

An Application of the Complier Average Causal Effect Analysis to Examine the Effects of a Family Intervention in Reducing Illicit Drug Use among High-Risk Hispanic Adolescents

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The Complier Average Causal Effect (CACE) method has been increasingly used in prevention research to provide more accurate causal intervention effect estimates in the presence of noncompliance. The purpose of this study was to provide an applied demonstration of the CACE analytic approach to evaluate the relative effects of a family-based prevention intervention, Familias Unidas, in preventing/reducing illicit drug use for those participants who received the intended dosage. This study is a secondary data analysis of a randomized controlled trial designed to evaluate the relative efficacy of Familias Unidas with high-risk Hispanic youth. A total of 242 high-risk Hispanic youth aged 12–17 years and their primary caregivers were randomized to either Familias Unidas or Community Practice and assessed at baseline, 6 months and 12 months postbaseline. CACE models were estimated with a finite growth mixture model. Predictors of engagement were included in the CACE model. Findings indicate that, relative to the intent-to-treat (ITT) analytic approach, the CACE analytic approach yielded stronger intervention effects among both initially engaged and overall engaged participants. The CACE analytic approach may be particularly helpful for studies involving parent/family-centered interventions given that participants may not receive the intended dosage. Future studies should consider implementing the CACE analysis in addition to ITT analysis when examining the effects of family-based prevention programs to determine whether, and the extent to which, the CACE analysis has more power to uncover intervention effects.

Keywords: Familias Unidas Intervention; Drug Use; CACE

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INTRODUCTION

Several analytic approaches have been applied to the field of prevention science to evaluate the efficacy or effectiveness of preventive interventions in randomized clinical trials, including intent-to-treat (ITT) and as-treated analytic approaches (Ellenberg, 1996;

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Newell, 1992). Of these, the ITT analysis has been the most widely used approach (Food & Drug Administration, 1997). The ITT method analyzes data by using data from all participants regardless of whether participants received the intended dosage of the intervention. In doing so, this analytic approach preserves the balance across conditions of randomized clinical trials and provides unbiased results of the effects of intervention assignment. Because of this, a strength of the ITT analysis is its ecological validity. That is, the ITT approach may have more utility to researchers and practitioners alike who are interested in examining the impact of preventive interventions in a real-world setting. A limitation of this approach, however, is that it may lack statistical power when evaluating the effects of interventions (Chene et al., 1998) in the presence of participants who received less than the intended dosage (i.e., noncomplier in intervention). For example, family-based interventions are often characterized by multiple intervention modules and it is likely that participants assigned to the experimental condition may not participate in some intervention modules or may not complete any modules at all (Prado, Pantin, Schwartz, Lupei, & Szapocznik, 2006). The ITT analytical strategy does not account for this noncompliance. This may underestimate the magnitude of the effects of the intervention because the intervention effects are diluted by those participants who did not receive the intended intervention dosage (Jo & Muthén, 2001). Alternatively, the as-treated analytic strategy compares only those participants who received the intended intervention dosage to the entire control group. However, a limitation to the as-treated analytic strategy is that this approach excludes noncomplier participants from the analysis, which may produce significant differences with respect to measured or unmeasured confounders between the intervention and control conditions and may thus result in biased comparisons due to the loss of randomization (Yau & Little, 2001).

