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The Efficacy of Structural Ecosystems Therapy for HIV Medication Adherence with African American Women

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Abstract

A systemic family therapy intervention, Structural Ecosystems Therapy (SET), has been shown to promote adaptation to living with HIV by reducing psychological distress and family hassles. This investigation examines the effect of SET on HIV medication adherence relative to a person-centered condition and a community control condition. Medication adherence was assessed on 156 trial participants. Results of a two-part model showed that SET was significantly more likely to move women to high levels of adherence (defined as at least 95% adherence) than a person-centered therapy. Family hassles was also significantly reduced by SET, though the effect of SET on medication adherence did not appear related to this change in family hassles.

Keywords

Ecosystemic; HIV; Adherence; Family Hassles; Two-Part Model

The HIV epidemic continues to be a major public health concern in the United States and across the globe with more than 56,000 new cases (22.8 per 100,000 individuals) reported in the United States during the year 2006 (Hall et al., 2008). African Americans, particularly African American women, are among the leading demographic groups for HIV prevalence (Centers for Disease Control and Prevention [CDC-P], 2006). Approximately 45% of new HIV infections in 2006 were among African Americans (Hall et al., 2008). Despite decreases in the rate of diagnoses for African American women, the estimated rates continue to be alarmingly higher than those of women in other ethnic and racial groups. Some estimate the rate of infection to be as much as 20 times as high for African American women when compared with Caucasian women (McDavid, Li, & Lee, 2006).

HIV seropositive individuals with appropriate medical care and adherence to medication regimens are, in many cases, leading long and productive lives. Highly active antiretroviral therapy (HAART) has been shown to be efficacious in reducing viral load, increasing CD4 cell count, slowing the clinical progression of HIV, and reducing HIV related morbidity and

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mortality (Cain et al., 2006; Cole, Hernan, Anastos, Jamieson, & Robins, 2007; Gulick et al., 1997; Palella et al., 1998). Despite these positive effects, many HIV-infected individuals do not adhere properly to their medication regimen (Nieuwkerk et al., 2001; Heckman et al., 2004). Inadequate adherence and sub-optimal levels of treatment represent risk for AIDS-related morbidity and mortality, and as a result, these issues are of major importance to the individual and are of substantial importance to society. Sub-optimal levels of treatment can lead to increases in viral load, reductions in CD4 cell counts, and to the development, and subsequent transmission, of medication-resistant HIV strains (Harrigan et al., 2005).

To address the low adherence rates observed in many HIV-infected individuals, several researchers have outlined the need to develop and test intervention strategies for improving medication adherence (cf. McPherson et al., 2000). There are a limited number of behavioral interventions with demonstrated efficacy in improving medication adherence rates among individuals with HIV (for reviews, see Simoni, Pearson, Pantalone, Marks, & Crepaz, 2006; Amico, Harman, & Johnson, 2006; Fogarty et al., 2002). A majority of the intervention strategies that have been developed and tested are cognitive behavioral interventions. Those studies reporting the largest effect sizes included samples from populations with demonstrated or anticipated problems with adherence (Amico et al., 2006). Studies employing interventions which focus on education and counseling showed improvements in medication adherence (Parsons, Golub, Rosof, & Holder, 2007; Johnson et al., 2007; Rathbun et al., 2005; Sommers et al., 2001). Another successful approach has been the use of scheduled reminder devices such as electronic pagers or calendars (Dunbar et al., 2002; Safren, Hendriksen, Desousa, Boswell, & Mayer, 2003).

Although some of these intervention modalities have been moderately effective in promoting HIV medication adherence, many of these strategies have not capitalized on an important correlate of HIV medication adherence: social support (cf. Freeman et al., 1996; Singh et al., 1999). In a review of adherence studies, Ammassari (2002) noted the research literature identified lack of social support as a significant predictor of nonadherence. Unfortunately, there are few examples in which social support was a planned component of the intervention to improve medication adherence for adults with HIV. In one study by Murphy et al. (2002), social support was measured throughout the group-based intervention and individual-based control condition. Intervention participants reported an increase in social support relative to a reported decrease in social support among the control group. Simoni, Pantalone, Plummer and Huang (2007) designed a social support intervention by establishing new peer relationships utilizing trained peers who were also HIV-positive and on highly active antiretroviral therapy. However, the authors reported null findings for effects on medication adherence.

