Published in final edited form as:
Epidemiology. 2018 July ; 29(4): 590–598. doi:10.1097/EDE.0000000000000832.

Mediation of neighborhood effects on adolescent substance use by the school and peer environments

Kara E. Rudolph[*,1], **Oleg Sofrygin**[2], **Nicole M. Schmidt**[3], **Rebecca Crowder**[1], **M. Maria Glymour**[4], **Jennifer Ahern**[1], and **Theresa L. Osypuk**[3]

[1]Division of Epidemiology, School of Public Health, University of California, Berkeley, California

[2]Division of Epidemiology, School of Public Health, University of California, Berkeley, California

[3]Department of Epidemiology and Community Health, University of Minnesota School of Public Health, Minneapolis, Minnesota

[4]Department of Epidemiology and Biostatistics, University of California, San Francisco, California

Abstract

Background—Evidence suggests that aspects of the neighborhood environment may influence risk of problematic drug use among adolescents. Our objective was to examine mediating roles of aspects of the school and peer environments on the effect of receiving a Section 8 housing voucher and using it to move out of public housing on adolescent substance use outcomes.

Methods—We used data from the Moving to Opportunity (MTO) experiment that randomized receipt of a Section 8 housing voucher. Hypothesized mediators included school climate, safety, peer drug use, and participation in an after-school sport or club. We applied a doubly robust, semiparametric estimator to longitudinal MTO data to estimate stochastic direct and indirect effects of randomization on cigarette use, marijuana use, and problematic drug use. Stochastic direct and indirect effects differ from natural direct and indirect effects in that they do not require assuming no post-treatment confounder of the mediator-outcome relationship. Such an assumption would be at odds with any causal model that reflects an intervention affecting a mediator and outcome through adherence to treatment assignment.

Results—Having friends who use drugs and involvement in after-school sports or clubs partially mediated the effect of housing voucher receipt on adolescent substance use (e.g., stochastic indirect effect 0.45% (95% CI: 0.12%, 0.79%) for having friends who use drugs and 0.04% (95% CI: −0.02%, 0.10%) for involvement in after-school sports or clubs mediating the relationship between housing voucher receipt and marijuana use among boys). However, these mediating effects were small, contributing only fractions of a percent to the effect of voucher receipt on probability of substance use. No school environment variables were mediators.

[*]Corresponding author: 13B University Hall, School of Public Health, Berkeley, CA 94720, kara.rudolph@berkeley.edu, tel. +15106431889.

Conflicts of interest: None

Data and analysis code: Researchers may apply for data access through the U.S. Census Bureau. Computing code required to replicate the results is provided here: https://github.com/cherrygarcia/code-for-papers/blob/master/MTOmediationpaper.R.

Conclusions—Measured school- and peer-environment variables played little role in mediating the effect of housing voucher receipt on subsequent adolescent substance use.

Keywords

mediation; stochastic intervention; neighborhood; substance use; adolescent

INTRODUCTION

Experimentation with substances is a common, yet risky, adolescent behavior. Nearly half (46%) of high school students report ever trying a tobacco product like cigarettes, and 44% of 12th-graders report ever using marijuana (1, 2). Regular, heavy, or problematic use of these substances can increase risk for a variety of health problems. For example, cigarette use during adolescence is associated with an increased risk of long-term addiction to and heavy use of tobacco (3, 4) and the attendant health consequences of poor lung function, cancer, heart disease, and pre-mature death (5). Long-term or heavy marijuana use in adolescence is associated with addiction, altered brain development, and poor educational outcomes (6). Drug use that is problematic or disordered is associated with lower educational attainment (7), increased risk of aggression and theft (8), and poor mental health (8, 9). Drug use disorders are estimated to affect nearly 9% of U.S. adolescents (10).

Neighborhoods are a promising point of intervention to alter substance use behaviors; mounting evidence suggests that aspects of the neighborhood environment influence risk of problematic drug use among adolescents (11–13). However, reducing exposure to neighborhood poverty has not resulted in uniformly beneficial effects on drug use and abuse among adolescents. For example, reductions in neighborhood poverty achieved via randomization to receive a housing voucher have been shown to improve drug use outcomes for girls but not for boys (14) and may be beneficial in some cities but not in others (15). To elucidate these inconsistent results, it may be useful to examine the potential mechanisms underlying the association between neighborhood poverty and adolescent substance use (16).

The Moving To Opportunity (MTO) experiment presents a unique opportunity to understand such mechanisms. MTO essentially randomized neighborhood context by randomizing families living in public housing to receive a Section 8 housing voucher that they could use to move to a private rental unit in a lower-poverty neighborhood (17). Moving also can induce change in multiple contexts important to adolescents, including the school and peer environments. Data on these contexts as well as on adolescent substance use were collected longitudinally.

The school environment may play a central role in mediating the effects of the MTO housing voucher intervention on adolescent substance use outcomes (18). Adolescents spend the majority of their day at school, and aspects of the school environment—including quality, connectedness, and climate—have been associated with adolescent externalizing behaviors and drug use (19–22). The peer environment may also play a mediating role, as peers are more influential during adolescence than at other points in the life course (23–25). For example, the smoking status of friends is associated with adolescent cigarette and marijuana use (26, 27), while participation in sports and extra-curricular activities is associated with lower likelihood of use (28–30).

Our objective was to examine the potential mediating roles of aspects of the school and peer environments on the effect of receiving a Section 8 housing voucher that was used to move out of public housing on adolescent substance use outcomes. We apply a robust and flexible causal mediation method (31) to estimate mediating effects.

METHODS

We used data from adolescents and their families who were enrolled in MTO at baseline (1994-1997) and followed up at the interim visit, which occurred 4-7 years later in 2001-2002. MTO has been described previously (17, 19, 32). Briefly, it was a randomized controlled trial sponsored by the U.S. Department of Housing and Urban Development in five U.S. cities (Baltimore, Boston, Chicago, Los Angeles, and New York) and enrolling 4,600 low-income families living in distressed public housing with children under 18. MTO can be thought of as an encouragement-design intervention where the randomized intervention of voucher receipt (the instrument) was designed to *encourage* intervention take-up (also called lease-up or adherence), which was moving with the voucher out of public housing and, typically, into a lower-poverty neighborhood.

