WEB APPENDIX 1

Pearl's Causal Mediation Formula for Natural Direct and Indirect Effects

Adapted from the work of Judea Pearl (1).

Consider an observational study in which *Y* denotes the outcome, *E* denotes the exposure, *M* denotes the mediator, and *C* denotes the set of pre-exposure variables that confound the relationship between (E,M) and Y.

The natural direct effect (NDE(*c*)) is defined as the expected change in Y within levels of *c,* induced by changing E from e to e* while keeping the mediator at the value it would have attained under E = e, before the change from e to e*. Pearl's mediation formula for NDE(*c*) is:

$$NDE_{e,e*}(c) = \sum_{m} [\mathbb{E}(Y|E = e^*, M = m, C = c) - \mathbb{E}(Y|E = e, M = m, C = c)]$$

$$\text{x} \quad P\,(M = m \mid E = e, C = c). \qquad (1)$$

The indirect effect, IE*(c)*, is defined as the expected change in Y within levels of *c* induced by keeping E constant at E = e, and changing M (for each individual) to the value it would have been attained had E been set to E = e*.

$$IE_{e,e*}(c) = \sum_{m} [\mathbb{E}(Y|E = \ e, M = m, C = c)\,[P(M = m|E = e^*, C = c) - P(M = m|E = e, C = c)]$$

(2)

WEB APPENDIX 2

Unmeasured Confounding Sensitivity Analysis

Discussed in Tchetgen Tchetgen and Shpitser (2, 3).

This sensitivity analysis documents how much bias there is in the direct effect and indirect effect given various levels of unmeasured confounding. To calculate the bias, we offset the outcome (Y) by subtracting a value that we calculated from a selection bias function and reestimated the direct effect. We continued to vary the selection bias function, reestimating the direct effect. Then we plotted the bias to see how quickly the curve changes across varying levels of the selection bias function. The offset was:

$$offset = t(1, M, C)\{1 - \Pr(M = M|E = 1, C)\} - t(0, M, C)\{1 - \Pr(M = M|E = 0, C)\}$$

e e

where $t(e, m, c) = \lambda(C) =$ $\mathbb{E}$ ($Y_{1,\mathrm{M}}$ |E; M=1; C) - $\mathbb{E}$ ($Y_{1,\mathrm{M}}$|E; M=0; C). Note that

$$offset = t(E, M, C)\{\Pr(M|E = 0, C) - \Pr(M|E = 1, C)\}.$$

t(E,M,C) is the selection bias function, which varies depending on the bias you want to introduce. We specified a simple functional form for illustrative purposes, so t(E,M,C) = λEM, (or one could alternatively use λE(2M - 1)). Thus:

$$offset = \lambda ME\{\Pr(M|E = 0, C) - \Pr(M\ |E = 1, C)\}.$$

λ is the sensitivity parameter, which varies depending on the scaling of the outcome. For our purposes, we varied λ from -1.5 to 1.5 by 0.1 increments. For simplicity, we did the sensitivity analysis on the continuous BMI outcome and a dichotomized mediator.

We calculated the offset as follows:

1) We selected a single component from the mediator vector (for this paper, the economic factor), and dichotomized this mediator at the median.

2) We estimated a logistic regression predicting the mediator from exposure and covariates to obtain the equation:

$$\text{Logit } P[M = 1|E, C] = \hat{\alpha}_0 + \hat{\alpha}_1 E + \hat{\alpha}_2 C.$$

3) Using the above equation, we calculated manually the following probabilities for each subject:

(1) $\widehat{\Pr}[M = 1|E = 0, C]$

and

(2) $\widehat{\Pr}[M = 1|E = 1, C]$.

Essentially, this step calculated a probability of M given no exposure (E=0) even for subjects who had an observed E=1, and a probability of M given exposure (E=1) even for subjects who had an observed E=0.

4) From the two equations above, we generated the probability for actual observed M as follows, for each level of E:

For E=0 (i.e., equation (1) above), if observed M=1, then the subject got the value of equation (1); if observed M=0, then the subject got the value of 1 – equation (1). This value is written as:

(3) $\widehat{\Pr}[M|E = 0, C]$,

where M = observed value of mediator.