Given the challenge of participants' noncompliance with the intervention in randomized controlled trials, the Complier Average Causal Effect (CACE) method (Bloom, 1984; Little & Rubin, 2000) was developed as a statistical method that takes noncompliance into account. The CACE approach postulates four types of compliance status: complier, never takers, defiers, and always takers (Angrist, Imbens, & Rubin, 1996; Little & Yau, 1998). Here, we consider the CACE compliance types in the context of a two-arm design with an active intervention arm and a placebo control condition. As seen from Table 1, Compliers are participants who comply with the study condition they were assigned, for example, participants who receive an intervention if assigned to the experimental condition or participants who do not receive the intervention if assigned to the control condition. Never takers are participants who, regardless of the condition assignment, would never receive the intervention. Defiers are participants who would do the opposite of the condition assignment. For example, participants would not receive the intervention if assigned to the experimental condition or participants who would receive the intervention if assigned to the control condition (e.g., contamination). Always takers are participants who would always receive the intervention regardless of the condition assignment. A strength of the CACE method is that it allows researchers to examine causal intervention effects of having received the intervention by comparing compliers in the intervention group to compliers in the control group who would have adhered to the experimental arm, if given the opportunity to do so (Jo, 2002). CACE may be more appropriate when the purpose of the study was to examine causal intervention effects by taking noncompliance into account. A limitation of the CACE method, however, is that it may not fully reflect the results expected in a real-world application due to noncompliance. Table 2 summarizes the advantages and disadvantages of the ITT and CACE approaches. It is worth noting that the choice of the ITT or CACE analytic approach should be guided by the research question. If the question is about the expected real-world impact of the intervention, ITT may be appropriate, whereas if the question is about causal intervention effects, CACE may be more appropriate.

TABLE 1
Classification of Participants in a CACE Study

	Received intended dosage	Did not receive intended dosage
Tx	Compliers Always takers	Never takers Defiers
Control	Always takers Defiers	Compliers Never takers

TABLE 2
Comparisons between the ITT and CACE Approach

	ITT	CACE
Overview	Uses data from all participants regardless of whether participants received the intended dosage of the intervention	Postulates four types of compliance status, including complier, never takers, defiers, and always takers. Compares compliers in the intervention group to compliers in the control group who would have adhered to the experimental arm, if given the opportunity to do so
Strengths	Preserves the balance across conditions in a randomized clinical trial Provides unbiased results of the effect of condition assignment Includes all individuals randomized to the experimental condition in the analyses, thus providing a more comprehensive picture of real-world application	In the presence of noncompliance, it yields causal estimates of the effects of intervention for individuals who comply with the experimental condition (i.e., the effect of receiving the intervention) Can examine factors associated with engagement in the intervention
Weaknesses	May lack statistical power when evaluating the effects of condition with noncompliance Intervention effects are diluted by those participants who did not receive the intended intervention dosage, therefore underestimating the effects of the active intervention components	May not reflect results expected in a real-world application due to noncompliance The underlying assumptions should be clearly specified and may be potentially invalid
Best used for	Testing the intervention effect that would happen in the real world	CACE may be more appropriate when the purpose of the study was to examine causal intervention effects by taking noncompliance into account

The CACE method has been increasingly used in prevention research to provide more accurate causal intervention effect estimates in the presence of noncompliance. In a recent study of a family-centered intervention, *Family Check-Up*, aimed at preventing antisocial behavior and substance use in youth (Stormshak et al., 2011), the authors found only 42% of families engaged in the intervention. Given the low engagement rate, the CACE method was utilized and significant intervention effects were found on antisocial behaviors and substance use among those participants who complied with the intervention. However, this study was limited by the lack of comparison in results between the CACE and ITT analysis. Lochman, Boxmeyer, Powell, Roth, and Windle (2006) evaluated an abbreviated version of the *Coping Power Program* for reducing children's aggressive behavior. In addition to the ITT analysis, two sets of CACE analysis were conducted with two complier

