IMPROVING ANTIRETROVIRAL MEDICATION ADHERENCE AMONG ADOLESCENTS WITH HUMAN IMMUNODEFICIENCY VIRUS (HIV): A CASE SERIES PILOT INTERVENTION STUDY

By

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To my husband, who has supported me through the years as I've pursued my goals

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IMPROVING ANTIRETROVIRAL MEDICATION ADHERENCE AMONG ADOLESCENTS WITH HIV: A PILOT STUDY

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Maintaining an adherence level of 95% or more is critical in optimizing treatment effectiveness, suppressing viral load, and preventing medication resistance in patients with HIV. Although adolescents are least likely to be adherent, they have been largely ignored by the intervention literature. The current study is the first-known prospective intervention designed to target adherence to antiretroviral medications among adolescents with HIV. Participants were four perinatally-infected adolescents who received a seven-week intervention focused on problem solving and family communication to improve adherence to their HIV regimen. The intervention was delivered through alternating home and telephone sessions and a multi-method adherence assessment approach was used to track adherence at baseline, during treatment, and at three-month follow-up. Viral load was obtained at all assessment points. All adolescents experienced an improvement in adherence levels following implementation of problem solving but, for the most part, these improvements were not maintained over time. Changes in the adolescent's routine were associated with declines in adherence. Seventy-five percent of the sample experienced a decrease in viral load by the end of treatment. Medication resistance and immune suppression affected the degree to which improvements in adherence affected viral load

in one participant. All participants reported a decrease in the severity of barriers experienced from pre- to post-treatment. Participant knowledge of their medication regimen was high at pre-treatment and did not change over time. Contrary to the initial hypothesis, parent perception of family conflict increased from pre- to post-treatment for some dyads. Adopting an individualized approach to help adolescents problem solve and overcome barriers may be promising strategy to improve their adherence. Interventions focused on improving adolescent adherence may benefit from helping the adolescent find ways to incorporate their regimen into their regular routine as opposed to encouraging the adolescent to bend their routine to the demands of their regimen. Adopting a proactive problem solving approach may help minimize the extent to which changes in routine result in declines in adherence. Further research, characterized by randomization to treatment, multi-site collaboration, and long-term monitoring of adherence are greatly needed.

CHAPTER 1
INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) is a life-threatening chronic illness that has reached epidemic proportions. Worldwide, it is estimated that between 34.1-47.1 million individuals have AIDS or are infected with the human immunodeficiency virus (HIV), the cause of AIDS (Joint United Nations Programme on HIV/AIDS, 2006). In 2005, up to 2.3 million children under the age of 15 were infected with HIV, and it is estimated that 1,500 children are infected with the virus daily (World Health Organization, 2006). In the United States, there are an estimated 45,669 individuals living with HIV/AIDS. Of these, 10,000 are children under the age of 13 (Centers for Disease Control and Prevention, 2005). A significantly large portion of those infected with HIV are children from ethnic minority groups (58% African American, 23% Hispanic), those living in poverty (Armstrong, Willen, & Sorgen, 2003), and in single-parent homes (Brown, Lourie, & Pao, 2000).

In 1982, the Centers for Disease Control and Prevention reported the first case of AIDS in children (Chadwick & Yogev, 1995); just one year after the illness was first identified in adults (National Institute of Allergy and Infectious Diseases, 2005). As both the adult and pediatric HIV populations have grown over the past two decades, much attention has been given to studying the viral structure and transmission of HIV in order to develop medications to slow down the disease's progression and find a cure.

HIV is a single-stranded ribonucleic acid (RNA) retrovirus that weakens the immune system through a process that begins by targeting T-cells, which help the immune system fight off infections (Armstrong et al., 2003). Once attached to a T-cell, the virus injects its genetic material and uses the cell's internal structure to replicate HIV-specific RNA proteins. This process leads to the eventual destruction of the T-cell and the release of additional viruses into

the bloodstream where they can attack other T-cells, replicate, and proliferate throughout the body. As the virus continues attacking the immune system by destroying T-cells, it weakens the body's ability to fight off opportunistic infections such as pneumonia, disseminated cytomegalovirus, and various cancers (National Institute of Allergy and Infectious Diseases, 2005).

HIV is transmitted through contact with blood and other bodily fluids via two methods of transmission. Vertical, or perinatal, transmission refers to mother-to-child viral transmission during pregnancy, birth, or breast feeding (National Institute of Allergy and Infectious Diseases, 2005). Approximately one-third to one-quarter of women infected with HIV who do not receive antiretroviral treatment during their pregnancy will pass on the virus to their infant (National Institute of Allergy and Infectious Diseases, 2005). Prior to the advent of preventative treatment for pregnant women who were HIV positive, perinatal transmission of HIV was the most common method of infection among children, accounting for 91% of all documented HIV cases (Armstrong et al. 2003). Fortunately, with the increased awareness of the importance of pre-natal preventative HIV testing and treatment, significantly fewer children are born with HIV (Centers for Disease Control and Prevention, 2005; Lindegren et al., 1999). Horizontal transmission refers to viral transmission through other modalities such as sexual activity, drug use, or blood transfusion (Armstrong et al., 2003). Currently, through risky sexual behavior, drug use, and limited access to HIV prevention services, adolescents and young adults are one of the most at-risk groups for contracting HIV, comprising half of all new infections (Secord & Cotronei-Cascardo, 2007; World Health Organization 2005).

Treatment of HIV in Children and Adolescents

Prior to the advent of antiretroviral medication, HIV was the leading cause of infant mortality in major American cities (Secord & Cotronei-Cascardo, 2007). Fortunately,

advancements in treatment over the past two decades have enabled a greater number of children born with HIV to survive into adolescence and adulthood (McConnell et al., 2005). Treatment for HIV first emerged in the late 1980's and consisted of single and dual agent nucleoside reverse transcriptase inhibitors (NRTI; Brogly, Williams, Seage, Oleske, Van Dyke, & McIntosh, 2005). With guidance from numerous clinical trials, treatment of HIV has evolved from a single agent approach to more effective multi-drug regimen (Borgly et al., 2005). These multi-drug approaches, also known as highly active antiretroviral therapy (HAART), suppress viral proliferation by targeting the various stages of HIV replication (Dong, 2007). Liquid formulations of many antiretroviral medications have helped increase the accessibility of these drugs to younger children and those with difficulty swallowing pills (Secord & Cotronei-Cascardo, 2006). Although there is no cure for HIV, existing treatments have helped "reduce HIV-related mortality and morbidity, improve quality of life, and restore and preserve immunologic function" by suppressing viral load (Panel on Antiretroviral Guidelines for Adult and Adolescents, 2006).

Currently, expert recommendations for antiretroviral treatment in adolescents and adults consist of either two NRTI's and one non-nucleoside reverse transcriptase inhibitor (NNRTI) or one protease inhibitor (PI) with two NRTI's (Panel on Antiretroviral Guidelines for Adult and Adolescents, 2006). It is important to note that this recommended regimen may not be appropriate for all patients and may vary based on other factors such as clinician judgment, patient age, and degree of viral suppression or medication resistance (Brogly et al., 2005; Panel on Antiretroviral Guidelines for Adult and Adolescents, 2006).

Most children and adolescents with HIV are prescribed several antiretroviral medications, often with multiple dosings per day (Steele & Grauer, 2003). In addition to being potentially

time-intensive, some medicines have unpleasant tastes and side-effects such as liver toxicity, hyperglycemia, hyperlipidemia, osteoporosis, and lactic acidosis (Panel on Antiretroviral Guidelines for Adult and Adolescents, 2006). Because of these and other factors discussed below, optimal adherence to these treatment regimens is a challenge for many children and their families.