For A=1 (i.e., equation (2) above), if observed M=1, then the subject got the value of equation (2); if observed M=0, then the subject got the value of 1 – equation (2). This value is written as:

(4) $\widehat{\Pr}[M|E = 1, C]$,

where M = observed value of mediator.

5) For each fixed level of λ, we calculated the offset, setting the offset to zero for subjects in the control group:

$$offset = \lambda ME[\widehat{\Pr}[M|E = 0, C] - \widehat{\Pr}[M|E = 1, C]],$$

i.e., $offset = \lambda EM[\text{equation (3)} - \text{equation (4)}]$

6) For each fixed level of λ, we generated a new outcome subtracting the offset from Y:

$$Y_{new,i} = Y_i - offset_i$$

7) Finally, we reestimated the direct effect, for each $Y_{new,\,i}$, recalculated the corresponding indirect effect, and plotted the series of direct and indirect effect coefficients with 95% confidence intervals (see below).

Web Table 1. Testing Mediation using Inverse Odds Weighting: Indirect, Direct, and Total Effects of MTO[a] intervention vs. Controls on Adult Obesity Prevalence in 2002

Treatment Effects[b,c]	All 4 Census Factors			Economic Factor Only		
	Relative Risk	95% CI	*P* Value	Relative Risk	95% CI	*P* Value
Obese						
Indirect effects	0.93	0.87, 1.00	0.05	0.95	0.90, 1.00	0.05
Direct effects	0.96	0.86, 1.07	0.48	0.94	0.85, 1.04	0.24
Total effects	0.89	0.82, 0.98	0.01	0.89	0.82, 0.98	0.01

Abbreviations: CI, confidence interval; MTO, Moving to Opportunity.

[a] *N* = 3,401 adult household heads.

[b] Four mediators derived from exploratory factor analysis: 1) Economic factor (median family income, % of people 25+ with college degrees, % owner-occupied housing units, % female-headed households with children, % of people 25+ with less than a high school degree, % unemployed in 16+ civilian labor force, % of households receiving public assistance, % people in poverty); 2) Business factor (number of businesses, annual payroll, number of employees); 3) Minority composition factor (% black, non-Hispanic, % Hispanic; % foreign-born); 4) Minority males and minority adults factor (% of population minority males 16+ civilian employed, % minority males 10-19 years, % minority adults 25+). Data source: 2000 census tract data linked to 1997 census tract locations of residential addresses of MTO participants.

[c] Covariates included adult baseline characteristics such as site, age, sex, race, ethnicity, marital status, employment status, receipt of welfare, education, school enrollment, no teens in baseline household, household member had a disability, had lived in baseline neighborhood for 5 or more years, felt very unsafe in the neighborhood, and had moved more than 3 times prior to baseline.

Binary treatment models the Section 8 voucher groups compared to public housing controls. The Section 8 voucher groups combine the two originally randomized groups of the low-poverty neighborhood section 8 plus regular section 8 group. MTO survey weights, adjusted for attrition and varying random assignment ratios across time. Randomization ratios are the relative proportions of participants assigned to each of the treatment arms. Because of higher-than-expected take-up of treatment (i.e., housing vouchers) in the MTO experimental treatment group, randomization ratios changed several times throughout the course of the 4-year participant enrollment period, to reduce the proportion of participants randomized to the voucher groups, and increase the proportions randomized to the control group. The randomization ratios also differed in the 5 sites. The weights reflect the probability of being assigned to each treatment group.