Measures

MTO randomized families into one of three groups: 1) receipt of a Section 8 housing voucher to be used to rent an apartment in a low-poverty neighborhood (<10% persons in poverty) and assistance finding housing (the restricted voucher group), 2) receipt of an unrestricted Section 8 housing voucher with no housing assistance (the unrestricted voucher group), and 3) no intervention or voucher but eligible to remain in public housing (the in-place control group). Partial F tests indicated estimates comparing the two voucher groups to the control group were similar for past 30-day cigarette use (p=0.42), marijuana use (p=0.58), and problematic drug use (p=0.13), measured at the follow-up timepoint. Therefore, we combined the two voucher groups and compared randomization to receive a housing voucher versus not, consistent with previous work (33). We include results without combining the voucher groups that compare the restricted voucher group to the control in the eAppendix.

We considered four binary mediators related to the school and peer environments that were measured at the interim assessment and had low levels of missingness: whether or not the adolescent 1) felt safe at school, 2) reported a positive school climate, 3) had friends who use drugs and 4) participated in an after-school sport or club himself/herself.

We considered three binary self-reported substance use outcomes that were measured at the interim assessment: 1) past 30-day cigarette use, 2) past 30-day marijuana use, and 3) problematic drug use, defined as any past-year use of hard drugs or using marijuana before school or work in the past 30 days. We include results for lifetime versions of these outcome measures in the eAppendix.

Covariates measured at the baseline survey included sociodemographic characteristics of the adolescent and family, behavior and learning characteristics of the adolescent, neighborhood characteristics at baseline, and reasons for participation in MTO. A full list of covariates is provided in the eAppendix.

A directed acyclic graph (DAG) depicting the relationships between these variable types is shown in Figure 1. The intervention of receiving a housing voucher (A) was randomized, so it is exogenous. The effect of intervention A is expected to act through adherence Z which is the actual use of the voucher to move out of public housing. Z may also be influenced by covariates, W. Mediators, M, are hypothesized to be influenced by Z and W. Outcomes, Y, may be affected by M, Z, and W. Voucher receipt is assumed not to have any effect on these mediators or future outcomes except through its use (Z), which is shown by no direct arrow from A to M or Y. This is aligned with the exclusion restriction assumption of an instrument (34) and is a reasonable assumption given that the voucher's only plausible effect would be through the move, as discussed in previous MTO analyses (e.g., 17, 35, 36).

Sample

We used youth in the MTO Tier 1 Restricted Access Dataset and who were successfully followed up and aged 12-17 at the interim assessment (N=2,242), as this is the subsample who answered school-related questions. MTO survey weights account for treatment arm random assignment ratios (which varied by site and year), sampling of children within households, and loss to follow-up (32). We excluded those in the Baltimore site as voucher receipt was not associated with a subsequent move to a low-poverty neighborhood (defined as < 25% poor), suggesting that the intervention differed in this site compared to others (N=1,882). Finally, we restricted our analysis to those with nonmissing mediator and outcome values (final sample size: N=1,644, 1,640, depending on the outcome), which means that our results only apply to this particular sample of adolescents. Covariate missingness was addressed using multiple imputation and is described below. This study was determined to be nonhuman subjects research by the University of California, Berkeley.

Statistical Approach

Our analysis proceeded in several steps. We first imputed missing covariate values (all had less than 5% missing) using multiple imputation by chained equations, which assumes the data are missing at random conditional on the variables in the imputation model (37). We generated 30 imputed datasets. The analysis was completed on each imputed dataset and the results pooled using Rubin's combining rules (38).

We then estimated the total effect of voucher randomization on each outcome (the intent-to-treat treatment effect) stratified by site and by gender, as previous MTO research has shown these to be important sources of effect heterogeneity (15, 33) (eFigures 1-3). Given theoretical rationale and empirical evidence (14, 39) for differential substance use responses to the MTO intervention between boys and girls, we estimated mediation effects separately by gender. However, a similar level of evidence for site heterogeneity in MTO is lacking (15). Consequently, since we lacked power to stratify analyses by gender and site, we combined sites with similar estimates within gender, using the same partial F test as described above for combining voucher groups. We focused our analyses on the subgroup with the largest sample size for each gender. Similar data-driven approaches have been used in combining other subgroups in MTO (40). We present results combining all sites in the eAppendix.

For each gender–mediator–outcome combination, we estimated statistical parameters of the data-dependent stochastic direct effect and indirect effect (31). The stochastic direct and indirect effects are analogous to the natural direct and indirect effects in the absence of confounders of the mediator-outcome relationship affected by prior exposure (41). However, unlike the natural direct and indirect effects, the stochastic direct and indirect effects will not generally sum to the total effect. The stochastic direct effect is defined: $E\left(Y_{a,\hat{g}_{M|a^*,W}}\right) - E\left(Y_{a^*,\hat{g}_{M|a^*,W}}\right)$, where $\hat{g}_{M|a^*,W}$ is a stochastic draw from an assumed known distribution of M conditional on a^* and W, estimated from the observed data. In words, it is the difference in the expected value of Y setting A to a versus a^* (in this case, a=voucher and a^*=no voucher) and stochastically drawing the value of M from the observed distribution of M conditional on a^* and W and accounting for adherence, Z, using sequential regression (42). This interpretation contrasts slightly with that of the natural direct effect, which is the difference in the expected value of Y setting A to a versus a^* and setting the value of M to level it would have been for the particular individual under a^* and assuming no Z. The stochastic direct effect is the combined path $\{a, b\}$ in Figure 1. The stochastic indirect effect is similarly defined: $E\left(Y_{a,\hat{g}_{M|a^*,W}}\right) - E\left(Y_{a^*,\hat{g}_{M|a^*,W}}\right)$. The stochastic indirect effect is the combined path $\{a,c,d\}$ in Figure 1. The stochastic direct and indirect effects can be identified using sequential regression as presented in VanderWeele and Tchetgen Tchetgen (41) and Rudolph et al. (31). The data-dependent versions of the stochastic direct and indirect effects that we estimate differ from the non-data-dependent versions in that they assume a known $\hat{g}_{M|a^*,W}$, estimated from the observed data. Reasons for choosing to estimate the data-dependent stochastic direct and indirect effects are technical and described in Rudolph et al. (31).