Adherence in Children and Adolescents with HIV

Adherence refers to the degree to which "a person's behavior coincides with medical or health advice" (Haynes, 1979, pp. 1-2). Although being adherent does not guarantee a positive health status, adherence tends to predict health in pediatric HIV (Steele & Grauer, 2003). Indeed, children who report being less adherent tend to have higher viral loads (Puga, 2006; Williams et al., 2006). Current recommendations suggest that the greatest chance of a person benefiting from treatment with HAART results from adherence of 95% or more (Paterson et al., 2001; Puga, 2006). Unfortunately, existing estimates of adherence to antiretroviral medications among the pediatric population are much lower. Only 34% of all families are over 90% adherent, with most adherence rates ranging from less than 50% up to 75% (Katko, Johnson, Fowler, & Turner, 2001; Steele et al., 2001). Half of all patients fail to take their medications as prescribed (Puga, 2006) and between 26-59% of patients report missing doses during a given week (Feingold, Rutstein, Meislich, Brown & Rudy, 2000; Murphy et al., 2001; Reddington et al., 2000). Alarmingly, a study of adolescents found that only 41% reported full adherence to their prescribed regimen (Murphy et al., 2001).

Although nonadherence has significant consequences in most pediatric conditions, the impact of nonadherence in HIV can be severe and possibly irreversible. Subtherapeutic levels of HAART medication may be ineffective at preventing viral proliferation which may lead to symptomatic HIV, replication of the HIV virus, and the development of medication resistance

(Gavin & Yogev, 2002; Sethi, Celentano, Gange, Moore, & Gallant, 2003). Children who become resistant to a particular medication may also develop resistance to other medications within the same therapeutic class, further limiting their treatment options (Altice & Friedland, 1998). Over time, those with chronic nonadherence may develop resistance to several, if not all, antiretroviral medications (Sethi et al., 2003).

Correlates of Adherence

Given the severity of nonadherence in HIV, research examining predictors of, and potential factors affecting, adherence is critically needed. Compared to the extensive adherence research in other pediatric medical conditions such as diabetes (De Civita & Dobkin, 2004), research on correlates and predictors of adherence in pediatric HIV is in its infancy (Steele & Grauer, 2003). Although the more extensive adult HIV literature on adherence (e.g., Adam, Maticke-Tynedale, & Cohen, 2003, Remien et al., 2003) has the potential to inform the pediatric knowledge base, various aspects of living with HIV, such as losing a parent from AIDS and growing up with a chronic, life-threatening illness, are unique to children and can potentially impact adherence (Steele & Nelson, 2007).

Similar to research in the general pediatric literature, certain characteristics of the treatment regimen have been found to negatively impact adherence in HIV. In general, medication adherence is a greater problem in the treatment of chronic medical conditions, such as HIV, than acute conditions (Rapoff, 1999). Length of treatment with antiretroviral therapy is negatively correlated with adherence, with children on lengthier courses of treatment being less likely to adhere (Martinez et al., 2000). Children who consider their regimen burdensome (e.g., too many pills, interferes with my schedule) tend to be less adherent than children who have less complex regimens or view their regimen as less intrusive (Belzer, Fuchs, Luftman, & Tucker,

1999; Goode, McMaugh, Crisp, Wales, & Ziegler, 2003; Rapoff, 1999). Finally, children who experience greater medication side-effects are less likely to be adherent (Belzer et al., 1999).

Child factors have also been associated with adherence. Specifically, children with a greater number of depressive symptoms tend to have poorer levels of medication adherence (Murphy et al., 2001). Children who view their HIV medication as a reminder that they are HIV positive are also less likely to be adherent (Belzer et al., 1999). Although medical providers believe that children who have been informed of their HIV status are less likely to be resistant to their treatment regimen (Brackis-Cott, Mellins, Abrams, Reval, & Dolezal, 2003), the data are mixed and do not allow for any definitive conclusions to be made (Wiener, Mellins, Marhefka, & Battles, 2007).

Child age has been found to be a significant predictor of adherence, with adolescents being less likely to adhere than younger children (Mellins, Brackis-Cott, Dolezal, & Abrams, 2004; Williams et al., 2006). This may be due to a premature shifting of responsibility for the medication regimen from the parent to the child as the child approaches adolescence (Steele & Grauer, 2003). The developmental and social challenges children face as they enter adolescence further contribute to non-adherence (Mellins et al., 2004; Steele & Grauer, 2003) as children experience tremendous changes in their biological and psychological functioning. During this time, adolescents attempt to establish their personal identity, increase their autonomy, and explore their sexuality through romantic relationships (Holmbeck, 2002). These processes may at times be at odds with adherence to the HIV medication regimen. Adolescents in close intimate relationships often struggle with disclosing their illness out of the fear of rejection (Wiener, Battles, & Heilman, 2000). This may lead to some adolescents hiding their HIV status by skipping doses when around others so as to avoid drawing unwanted attention to themselves

(Rao, Kekwaletswe, Hosek, Martinez, & Rodriguez, 2007). Because adolescence is a critical time in which lifelong positive and risky health behaviors are established, intervening with adolescents who have poor adherence to their HIV regimen is extremely important (Holmbeck, 2002).

Certain caregiver characteristics have also been associated with nonadherence. Parents with less ability to name their child's medications, a reduced sense of self-efficacy with regard to their ability to correctly administer their child's medications, lower perceptions of medication efficacy, and a greater concern of others discovering their child's medical condition are more likely to have children with poor adherence (Reddington et al., 2000). It may be that parents who are afraid of other's discovering their child's HIV status limit their ability to take advantage of adherence-enhancing social support networks such as their child's school nurse who can assist with administering medications within the school setting (Steele & Grauer, 2003).

Specific family characteristics have been associated with non-adherence in children and adolescents with HIV. Parent-child communication is positively associated with adherence, with dyads reporting poorer parent-child communication being more likely to be non-adherent (Mellins et al., 2004). Other family factors such as parent-child relationship quality and caregiver-perceived quality of life and stress are also strongly associated with adherence (Mellins et al., 2004; Miller, Bishop, Herman, & Stein, 2007). These relationships make intuitive sense as so much of a child's functioning occurs within and is affected by the larger family system (Cunningham, Naar-King, Ellis, Pejuan, & Secord, 2006). Given that parent-child conflict tends to increase during adolescence (Robin & Foster, 1989), it is possible that targeting family factors, such as parent-child communication and joint problem solving, may help to improve adolescent adherence to antiretroviral medications. Indeed, these family factors are highly

amenable to intervention and should be targeted when addressing adherence in children and adolescents with HIV (Mellins et al., 2004).

Limitations of Adherence Literature

In a recent review of the literature, Steele and Grauer (2003) noted three major challenges facing the integration of existing research on adherence in pediatric HIV: the cross-sectional nature of the current literature, a lack of coherence in adherence conceptualization, and the high variability in adherence assessment methodologies. These issues have significantly impacted the design of intervention programs to improve adherence as no coherent picture of adherence to antiretroviral medications can be drawn to guide research (Steele & Grauer, 2003).

As previously mentioned, treatment for HIV requires multiple drug regimens over extended periods of time. Because adherence is a dynamic process that is multiply determined (Brown, 2002), cross-sectional studies may be inadequate in assessing the complexity of adhering to a long-term medication regimen (La Greca & Bearman, 2003). Prospective longitudinal assessment is greatly needed to better understand the process of adherence in youth with HIV (Liu et al., 2001; Steele & Grauer, 2003).

Adherence varies greatly by how it is conceptualized (Rapoff, 1999). Categorical conceptualizations of adherence, often used in initial studies, use specified criteria and labels (e.g., poor, fair, good) to classify patient adherence (La Greca & Bearman, 2003). In the pediatric HIV literature, categorical conceptualizations have made it difficult to compare results across studies as arbitrary cutoffs with no physiological basis have been used (Steele & Grauer, 2003). Because of this, studies which conceptualized adherence as a categorical variable, such as that conducted by Feingold and colleagues (Feingold et al., 2001), have a limited ability to inform the literature. Recently, a move toward conceptualizing adherence as a continuous, multidimensional variable has emerged in the pediatric literature (La Greca & Bearman, 2003). A greater number

of studies in pediatric HIV now report adherence as a continuous variable in the form of a percent by dividing the number of adherence behaviors completed by the number of behaviors prescribed (La Greca & Bearman, 2003). Despite the move toward viewing adherence as continuous variable, there remains high variability in what constitutes adherence, with no two studies in Steele and Grauer's (2003) comprehensive review conceptualizing adherence in the same way.

The high variability in how adherence is measured serves as another barrier in integrating the existing literature. Adherence in pediatric populations has been assessed in various ways. Drug assays, self-report, pill counts, pharmacy refill history, provider rating, and electronic monitoring are among the most commonly used assessment methods in pediatric HIV (Farley, Hines, Musk, Ferrus, & Tepper, 2003; Simoni, Montgomery, Martin, New, Demas, & Rana, 2007). Although each method is able to provide some measurement of adherence, assessment methods vary in the accuracy and quality of information they can provide as well as in the costs of using them.