Family and close friends may provide a different level of social support when compared with other group participants, or peers assigned through research intervention. Freeman and colleagues point out that social support from family and friends influences patients' adherence to their HIV medication (Freeman et al., 1996). Others have suggested that family and friends may have a positive effect on medication adherence through encouragement, underscoring the importance of adherence and serving as a reminder mechanism to the HIV-infected individual (Vervoort, Borleffs, Hoepelman, & Grypdonck, 2007). Although family and friends may also negatively affect adherence through conflictual and counterproductive interactions (Remein et al., 2006), the focus of family-based interventions is on encouraging positive, rather than negative, interactions. Whereas other modalities depend on the individual to monitor his/her own adherence at the conclusion of the intervention, family-based modalities may enhance long-term treatment adherence by engaging family members who will be present after the intervention ends. Such interventions may therefore prevent harmful family interactions and reduce family-related stressors that hinder adherence.

Few studies have focused on the efficacy of family-based interventions to improve medication adherence. Searches in PubMed and PsychINFO crossing the terms HIV, adherence, family and intervention produced few studies in which interventions with the family were used to address HIV medication adherence in adults. In an intervention study targeted at serodiscordant couples, Remien et al. (2005) reported that treatment focused on improving communication, enhancing problem-solving and educating participants on the importance of adherence led to improvements in medication adherence. Rawlings et al. (2003) designed an intervention that invited both participants and their caregivers to treatment sessions, but were unable to successfully retain caregivers and ultimately found no significant difference on adherence between the intervention and control groups. Given the importance of family members as sources of support and empowerment, interventions designed to improve family interactions may serve as a means of promoting and maintaining HIV medication adherence. In the present analyses, we examine the efficacy of Structural Ecosystems Therapy (Mitrani, Szapocznik, & Robinson-Batista, 2000; Szapocznik et al., 2004) in increasing medication adherence in African American women infected with HIV.

The present study was a secondary data analysis of a randomized clinical trial designed to test the efficacy of a family-based intervention on improving psychosocial functioning for low-income, African American women with HIV (Szapocznik et al., 2004). It should be noted that medication adherence was not a targeted outcome in the parent trial. An adherence measure was added to the study approximately midway through because of the emerging focus in the research literature at that time on adherence as an important outcome for persons with HIV/AIDS. Two primary hypotheses guided the present study. First, we hypothesized that SET, as a family-based ecological intervention, would be efficacious, relative to individual therapy and community control conditions, in improving adherence to antiretroviral medications among a sample of urban, low-income African American women with HIV. Second, we hypothesized that the effects of the family-ecological condition on adherence to antiretroviral medication would be mediated by the known effects of the family-based ecological intervention on family hassles and psychological distress. The direct effects of the intervention on these hypothesized mediators have already been established (Szapocznik et al., 2004).

METHODS

Design

The present study uses data from a randomized clinical trial testing the efficacy of Structural Ecosystems Therapy (SET) relative to an attention-control person-centered condition (PCA), and a community control condition (CC). Detailed information on the methods, including design, participants, recruitment, and intervention conditions can be found in Szapocznik et al. (2004). However, a brief overview is provided here.

This study used a mixed design with three conditions and five assessment points. Participants were randomized to condition, assessed at baseline and reassessed at 3, 6, 9, and 18 months post-baseline. The study used an intent-to-treat design, where participants continued to be assessed even if they had dropped out of the SET or PCA interventions, and where data from all participants were used in the analysis. Participants were assigned to condition based on an urn randomization procedure (Wei & Lachin, 1988). This procedure was utilized to balance the conditions with regard to age, number of psychiatric diagnoses, number of children, and history of drug use.