WEB APPENDIX 3

Example Stata Program for Inverse Odds Weighting: Estimating Total, Direct, and Indirect Effects, Applying Bootstrapping to Derive Standard Errors

NOTE: Gray sections are variables names, lists, or parameters chosen by the user.

```
*Define a user-written program ;
capture program drop IOW
  program IOW , rclass

*Retain estimates of predicted probability, inverse odds, and inverse odds weights for later use ;
capture drop  predprob inverseodds  wt_iow

*Insert regression of binary treatment on mediators and covariates, using a logit model weighted by the
original sample weight (if the treatment is a normally distributed continuous variable, use a linear
regression model instead) ;
logit treatment mediator1 mediator2 covariate1 covariate2

*Obtain predicted probability for each individual based on the above regression model;
predict predprob , p

*Calculate each individual's inverse odds from the predicted probability ;
gen inverseodds = ((1-predprob)/predprob)

*Calculate inverse odds weights; for control members (i.e., people without the treatment or exposure),
inverse odds weight = the original sampling weights (or 1 if there are no sample weights). For treatment
members, inverse odds weight = inverse odds x original sampling weights (or simply the inverse odds if
there are no sample weights) ;
gen wt_iow = 1if treatment==0
replace wt_iow = inverseodds if treatment==1

 * Insert the total effect regression here and retain estimate of total effects for later use. Here we use
Poisson regression, but other weighted regression models can be utilized instead ;
glm outcome treatment covariate1 covariate2 ,  fam(poisson) link(log) vce(robust)

matrix bb_total= e(b)
scalar b_total=bb_total[1,1]
return scalar b_total=bb_total[1,1]

 * Insert the direct effect regression, which is the same as the total effect regression but applying the
inverse odds weight. Retain estimate of direct effects. Calculate indirect effects as the difference
between total effects and direct effects.  Any alternative expression of the indirect effects could also be
used (for example the % of the total effect that is indirect could be calculated as: (b_total-
b_direct)/b_total ;
glm outcome  treatment covariate1 covariate2  [pweight=wt_iow] ,  fam(poisson) link(log) vce(robust)

matrix bb_direct = e(b)
scalar b_direct=bb_direct[1,1]
```

```
return scalar b_direct=bb_direct[1,1]
return scalar b_indirect = b_total-b_direct

end

* Request bootstrapped estimates of indirect, direct and total effects.  Provide initial value of the
random-number seed so estimates can be replicated at a later time. Request 1000 bootstrap
replications ;
 bootstrap r(b_indirect) r(b_direct) r(b_total), seed(32222) reps(1000): IOW
```

WEB APPENDIX 4

Example Stata Program for Inverse Odds Weighting: Estimating Total, Direct, and Indirect Effects; Using Multiple Imputation via Chained Equations (MICE) to Impute Missing Data; Bootstrapping to Derive Standard Errors

NOTE: Gray sections are variables names, lists, or parameters chosen by the user.

```
*define a user-written program;
capture program drop IOWMICE
program IOWMICE, rclass


*tell Stata to preserves the data. Data is restored after program termination ;
preserve

*Insert equation to impute missing data. We request 20 imputed datasets ;
ice outcome mediator1 mediator2 covariate1 covariate2 , saving("filelocation\nameofdataset.dta" ,
replace)   m(20)

use " filelocation\nameofdataset.dta " , clear

*Retain estimates of predicted probability, inverse odds, and inverse odds weights for later use ;
capture drop logodds predprob inverseodds wt_iow

*Insert regression of treatment on mediators and covariates. Mim command analyzes multiply imputed
data. Storebv command stores regression results for later use;
mim, storebv: logit treatment mediator1 mediator2 covariate1 covariate2

*Calculate predicted log odds and use that to calculate predicted probabilities and inverse odds;
predict logodds, xb
gen predprob = exp(logodds)/(1+exp(logodds))
gen inverseodds = ((1-predprob)/predprob)

*Calculate inverse odds weights;
gen wt_iow = 1if treatment==0
replace wt_iow = inverseodds if treatment==1

* Insert the total effect regression here and retain estimate of total effects for later use ;
mim, storebv: glm outcome_treatment covariate1 covariate2 ,  fam(poisson) link(log) vce(robust)

matrix bb_total= e(b)
scalar b_total=bb_total[1,1]
return scalar b_total=bb_total[1,1]

* Insert the direct effect regression here. Retain estimate of direct effects. Calculate indirect effects as
the difference between total effects and direct effects;
mim, storebv: glm outcome treatment covariate1 covariate2  [pweight=wt_iow],  fam(poisson) link(log)
vce(robust)
```

```
matrix bb_direct = e(b)
scalar b_direct=bb_direct[1,1]
return scalar b_direct=bb_direct[1,1]
return scalar b_indirect = b_total-b_direct

end
```