Blood assays measure a drug's concentration or presence in the bloodstream (La Greca & Bearman, 2003). They provide a direct and objective measure of drug exposure and can be used to reliably determine adherence over short periods of time (La Greca & Bearman, 2003; Liu et al., 2001). Although drug assays are informative they can also be misleading. They are highly influenced by short-term adherence and are thus only a snapshot of behavior (Liu et al., 2003). Thus, a patient who is generally nonadherent but takes all of their medication just prior to having a drug assay will appear highly adherent (La Greca & Bearman, 2003). Additionally, because the therapeutic drug concentration levels for antiretroviral medications are ill-defined in pediatric populations, blood assays are somewhat limited in their ability to measure adherence in HIV

(Puga, 2006). This, in addition to the high cost of this assessment method and limited insurance reimbursement rates, make drug assays an impractical method for assessing adherence in this population (Puga, 2006).

Self-report is able to span a greater period of time than drug assays and serves as an inexpensive method of measuring adherence (La Greca & Bearman, 2003). It comes in various forms and can be collected through interviews, questionnaires, and self-monitoring (La Greca & Bearman, 2003, Marhefka, Farley, Rodrigue, Sandrik, Sleasman, & Tepper, 2004; Wiener, Riekert, Ryder, & Wood, 2004). Self-report spanning a shorter amount of time (e.g., 24-hour recall) resulting from direct and objective questioning tends to provide more reliable reports than recalls of greater time spans (La Greca & Bearman, 2003; Marhefka, Tepper, Farley, Sleasman, & Mellins, 2006). Although relatively easy to obtain, questions about the validity of self-report have arisen as several studies have found that self-report is highly influenced by social desirability, tends to overestimate adherence, and has an inconsistent association with virologic response (Farley et al., 2003; Frey & Naar-King, 2000; Melbourne, Geletko, Brown, Willey-Lessne, Chase, & Fisher, 1999; Naar-King, Frey, Harris, & Arfken, 2005). Though few studies have been able to demonstrate the external validity of self-report data (Steele & Grauer, 2003), self-report remains one of the most utilized methods for assessing adherence in HIV. Self-report can provide information about various adherence-related behaviors such as dietary intake, which may enhance medication absorbency, sleep patterns, and division of family responsibility for disease management (La Greca & Bearman, 2003; Naar-King et al., 2005, Simoni et al., 2007; Wiener et al., 2004). Several measures, such as the 24-hour recall interview (Marhefka et al., 2006) and the Treatment Interview Protocol (Marhefka et al., 2004), have been developed to

improve the accuracy of self-report data and have been found to correlate with data from electronic monitoring and pharmacy records (Farley et al., 2003; Watson & Farley, 1999).

Two studies in the pediatric HIV literature support the use of medical provider rating as a form of assessing medication adherence (Farley et al., 2003; Naar-King et al., 2005). Health providers in pediatric HIV are in a good position to assess adherence as they tend to have connected and long-lasting relationships with their patients and their families (Naar-King et al., 2005). Provider ratings of adherence are often lower than self-report ratings and have been associated with viral load (Farley et al., 2003, Naar-King et al., 2005). Though a potential source of adherence assessment, provider reports still overestimate adherence (Wiener et al., 2004). Ratings can be influenced by other factors such as patient report, or judgments about adherence based on history or family knowledge (La Greca & Bearman, 2003; Naar-King et al., 2005).

Pill counts measure adherence by comparing the amount of medication remaining in a container with the amount that would be expected to be remaining if the patient had taken the medication as prescribed (La Greca & Bearman, 2003). Though they are considered more reliable than self-report (La Greca & Bearman, 2003), pill counts have significant disadvantages. As with self-report, pill counts tend to overestimate adherence (Steele et al., 2001). They are difficult to accurately obtain when patients forget to bring in their pill bottles to clinic appointments (Naar-King et al., 2005) and do not guarantee that the pills missing have been ingested (La Greca & Bearman, 2003). Because they are computationally complex and time-consuming, pill counts are better suited for research purposes and short-term regimens (La Greca & Bearman, 2003; Liu et al., 2001).

Pharmacy refill history measures adherence by examining the extent to which prescribed medications are ordered on time (La Greca & Bearman, 2003). They are less cumbersome than

pill counts and are relatively easy and inexpensive to obtain (Liu et al., 2001). Recent studies show a significant association between pharmacy refill data and viral load among children (Farley et al., 2003; Katko et al., 2001; Marhefka et al., 2004; Marhefka et al., 2006). Despite the superiority of pharmacy refill data over other forms of adherence assessment, data can easily be invalidated if a patient frequently uses different pharmacies or stores medication at home (Marhefka et al., 2004). Additionally, pharmacy data is only able to provide a general picture of adherence. As such, it cannot provide detailed information on day-to-day adherence behaviors or whether missing medications have been actually consumed by the patient (Marhefka et al., 2004; Melbourne et al., 1999).

Electronic monitoring is the most recent innovation in adherence measurement. Through the use of a microchip embedded in prescription pill caps, medication dosing events are recorded each time the patient opens their bottle to retrieve medication (APREX, 1998). In addition to providing information on overall dosing behavior, electronic monitoring can provide real-time information about the time and date of each dosing event (Melbourne et al., 1999). This may help identify patterns and deviations of medication use (e.g., patient is non-adherent on weekends, patient adherence increases just prior to their appointment) that self-report and pill counts are not able to detect (Farmer, 1999; Schwed et al., 1999). Despite the abundance of information that can be obtained from electronic monitoring, several disadvantages have limited its use. The biggest barrier to implementing electronic monitoring is cost (Wiener et al., 2004). The high price of each monitoring cap combined with the numerous medications prescribed for children with HIV limits the clinical utility of electronic monitoring (Naar-King et al., 2005). Some researchers have made methodological accommodations such as monitoring adherence to only one antiretroviral medication in order to incorporate the advantages of electronic monitoring

(Farley et al., 2003; Liu et al., 2001; Melbourne et al., 1999). Though this strategy is able to provide some information on patient adherence patterns, this information is limited to only the medication being monitored as patients may be more adherent to some medications than others (De Civita & Dobkin, 2004). A second limitation of electronic monitoring is its inability to monitor other common medication forms in children, such as liquid and powder formulations (Bova et al., 2005; Farley et al., 2003; Simoni et al., 2007). Finally, it has been suggested that electronic monitoring may actually underestimate adherence as it is only able to document when pill bottles are opened (LaFleur & Oderda, 2004; Naar-King, Frey, Harris, & Arfken, 2005). Thus, a patients who opens their pill bottle once but retrieves several dosings for use in a pill box or to lay out pills in advance will be seen as less adherent despite actual medication taking behaviors (Bova, Fennie, Knafl, Dieckhaus, Watrous, & Williams, 2005; La Greca & Bearman, 2003, Liu et al., 2001). As with pill counts and pharmacy refill history, electronic monitoring cannot guarantee that patients actually ingest the medication prescribed (Liu et al., 2001). Despite these limitations, electronic monitoring has been found to have higher specificity and predictive value than other forms of assessing adherence and is associated with virologic response (Farley et al., 2003).

As previously mentioned, all of the above methods of assessing adherence have disadvantages in terms of accuracy and/or cost. Currently, there is no gold standard for measuring adherence in this population (Marhefka et al., 2004). As such, no method should be used in isolation (Dolezal, Mellins, Brackis-Cott, & Abrams, 2003; Liu et al., 2001). Instead, assessment methods should be combined to provide a more accurate estimate of adherence (Puga, 2006). Research by Liu and colleagues (Liu et al., 2001) has advocated the use of a composite adherence score based on the combination of information from electronic monitoring,

pill counts, and self-report. Preliminary data support the superiority of a composite score over individual assessment methods such as self-report and pill count (Liu et al., 2001). However, given that Liu's composite score calculations rely upon repeated measures longitudinal growth modeling, which requires a far greater number of participants than those commonly found in pediatric research studies, the use of this model in the pediatric literature is somewhat limited.

