Supplemental Table 1. First-Stage Mediation Results, MTO Treatment Effect Regressed on Mediators Individually

	Boys					Girls				
	+/–	**b**	**SE**	**p**	**N**	**+/–**	**b**	**SE**	**p**	**N**
Lifetime Substance Use										
Lifetime Alcohol Use		0.123	0.172	0.474	1390		-0.246	0.168	0.144	1420
Lifetime Cigarette Use	–	0.415	0.204	0.042	1390		-0.199	0.177	0.260	1422
Lifetime Marijuana Use		0.149	0.195	0.444	1385	+	-0.341	0.185	0.066	1417
Past 30 Day Alcohol Use										
Alcohol Use Yes/No	–	0.459	0.227	0.043	1386	+	-0.481	0.205	0.019	1416
Number of Days Used Alcohol					1386					1416
1-2 Days vs. Never		0.445	0.284	0.117		+	-0.411	0.224	0.066	
3 or More Days vs. Never		0.518	0.358	0.148		+	-0.654	0.397	0.100	
Past 30 Day Cigarette Use										
Cigarette Use Yes/No	–	0.764	0.234	0.001	1384	+	-0.397	0.219	0.070	1414
Number of Cigarettes Smoked per Day					1384					1414
Less than Daily vs. Never	–	0.481	0.281	0.088			-0.365	0.279	0.191	
Daily, 1-19 Cigarettes vs. Never	–	1.187	0.419	0.005		+	-0.571	0.321	0.075	
Pack/Day or More vs. Never		0.870	0.642	0.175			0.248	0.712	0.728	
Past 30 Day Marijuana Use										
Marijuana Yes/No		0.170	0.253	0.502	1379	+	-0.597	0.249	0.017	1415
Number of Days Smoked Marijuana †		0.287	0.259	0.266	1379	+	-0.607	0.271	0.025	1415
Past 30 Day Number of Substances Used					1356					1394
One Substance vs. None		0.228	0.253	0.368			-0.134	0.219	0.541	
Two Substances vs. None	–	0.534	0.282	0.058		+	-1.026	0.276	0.000	
3-4 Substances vs. None	–	0.924	0.443	0.037			-0.027	0.430	0.951	
Social Connectedness										
Number of Adults Youth can Confide in					1391					1420
3-4 vs. 5+ Adults		0.016	0.217	0.942			-0.122	0.223	0.585	
2 vs. 5+ Adults		0.246	0.228	0.280		+	-0.486	0.227	0.032	
1 vs. 5+ Adults		-0.239	0.245	0.329		+	-0.510	0.217	0.019	
0 vs. 5+ Adults		0.096	0.310	0.756			-0.280	0.366	0.445	
Number of Adults to Help Youth					1382					1414
5-6 vs. 7+ Adults		0.030	0.216	0.888		+	-0.468	0.219	0.032	
3-4 vs. 7+ Adults		0.128	0.203	0.529			-0.123	0.194	0.525	
2 vs. 7+ Adults	–	0.399	0.226	0.078		+	-0.651	0.220	0.003	
1 vs. 7+ Adults		-0.335	0.259	0.196		+	-0.584	0.249	0.019	
0 vs. 7+ Adults		0.156	0.731	0.831			0.544	0.767	0.479	
Youth Has No Friends	+	-0.570	0.341	0.095	1256		0.208	0.389	0.592	1423
Youth Has Less Than 3 Friends		-0.271	0.178	0.129	1382		-0.026	0.160	0.873	1423
Youth Has Less Than 5 Friends		-0.162	0.151	0.283	1382		-0.192	0.150	0.202	1423
Youth Has Friends from Baseline Neighborhood	+	-0.455	0.162	0.005	1354	+	-0.611	0.159	0.000	1369
Peer Deviance										
Friends Use Drugs	–	0.461	0.182	0.011	1286		0.099	0.157	0.527	1373
Friends In a Gang	+	-0.445	0.212	0.036	1325		0.035	0.189	0.851	1371
Friends Carry Weapons		0.221	0.221	0.318	1320		0.125	0.212	0.557	1391
Maternal Mental Health										
Psychological Distress		0.078	0.071	0.273	1368	+	-0.142	0.083	0.088	1377
Lifetime MDD		-0.068	0.212	0.749	1367		-0.262	0.214	0.221	1375
Generalized Anxiety Disorder		-0.099	0.158	0.531	1346		-0.090	0.163	0.580	1350
Not Calm/Peaceful		-0.052	0.156	0.738	1366	+	-0.323	0.158	0.042	1377