Participants were excluded from the study if they had used illicit drugs in the previous 6 months and if they had ever been hospitalized for any psychiatric illness, with the exception of drug use, and if they had participated in the pilot phase of the study or were enrolled in another behavioral intervention trial for HIV+ women. Individuals who were homeless, or residing in

an institution that prohibited outside contact, were not included. Recruiters assessed and excluded individuals with cognitive impairment. If the individual did not endorse at least two interpersonal problems, including a family-related problem, they were excluded. Finally, at the start of the study individuals with CD4 cell counts below 200 were excluded. This condition was relaxed to exclude only those individuals with CD4 cell counts below 50 after 60 women had been admitted to the study (Szapocznik et al., 2004). Whereas taking antiretroviral medications was not required to be included in the SET clinical trial, to be included in analysis of HIV medication adherence in the present investigation, women must have been taking antiretroviral therapy.

Intervention Conditions

Structural Ecosystems Therapy (SET)—SET targets maladaptive interpersonal interactions within the family, as well as interactions between the family and other important systems (e.g., health care providers). SET therapists work in the present to restructure these interactions and to promote healthy relationships within and outside the family. As an extension of Brief Strategic Family Therapy (BSFT; Szapocznik, Hervis, & Schwartz, 2003), SET consists of three primary techniques: joining (gaining entry into the family and building trust with family members), diagnosing (identifying the patterns of interactions, both within the family and between the family and outside systems, that prevent the family from being more supportive to the HIV-seropositive woman), and restructuring (implementing therapeutic techniques to correct these maladaptive patterns of interactions). Eight therapy sessions were considered a minimum dosage of therapy (Mitrani, Prado, Feaster, Robinson-Batista & Szapocznik, 2003); though as a psychotherapeutic intervention, therapy and/or booster sessions could continue up to 9 months with agreement of participant and therapist that it was necessary. More detail on the SET model can be found in Mitrani et al. (2000).

Person-Centered Approach (PCA)—PCA was incorporated to control for common factors in therapy such as attention, supportiveness, and empathy. The aim of this condition was to implement an intervention that was distinct from the central techniques and active ingredients of SET. PCA is non-directive whereas SET is directive; PCA targets the individual whereas SET targets the family and ecosystem; PCA targets the self whereas SET targets family interactions; and PCA sets no goals for the client, while SET is strategic/goal directed. The focus in PCA is the quality of the relationship between the therapist and the client, in which the therapist demonstrates empathy, unconditional positive regard, and congruence (Rogers, 1959). By definition, the Person-Centered Approach does not incorporate any specific therapeutic *techniques*; rather, it is the therapeutic *relationship* that is the active ingredient. Dosing opportunity for PCA was the same as for SET.

Community Control (CC)—The community control condition was intended to reflect (and control for) the baseline services that HIV-infected African American women receive in the local community. Women in this condition received no services from the study.

Therapist Training, Fidelity—Therapists were nested within the SET and PCA conditions. Therapists in both conditions had at least a master's degree in counseling, social work, or marriage and family therapy and at least 1 year of clinical experience. Details of training and monitoring procedures are described in Szapocznik, et al. (2004). Briefly, all therapists were trained using the respective manual of the condition (SET or PCA) and attended numerous trainings. The training period lasted from three months (SET) to one year (PCA) during a pilot period prior to study initiation. Both conditions had their own clinical supervisors and both teams of therapists met with the supervisor weekly to review case notes and videotapes of therapy. A total of 175 videotapes were rated by independent raters and mean ratings showed

that the two therapies were faithful to their prescribed and proscribed intervention behaviors (Szapocznik, et al. 2004).

Comparability of Contact—There was no difference in the rate of engagement to treatment across conditions. Engagement in treatment was defined as attending at least two therapy sessions. Of the women randomized to SET, 75% engaged in treatment. By comparison, 61% of the women randomized to PCA engaged (Prado, Szapocznik, Mitrani, Mauer, Smith & Feaster, 2002). SET was more likely to retain participants than PCA. Women assigned to the SET condition received more hours of therapy contact (SET: $M=12.45$, $SD=12.85$; PCA: $M=5.74$, $SD=5.23$; $F(1,129)=15.24$, $p<.0001$).