Interventions to Improve Adherence in Pediatric HIV

Difficulty integrating the extant adherence literature in HIV has limited its ability to inform adherence-improving intervention studies. To our knowledge, the first published intervention study was conducted by Rogers and colleagues (Rogers, Miller, Murphey, Tanney, & Fortune, 2001) to improve future adherence to medications by targeting the acceptability of HAART treatment among a group of HIV positive adolescents who had never been treated with antiretroviral medications. Guided by the Transtheoretical Model of Change (Prochaska & DiClemente, 1983), Rogers and colleagues designed a 6-8 session intervention program delivered on a weekly basis during each patient's medical appointment. The intervention consisted of presenting the patient with audio and videotapes depicting a newly diagnosed HIV positive adolescent female as she joined a support group to help her cope with the impact of her illness and adjusted to the demands of her medical treatment. Despite the innovative approach of this study, several methodological weaknesses must be noted. Of the 65 adolescents who agreed to participate in the study, only 18 (28%) completed the program. Of these 18, only seven (38%) participants received the program as it was intended to be delivered. At times, study sessions were not administered because they interfered with the patient's health care delivery, as all sessions were delivered during patient medical appointments. Because the study treatment schedule was more intensive than what patients typically received through their standard medical

care (i.e., weekly clinic-based appointments), treatment burden was an issue and contributed to the study's high attrition rate.

The methodological weaknesses of the Rogers et al. (2001) study reflect the difficulty of conducting clinic-based interventions with this population. Since this time, researchers have shifted to the delivery of home-based interventions. Home-based interventions minimize treatment burden in multiple ways. First, by bringing the treatment to the patient, home-based interventions limit the need for superfluous clinic visits. Through the elimination of unnecessary clinic-related expenses, home-based interventions may serve as a more cost-effective approach to the delivery of services. Home-based visits may also be helpful in reducing study attrition as they increase participant convenience by minimizing participant travel burden. Finally, home-based treatments can be delivered without interfering with the delivery of standard medical care, an issue that repeatedly came up in the Rogers et al. (2001) study. Because of the multiple advantages associated with home-based treatments, interventions since Rogers et al. (2001) have primarily been home-based.

Using the well-researched Health Belief Model (Becker, Drachman, & Kirscht, 1972; Becker, Maiman, Kirscht, Haefner, & Draschman, 1977) as a guide, Berrien and colleagues (Berrien, Salazar, Reynolds, & McKay, 2004) conducted a randomized, home-based, non-blind pilot study to improve the adherence of 18 children (ages 1.5-19 years) with HIV. The study focused on improving patient/caregiver knowledge and adherence by providing education for the HIV regimen through eight structured home visits over a three month period. The intervention was guided by a medication knowledge questionnaire completed at the beginning of the study which identified barriers to adherence and misconceptions or lack of knowledge regarding the child's HIV regimen. When compared to the control group, significant differences were noted in

participant knowledge of their regimen at post-treatment, with the treatment group reporting greater knowledge and understanding of their medications. No significant differences were noted in self-reported adherence or pharmacy refill history. No significant differences were noted in either viral load or CD4 count. Six to eleven month follow-up assessments suggested that those few participants who experienced significant improvements in their viral load were able to maintain their health status over time. Although this study had several methodological improvements over the previously described Rogers and colleagues (2001) study, such as the inclusion of methods to assess adherence, laboratory results, and a follow-up assessment, results suggest that the study was unable to demonstrate clinically significant change in health status. No criteria for poor adherence were specified and only one child over the age of 16 completed the protocol, limiting the study's generalizability to adolescents with chronic non-adherence.

Although the above two studies served as important stepping stones for the development of future intervention studies, they failed to account for many of the complex behaviors and system-level factors that comprise adherence such as child characteristics and family functioning (Cunningham et al., 2006). With the belief that child nonadherence is multiply determined, Cunningham and colleagues (Cunningham et al., 2006) reported on the adaptation of Multisystemic Family Therapy (MST; Henggeler, Schoenwald, Borduin, Rowland, & Cunningham, 1998) to improve antiretroviral medication adherence in P.D.S., a 12 year-old African American male. Drawing from evidence-based treatments such as cognitive-behavioral therapy, parent training, and structural family therapy, MST was used to change the systems (e.g., individual, family, community) affecting or maintaining P.D.S.'s nonadherence. After five months of intensive MST home and community-based visits 2-3 times per week, P.D.S.'s viral load declined, and remained at, undetectable levels for 12 months. MST was reinstituted when

P.D.S.'s viral load increased and similar reductions were noted at the end of treatment. Given the single-case nature of this intervention, the authors noted their inability to determine if changes in P.D.S.'s viral load were the result of the intervention or other non-specific factors such as the mere presence of the research team. Adherence was not measured in the study.

Multisystemic therapy was also applied in a larger study by Ellis, Naar-King, Cunningham, and Secord (2006) with 19 children and their families. Participants received home-based MST sessions 2-3 times per week. Because MST is goal-driven, the intervention was not time-limited. Instead, treatment was only discontinued when treatment goals were met. On average, participants received MST for almost seven months (46 sessions). No changes in caregiver-reported adherence were seen upon completion of the intervention but statistically significant improvements were noted in caregiver knowledge. Clinically significant reductions were seen in viral load, with these changes maintained at three-month follow-up. Although Ellis's intervention shows promise, several methodological weaknesses must be noted. First, this study was conducted via retrospective chart review. The authors were limited in their ability to examine the process of adherence as all data were archival. Second, only one method of measuring adherence was used. The authors noted a ceiling effect with regard to self-report adherence as caregivers reported high levels of adherence at the beginning of the study despite contradictory laboratory data. Finally, the authors acknowledged the cost of MST ($5,500 to $6,000 per patient) as a significant barrier to the implementation of treatment.

Preliminary studies of MST have supported its use as a viable treatment option to improve adherence in the pediatric HIV population. Adopting a socioecological framework such that used in MST provides significant advantages over the cognitive or education-only programs previously used in this population. By acknowledging adherence to be a complex and multiply-

determined behavior, a socioecological approach is able to target several system-level domains of adherence, such as child and family-system factors previously discussed (Cunningham et al., 2006). Another advantage over prior interventions is MST's ability to maintain positive adherence behaviors by helping patients develop life-long skills such as improved problem-solving. These skills may enable the maintenance of good adherence long after the withdrawal of an intervention.

Limitations of the Intervention Literature

A general criticism of the existing intervention literature, including MST, is the lack of prospective studies employing multiple methods of assessing adherence (Simoni et al., 2007). At best, existing interventions have adopted single-method approaches. Some interventions have failed to include even one measure of adherence. When adherence is measured, self-report tends to be the most commonly used method, with self-reports ranging from 24-hour recalls to recall periods of over a month or more. Given the consistent finding that self-report tends to overestimate adherence (Farley et al., 2003; Frey & Naar-King, 2000; Melbourne et al., 1999; Naar-King et al., 2005), future studies employing multiple methods of measuring adherence would have several methodological advantages over the existing literature (Steele & Grauer, 2003).

The extant intervention literature has also been criticized for its universal application of one specific treatment to children from very different age ranges without consideration of the unique needs of participants from various developmental stages (Simoni et al., 2007, Steele & Grauer, 2003). A consequence of this approach has been that little to no attention has been given to the high variability in normative developmental tasks across age groups (Simoni et al., 2007; Steele & Grauer, 2003). Thus, issues that are salient to one age group, such as adolescence, may not be adequately targeted in an intervention with participants ranging from infancy through

young adulthood (Steele & Grauer, 2003). Interventions targeting a specific age range may be an improvement over existing interventions as they would allow for targeting of normative developmental tasks (Holmbeck, 2002). Such interventions have been limited by the small number of children with HIV who are of the same developmental stage and living in the same geographical area (Simoni et al., 2007). Single-case experimental designs may be an effective approach to dealing with small participant sample sizes and may prove to be an informative precursor to larger, multi-site studies.