definitions: attended at least one session out of 10 parent group sessions (70.5% cases) and attended eight or more sessions (24.1% cases). The results showed that decreases on externalizing scores were more substantial in the CACE analyses, compared to the ITT analysis. However, despite the increased use of CACE in prevention science, few studies have applied the CACE method to evaluate the relative effects of family-based preventive interventions (Connell, Dishion, Yasui, & Kavanagh, 2007). Therefore, the purpose of this study was to provide an applied demonstration of the CACE analytic approach to evaluate the relative effects of a family-based prevention intervention, Familias Unidas, in preventing/reducing illicit drug use for those participants who received the intended dosage. Familias Unidas was found efficacious in reducing the probability of past 90-day illicit drug use in a recent randomized trial among 242 high-risk Hispanic adolescents utilizing the ITT analysis (Prado et al., 2012). Given the fact that in a previous study (Prado et al., 2012), some participants had a lower than optimal intervention dosage, this study will compare the effects of the Familias Unidas intervention as analyzed through the use of CACE versus ITT. We hypothesize that the CACE method will reveal stronger intervention effects in reducing past 90-day illicit drug use for Familias Unidas, compared to the effects resulting from the use of the ITT analysis. To our knowledge, this is the first study to use CACE analysis for evaluating the effects of a family-based preventive intervention, such as Familias Unidas, in preventing/reducing illicit drug use among adolescents.

METHOD

Participants

This study is a secondary data analysis of a randomized controlled trial designed to evaluate the relative efficacy of Familias Unidas with high-risk Hispanic youth (Prado et al., 2012). Eligibility criteria for this study included adolescents who: (a) self-identified as Hispanic or Latino; (b) were between the ages of 12–17 years; (c) had plans to remain a resident of South Florida during the duration of the study; and (d) had been identified as a high-risk youth. For recruitment, research staff screened potential participants over the phone to identify those who met all of the eligibility criteria, and those potential participants were scheduled for a face-to-face meeting to have the study explained to them, sign informed consent/assent, and complete the baseline assessment. A total of 242 youth and their primary caregivers were recruited through the Miami-Dade County Department of Juvenile Justice and the Miami-Dade County Public School (MDCP-S) system. For this study, high risk was defined as having been arrested or as having committed at least one “Level III Behavior Problem,” described by MDCP-S as assault/threat against a nonstaff member, breaking and entering/burglary, fighting (serious), hazing, possession or use of alcohol and/or controlled substances, possession of simulated weapons, trespassing, and vandalism. Participants were 156 boys and 86 girls (mean age = 14.7, $SD = 1.38$). The median household income was \$15,000 to \$19,999. The majority (65.3%, $n = 158$) of adolescents were born in the United States. Immigrant adolescents ($n = 84$) and parents were primarily born in Cuba (25.0%), Honduras (15.5%), and Nicaragua (9.5%). Of foreign born adolescents, 21.4% ($n = 18$) had been living in the United States for less than 3 years, 58.3% ($n = 49$) between 3 and 10 years, and 20.2% ($n = 17$) for more than 10 years.

Study Design

The study design consisted of a 2 (Condition) \times 3 (Time) randomized controlled trial.

All participants in the study were randomly assigned to either the Familias Unidas intervention ($n = 120$) or Community Practice condition ($n = 122$), where participants

were referred to standard of care services through the Department of Juvenile Justice or a community-based organization. Participants were followed up at 6 months ($n = 232$) and 12 months ($n = 229$) postbaseline (Figure 1). At each assessment, adolescents were asked whether they had used an illicit substance in the 90 days prior to assessment. For this study, binary variables were created to indicate any illicit drug use in the past 90 days. Additional study design and procedural details for the parent study have been described and can be found elsewhere (Prado et al., 2012).

Study Conditions

Experimental condition

Familias Unidas is guided by ecodevelopmental theory, which posits that adolescents are situated within a network of overlapping and mutually interacting systems (Pantin, Schwartz, Sullivan, Prado, & Szapocznik, 2004; Szapocznik & Coatsworth, 1999). Administered over a 12-week period, eight 2-hour sessions are delivered to parents in a group format that focuses on (a) building parental investment in the adolescents' worlds; (b)