+ = Beneficial effect of treatment; – = Harmful effect of treatment

† Poisson Model

NOTE: Models adjusted for all covariates in second-stage models. Includes all sites

Appendix A: Unmeasured Confounding Sensitivity Analysis

We estimated the unmeasured confounding sensitivity analysis, as discussed in Tchetgen Tchetgen & Shpitser (2009) and Nguyen et al. (2015), to document the extent of potential bias in the direct and indirect effects given various levels of unmeasured confounding. The bias was calculated by subtracting from the outcome (Y) a value calculated from a selection bias function, t(a,m,x), where t=the selection bias function, m=mediator, a=exposure, and x=covariates. The selection bias function, t(a,m,x), varies depending on the bias you want to introduce, and captures the extent to which confounding may lead to differences in the average potential outcome in individuals with the mediator compared to those without. We have specified t(a,m,x) as:

$$t(a, m, x) = \lambda m$$

λ is the sensitivity parameter, and estimates:

$$\lambda = \mathbb{E}\left(Y_{a=1,m} \middle| A = 1; M = 1\right) - \mathbb{E}\left(Y_{a=1,m} \middle| A = 1; M = 0\right)$$

Thus, λ is zero when the mediator is unconfounded, positive values of λ indicate that individuals with higher outcomes are more likely to exhibit the mediator, and negative values of λ indicate individuals with higher outcomes are less likely to exhibit the mediator. We varied λ from -1.5 to 1.5 by .1 increments, calculated the offset for each λ, subtracted the offset from the outcome, and reestimated the direct and indirect effects. Then we plotted the bias to see how quickly the curve changed across varying levels of the selection bias function. For our analysis, the offset was calculated as:

$$offset = t(\underset{a}{1}, m, x)[1 - \Pr(M = m|A = 1, x)] - t(\underset{a}{0}, m, x)[1 - \Pr(M = m|A = 0, x)]$$

which simplifies to:

$$offset = t(a, m, x)[\Pr(M = m|A = 0, x) - \Pr(M = m|A = 1, x)]$$

Since t(a,m,x)=λm, the offset is:

$$offset = \lambda m[\Pr(M = m|A = 0, x) - \Pr(M = m|A = 1, x)]$$

To calculate the offset we:

1) Selected a mediator, and, if not already binary, dichotomized the mediator.

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

$$Logit\ P[M = 1|A, X] = \hat{\alpha}_0 + \hat{\alpha}_1 A + \hat{\alpha}_2 X$$

3) Using the above equation, manually calculated the following probabilities for each subject (i.e., (1) the probability of M given no exposure (A=0) even for subjects who have an observed A=1, and (2) the probability of M given exposure (A=1) even for subjects who have an observed A=0):

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

and

$$(2)\ \widehat{\Pr}[M = 1|A = 1, x]$$

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

   For A=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):

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

   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):

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

   where M= observed value of mediator

5) For each fixed level of λ, calculated the offset, with the offset equal to zero in the control group:

   $$offset = \lambda M[\widehat{\Pr}[M|A = 0, x] - \widehat{\Pr}[M|A = 1, x]]$$

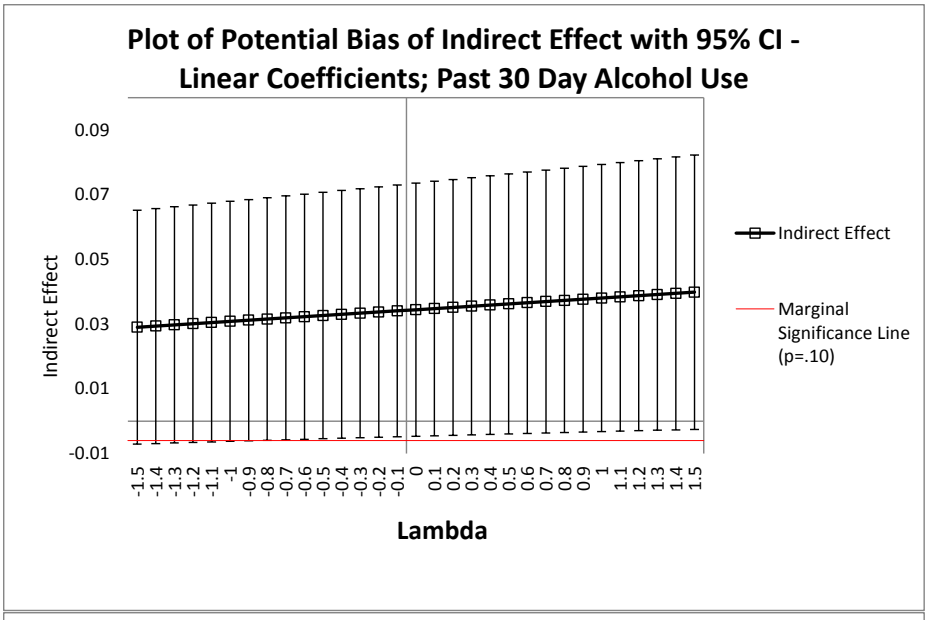
   i.e., $offset = \lambda M[\text{equation } (3) - \text{equation } (4)]$