*Request bootstrapped estimates of indirect, direct and total effects. Provide initial value of the random-number seed so estimates can be replicated at a later time. Request 1000 bootstrap replications ;

```
bootstrap r(b_indirect) r(b_direct) r(b_total), seed(32222) reps(1000): IOWMICE
```

WEB APPENDIX 5

Constructing Inverse Odds Ratio Weights

Web Appendices 3 and 4 utilize inverse odds weights, which can at times produce more efficient effect estimates than inverse odds ratio weights. This Web appendix presents Stata code for how to construct inverse odds ratio weights.

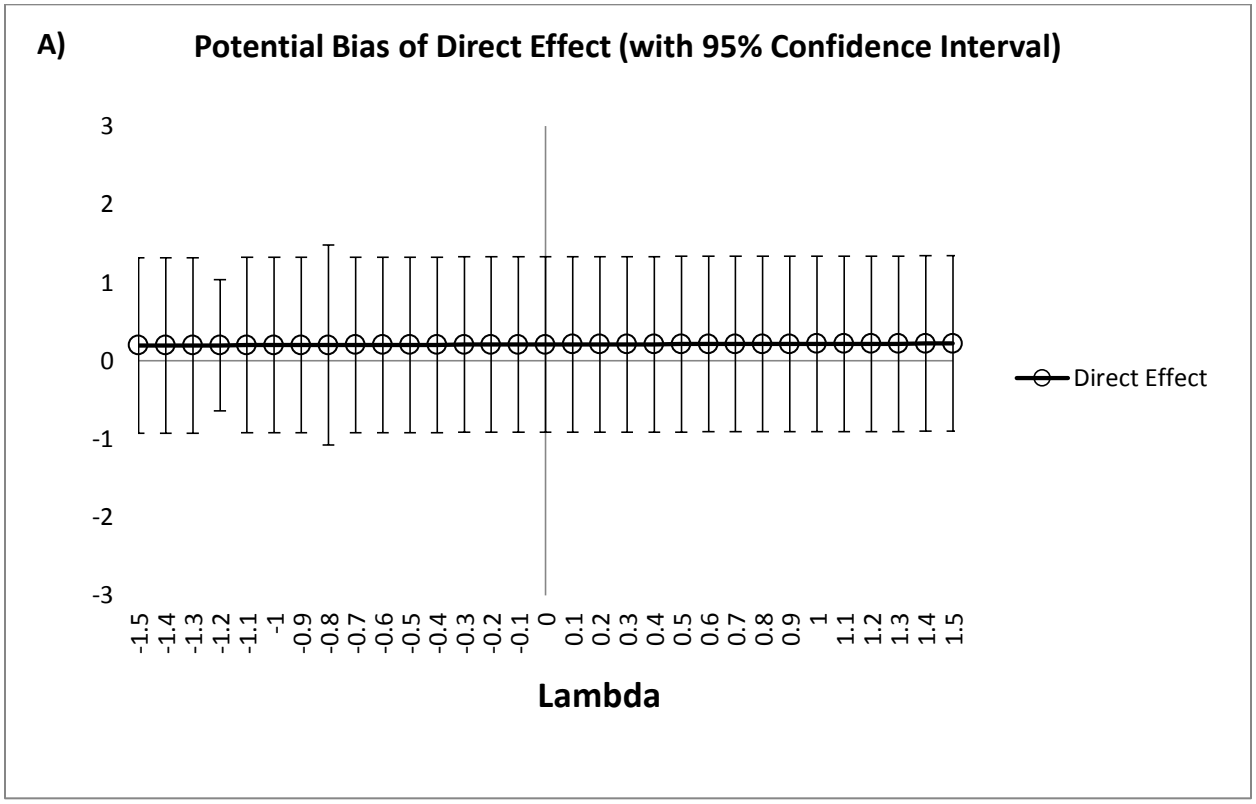
NOTE: Gray sections are variables names, lists, or parameters chosen by the user.