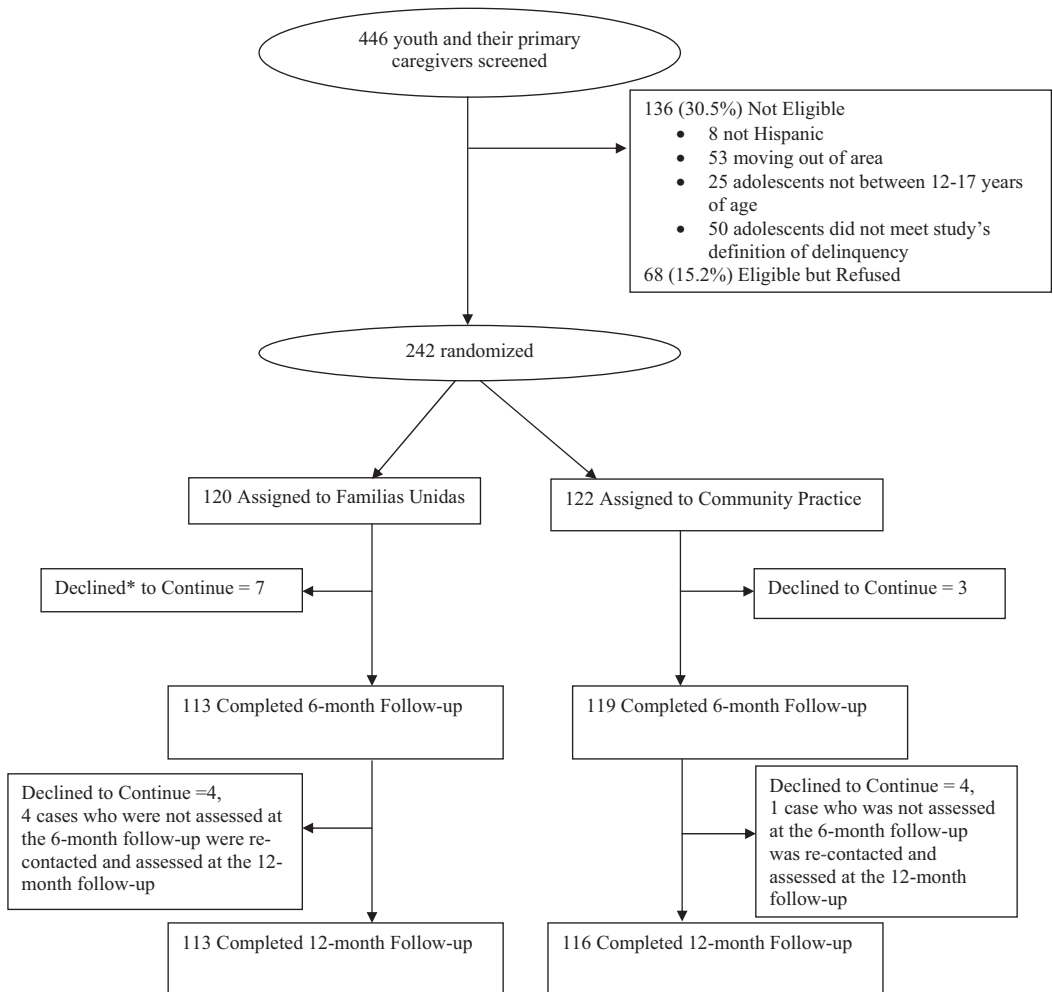


FIGURE 1. Flow of Study Participants. *Participants declined to participate or lost to follow-up.

enhancing communication skills; (c) improving family support; (d) increasing parental investment in the school world; (e) increasing monitoring of the peer world; (f) preventing and reducing adolescent substance use by enhancing communication skills around drug use; (g) preventing and reducing adolescent risky sexual behavior by enhancing communication skills around risky sexual behavior; and (h) prevention as a continuous and ongoing process. In addition, four 1-hour family sessions allow for parents to practice with their adolescent the skills they learned in the group sessions.