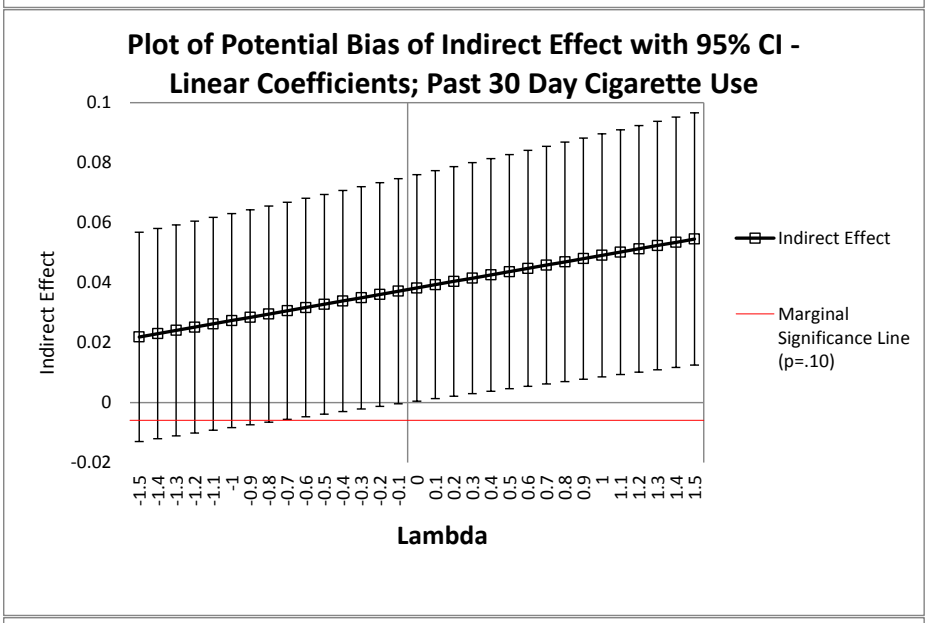
6) For each fixed level of λ, generated a new outcome subtracting the offset from Y:

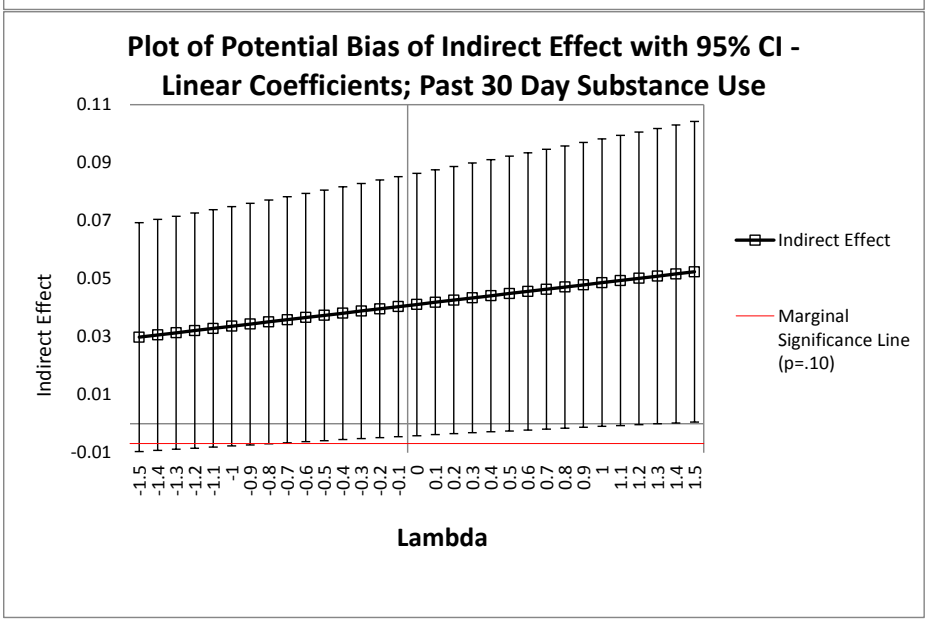
   $$Y_{new,i} = Y - offset_i$$

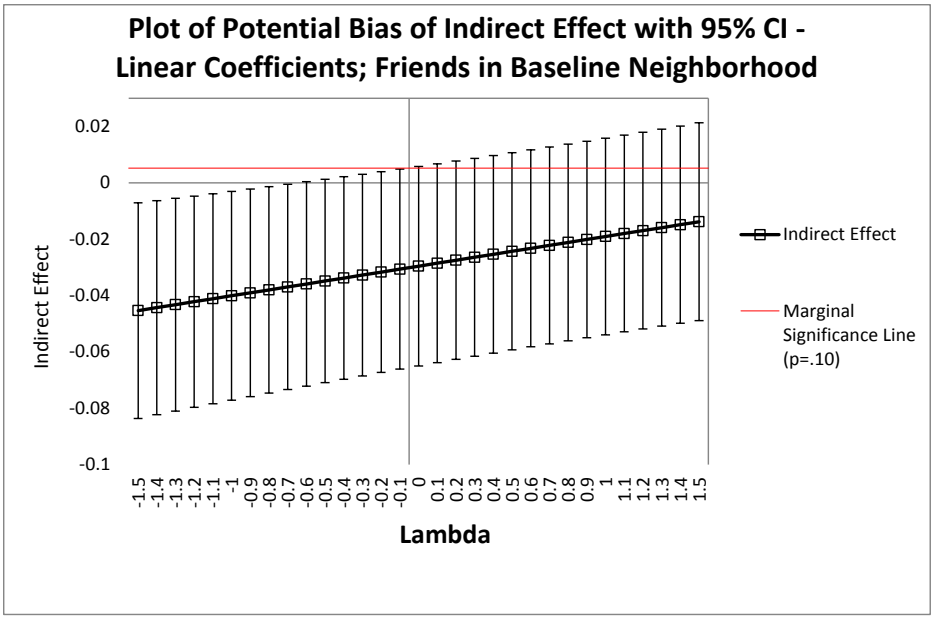
7) Reestimated the direct and indirect effects, for each $Y_{new,\,i}$.

Below are the indirect effect plots for mediators that had significant or suggested marginally significant findings on mental health. When recoding categorical number of cigarettes smoked to a dichotomy, it was the same measure as past 30 day cigarette use, so we estimated this equation only for the original dichotomy.


Plot of Potential Bias of Indirect Effect with 95% CI - Linear Coefficients; Past 30 Day Alcohol Use
Indirect Effect
0.09
0.07
0.05
0.03
0.01
-0.01
-1.5 -1.4 -1.3 -1.2 -1.1 -1 -0.9 -0.8 -0.7 -0.6 -0.5 -0.4 -0.3 -0.2 -0.1 0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1 1.1 1.2 1.3 1.4 1.5
Lambda
Indirect Effect
Marginal Significance Line (p=.10)


Plot of Potential Bias of Indirect Effect with 95% CI - Linear Coefficients; Past 30 Day Cigarette Use
Indirect Effect
0.1
0.08
0.06
0.04
0.02
0
-0.02
-1.5 -1.4 -1.3 -1.2 -1.1 -1 -0.9 -0.8 -0.7 -0.6 -0.5 -0.4 -0.3 -0.2 -0.1 0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1 1.1 1.2 1.3 1.4 1.5
Lambda
Indirect Effect
Marginal Significance Line (p=.10)


Plot of Potential Bias of Indirect Effect with 95% CI - Linear Coefficients; Past 30 Day Substance Use
Indirect Effect
0.11
0.09
0.07
0.05
0.03
0.01
-0.01
-1.5 -1.4 -1.3 -1.2 -1.1 -1 -0.9 -0.8 -0.7 -0.6 -0.5 -0.4 -0.3 -0.2 -0.1 0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1 1.1 1.2 1.3 1.4 1.5
Lambda
Indirect Effect
Marginal Significance Line (p=.10)


Plot of Potential Bias of Indirect Effect with 95% CI - Linear Coefficients; Friends in Baseline Neighborhood
Indirect Effect
0.02
0
-0.02
-0.04
-0.06
-0.08
-0.1
-1.5 -1.4 -1.3 -1.2 -1.1 -1 -0.9 -0.8 -0.7 -0.6 -0.5 -0.4 -0.3 -0.2 -0.1 0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1 1.1 1.2 1.3 1.4 1.5
Lambda
Indirect Effect
Marginal Significance Line (p=.10)