We estimated stochastic direct and indirect effects instead of the more common natural direct and indirect effects, because the stochastic effects do not require the absence of post-treatment confounding of the mediator-outcome relationship, $M_{a^*} \perp Y_{a,m} | W$, an assumption that is required for identifying their natural counterparts (43). Assuming no post-treatment confounder of the mediator-outcome relationship is at odds with any DAG that reflects an intervention affecting a mediator and outcome through adherence to treatment assignment. This is because in a trial where the randomized treatment acts through the treatment actually received, adherence, Z, is a confounder of the M-Y relationship that is affected by A (see Figure 1). This assumption is also problematic, because it invokes worlds under a and a^* simultaneously (the cross-worlds assumption) and so is never empirically verifiable. Previously, researchers had limited options when this assumption was not met. There may also be substantive reasons to choose to estimate stochastic instead of natural direct and indirect effects. For example, it may be easier to imagine counterfactual distributions of mediator values under certain types of a's and a^*'s—like where A represents race or sex—than it would be to imagine individual counterfactual mediator values where one would need to imagine that an individual changes sex or race (41). The data-dependent stochastic direct and indirect effect estimands require two assumptions for identification: 1) $Y_{am} \perp A/W$ and 2) $Y_{am} \perp M|W, A = a, Z$ (31), which are the same as for controlled direct effects. (Note that the third identification assumption of stochastic direct and indirect effects, $A \perp M_a|W$, is not technically required for the data-dependent versions that assume a known $\hat{g}_{M|a^*, W}$.)

We use a recently developed targeted minimum loss-based estimator to estimate stochastic direct and indirect effects (31). We note that both the estimator and estimands extend to observational studies with non-random treatment assignment (31). This estimator is doubly robust and incorporates machine learning in fitting models for Z, M, and Y. Specifically, in fitting each of these models, we used the least absolute shrinkage and selection operator (lasso) (44) in the glmnet R package (45). This algorithm selects covariates to include in each model from a high-dimensional list of main terms and two-way interactions (e.g, predicting $P(Z = 1/a, W)$, $P(M = 1/z, W)$, and $P(Y = 1/Z, M, W)$). Age, race/ethnicity, site, and gender were included in all models. The lasso algorithm included additional covariates that improved model fit by more than one standard error and we used 5-fold cross-validation to minimize the risk of over-fitting. We chose to use lasso to help prevent overfitting given our small sample size but note that any machine algorithm or ensemble learner could be used.

The first step in this process is to estimate the data-dependent, stochastic interventions for each mediator. Taking the difference of these stochastic interventions comparing voucher receipt to not, $E\left(\hat{g}_{M|a, W} - \hat{g}_{M|a^*, W}\right)$, is an estimate of the first-stage effects—the effect of voucher receipt on the mediator, through adherence. The next step is to plug the $\hat{g}_{M|a, W}$ and $\hat{g}_{M|a^*, W}$ values into the targeted minimum loss-based estimator to estimate the data-dependent stochastic direct and indirect effects.

R version 3.3.1 was used for all analyses. Code to implement the targeted minimum loss-based estimator is given in Rudolph et al. (31) and code to replicate these analyses is provided: https://github.com/cherrygarcia/code-for-papers/blob/master/MTOmediationpaper.R.

Sensitivity Analyses

We conducted three sensitivity analyses. First, we repeated our analyses without combining voucher groups—we compared the restricted voucher group to the control group. Those in the restricted voucher group tended to move farther with the voucher, and children in those families were more likely to change school districts as compared to the unrestricted Section 8 voucher group (19). Farther moves and school district changes would more likely result in changes in aspects of the school and peer environments.

Second, we repeated our analyses using lifetime outcome measures instead of past 30-day measures. It is possible that the low substance use levels captured in past 30-day measures impact our ability to detect effects. Lifetime use may a more sensitive measure. It is theoretically possible that using lifetime measures could result in the outcome having occurred prior to randomization. We believe this would not affect much of the sample, though, because most children in our analytic sample were randomized at an age (median age: 8 years, range: 5-14 years) much earlier than most first use cigarettes or marijuana (14-15 years and 16 years, respectively) (46, 47). Furthermore, because voucher receipt was random, we would expect the outcomes at baseline to be balanced between the intervention groups.

Third, we repeated our analyses forming gender-specific subgroups that included all four sites.

RESULTS

The analytic samples for boys and girls for the cigarette use, marijuana use, and problematic drug use outcomes are shown in eTables 1-3. Boys from Boston, Chicago, and NYC (N=664) and girls from all four sites (N=997) were included in the cigarette use sample. Boys from Boston, LA, and NYC (N=640) and girls from Boston and Chicago (N=507) were included in the marijuana use sample. Boys from all four sites sites (N=861) and girls from Chicago, LA, and NYC (N=731) were included in the problematic drug use sample. Sites comprising the analytic samples for each sensitivity analysis are given in eTable 4.

eTables 1-3 show survey-weighted baseline characteristics by voucher status for each of the gender-outcome samples. Because voucher status was randomized, we would expect baseline characteristics to be balanced across groups, though imbalances may occur by chance in finite samples like this one. The results confirm similar baseline characteristics across voucher groups; differences, where they exist, tend to be small. The bottom portions of eTables 1-3 show survey-weighted follow-up characteristics by randomization status, including adherence, mediators, and outcomes.

Total effects are presented in Figures 2–4. Voucher receipt increased the probability of cigarette use at follow-up among boys (risk difference (RD): 0.047, 95% CI: −0.011, 0.105) but decreased the probability among girls (RD: −0.066, 95% CI: −0.138, 0.006) (Figure 2). Voucher receipt was not associated with marijuana use or problematic drug use at follow-up, though point estimates for girls and boys were in opposite directions (Figures 3 and 4).

First-stage estimated effects are shown in Table 1. (See eTables 5-7 for first-stage effects for each of the sensitivity analyses.) Using the mediator of feeling safe at school among boys in the marijuana and drug-use samples as an example, we compare the observed distribution of the probability of feeling safe at school, conditional on covariates and accounting for adherence, under the scenario that everyone receives a voucher versus no one receives a voucher. For this mediator, the difference in the means of the distributions comparing voucher receipt versus not is a risk difference of 0.030; a boy has a 0.030 greater probability of feeling safe at school if he receives a housing voucher versus does not receive a housing voucher.

Using the above data-dependent stochastic interventions, we estimated the direct and indirect effects of voucher receipt on each of our three outcomes, shown in Figures 2–4. Results for the three sensitivity analyses are presented in the eFigures 4-12, and do not substantively differ from the main analysis results presented in the text.

We found evidence of mediation by two variables: having friends who used drugs and participation in an after-school sports team or club (see the *SIE* panel in Figures 2–4). No school environment variables mediated the total effects. For girls, receiving a voucher led to a 0.42% (95% CI: 0.11%, 0.73%) increased probability of cigarette use through having friends who used drugs, a 0.37% (95% CI: −0.15%, 0.90%) increased probability of marijuana use through having friends who use drugs, and a 0.10% (95% CI: −0.03%, 0.23%) increased probability of problematic drug use use through having friends who use drugs. For boys, receiving a voucher led to a 0.45% (95% CI: 0.12%, 0.79%) increased probability of marijuana use through having friends who use drugs and a 0.07% (95% CI: −0.01%, 0.15%) increased probability of problematic drug use through having friends who use drugs. There was no indirect effect on cigarette use among boys.