As a group, adolescents have been largely ignored by the intervention literature. This is surprising given research showing that adolescents are at greatest risk for non-adherence (Mellins et al., 2004; Williams et al., 2006). Adolescents and young adults comprise the largest group of newly infected individuals with HIV (Secord & Cotronei-Cascardo, 2007; World Health Organization 2005). Additionally, the relative aging of the pediatric HIV population, with many children exposed to the virus in the late 1980's and early 1990's surviving into adolescence and young adulthood, further contributes to the large numbers of adolescents currently living with HIV (McConnell et al., 2005). The increased number of adolescents currently infected, coupled with greater rates of non-adherence among this age group (Murphy et al. 2001, Williams et al., 2006), implies a critical need for interventions targeting adherence among adolescents.

Despite being the most promising approach to improving adherence in children with HIV, MST is limited in its applicability to the greater pediatric HIV population. Although several researchers have supported the utility of home visits among this population (e.g., Berrien et al., 2004; Cunningham et al., 2006; Ellis et al., 2006) the time-intensive nature of MST (2-3 home visits per week) contribute to high treatment cost and limited feasibility outside of the research

setting. Thus, there is a critical need for the development of a more cost-effective and less time-intensive home-based intervention to improve adherence among adolescents with HIV.

A behavioral-family systems model (BFST; Robin & Foster, 1989) may be an alternative, yet efficacious, approach to targeting adherence in adolescents with HIV. Behavioral-family systems therapy targets parent-adolescent communication and problem-solving skills to improve overall functioning in distressed families (Robin & Foster, 1989). Traditionally used with families experiencing high levels of conflict, successful applications of BFST have been reported in other problematic areas of adolescent functioning such as eating disorders (Robin, 2003), and Attention-Deficit/Hyperactivity Disorder (Robin, 1998).

With notable exceptions (e.g., Harris, & Mertlick, 2003; Quittner, Drotar, Iveres-Landis, Slocum, Seidner, & Jacobson, 2000; Wysocki, Harris, & Buckloh, 2006; Wysocki, Greco, & Harris, 2000), applications of BFST to children and adolescents with chronic illnesses have been limited. Adapting a behavioral-family systems approach to target adherence in adolescents with HIV may be an efficacious treatment. It has been suggested that focusing specifically on improving family functioning by helping dyads build positive and effective communication skills may positively impact adherence to antiretroviral medications (Mellins et al., 2004). BFST places specific emphasis on this aspect of family functioning and also incorporates problem-solving skills training to help reduce the frequency and severity of conflict within the family system.

Though research finding poorer parent-child communication and relationship quality to be associated with non-adherence among adolescents with HIV supports the application of a BFST-oriented intervention to this population, no known research has examined the extent to which adolescent problem-solving abilities may impact adherence. Support for incorporating a

problem-solving approach comes from the adult HIV literature. Problem-solving has been consistently and successfully used in several intervention studies aimed at improving adherence to antiretroviral medications in adults (e.g., Davies et al., 2006; Johnson, Gamarel, & Rose, 2006; Remien et al., 2005). Incorporating problem-solving skills training in an adherence-improving intervention for adolescents may have similar benefits. An additional benefit of including problem-solving skills training is that it provides adolescents with lifelong conflict-resolution skills that can be applied to the many challenges they will face in life (Robin & Foster, 1989). The two principal components of a behavioral-family systems-oriented approach (problem-solving and family communication) are well suited for an intervention to improve adherence among adolescents with HIV.

Current Study Aims and Hypotheses

The current study expands upon the existing intervention literature in several ways. It is the first-known prospective, behavioral-family systems-oriented intervention approach designed to target adherence to antiretroviral medications among adolescents with HIV. Through alternating weekly home and telephone sessions, the current intervention targets both the adolescent and the family system to improve adherence through the development of effective problem-solving and communication skills as they relate to the HIV regimen. A second advantage over the extant literature is the narrower focus on the adolescent age group. By focusing solely on adolescents with HIV, this study targets an important yet greatly understudied population. Finally, the use of multiple methods for assessing adherence (ex., electronic monitoring, self-report, pill count, and laboratory results) serves as a significant improvement over previous research which has predominantly utilized single-method approaches.

Study aims and hypotheses are as follows:

Aim 1: To conduct a family-oriented intervention to improve family communication and problem-solving skills to increase adherence to prescribed antiretroviral medications among adolescents with HIV.

Hypothesis 1.1: Adolescents will have improved rates of adherence from pre-to post-treatment as determined by an adherence composite score.

Hypothesis 1.2: Adherence rates will be maintained at three-month follow-up.

Aim 2. To examine the effect of the intervention on patient virologic functioning.

Hypothesis 2.1: Adolescents completing the intervention will experience a 1 $\log_{10}$ reduction in viral load from pre- to post-treatment.

Hypothesis 2.2: Viral load at post-treatment will either be maintained or decreased at three-month follow-up.

Aim 3. To improve caregiver and patient knowledge of the medication regimen.

Hypothesis 3: Participants completing the intervention will have improved knowledge of their medication regimen at post-treatment compared to their knowledge at pre-treatment.

Aim 4. To identify and reduce barriers to adherence to the treatment regimen as a result of the intervention.

Hypothesis 4: Participants will report a significant decline in the number of barriers to adherence from pre- to post-treatment.

Aim 5. To identify and remediate family conflict around treatment tasks.

Hypothesis 5: Participants will report a significant decline in their degree of family conflict, as determined by the Conflict Behavior Questionnaire (Robin & Foster, 1989), from pre- to post-treatment.

CHAPTER 2
METHOD

Participants

Participants were four adolescents (ages 13, 15, 17, and 17 years) with a diagnosis of HIV and their parent/legal guardian attending a regularly scheduled appointment at the Pediatric Infectious Disease Clinic directed by Robert Lawrence, M.D. at University of Florida.

Inclusion Criteria

Child eligibility for participation included: (1) currently receiving medication for treatment of a diagnosis of HIV with no planned change in medication type (dosing changes were allowed), (2) being aware of their HIV diagnosis, (3) between the ages of 11-18, (4) accompanied by a parent/legal guardian, (5) able to speak, read, and understand English, (6) having at least one medication amenable to electronic monitoring, and (7) referred to the study by their physician for problems with adherence to their current medication regimen. Parent eligibility for participation included: (1) having legal guardianship of the child, (2) living in the same household as the participating child for the duration of the study, (3) living within a 90-minute driving distance of Gainesville, Florida, (4) not planning to move out of the area within the next year, and (5) able to be contacted by telephone on a weekly basis.

Exclusion Criteria

Children and/or parents were excluded from the study for any factors that could negatively impact their ability to successfully complete a telephone-based intervention designed to improve adherence to antiretroviral medications. Exclusion criteria included the presence of: (1) significant cognitive or developmental delay, (2) an inability to communicate via telephone, (3) the presence of a major psychiatric illness or medical condition in either the child or parent that impaired judgment, (4) current participation in another intervention designed to improve

adherence, (5) any other medical or behavioral condition that, in the opinion of staff, would adversely affect participation in the intervention.

Criteria for Identifying Nonadherent Patients.

All potential participants were considered nonadherent based upon physician referral. To identify nonadherent patients, physicians had access to patient self-reported adherence, laboratory data, and pharmacy refill records.

Experimental Design

Although randomized clinical trials provide the strongest evidence for the causal relationship between an intervention and patient outcome (Clingempeel & Henggeler, 2002), the small number of adolescents with HIV living in the north-central Florida area limited the feasibility of this approach. A single-case design was used.

Single-case experimental designs are well-suited to small sample sizes as they involve the intensive study of individual subjects with the purpose of learning and measuring the effects of treatment on different individuals (Barlow & Hersen, 1984). Through their controlled and reliable measurement of clinical change, single-case designs contribute significantly to our understanding of the effectiveness of interventions and can serve as informative precursors to larger group-based interventions (Barlow & Hersen, 1984; Tervo, Estrem, Bryson-Brockmann, & Symons, 2003).

Due to the longitudinal nature of this study, the following steps were taken to minimize attrition: (1) increasing compensation across time to encourage continued study enrollment, (2) alternating weekly home and phone sessions to minimize participant burden, and (3) coordinating regular clinic appointments into the study protocol to reduce participant travel for study-related assessments.

Procedure

Recruitment

Eligible study participants were approached while attending a regularly scheduled appointment at the Pediatric Infectious Diseases Clinic by a trained member of the research team. Interested participants were provided with detailed study information. Parent informed consent and child assent were obtained prior to all data collection. All potential participants were informed that study refusal would not adversely affect their medical care.