In SET, the therapist worked with the woman to identify family members she wanted to invite to participate in session with her. Family members were identified by their relationship to the index woman and included children, significant others, siblings, parents, extended family, health care workers and friends. Of those women who engaged, 91.8% had at least one family member attend a treatment session. Children attended at least one treatment session for the largest percentage of the engaged women (71%), followed by significant others (31%), siblings (31%), extended family members (31%), health care workers (24%), and friends (16%).

Procedures

Study procedures were approved and overseen by an Institutional Review Board. Participants were seen in this study from 1996 until 2000. Informed consent was obtained from the woman to conduct assessments and therapy sessions. For women randomized to the SET condition, informed consent was obtained for family members participating in therapy sessions. Participants were recruited from community-based agencies that provide health care and social services to individuals with HIV. All participants were recruited in South Florida. After explaining the study to each woman and her family members, the interviewer read and obtained informed consent from the woman and her participating family members.

Assessments and therapy sessions were conducted at the woman's home or other locations convenient to the woman. Assessors and therapists contacted each woman to set and confirm appointments for each assessment or therapy session. For women in the SET condition, therapists also contacted family members to remind them to be available for therapy sessions.

Measures

Demographics—Each participant completed a 22-item demographic instrument. Among the information provided by participants were age, marital status, level of education, personal income, number of children, number of years living with HIV, and self-reported CD4 cell count (at the last medical visit).

Psychological Distress—The Global Severity Index from the Brief Symptom Inventory (Derogatis, 1993) was used to measure psychological distress. The Brief Symptom Inventory consists of 53 self-report items that assess the respondent's psychological symptoms within the past seven days. The Global Severity Index includes the following nine dimensions: (a) depression, (b) anxiety, (c) paranoid ideation, (d) psychoticism, (e) somatization, (f) interpersonal sensitivity, (g) hostility, (h) phobic anxiety, and (i) obsessive-compulsive behavior. Each item is rated on a 5-point Likert scale ranging from 'not at all' to 'extremely.' The Global Severity Index is calculated by deriving an item mean response (i.e., 1–5) across the 53 items. In this study, Cronbach's α for scores on the Global Severity Index was .96.

Family Hassles—The Hassles Scale (DeLongis, Folkman, & Lazarus, 1988), revised for African American women, was used to assess daily hassles in a number of areas. In the version

of the scale used in this study, we omitted items that would not be relevant to poor, urban women (e.g., financial investments) and added items not in the original scale that would apply to the current sample (e.g., your ex-spouse; see Smith et al., 2001). The family hassles score was obtained by counting the number of family-related hassles items that the woman endorsed (maximum 12).

Medication Adherence—Adherence was measured using the AIDS Clinical Trial Group Adherence Interview Questionnaire (Chesney et al., 2000). This self-report measure asks participants to (a) list the HIV medications that they have been prescribed, (b) the number of prescribed doses and pills per dose that they are supposed to take, and (c) the number of pills missed per dose for each medication. Participants responded to items (b) and (c) above with respect to the four days prior to assessment. In this study, the percent of pills missed (i.e., the ratio number of pills missed to the total number of pills that were supposed to be taken) over the past four days was used.

As noted above, the success of HAART led to increased emphasis on medication adherence during the recruitment and enrollment period for the parent study. As a result, adherence measures were added to the assessment battery after 24 women of the total 209 had already completed the study. Adherence measures were added to the study for newly enrolled participants ($n=106$) as well as for those participants who were attending follow-up sessions ($n=79$). A total of 29 of these women were not taking HIV medications and are excluded from the analysis. The resulting data represents 156 participants.

At the first adherence assessment, 5.1% of participants reported taking one medication, 16.1% reported two medications, 69.3% reported three medications and 9.5% reported four medications. Eighteen different medications were identified by participants. Those reported most frequently included lamivudine (43%), stavudine (38%), nelfinavir (26%), nevirapine (25%), idinavir (20%) and didanosine (13%).