Participating in after-school sports or clubs also appeared to mediate the relationships for boys. Among boys, receiving a voucher led to a 0.03% (95% CI: −0.00%, 0.05%) increased probability of cigarette use through sport/club participation, a 0.04% (95% CI: −0.02%, 0.10%) increased probability of marijuana use through sport/club participation, and a 0.01% (95% CI: 0.00%, 0.01%) increased probability of problematic drug use use through sport/club participation. It may seem counter-intuitive that participating in sports or clubs would increase substance use outcomes, but this can be understood by the voucher decreasing rather than increasing participation in an after-school sport or club among boys (Table 1). Thus, participating in sports or clubs acts to decrease substance use in these samples. No mediators related to the school environment were identified. The direct effects showed few differences between mediators given the relatively small indirect effects.

DISCUSSION

We found that two aspects of the peer environment weakly mediated the effect of housing voucher receipt on cigarette use, marijuana use, and problematic drug use: peer drug use and participation in after-school sports of clubs. However, these mediating effects were small, contributing only fractions of a percent to the effect of voucher receipt on probability of substance use. We had hypothesized that aspects of the school environment would mediate the effect of voucher receipt on substance use outcomes, but both of the school environment variables were estimated to have null indirect effects with point estimates close to zero. These findings suggest that, in this particular population, housing voucher receipt and subsequent move out of public housing may affect substance use in small part by affecting aspects of the peer environment but not by affecting the particular aspects of the school environment we examined.

Our identification of mediators of the housing voucher receipt–adolescent substance use relationship contributes to the literature both substantively and methodologically. Substantively, we show that although moving affects both the school and peer environments, the school environment does not appear to be a mediator on the pathway from housing voucher receipt to substance use. While we do not know of any previous research estimating these same pathways, our results are supported by previous research documenting associations between similar aspects of the peer environment and substance use. For example, participating in sports has been found to be associated with lower odds of drug use in multiple studies (28), participation in after-school programs have been associated with lower substance use (29, 30), and the link between peer drug use and adolescent substance use has been consistently demonstrated (27, 48, 49). Our finding that school factors do not mediate the effect of the MTO intervention substance use was unexpected given previous research suggesting associations (including dose-response associations) between school-related factors—such as climate, connectedness, and perceived teacher support—and adolescent cigarette and drug use (22, 25, 50).

Methodologically, we demonstrate a causal mediation approach that avoids the problematic assumption of no post-treatment confounder of the mediator-outcome relationship. This assumption is required for estimating natural direct and indirect effects but is violated by the DAG in Figure 1, which reflects a randomized trial where an intervention’s effect on the mediator and outcome acts through adherence (31). Recent work on stochastic (or interventional) direct and indirect effects have relaxed the problematic assumption required of natural direct or indirect effects of no post-treatment confounder of the mediator-outcome relationship (41, 51–56). However, we know of no alternative stochastic direct and indirect effects estimator that would be useful in an instrumental variable scenario where there is no direct effect of A on M.

Another strength of our causal mediation approach is doubly robust estimation. The data-dependent stochastic direct and indirect effects targeted minimum loss-based estimator we use is appropriate for either randomized trials or observational studies. It is double robust in the sense that if one correctly specifies either the Y model or the A and M models, then the estimator is consistent. In the case of MTO, A is randomized, so misspecification of the treatment model does not apply. The estimator we use also easily incorporates machine learning approaches, thereby further reducing our reliance on correct specification of multiple parametric models. In addition, the MTO data are unique in that MTO randomized moving, typically to lower-poverty neighborhoods (through the instrument of housing voucher receipt), and consequently, the exposure is not challenged by endogeneity with numerous sociodemographic factors. In addition, the use of multiple waves of MTO data mean that the intervention measure is temporally prior to when the mediator and outcomes were assessed.

Because the mediators and outcomes were both measured at the interim follow-up, it is possible that the outcome could have temporally preceded the mediator. However, we believe it to be less likely that current cigarette or marijuana use would influence school climate or feeling safe at school. It is perhaps more likely that current substance use, which could also serve as a proxy for past substance use, could influence aspects of the peer environment, especially peer drug use. Resolving the directionality of the mediators and outcomes is an area for future work pending the release of the final wave of MTO data.

This study was limited by small sample size. Statistical power is a challenge in any mediation analysis, but poses an even greater challenge in the case of an encouragement-design like MTO where the treatment intervention does not directly affect the mediator but instead affects it through a causal intermediate. Although we could not increase our sample size, we used two approaches to minimize our risk of overfitting. We used five-fold cross validation coupled with the lasso algorithm to select a small subset of variables to include for each of the models.

Our results could have also been biased by unobserved confounding. Because this was an experimental study, substantial unobserved confounding of the treatment–outcome relationship is unlikely, but our results would still be vulnerable to unobserved post-treatment confounders of the mediator–outcome relationship.

It is also possible that the assumption of no interference between individuals could be violated given the social nature of the experiment (57). This would be the case if an adolescent's potential outcome depends on another participating adolescent's intervention assignments. This could happen if individuals interact in ways that are not captured by the full set of covariates and mediators over the years of the MTO experiment. MTO's principal investigators posited that interference is likely minimal because: 1) most participating families were socially isolated at baseline, 2) few families living in the public housing developments participated in MTO, and 3) the intervention deliberately avoided relocating families to the same neighborhoods, which resulted in little clustering of families at follow-up (36).

The indirect effects we estimated were small, increasing or decreasing the risk of substance use by tenths or hundredths of a percent. There are likely multiple contributors to such small effects, including weak mediators, weak first-stage effects (which could be due to incomplete measurement of adherence, families not moving far enough away from their original neighborhoods, and mismeasurement of mediators), as well as measurement error in outcomes and covariates. We further discuss each of these contributors in the eAppendix.

In summary, we found evidence that aspects of the peer environment weakly mediated the relationship between Section 8 voucher receipt and subsequent move out of public housing and substance use among adolescents. Despite the apparent beneficial effects of MTO on several aspects of the peer and school environments, these factors do little to explain the total effects of housing voucher randomization on substance use.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Sources of financial support: The results reported herein correspond to specific aims of grant K99DA042127 to PI Rudolph from the National Institute on Drug Abuse. NMS, MMG, and TLO's time was supported by grant

R01MD006064 from the National Institute on Minority Health and Health Disparities and by grant R03HD082679 from the National Institute of Child Health and Human Development.