Community practice

Participants randomized to the Community Practice condition were offered referrals for standard care services provided by the Department of Juvenile Justice or community-based organizations in Miami-Dade County. Standard care services consisted of various therapeutic approaches, including individual and family therapy, aimed at preventing and reducing substance use and sexual risk behaviors in adolescents and their families.

Statistical Analyses

Categorization of participants into complier categories

Due to the exploratory nature of this study and the lack of prior determination regarding the exact definition of Familias Unidas compliance, two definitions of complier were utilized to classify participation in the intervention: initially engaged and overall engaged. First, consistent with our prior engagement research (Perrino, Coatsworth, Briones, Pantin, & Szapocznik, 2001; Prado et al., 2006), participants were classified as “initially engaged” if a caregiver attended at least one of the first three parent group sessions. This engagement definition focuses on initial participation, which is typically affected by factors and processes such as recruitment strategy, parental motivation, and parental beliefs about the usefulness of the intervention. Using this definition, 83 (69.2%) of the families in the intervention group were classified as “initially engaged” and the remainder as “not engaged.” The dosage of initially engaged participants ranged from 1 to 12 sessions ($M = 8.9$, $SD = 2.75$).

Second, we defined families as overall engaged if a caregiver attended at least 50% of the intended dosage. This definition is consistent with the work of Dishion (2012). To do so, we calculated the total dosage received by summing up the sessions that a participant attended. The possible dosage for the intervention group ranged from 0 to 12 sessions ($M = 6.88$, $SD = 4.05$); thus, caregivers who attended at least six sessions were classified as overall engaged and the remainder as not engaged. The dosage of overall engaged participants ranged from 6 to 12 sessions ($M = 9.46$, $SD = 1.89$). The complier definitions described above utilized multiple sources of information including initial entry and dosage (i.e., subsequent attendance).

Validation of CACE assumptions

There are five assumptions underlying the CACE methodology (Jo, 2002). In the following section, we describe each of these assumptions and how they were addressed:

- 1 *Random assignment.* The CACE method requires the presence of random assignment. In this study, participants were randomly assigned to intervention or Community Practice.
- 2 *Stable Unit Treatment Value Assumption.* This assumption requires that the outcomes for each participant be independent from the outcomes of other participants.

Given that Familias Unidas was delivered to parents through parent group sessions and family visits, and only one adolescent in each family participated in this study, we can safely assume this assumption was met.

- 3 *No defiers.* As stated above, defiers are participants who do the opposite of the condition assignment they were randomized to. In this study, it is unlikely that participants assigned to the control group received any Familias Unidas intervention content. Accordingly, there are no defiers in the control group. Due to the random assignment, we assume that the same lack of defiers would be found in the intervention group. For the same reason, in this study, always-taker membership is also zero due to the design of the study, where participants do not have access to the intervention unless they were randomly assigned to it.
- 4 *Rate of compliance is not zero.* This assumption implies that the rate of compliance cannot be zero. As mentioned above, engagement analysis indicated that 69.2% of participants were initially engaged compliers and 65.8% were overall engaged compliers in the experimental group, which satisfies the rate of compliance.
- 5 *Exclusion restriction assumption.* The exclusion restriction assumption denotes that the intervention effect is assumed to be zero for noncompliers (i.e., no effect of intervention). For this study, because the noncompliers in the intervention group did not receive the targeted intervention dosage, we assume the intervention effect was zero for noncompliers. However, this assumption can be problematic because noncompliers randomized to the intervention condition do possibly participate in some of the group sessions or family visits. However, studies show that including pretreatment covariates to predict compliance status can relax this assumption (Frangakis & Rubin, 1999; Jo, 2002).