Compensation

Participants were given $15 in recompense for completion of the pre-treatment assessment, $20 for completion of the treatment midpoint (session four), $25 for completion of the post-treatment assessment, and $45 for completion of the three-month follow-up. Participants were given an additional $20 for returning functioning electronic monitoring caps at the end of the study. Thus, participants were eligible to receive up to $125, but no less than $105, for successful completion of the entire study.

Initial Screening and Assessment

Dyads meeting initial eligibility criteria completed a semi-structured interview designed to assess current adherence beliefs and practices. Parents and children also completed self-report questionnaires designed to obtain basic demographic and contact information. Adolescents were given one Medication Event Monitoring System (MEMS) cap for their selected medication to be monitored and received instruction on proper MEMS cap use.

Monitoring was limited to an antiretroviral medication that was in pill form and was currently contained in standard prescription plastic vial. Medications not housed in plastic vials (e.g., pill box), liquid, and powder medications were not eligible for MEMS cap use. Physician

rating of adherence was obtained via a visual analog scale. Information regarding patient viral load and medication regimen were obtained from medical records.

Baseline Monitoring

During the initial assessment, participants identified a day and time in which they would be available each week for contact by the research team in order to obtain baseline adherence data. MEMS cap and pill count data were collected during weekly scheduled home visits by research team members trained in the proper MEMS cap data collection and pill count procedures who were not directly involved with the intervention and were blind to study aims. Self-report adherence data were obtained via a participant-completed questionnaire.

Schedule for Assessment

Participants completed four major assessments throughout their participation in the study (See Table 1). The first assessment occurred immediately following informed consent and was used to determine study eligibility. Participants who met initial study criteria were provided with a MEMS cap and were informed that their adherence would be monitored on a weekly basis throughout the entire intervention via self-report, pill counts, and MEMS cap data. Pre-arranged weekly home visits by a member of the research team were required to obtain MEMS cap and pill count data. An adherence composite score based on MEMS cap, pill count, and self-report data were used to determine the starting time for the pre-treatment assessment. The pre-treatment assessment occurred at the participant's next scheduled clinic appointment after a stable adherence pattern (i.e., two data points in which adherence was not improving), was obtained. Thus, participants had varying lengths of baseline monitoring prior to initiating the intervention.

A post-treatment assessment occurred at the end of the intervention program. Participants also completed a follow-up assessment approximately three months after their post-treatment assessment. Viral load data were obtained at each clinic visit as part of the patient's regular care.

Measures

Demographic Questionnaire

A demographic questionnaire designed for this study was used to obtain information regarding family background information such as: child age, gender, race, age at diagnosis, age of disclosure, and parent marital status, education, and family income. The participating parent completed the demographic questionnaire during the initial visit.

Treatment Interview Protocol

The Treatment Interview Protocol (TIP; Marhefka et al., 2004) is a qualitative structured interview designed to assess a patient's typical adherence to their prescribed medical regimen. The TIP assesses adherence behaviors by asking caregivers about their child's *actual* regimen behaviors prior to soliciting caregiver knowledge of their child's *prescribed* regimen. Caregiver knowledge of the prescribed regimen, as measured by the TIP, is associated with pharmacy refill history, a proxy of medication adherence. For the purpose of this study, participants completed the portion of the TIP designed to assess knowledge of the medication regimen. This information was used to inform and guide the current intervention program and took approximately five minutes to complete. The TIP was also administered at post-treatment to examine changes in medication regimen knowledge as a result of the intervention.

Conflict Behavior Questionnaire

The Conflict Behavior Questionnaire (CBQ, Robin & Foster, 1989) assesses parent-child conflict, arguments, and disagreements over the past two weeks via a 20-item true or false scale. Parent and child-report versions of the CBQ were used in this study. The CBQ has been used extensively throughout the literature, has adequate internal consistency, and has been found to discriminate between distressed and nondistressed families (Robin & Foster, 1989). The CBQ

was administered at both pre- and post-treatment to examine changes in parent-adolescent conflict.

Pediatric AIDS Clinical Trials Group Adherence Module 2

The Pediatric AIDS Clinical Trials Group (PACTG) Adherence Module 2 is designed to assess general reasons for non-adherence to prescribed medications. Because a patient's level of adherence may vary across medications (De Civita & Dobkin, 2004), participants are asked to identify reasons for non-adherence for each individual medication. Patients are asked to endorse their reasons for non-adherence from a list provided in Module 2 and are given the opportunity to identify any reasons not listed in the module. This information was used to inform and guide the current intervention program and was administered at pre-treatment, post-treatment, and at three-month follow-up.

Client Satisfaction Questionnaire

The Client Satisfaction Questionnaire (CSQ; Larsen, Attkisson, Hargreaves, & Nguyen, 1979) is an eight-item measure designed to measure client satisfaction with services. Items for the CSQ were selected on the basis of ratings by mental health professionals of a number of items that could be related to client satisfaction as well and by subsequent factor analysis. The CSQ-8 is uni-dimensional, yielding a homogeneous estimate of general satisfaction with services. Adolescent and caregiver treatment satisfaction were measured by the CSQ-8 immediately after completing the intervention. Participating caregivers and children completed this measure separately.

Medication Use

Medication use was measured through electronic monitoring, pill counts, and self-report. Because the cost of electronic monitoring of all medications exceeded the financial resources of this study, only one medication was selected for electronic monitoring at the physician's

discretion. However, all patient antiretroviral medications were measured via pill counts and self-report.

Electronic monitoring

Medication Event Monitoring System (MEMS) TrackCaps (APREX, 1998) are considered a reliable and innovative method for assessing patient adherence (La Greca & Bearman, 2003). MEMS caps fit most pharmacy bottles and monitor vial openings (events) via a microprocessor imbedded in the bottle cap. Each event is date and time-stamped with an accuracy of ± 30 seconds. Each MEMS cap is waterproof, can store up to 3800 medication events, and is capable of retaining stored data for years after loss of battery power.

MEMS caps were placed on one plastic medication vial prescribed to the patient for the management of their HIV. The medication selected for monitoring was at the discretion of the medical team. When the patient's medical regimen consisted of medications of different dosing frequencies, the medication with the highest dosing frequency was selected. When dosing frequencies were the same among two or more medications, the medication perceived to have the lowest adherence rate was selected for electronic monitoring.

MEMS cap data were collected on a weekly basis during baseline monitoring. Encrypted MEMS cap data were downloaded onto a battery-powered portable communication device while in the participant's home. Data were later uploaded onto the Aardex Ltd. HIPPA-compliant PowerView Version 3 software on a personal computer to obtain numerical and graphical representation of the data. A sample graph from the PowerView software is included in Appendix A.

Participants were instructed on MEMS cap use at the initial screening visit and additional MEMS caps were available during each home visit to replace any malfunctioning caps. All caps were collected at the post-treatment assessment and were returned to participants one month

prior to their three-month follow-up appointment to complete the one month of monitoring required for the follow-up assessment.

Pill counts

Pill counts were obtained by a member of the research team who was trained by the pharmacist of the UF/Shands Infectious Disease Clinic or the Principal Investigator in the proper procedure for counting pills. Pill counts were obtained on a weekly basis during baseline monitoring and on a bi-weekly basis during treatment to coincide with scheduled home visits. Pill counts were also obtained one month prior to, and during, the patient's three-month in-clinic follow-up visit. Patients received a reminder call the day before their clinic visit to help minimize the number of patients who forgot to bring their pill bottles. A home visit was scheduled for those patients forgetting to bring in their medications to the clinic.

Self-reported adherence

Self-report medication use was collected on a weekly basis. Participants completed a paper-based monitoring log once a week that was customized for their specific regimen (e.g., number of pills, and frequency of dosing). For each expected dose, participants were asked to indicate: (1) "yes" or "no" if they took the dose as prescribed and (2) if "no", participants were asked to write down why they did not take the dose. Asking participants to provide a reason for missed doses helped inform treatment by identifying any additional barriers that needed to be addressed by the intervention.