Analysis Plan—The first step of the analysis was to examine mean adherence across time using a mixed model. This model was used to predict adherence (measured as percent of pills taken as prescribed) as a function of condition, time, and the condition by time interaction. A random effect was included for participant to control for the nesting of time points within participants (Singer & Willett, 2003). These analyses were conducted using SAS Proc Mixed, which can estimate multilevel models in analysis of variance format. SAS Proc Mixed uses full-information maximum likelihood estimation so that cases with missing data can be included in the analysis.

The second step of the analysis plan utilized a two-part random-effects regression model (Olsen & Schafer, 2001) to ensure that results were not affected by the distribution of adherence, which did show clustering at high and very low levels of adherence. The outcome variable was partitioned into three adherence categories: 1 for no adherence (did not take any pills in the last 4 days), 2 for low to moderate adherence ($0 < Y < 95\%$ of pills) and 3 for highly adherent ($\geq 95\%$ of pills). The repeated measures variable, time, was centered at the baseline assessment so that the model examines baseline and change from baseline. The first part of the model was a random-effects ordered logistic growth model predicting adherence category as a function of time, treatment condition and their interaction. The second part of the model was a random-effects growth curve model for adherence among those participants who reported taking at least one pill but less than 95% of their prescribed dose in the last four days prior to assessment (adherence category 2). The distribution of the outcome variable within this moderate category of adherence more closely approximated normality.

This model, then, decomposes the outcome (% of pills taken) into a categorical piece and a continuous piece and estimates two different growth curves for these two components. However, these two growth models were estimated jointly as recommended by Olsen and Schafer (2001) to prevent possible bias induced by subsetting the data for analysis (if, for example, the level of adherence was estimated just on those participants that were not completely adherent or non-adherent). This model was estimated using a maximum likelihood procedure of Mplus Version 5.1 (Muthen & Muthen, 1998–2008).

The third part of the analyses was to test for potential mediating factors of any results. The primary findings from the parent trial showed that the SET intervention significantly decreased family hassles and psychological distress relative to the other two conditions. Therefore, these two factors were tested as potential mediators of any intervention effect. The test of mediation was done by examining the significance of the product of the pathways from the intervention to the slope of the hypothesized mediator and from the slope of the mediator to the slope of the adherence outcome. This test utilized the delta-method standard errors for this product (Muthen & Muthen, 1998–2008).

These models are robust to data missing-at-random which implies that results are not affected by any observed variables that predict missing data. Because data for this secondary analysis was initiated after more than half of the trial participants had begun the study, there is a significant amount of missing data with some participants first being assessed in the later assessments of the study. This pattern of missing data was the result of study-related factors and not participant factors.

RESULTS

Participants

Participants in the current study included 156 urban, low-income (median income = \$9338 IQR=\$8592) HIV-seropositive African American mothers enrolled in the randomized controlled trial. The mean age of the participants was 36.4 ($SD = 8.9$). The modal level of education was less than high school, with 19% of the sample completing a high school degree and less than 1% completing a college degree. Forty-three percent identified as never married and not living with a significant other; 9.7% identified as married but living apart from their spouse, 11.0% were married living together, 16.2% were living with a partner and 20.1% were divorced or widowed. Seventy-eight percent of the women in the sample reported living with HIV for at least 3 years and more than half had been living with HIV for more than 5 years. At baseline, the mean self-reported CD4 cell count for the sample was 412.8 ($SD=58.3$).

Attrition rates were 9.0%, 4.9%, 10.4% and 45.5% at 3, 6, 9 and 18 months, respectively. The low response rate for the 18-month assessment was due to discontinuation of the study assessments as a result of a lack of funding (Szapocznik et al., 2004). To ensure that results were not affected by the high amount of attrition at the 18 month follow-up, we explored models which tested for differences in the women with and without data at 18 months in mean levels across the earlier times. There was a significant difference by condition in the amount of attrition at 3 months ($\chi^2(2)=8.38, p<.02$), with women assigned to SET comprising 10 of the 14 that dropped out at 3 months (note that this pattern was not apparent in the full study, only within the subset of participants with adherence measures). There were no differences in the rates of attrition by condition at the later time points. Of the 10 women in SET that only had data at baseline, 6 of these women reported adherence at greater than 95%.