References

1. Arrazola RA, Neff LJ, Kennedy SM, et al. Tobacco use among middle and high school students—united states, 2013. MMWR Morb Mortal Wkly Rep. 2014; 63(45):1021–1026. [PubMed: 25393220]
2. on Drug Abuse NI, Marijuana. https://www.drugabuse.gov/drugs-abuse/marijuana, accessed: 2017-06-12
3. Khuder SA, Dayal HH, Mutgi AB. Age at smoking onset and its effect on smoking cessation. Addictive behaviors. 1999; 24(5):673–677. [PubMed: 10574304]
4. D'Avanzo B, La Vecchia C, Negri E. Age at starting smoking and number of cigarettes smoked. Annals of epidemiology. 1994; 4(6):455–459. [PubMed: 7804500]
5. of Health UD, Services H. et al. Preventing tobacco use among youth and young adults: A report of the surgeon general. Vol. 3. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2012.
6. Volkow ND, Baler RD, Compton WM, et al. Adverse health effects of marijuana use. New England Journal of Medicine. 2014; 370(23):2219–2227. [PubMed: 24897085]
7. Macleod J, Oakes R, Copello A, et al. Psychological and social sequelae of cannabis and other illicit drug use by young people: a systematic review of longitudinal, general population studies. The Lancet. 2004; 363(9421):1579–1588.
8. Kandel DB, Davies M, Karus D, et al. The consequences in young adulthood of adolescent drug involvement: An overview. Archives of General Psychiatry. 1986; 43(8):746–754. [PubMed: 3729669]
9. Brook JS, Cohen P, Brook DW. Longitudinal study of co-occurring psychiatric disorders and substance use. Journal of the American Academy of Child & Adolescent Psychiatry. 1998; 37(3): 322–330. [PubMed: 9519638]
10. Merikangas KR, He Jp, Burstein M, et al. Lifetime prevalence of mental disorders in us adolescents: results from the national comorbidity survey replication-adolescent supplement (ncs-a). Journal of the American Academy of Child & Adolescent Psychiatry. 2010; 49(10):980–989. [PubMed: 20855043]
11. Leventhal T, Brooks-Gunn J. The early impacts of moving to opportunity on children and youth in new york city. Choosing a better life: Evaluating the Moving to Opportunity social experiment. 2003:213–44.
12. Theall KP, Sterk CE, Elifson KW. Perceived neighborhood fear and drug use among young adults. American journal of health behavior. 2009; 33(4):353–365. [PubMed: 19182981]
13. Leifheit KM, Parekh J, Matson PA, et al. Is the association between neighborhood drug prevalence and marijuana use independent of peer drug and alcohol norms? results from a household survey of urban youth. Journal of Urban Health. 2015; 92(4):773–783. [PubMed: 25900150]
14. Gennetian LA, Sanbonmatsu L, Katz LF, et al. The long-term effects of moving to opportunity on youth outcomes. Cityscape. 2012:137–167.
15. Rudolph KE, Schmidt NM, Glymour MM, et al. Composition or context:6 using transportability to understand drivers of site differences in a large-scale housing experiment. Epidemiology. 2017 In Press.
16. Harding, DJ., Gennetian, L., Winship, C., et al. Unpacking neighborhood influences on education outcomes: Setting the stage for future research. National Bureau of Economic Research; 2010. Technical report
17. Kling JR, Liebman JB, Katz LF. Experimental analysis of neighborhood effects. Econometrica. 2007; 75(1):83–119.
18. Leventhal T, Fauth RC, Brooks-Gunn J. Neighborhood poverty and public policy: A 5-year follow-up of children's educational outcomes in the new york city moving to opportunity demonstration. Developmental Psychology. 2005; 41(6):933. [PubMed: 16351338]

19. Orr L, Feins J, Jacob R, et al. Moving to opportunity: Interim impacts evaluation. 2003
20. Wang MT, Dishion TJ. The trajectories of adolescents' perceptions of school climate, deviant peer affiliation, and behavioral problems during the middle school years. Journal of Research on Adolescence. 2012; 22(1):40–53. [PubMed: 22822296]
21. Klein J, Cornell D, Konold T. Relationships between bullying, school climate, and student risk behaviors. School Psychology Quarterly. 2012; 27(3):154. [PubMed: 22889138]
22. LaRusso MD, Romer D, Selman RL. Teachers as builders of respectful school climates: Implications for adolescent drug use norms and depressive symptoms in high school. Journal of Youth and Adolescence. 2008; 37(4):386–398.
23. Kulis S, Marsiglia FF, Sicotte D, et al. Neighborhood effects on youth substance use in a southwestern city. Sociological Perspectives. 2007; 50(2):273–301. [PubMed: 21339890]
24. Leventhal T, Brooks-Gunn J. The neighborhoods they live in: the effects of neighborhood residence on child and adolescent outcomes. Psychological bulletin. 2000; 126(2):309. [PubMed: 10748645]
25. Mayberry ML, Espelage DL, Koenig B. Multilevel modeling of direct effects and interactions of peers, parents, school, and community influences on adolescent substance use. Journal of youth and adolescence. 2009; 38(8):1038–1049. [PubMed: 19636769]
26. Hoffman BR, Monge PR, Chou CP, et al. Perceived peer influence and peer selection on adolescent smoking. Addictive behaviors. 2007; 32(8):1546–1554. [PubMed: 17188818]
27. Maxwell KA. Friends: The role of peer influence across adolescent risk behaviors. Journal of Youth and adolescence. 2002; 31(4):267–277.
28. Lisha NE, Sussman S. Relationship of high school and college sports participation with alcohol, tobacco, and illicit drug use: A review. Addictive behaviors. 2010; 35(5):399–407. [PubMed: 20100638]
29. Elder C, Leaver-Dunn D, Wang MQ, et al. Organized group activity as a protective factor against adolescent substance use. American Journal of Health Behavior. 2000; 24(2):108–113.
30. Schinke SP, Fang L, Cole KC. Substance use among early adolescent girls: risk and protective factors. Journal of Adolescent Health. 2008; 43(2):191–194. [PubMed: 18639794]
31. Rudolph KE, Sofrygin O, van der Laan MJ. Robust and flexible estimation of stochastic mediation effects: a proposed method and example in a randomized trial setting. arXiv preprint.
32. Sanbonmatsu L, Ludwig J, Katz LF, et al. Moving to opportunity for fair housing demonstration program–final impacts evaluation. 2011
33. Osypuk TL, Schmidt NM, Bates LM, et al. Gender and crime victimization modify neighborhood effects on adolescent mental health. Pediatrics. 2012; 130(3):472–481. [PubMed: 22908105]
34. Angrist JD, Imbens GW, Rubin DB. Identification of causal effects using instrumental variables. Journal of the American statistical Association. 1996; 91(434):444–455.
35. Leventhal T, Brooks-Gunn J. Moving to opportunity: an experimental study of neighborhood effects on mental health. American Journal of Public Health. 2003; 93(9):1576–1582. [PubMed: 12948983]
36. Ludwig J, Liebman JB, Kling JR, et al. What can we learn about neighborhood effects from the moving to opportunity experiment? American Journal of Sociology. 2008; 114(1):144–188.
37. Buuren S, Groothuis-Oudshoorn K. mice: Multivariate imputation by chained equations in r. Journal of statistical software. 2011; 45(3)
38. Rubin, DB. Multiple imputation for nonresponse in surveys. Vol. 81. John Wiley & Sons; 2004.
39. Clampet-Lundquist S, Edin K, Kling JR, et al. Moving teenagers out of high-risk neighborhoods: How girls fare better than boys. American Journal of Sociology. 2011; 116(4):1154–1189.
40. Nguyen QC, Rehkopf DH, Schmidt NM, et al. Heterogeneous effects of housing vouchers on the mental health of us adolescents. American journal of public health. 2016; 106(4):755–762. [PubMed: 26794179]
41. VanderWeele TJ, Tchetgen Tchetgen EJ. Mediation analysis with time varying exposures and mediators. Journal of the Royal Statistical Society: Series B (Statistical Methodology). 2017; 79(3):917–938. [PubMed: 28824285]
42. Bang H, Robins JM. Doubly robust estimation in missing data and causal inference models. Biometrics. 2005; 61(4):962–973. [PubMed: 16401269]