Medication Adherence

Information obtained from participant MEMS cap data, pill counts, and self-report were used to generate a composite medication adherence score guided by the theoretical underpinnings of Liu et al.'s (2000) composite adherence score. In the event that MEMS cap data were missing or invalid, CAS values were obtained from pill count adherence data. In the

event that MEMS cap and pill count data were both missing or invalid, self-report data were used. MEMS, pill count, and self-report data were considered invalid if: 1) the data were missing, 2) visual inspection suggested that the data were clearly discrepant from all other adherence values obtained.

Viral Load

A patient's viral load refers to the estimated amount of HIV RNA copies per milliliter of blood plasma (AIDSinfo, 2005). Viral load serves as an indicator of disease progression and to what extent treatment is working (AIDSinfo, 2005). The patient's estimated viral load was obtained as a part of the patient's usual medical care and was taken from medical records corresponding to the patient's initial, pre-treatment, post-treatment, and three-month follow-up assessment visits.

Intervention Program

The current intervention program used a behavioral-family systems-oriented approach targeting family communication and problem-solving skills to improve adherence to antiretroviral medications among adolescents with HIV. Dyads received seven sessions focusing on improving parent-adolescent communication and using a problem-solving approach to reduce barriers to adherence. Throughout the intervention, participants were reinforced for positive self-care behaviors. All sessions occurred during an agreed upon time by the interventionist and the participants and lasted approximately 40-50 minutes. Both the participating parent and child were required to be present for each session.

The intervention was delivered by an advanced graduate student with a background in pediatric psychology who also had over two years of experience working in a pediatric HIV clinic. Beyond the possibility of having briefly encountered families through the delivery of

consultative services in the HIV clinic, the interventionist did not have a prior relationship with any of the participating adolescents or caregivers.

Session Format

During the intervention, children and parents participated in alternating weekly phone calls and in-person sessions with a behavioral family systems therapy orientation (Robin & Foster, 1989) to assess their adherence and address any barriers to following their treatment regimen. Participants received alternating in-person and telephone sessions. For a listing of session format and content, please see Table 2.

Treatment sessions

The first treatment session occurred in person at the participant's regularly scheduled clinic appointment after at least two data points in which adherence was not improving were obtained through baseline monitoring. The main purpose of this session was to provide the family with a constructive experience to discuss their difficulties, reframe any attributions or beliefs that may interfere with future treatment, gather information related to current adherence, parent-adolescent conflict, and family processes, and establish appropriate expectations for treatment. At this visit, participants completed a structured adherence interview (TIP) and self-report questionnaires. Participants were provided with educational information about HIV through an interactive quiz format. All information was presented at a developmentally-appropriate level and participants were given written information of the session content (Appendix B). Participants were provided with a written list of their medication regimen which included each medication name (brand name and generic), dosage, frequency of dosage, time frame when medication should be taken, and any special instructions (e.g., take with food). A pictorial adherence sheet (Appendix C) was also provided to assist patients who preferred a visual representation of their medication regimen.

At the end of the session, participants were provided with summary feedback from their therapist and information about their future treatment.

The second session occurred in the family's home approximately one week after the first treatment session. This session incorporated information obtained from the initial and pre-treatment assessment to help families identify regimen-specific barriers to adherence. Families reviewed all of the barriers listed from their completion of the PACTG Adherence Module 2 measure and rated each barrier in terms of: (1) how difficult they believe each barrier would be to overcome, and (2) the importance of overcoming each barrier.

Participants then targeted a barrier believed to be important, but of lesser difficulty to overcome using the problem-solving framework outlined by Robin and Foster (1989). Participant materials for session two are presented in Appendix D. Instructions, modeling, role playing, and corrective feedback were provided to guide the family through the following problem-solving process targeting their selected barrier to adherence:

Problem Definition: During this phase, both the adolescent and their parent were allowed to express their perspective on the selected barrier to adherence. Each family member was guided by their therapist in stating their view of the problem in a precise, concise, and non-accusatory manner. Each family member was then asked to verify their understanding of each other's perspective through reflection. Inaccurate reflections were clarified by the person stating the problem so that family members would be able to understand each other's perspectives and have a clear understanding of the problem to be addressed in the following phases.

Generation of alternative solutions: This phase provided family members the opportunity to suggest a variety of strategies to overcome their identified barrier to adherence. During this phase, family members were instructed to list as many ideas as possible, no matter how

outlandish or ridiculous they may seem. The adolescent was asked to record all ideas generate on a problem-solving worksheet (Appendix D) in order to maintain their engagement in the process. Family members were specifically instructed to defer evaluation of any ideas until a later phase, as evaluation could interfere with the generation of high quality and novel solutions. Thus, the therapist interrupted any pre-mature evaluations during this phase in an effort to keep the conversation on task and maintain a non-evaluative atmosphere with balanced participation among family members. Participants progressed to the decision making phase once they generated a workable list of potential solutions. A minimum of 3-4 solutions that went beyond each family member's initial position on the problem were required to move to the next phase. The therapist occasionally interjected a suggestion to help diffuse any tense situations and encourage the generation of creative alternatives.

Decision making: The therapist began this phase by providing the parent and adolescent with a brief discussion of the rationale for the decision-making process. During this phase, the parent and adolescent took turns evaluating each idea generated from the previous phase. Participants were asked to evaluate and clearly state the perceived negative and positive consequences of each idea for themselves and for the rest of their family. Participants were prompted to comment on the feasibility of each idea in addition to the short- and long-term consequences of implementing each idea. Parents and adolescents then independently rated each idea with either a plus or a minus. After all solutions were evaluated, dyads reviewed their ratings to identify any solutions that were rated positively by everyone. Participants who reached a consensus on one or more ideas either selected one idea, or combined several ideas, to implement. Participants who were not able to reach a consensus were assisted by the therapist in negotiating a compromise. A solution rated positively by either the adolescent or parent was

chosen for discussion. Participants were asked to restate their evaluation of the solution and note areas of disagreement between them. The person who was viewed as making the greatest compromise through the implementation of the solution was prompted to provide a variation of the current solution for further consideration. Family members evaluated the new proposed solution while the therapist played an active mediating role to help the family arrive at a consensus.

Planning implementation: During this phase, adolescents and parents generated a step-by-step plan for implementing the chosen solution. A thorough plan outlined specific responsibilities/behaviors for each family member (e.g., parent will check to make sure child takes medicine), identified any resources that may be needed (e.g., use of a wrist watch or cell phone alarm to remind child to take medicine), and anticipated any difficulties that may arise in implementing the agreed upon solution. Family members were asked to monitor each other's compliance to the terms outlined in the plan.

Renegotiation: The renegotiation phase of problem-solving was only invoked when the family had been unsuccessful at using their initial solution to reach their goal. The therapist engaged in a thorough review of each person's attempts at implementation. Information obtained form this review helped place the failure in the context of the problem-solving framework and assisted in revising the current plan.

Problem-solving played a role throughout the entire intervention as additional barriers arose. Negative communication habits which interfered with productive verbal interchanges were identified and modified by the therapist during all problem-solving sessions.

The third session occurred over the telephone. This session focused on evaluating the success of the problem-solving approach implemented in session two. Participants evaluated the

success or failure of their previously established goal. Those reporting problem resolution/goal attainment were asked to identify and target a barrier of slightly greater difficulty and importance to overcome using the problem-solving framework described above. Participants who did not reach their goal re-evaluated their current plan, identified any barriers they experienced, and implemented the problem-solving framework to either revise their current goal or revise their plan. Problem-solving exercises were used to assist participants in need of additional experience with problem orientation and the problem-solving process.

The fourth session was conducted in-person. Participants reported on their degree of success with the problem-solving approach outlined in the previous session. If the previously agreed upon plan was unsuccessful, the problem-solving process was conducted to either revise the plan or the goal or to break down the problem into smaller, more manageable components. Participants reporting successful resolution of their previously targeted problem were asked to target the next barrier on their list in terms of difficulty and importance. The main goal of this session was to provide the family with communication skills training. Families participated in a didactic session that provided rationale for communication training and discussed common parent/child communication errors. Various family communication patterns (ex. verbal, nonverbal, and mixed) were discussed and positive family communication strategies were emphasized. Participants were provided a written copy of the session materials (Appendix E). With guidance from their therapist, participants identified their own problematic communication patterns and practiced positive communication alternatives via role-playing. Participants received feedback from their therapist and agreed to target these specific communication strategies throughout the week.