Mean Adherence over Time—Analyses indicated a significant main effect of time ($F(4,338)=2.58, p<.04$) and a significant condition by time interaction ($F(8,337)=2.19, p<.03$). Figure 1 displays the results of this analysis in the form of average adherence by treatment

group at each time point. Results indicated that whereas PCA and CC had higher rates of adherence initially, at the 18 month follow-up, individuals in the PCA condition reported significantly lower levels of medication adherence than those in either CC or SET. There were no differences in mean levels between the women with and without data at the 18 month timepoint ($F(3,174)=1.09$, $P=.38$) and the time by treatment interaction remained significant in this model ($F(8,174)=2.23$ $p<.03$).

Two-Part Model—The categorical part of the model indicated that women assigned to SET were more likely to be in the higher category of adherence over time (i.e., $> 95\%$). For individuals in SET, the expected ordered odds ratio for moving to the next higher category of adherence was 1.45 (95% CI: 1.04 2.01), indicating that, at each 3-month assessment period, individuals in SET were 1.45 times as likely as those in PCA to transition into the high adherence group. The expected ordered odds ratio for SET versus the CC condition was 1.29 (95% CI: .97, 1.72) and was not statistically significant. Figure 2 plots the predicted probability of membership in the highest level of adherence for all three conditions. The probability of being in the most adherent group increases for SET over time and decreases for both PCA and CC. The second part of the model, the random-effects growth curve, demonstrated no significant differences across conditions. Women who had missing data at 18 months had no difference in the probability of being in higher categories in the earlier times ($\chi^2(4)=5.6$, $p<.24$) and the difference between PCA and SET in the slope of the growth curve remained significant ($t(448)=2.05$, $p<.04$).

Mediation Analyses—Because the results of the primary analyses showed that the significant effect of SET was primarily in increasing the probability of being highly adherent, and because movement within the moderate adherence category did not differ significantly by condition, only the categorical portion of the two-part model was included in the mediation models.

As reported in Szapocznik et al., (2004) using the full sample, the SET intervention was characterized by a significant rate of decline in negative family hassles relative to the PCA condition ($\beta=-.282$, $t(448)=-2.16$, $p<.04$) and relative to the CC condition ($\beta=-.297$, $t(448)=-2.27$, $p<.03$). Similarly, the SET condition was characterized by a significantly greater rate of decline in psychological distress relative to the PCA condition ($\beta=-22.2$, $t(448)=-2.26$, $p<.03$) and relative to the CC condition ($\beta=-24.5$, $t(448)=-2.48$, $p<.02$) in the sub-sample of participants who completed medication adherence measures. Participants in the CC condition did report significantly fewer hassles at baseline than did those in the SET condition ($\beta=-.95$, $t(448)=-2.08$, $p<.04$). There were no differences across conditions in psychological distress at baseline. There were no significant relationships between rates of change in family hassles or psychological distress on change in adherence, thus the conditions for mediation are not met.

DISCUSSION

Results of the present secondary analysis demonstrated that Structural Ecosystems Therapy significantly improved HIV medication adherence in HIV+ African American women compared to those women assigned to a person-centered counseling condition. Specifically, the two-part model showed that over time, women in the SET condition demonstrated increased probability of being at least 95% adherent whereas women in the PCA condition demonstrated decreased probability of being 95% adherent. The third condition, a community control group, also showed declines in the likelihood of being 95% adherent over time, though these declines were not significantly different than the other two conditions. These results point to the possibility that an ecosystemic approach to medication adherence may benefit low-income urban minority women, and lends support to the call for ecological and family-based

approaches for persons with HIV/AIDS (Crepaz et al., 2006; Rotheram-Borus, Flannery, Rice, & Lester, 2005).

The SET intervention focuses on the HIV seropositive woman's family and the various systems in which she and her family are embedded. The general goal is to improve the woman's and family's adaptation to HIV infection by reducing problematic interactions and supporting adaptive connections within the family and between the women, family and other key systems that impact the woman's life (such as the health provider). This intervention is process-focused and does not emphasize any particular content. Instead, it is theorized that improving family functioning, regardless of content area, and improving the efficacy of the woman and the family in interacting with resources, will lead to improved psychosocial functioning, which in turn, can result in improved adherence. As such, the intervention does not focus on medication adherence. Instead, the therapist uses any issues that are relevant to the family as a vehicle to change interaction patterns. The changes brought about by the intervention include reductions in family-related hassles – evidence that SET operates through improving family interaction patterns.