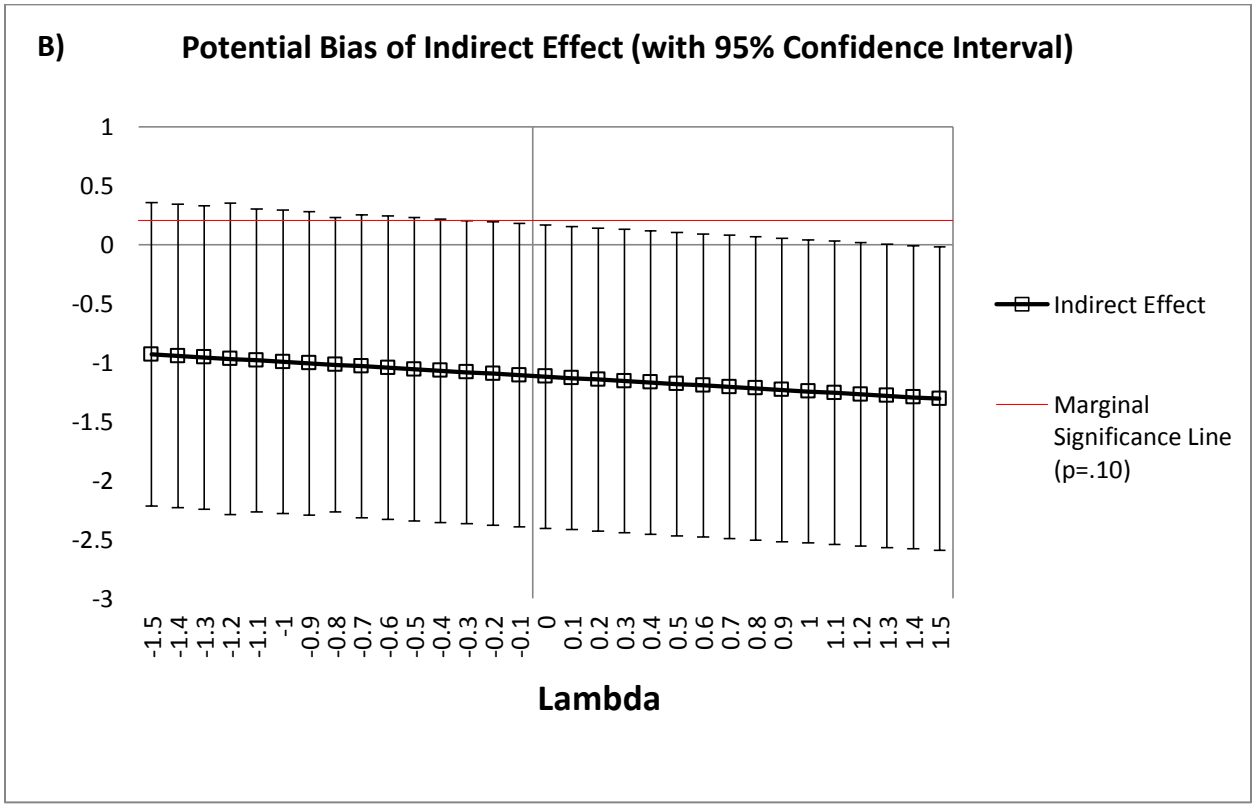
```
*Insert regression of treatment on mediators and covariates ;
logit treatment mediator1 mediator2 covariate1 covariate2

*Calculate inverse odds ratio ;
gen inverseoddsratio = 1/(exp(betacoefficientofmediator1*mediator1 +
betacoefficientofmediator2*mediator2))

*Calculate inverse odds ratio weights; for control members (i.e., people without the treatment or
exposure), inverse odds ratio weight = the original sampling weights. For treatment members, inverse
odds ratio weight = inverse odds ratio x original sampling weights ;
gen wt_iorw = 1if treatment==0
replace wt_iorw = inverseoddsratio if treatment==1
```

Web Figure 1. Unmeasured Confounding Sensitivity Analysis (Linear Coefficients)





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