Estimation of CACE models

We estimated a linear growth model with intercept and slope because this study was limited to three time points. CACE models were estimated with a finite growth mixture model with two classes (i.e., complier and never taker, per assumption 2). The compliance status (compliers or never takers) was directly observed (per engagement definition) in the experimental group and was estimated for the control group. In this study, the unknown compliance status in the control group (compliers or never takers) is treated as missing data, which was estimated using maximum likelihood estimation via the Expectation-Maximization (ML-EM) algorithm estimation (Jo & Muthén, 2003) with Mplus (Muthén & Muthén, 1998–2012). The ML-EM estimation method is more efficient than the traditional instrumental variable (IV) method. More specifically, two dummy class membership variables were used to indicate compliance status. In the intervention group, compliers (based on observed compliance) were assigned 1 for dummy class variable 1, and 0 for dummy class variable 2; noncompliers (based on observed compliance) were assigned 0 for dummy class variable 1, and 1 for dummy class variable 2. In the control condition, because compliance status was unknown, both dummy class variables were assigned 1 to allow their compliance status to be estimated. When specifying the intervention effect for the noncomplier class, the intervention effect (e.g., regression of slope on condition) was fixed at zero under the exclusion restriction assumption that the intervention effect is zero. Second, to increase the precision of the CACE estimates and also to identify predictors of engagement, we then included baseline covariates, including family income, family stress, parent report of positive parenting, and adolescent behavior problems as predictors of compliance status in the CACE model. These covariates were included because they were all tested as potential predictors of compliance in a previous study (Prado et al., 2006). The sample Mplus input syntax for this study is available upon

request. In addition, a sample Mplus CACE analysis input syntax can be found at <http://www.statmodel.com/examples/mixture/mix12.html>.

RESULTS

As reported in our previous publication (Prado et al., 2012), the ITT analysis (using growth curves) showed a significant difference in past 90-day illicit drug use between Familias Unidas and Community Practice ($b = 0.72, SE = 0.34, z = 2.11, p = .04$).

For the CACE analysis, using the initially engaged definition, the intervention was significantly related to the linear slope ($b = 1.04, SE = 0.53, z = 1.97, p = .05$), which was higher than the ITT estimate ($b = 0.72$). The CACE results showed that the estimates of intervention effects among participants who attended at least one of the first three parent group sessions were stronger than that of the ITT analysis. Using the overall engaged definition, the intervention was significantly related to the linear slope ($b = 1.14, SE = 0.55, z = 2.08, p = .04$). On the basis of the CACE model using the overall engaged definition, we then included baseline covariates to predict the compliance status. The intervention effect was comparable to the model without covariates ($b = 0.99, SE = 0.40, z = 2.49, p = .01$). The results showed that higher positive parenting was negatively and significantly related to engagement ($OR = 0.82, p = .004$).

We then compared the ITT results with this CACE analysis results. As shown in Figure 2, for compliers, the observed proportion of youth reporting illicit drug use in Familias Unidas decreased from 33.8% at baseline to 22.1% at 12-month postbaseline, while for youth in the Community Practice condition it increased from 33.7% at baseline to 45.5% at 12-month postbaseline. In the ITT analysis, the observed proportion of youth reporting illicit drug use in Familias Unidas decreased from 29.1% at baseline to 22.5% at 12-month postbaseline, while for youth in the Community Practice condition it increased from 23.1% at baseline to 31.3% at 12-month postbaseline. Relative to the ITT analysis, the observed differences in trajectories across conditions were more substantial in the CACE analysis.