43. Pearl, J. Proceedings of the seventeenth conference on uncertainty in artificial intelligence. Morgan Kaufmann Publishers Inc; 2001. Direct and indirect effects; p. 411-420.

44. Tibshirani R. Regression shrinkage and selection via the lasso. Journal of the Royal Statistical Society Series B (Methodological). 1996:267–288.

45. Friedman J, Hastie T, Tibshirani R. Regularization paths for generalized linear models via coordinate descent. Journal of statistical software. 2010; 33(1):1. [PubMed: 20808728]

46. Clark TT, Doyle O, Clincy A. Age of first cigarette, alcohol, and marijuana use among us biracial/ethnic youth: A population-based study. Addictive behaviors. 2013; 38(9):2450–2454. [PubMed: 23688908]

47. Swendsen J, Anthony JC, Conway KP, et al. Improving targets for the prevention of drug use disorders: sociodemographic predictors of transitions across drug use stages in the national comorbidity survey replication. Preventive medicine. 2008; 47(6):629–634. [PubMed: 18926848]

48. Norton EC, Lindrooth RC, Ennett ST. Controlling for the endogeneity of peer substance use on adolescent alcohol and tobacco use. Health Economics. 1998; 7(5):439–453. [PubMed: 9753378]

49. Lundborg P. Having the wrong friends? peer effects in adolescent substance use. Journal of health economics. 2006; 25(2):214–233. [PubMed: 15964090]

50. Bond L, Butler H, Thomas L, et al. Social and school connectedness in early secondary school as predictors of late teenage substance use, mental health, and academic outcomes. Journal of Adolescent Health. 2007; 40(4):357–e9.

51. Didelez, V., Dawid, AP., Geneletti, S. Proceedings of the Twenty-Second Conference on Uncertainty in Artificial Intelligence. AUAI Press; 2006. Direct and indirect effects of sequential treatments; p. 138-146.

52. van der Laan MJ, Petersen ML. Direct effect models. The International Journal of Biostatistics. 2008; 4(1)

53. Zheng W, van der Laan MJ. Causal mediation in a survival setting with time-dependent mediators. 2012

54. VanderWeele TJ, Vansteelandt S, Robins JM. Effect decomposition in the presence of an exposure-induced mediator-outcome confounder. Epidemiology (Cambridge, Mass). 2014; 25(2):300.

55. Vansteelandt S, Daniel RM. Interventional effects for mediation analysis with multiple mediators. Epidemiology (Cambridge, Mass). 2017; 28(2):258.

56. Zheng W, van der Laan M. Longitudinal mediation analysis with time-varying mediators and exposures, with application to survival outcomes. Journal of Causal Inference. 2017

57. Sobel ME. What do randomized studies of housing mobility demonstrate? causal inference in the face of interference. Journal of the American Statistical Association. 2006; 101(476):1398–1407.

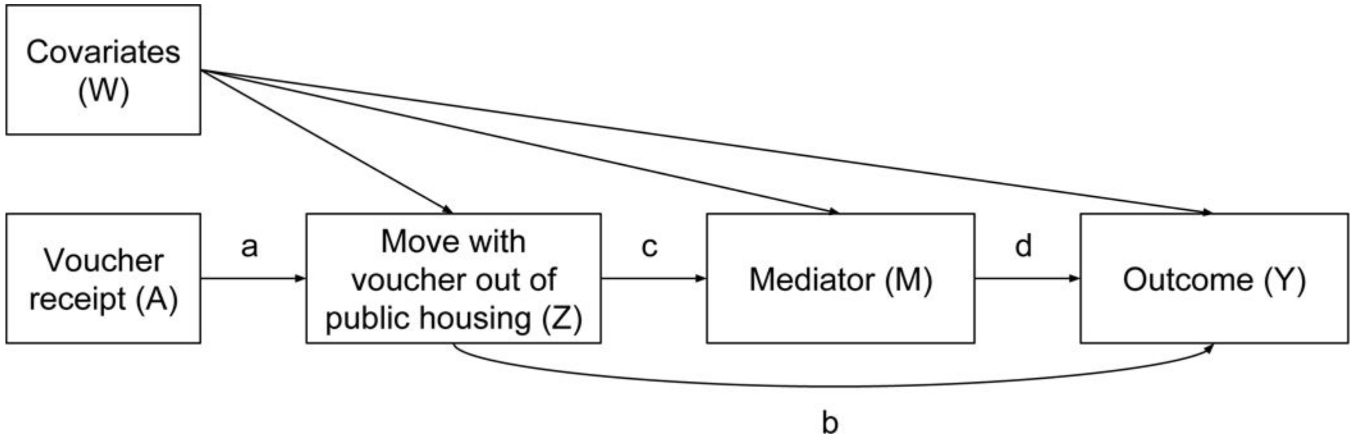

Figure 1.
Directed acyclic graph (DAG) of Moving to Opportunity's causal model of mediation.