It is encouraging that this intervention had an impact on medication adherence although adherence was not a specified intervention focus. The intervention did demonstrate reductions in family conflict (as measured by family hassles). A hypothesized mechanism is that this reduction in family conflict provided the woman (and her family members) with the freedom to focus on managing her HIV care. Although, SET significantly decreased family hassles relative to both other conditions the test of mediation was not significant. Similarly, work to improve relationships with key resources, including health care providers, may be a mechanism through which improvements in medication adherence were made. There is evidence to suggest that the patient-provider relationship is a key component to good medication adherence for HIV and other chronic diseases (Beach, Keruly, & Moore, 2006; Furtres et al., 2007; Ingersoll & Heckman, 2005). Unfortunately, the design of the parent study did not include measures to assess the relationship between the participants and their health care providers nor family members' focus on health issues.

Regardless of the promising results of SET in this investigation, it is important to note that SET was not significantly different from the community control condition. Further it is clear that there remains a sizable number of women who need to improve their adherence to maintain antiretroviral efficacy even in SET, which had the highest probability of women being over 95% adherent. Any further investigations of SET for medication adherence should add a specific focus on medication adherence.

It should be noted that this investigation extended two-part modeling (originally put forward by Olsen & Schaffer, 2001) to accommodate the clustering of participants at both the completely non-adherent level and the highly adherent (greater than 95%) level. These models are frequently used for variables such as illegal drug use where there are more participants reporting scores of zero than would be expected within the Poisson distribution (the distribution commonly used for count data). In most instances, these models have been used for data with clustering of observations at zero (the bottom of the scale) by estimating a growth model explaining the probability of scoring above zero, along with a growth curve for the non-zero data. In this study, the adherence data were parsed into 3 levels: zero adherence, partial (and continuously varying levels of) adherence and full adherence. Thus, the model was adapted to account for clustering of data at both the top and bottom of the scale.

As a secondary analysis this study is characterized by several limitations. First, because the parent study did not focus on adherence, the sole measure for assessing adherence was self-report. Whereas more objective measures of adherence are desirable, the validity of self-report

measures has been established (Walsh, Mandalia & Gazzard, 2002, Simoni, Kurth, Pearson, Pantaloni, Morrill, et al. 2006). It has been shown that self-report tends to over-estimate adherence (DeMasi, Graham, Tolson, Pham, Capuano et al., 2001) though there is no reason to think this over-reporting would be different by treatment assignment. Second, the assessment of adherence began after the protocol was initiated and only a subset of the original study was included. This has implications for the power to uncover significant effects and may explain the lack of a mediating effect of family hassles and psychological distress. Third, the SET condition did have a higher rate of attrition at the 3 month time point (which was not significant in the parent study). The presence of differential attrition can be worrisome because it brings into question whether results are a function of the change in composition in the sample. In this case, the majority of the women assigned to SET that were lost to follow-up at 3 months showed the highest level of adherence at baseline. Therefore, their drop out would have inflated the baseline level of adherence; yet, SET had low initial adherence and demonstrated a significant increase in the rate of adherence over time. A final limitation is that many theoretically important precursors and determinants of adherence were not assessed (e.g., self-efficacy, intentions, family support for adherence, health care interactions), preventing a more complete understanding of the potential mechanism(s) leading to the results.

This study suggests that a family-focused, ecosystemic approach may be a useful foundation for an intervention to improve HIV medication adherence. Most interventions on HIV medication adherence have shown very modest effects (Simoni et al., 2006). Clearly, future work on ecosystemic approaches for HIV medication adherence should add a specific focus on HIV medication adherence to increase effectiveness.

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Figure 1.
Mean Adherence Levels Across Time by Condition

Figure 2.
Probability of Being Highly Adherent ($\geq 95\%$)