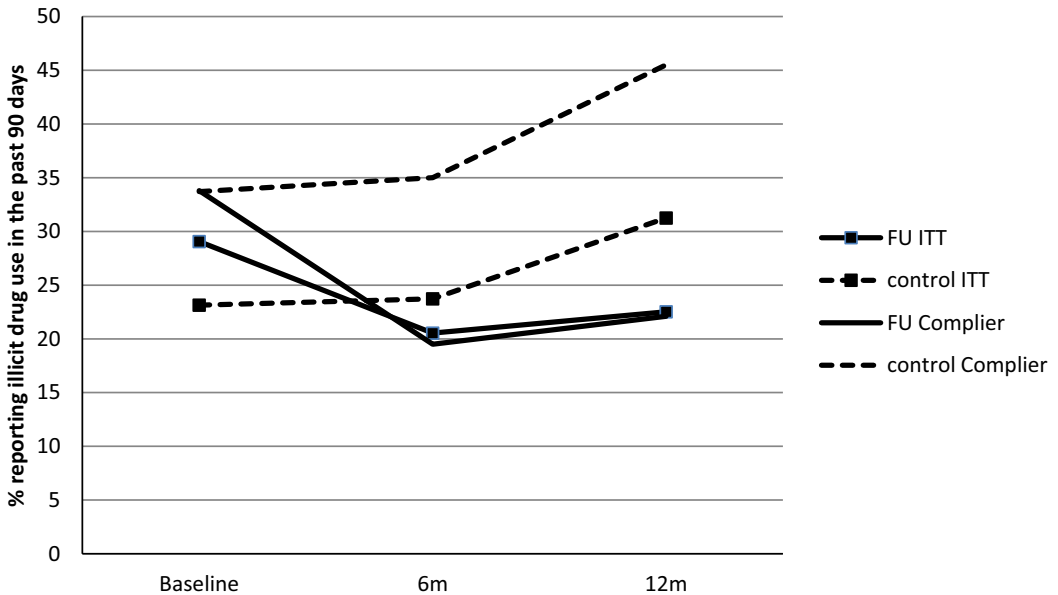


FIGURE 2. Observed % of Illicit Drug Use for ITT and CACE Analysis with Covariates.

DISCUSSION

In this study, we explored the utility of the CACE analytic approach in examining the relative efficacy of Familias Unidas on decreasing past 90-day illicit drug use. Findings indicate that, relative to the ITT analytic approach, the CACE analytic approach yielded stronger intervention effects among both initially engaged and overall engaged participants. Specifically, results suggest that the intervention effects estimates increased from 0.72 to 1.04 (with initially engaged) and to 1.14 (with overall engaged), respectively. Therefore, one advantage of the CACE analytic strategy might be to produce more precise findings when testing for causal intervention effects by examining effects for participants who actually received the targeted dosage. This is especially appropriate for family-based prevention programs with multiple intervention modules, where participants in the experimental condition are likely to not participate in some intervention sessions or may not complete any sessions at all. When compliance is less than optimal in randomized trials, the ITT analysis may not be able to reveal significant intervention effects. Thus, the CACE analytical strategy provides an opportunity for researchers to reveal causal intervention effects that take noncompliance into account. This is particularly important for preventive family-based interventions with minority populations, given the underrepresentation of these groups in randomized controlled trials. The CACE methodology provides an additional tool for uncovering effects for an often difficult to engage and retain population, therefore maximizing the opportunity for identifying what works for these groups. Given today's best practices and managed health care system, practitioners are now more than ever being required to deliver research-informed interventions and standards of care. These demands necessitate that clinicians develop a knowledge base to understand for whom interventions work, under what conditions, and the mechanisms by which these interventions have an impact. The CACE method provides clinicians with another perspective to critically evaluate the efficacy of a family-based intervention and determine for themselves if this intervention may be appropriate for the populations they serve. Although an intervention may otherwise have been discarded as a possibility, the CACE approach provides an additional level of analysis for clinicians to consider by taking intervention noncompliance, a real-world challenge that many clinicians experience, into account when evaluating an evidence-based intervention program. This is important given the low levels of participation that are common and the low number of interventions available to minority populations.