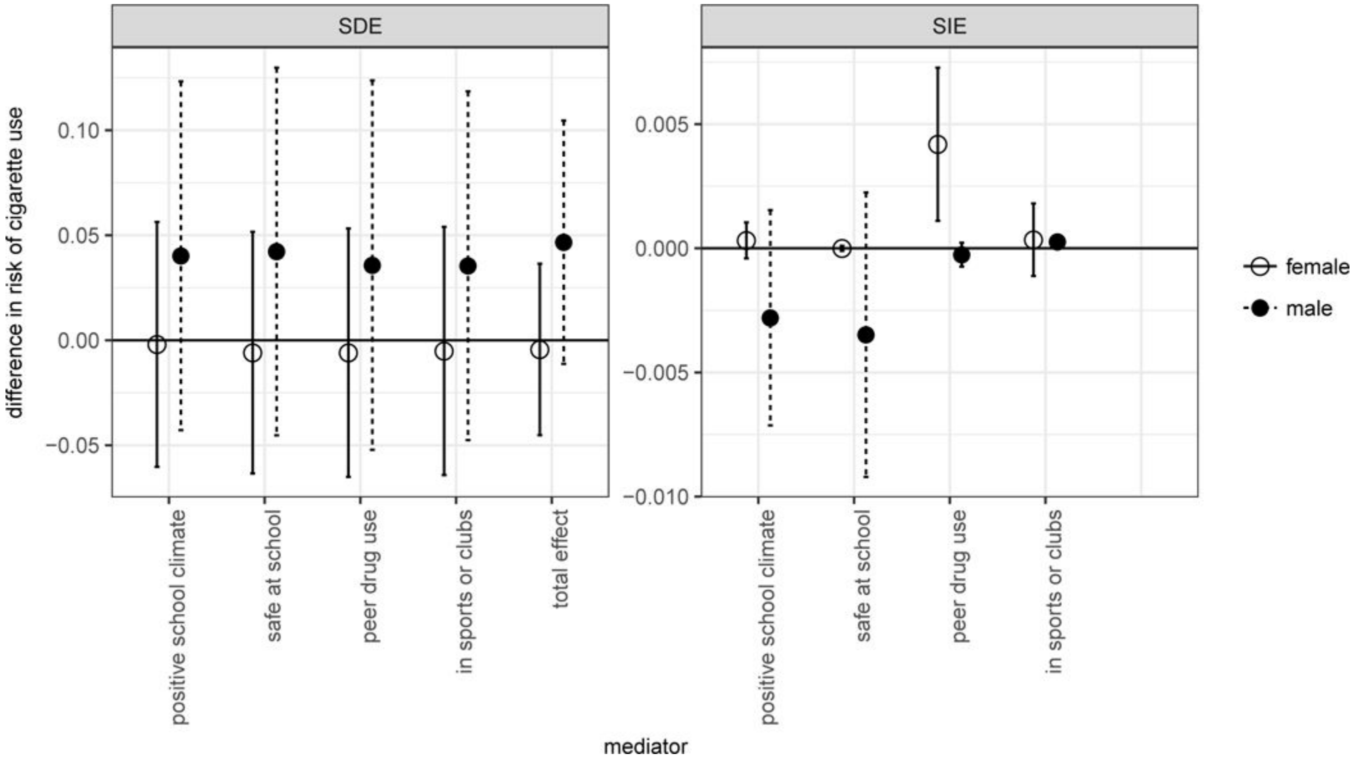

Figure 2.
Data-dependent stochastic direct (SDE) and indirect effect (SIE) estimates and 95% confidence intervals on cigarette use by mediator. The total effect is provided for reference in the SDE panel. Note that the SDE and SIE are graphed on different scales. Data from the Moving to Opportunity experiment, interim follow up.

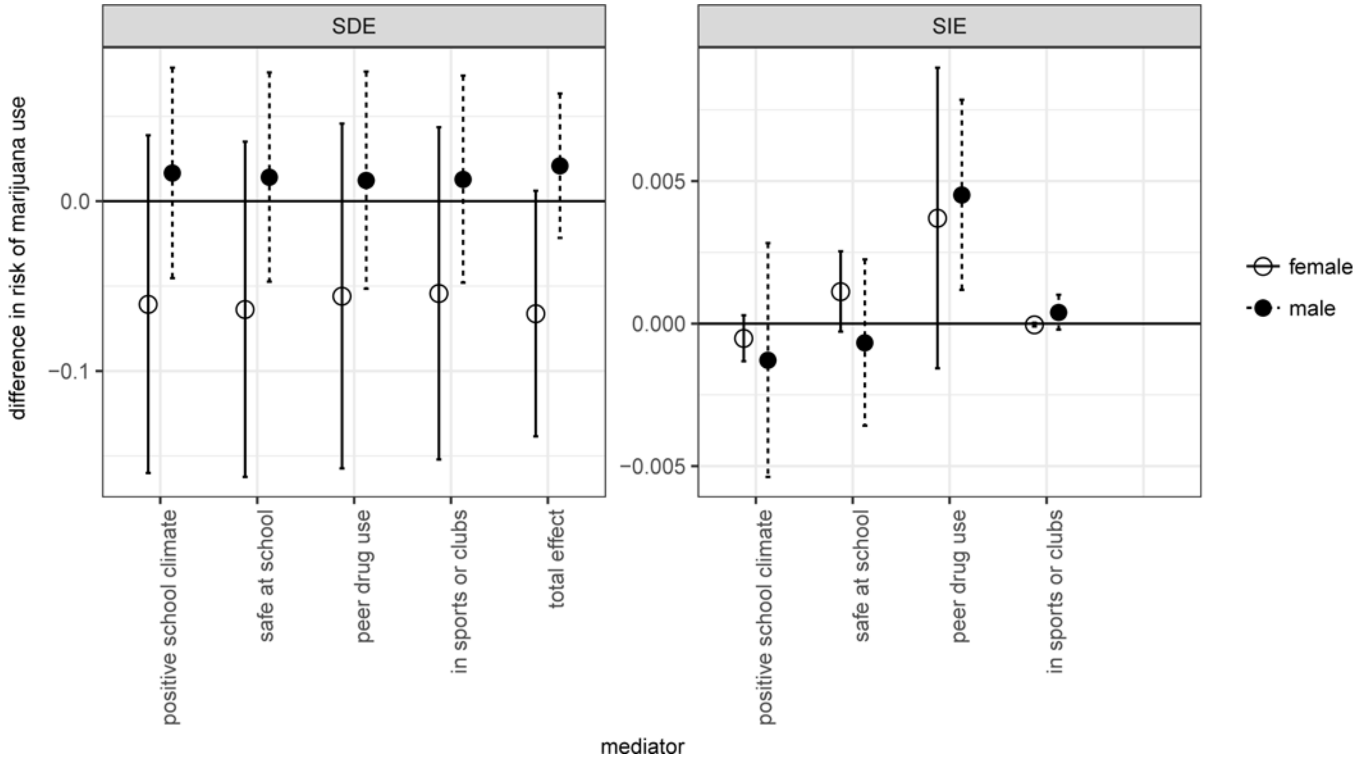

Figure 3.
Data-dependent stochastic direct (SDE) and indirect effect (SIE) estimates and 95% confidence intervals on marijuana use by mediator. The total effect is provided for reference in the SDE panel. Note that the SDE and SIE are graphed on different scales. Data from the Moving to Opportunity experiment, interim follow up.

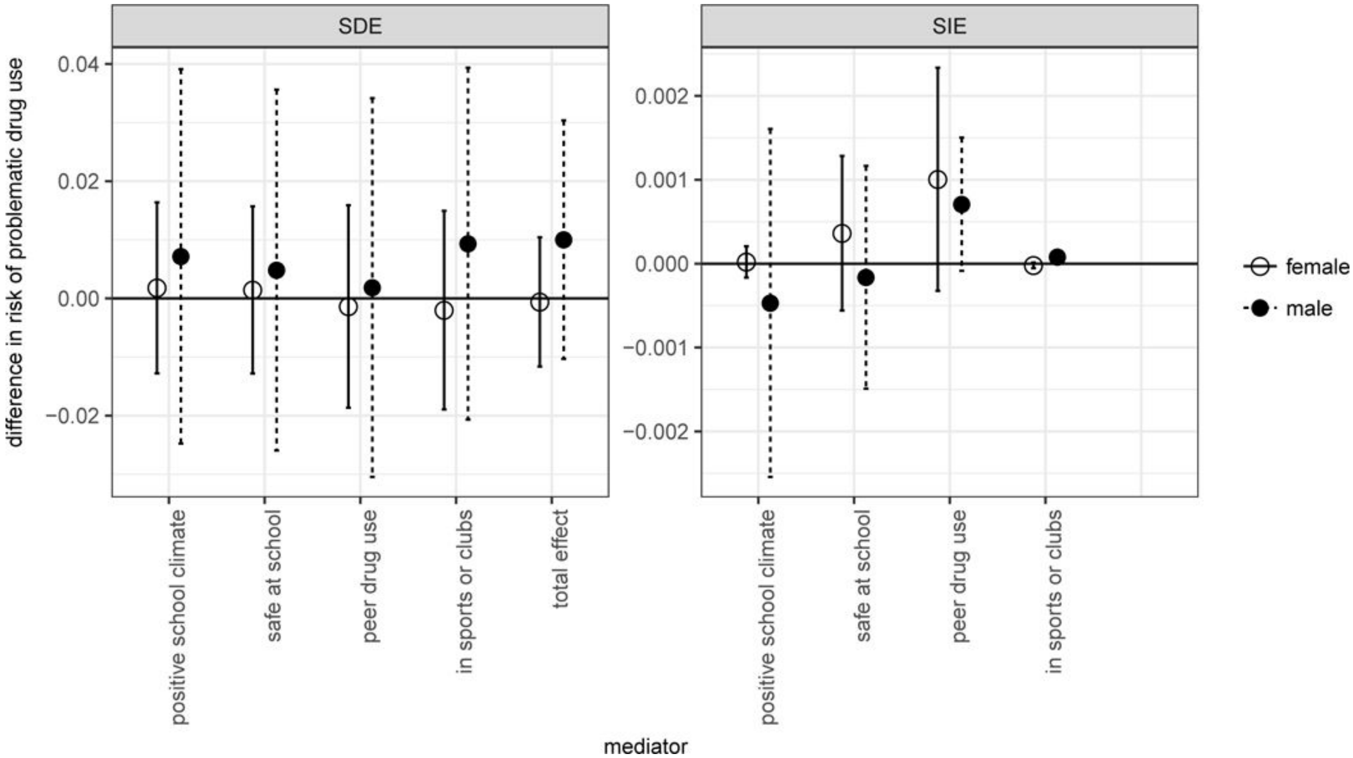

Figure 4.
Data-dependent stochastic direct (SDE) and indirect effect (SIE) estimates and 95% confidence intervals on problematic drug use by mediator. The total effect is provided for reference in the SDE panel. Note that the SDE and SIE are graphed on different scales. Data from the Moving to Opportunity experiment, interim follow up.

Table 1

Risk differences (RD) of the effect of voucher receipt on the mediator by outcome sample (marginal effects, adjusting for baseline covariates and adherence, *Z*). CI indicates confidence interval.

Mediator	**Boys RD (95% CI)**	**Girls RD (95% CI)**
Cigarette Use Sample		
Feels safe at school	0.033 (0.023, 0.043)	0.001 (−0.002, 0.005)
Positive school climate	0.036 (0.027, 0.046)	−0.008 (−0.012, −0.005)
Participates in after-school sport or club	−0.004 (−0.007, −0.000)	0.006 (0.005, 0.008)
Has friends who use drugs	−0.004 (−0.023, 0.016)	0.032 (0.019, 0.044)
Marijuana Use Sample		
Feels safe at school	0.030 (0.026, 0.034)	0.026 (0.021, 0.032)
Positive school climate	0.042 (0.036, 0.047)	−0.012 (−0.020, −0.005)
Participates in after-school sport or club	−0.008 (−0.014, −0.002)	0.001 (−0.004, 0.005)
Has friends who use drugs	0.027 (0.012, 0.041)	0.048 (0.028, 0.068)
Problematic Drug Use Sample		
Feels safe at school	0.030 (0.024, 0.037)	−0.028 (−0.032, −0.025)
Positive school climate	0.035 (0.028, 0.042)	−0.008 (−0.011, −0.004)
Participates in after-school sport or club	−0.003 (−0.005, 0.000)	0.003 (0.002, 0.004)
Has friends who use drugs	0.014 (−0.001, 0.028)	0.032 (0.019, 0.044)