Although it should not be surprising, study findings suggest that participants who were classified as initially or overall engaged benefited the most from the effects of a family-based preventive intervention on past 90-day drug use. From a preventive intervention perspective, identifying barriers to participation in family-based prevention programs may aid in improving session attendance. Improving session attendance might be particularly important as, similar to previous research (Prado et al., 2006), study findings indicate that higher rates of compliance (i.e., session attendance), relative to lower rates of compliance, improve behavioral outcomes. In addition, findings indicate that higher levels of positive parenting were negatively related to engagement (i.e., complied with intervention). Therefore, although it is important to engage all families and especially those who might benefit most from prevention services (e.g., high risk), it is important to engage families who report higher levels of positive parenting as these families may receive less than the intended dosage. Doing so may yield optimal intervention outcomes. Thus, prevention interventionists should acknowledge the families' positive parenting efforts, as well as highlight the need to maintain and potentially improve positive parenting aimed at preventing and reducing drug use among Hispanic adolescents.

The CACE analytic approach provides accurate estimates only when the underlying assumptions are met (Jo, 2002), therefore, researchers should carefully examine these

assumptions before conducting CACE analysis. In our case, the exclusion restriction assumption was particularly problematic given that the exclusion restriction assumes a lack of intervention effect for any participant who received less dosage than those participants defined as engaged. However, depending on how engagement is defined, which of course varies from study to study, noncompliers in the experimental condition may receive substantial intervention dosage, which can make it more difficult to justify exclusion restriction assumptions. However, our definitions of engagement were based on our past research and that of others. In addition, in this study, we included covariates to predict engagement status to improve the precision of compliance status and ameliorate the bias that may be caused by the possible violation of the exclusion restriction assumption (Jo, 2002). We also assume no defiers in this study. Although it is unlikely that a participant randomized to the control group received any Familias Unidas content from another participant, it is theoretically possible that two parents from both conditions could speak about the Familias Unidas intervention. Unfortunately, we did not collect any data on this potential source of contamination.

Given the novelty of applying the CACE analytic approach to the evaluation of family-based preventive interventions, several challenges exist, including the definition of engagement. Our findings are similar to previous studies, suggesting that more stringent definitions of engagement yield larger CACE estimates, whereas less stringent definitions produce smaller CACE estimates (Connell, 2009). However, with a more stringent definition of engagement, the exclusion restriction assumption may more likely be invalid, as the noncompliers would theoretically receive a substantial dosage of the intervention. Additional research is needed to identify optimal definitions of dosage which may prove valuable in obtaining robust findings and in making comparisons across studies.

As previously mentioned, utilizing the ITT or CACE analytic approach should be guided by the research question. The ITT analysis has been implemented in our previous studies (e.g., Prado et al., 2012) because we intended to examine intervention effects on illicit drug use regardless of dosage received by participants. In this study, the CACE analysis was used because we wanted to examine causal intervention effects that take noncompliance into account by examining intervention effects only for participants who complied with the intended intervention dosage.

There were several limitations in this study. First, the exclusion restriction assumption was particularly problematic, as we mentioned above. Second, we did not collect data on whether, what type, or how many services participants in the Community Practice group received. Given that participants came from the Department of Juvenile Justice or had committed a Level III offense in the MDCP-S system and that they were provided with a referral, it is very likely that participants in the control condition received some type of intervention. Thus, the estimate of the intervention effect could be underestimated. However, we cannot confirm if participants followed through with services they were referred to. Finally, the self-report measure of illicit drug use may also be biased as there is evidence that some adolescents provide false-negative reports of drug use (Santisteban et al., 2003). However, in this study, audio computer-assisted self-interviews were used to collect data. It has been found that this method can increase accuracy of reporting sensitive information, including adolescent illicit drug use (Metzger et al., 2000).

To summarize, few studies have applied the CACE analytic approach to evaluate prevention programs, and even fewer to preventive family-based programs (Stormshak et al., 2011, Connell et al., 2007). This approach may be particularly helpful for studies involving parent/family-centered interventions given that participants may not receive the intended dosage. Thus, future studies should consider implementing the CACE analysis in addition to ITT analysis when examining the effects of family-based prevention programs to

determine whether, and the extent to which, the CACE analysis has more power to uncover intervention effects.

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