The fifth session occurred over the telephone and focused on reviewing the previous week's homework on problematic communication patterns and the problem-solving process. Each participant was allowed to express their opinion on what went well and needed additional work with regard to their targeted communication patterns. Participants were asked to reflect on their own progress as well as problem-solving any additional issues the family wanted to address.

The sixth session occurred in person and focused on defining family roles. Participants identified their specific roles within the family in general, as well as in regard to the teen's HIV regimen (e.g., who is responsible for refilling the medication) and used positive communication strategies to resolve ambiguous roles pertaining to the HIV regimen (Appendix F). Parents were given information about the developmental changes from childhood to adolescence and the potential impact of these changes on their teen's adherence (Appendix G).

The seventh session occurred over the phone and was led by the dyad as they reviewed their recent problem solving efforts. Dyads were encouraged to provide feedback and model appropriate problem-solving and communication skills. The therapist served as a passive listener throughout most of the telephone session. The session concluded with feedback from the therapist.

Data Analyses

For Hypothesis 1.1, that adolescents would have improved rates of adherence from pre-to post-treatment as determined by an adherence composite score, data were graphically displayed in percent adherence form and visually inspected according to guidelines set forth by Kazdin (1982).

Autocorrelations were run to identify serial dependency in the data before all statistical analyses. Significant autocorrelations indicate the presence of serial dependency and dictate the

need for specialized statistical techniques such as time series analysis.An autocorrelation is computed by correlating each data point with another data point later on in the series. Correlating a data point with the point immediately after it is referred to a lag-1 correlation. The correlation of a data point with another point two positions after it in the series is known as a lag-2 correlation. Depending upon the number of data points available, autocorrelations of numerous lags can be calculated. Though a lag-1 correlation is usually sufficient in identifying serial dependency in the data, autocorrelations of greater than lag-1 allow for a finer grained analysis of serial dependency (Barlow & Hersen, 1984). In the current study, autocorrelations of numerous lags, as allowable by the data, were calculated. Data not serially dependent were subject to Mann-Whitney U-tests.

For Hypothesis 1.2, that adherence treatment gains would be maintained at three-month follow-up, data were graphically displayed and visually inspected. Changes between phases were evaluated using Mann-Whitney U-tests.

For Hypothesis 2.1, that adolescents completing the intervention would experience a reduction in viral load from pre- to post-treatment, a 1 log10 reduction in viral load was considered to be a clinically significant change.

For Hypothesis 2.2, that viral load at post-treatment would either be maintained or decreased at three-month follow-up, a 1 log10 increase in viral load was considered a clinically significant increase in viral load.

For Hypothesis 3, that participants completing the intervention would have improved knowledge of their medication regimen at post-treatment compared to their knowledge at pre-treatment, data were compared across phases. An improvement in regimen knowledge was

identified by an increase in percent of medications correctly named, percent of doses correctly identified, and percent of dosing frequencies correctly identified.

For Hypothesis 4, that participants would report a significant decline in the number of barriers to adherence from pre- to post-treatment, barrier severity scores were compared across phases. Decreases in barriers were identified by a decline in barrier severity score from pre- to post-treatment.

For Hypothesis 5, that participants would report a significant decline in their degree of family conflict, as determined by the Conflict Behavior Questionnaire (CBQ; Robin & Foster, 1989), from pre- to post- treatment, CBQ scores were compared across phases. Decreases in family conflict were identified by a decline in CBQ scores from pre- to post-treatment. For those families reporting clinically elevated scores on the Conflict Behavior Questionnaire (Robin & Foster, 1989) at pre-treatment, a reduction in reported conflict to non-clinical levels was considered a clinically significant change.

Table 2-1. Intervention schedule of assessment

Study Phase	Length of Phase	Measures Completed
Initial Screening & Assessment	1 hour in-clinic assessment	Informed Consent Demographic questionnaire Medication use (physician rating) Viral load
Baseline Monitoring	Until a consistent pattern of adherence is obtained	Medication use (self-report, MEMS, pill counts)
Pre-Treatment Assessment/Session 1	50-minute in-clinic assessment	Adherence Interview (TIP) PACTG Adherence Module 2 Conflict Behavior Questionnaire Viral load Medication use (self-report, MEMS, pill counts, physician rating)
Treatment Assessment	8 weekly sessions Note: Session 1 occurs during pre-treatment assessment	Medication use (self-report, MEMS, pill counts)
Post-Treatment Assessment	30-minute in-clinic assessment	Medication use (self-report, MEMS, pill counts, physician rating) Conflict Behavior Questionnaire PACTG Adherence Module 2 Viral load
Follow-up Assessment	Approximately 3 months	PACTG Adherence Module 2 Viral load Medication use (self-report, MEMS, pill counts, physician rating)

Table 2-2. Intervention sessions by format and topic

Session #	Session Format/ Location	Topic
1	In-clinic visit	Introduction to treatment program, HIV education, medication regimen review
2	In-person home visit	Introduction to problem-solving
3	Telephone	Review of problem-solving progress
4	In-person home visit	Family communication skills training
5	Telephone	Review of problem-solving and communication progress
6	In-person visit	Defining family roles and expectations
7	Telephone	Family-led problem-solving session, self-evaluation of progress

CHAPTER 3
RESULTS

Participant Data

Participant 1

Background information

Participant 1 (P1) was a 17-year-old African-American female in the custody of her maternal aunt. Caregiver reported annual family income fell between $20,000 and $29,999. Participant 1 was diagnosed with HIV at birth and was informed of her diagnosis at age 14. Her prescribed treatment regimen consisted of two NRTI's (Viread 300 mg once a day; Epzicom 1 tablet once a day) and two PI's (Norvir 100mg once a day; Reyataz 300 mg once a day), all of which were taken at night. According to the medical team, P1 had a longstanding history of poor adherence to her treatment regimen. Pharmacy records indicated that prior to enrolling in the current study, P1 had not refilled her medications in over three months. At the time of enrollment, physician estimated adherence for the past month was 36%.

Construction of composite adherence score

Per the suggestion of her physician, Reyataz was selected as the medication to be monitored electronically throughout the entire study. Adherence data as measured by MEMS, pill count, and self-report for Reyataz are presented in Figure 1. As seen in Figure 1, MEMS cap estimates were significantly below pill count and self-report estimates during the treatment and follow-up phases of the study. Midway through treatment the researchers became aware that the MEMS had been dropped several times on a hard surface. Participant 1's MEMS was then replaced with a new MEMS and additional education on proper MEMS cap use was provided. Despite this, MEMS estimates continued to be significantly below pill count and self-report data. Though pill count and self-report data were highly correlated with one another (95.2%), MEMS

cap associations with pill count data (-0.7%) were trivial. Correlations between MEMS and self-report data were low (19.2%). Using previously described guidelines for identifying missing or invalid data, MEMS cap data were only used for baseline week two and week four in constructing the composite adherence score. Pill counts, which were more consistent with self-report as well as with viral load data, were used for the majority of composite adherence score calculations (baseline weeks one & three, treatment sessions two, four, & six). During the weeks in which phone sessions were conducted and pill counts could not be obtained (sessions three, five, & seven), self-report data were used as the foundation for CAS. As MEMS cap data were deemed invalid for the follow-up period and pill count data did not capture week-to-week variability in adherence rates, self-report data were used for all follow-up CAS. It must be noted, however, that average self-reported adherence during the follow-up period (95%) was similar to estimated monthly pill count adherence (92.6%).

Treatment and adherence

Composite adherence data for P1 are presented in Figure 2. During the baseline monitoring period, her adherence ranged from 0% to 100%, with an average adherence rate of 64.7%. Physician estimate of adherence for the baseline period was 86%.

According to self-report adherence sheets completed throughout the baseline monitoring period, “forgetting” was the most commonly cited reason for missing a dose. This barrier was specifically targeted during treatment. In session two, P1 and her guardian agreed to implement a new incentive system to help improve her adherence. According to this system, P1 would earn points toward being allowed to redecorate her room each time she remembered to take her medication. Unfortunately, this system was not implemented during the week and adherence rates dropped from 87.5% at the end of baseline monitoring to 71.4% and 75% during treatment weeks one and two. In session three, a reevaluation of the previously designed plan was

conducted and both P1 and her guardian decided to devise a new plan. Through use of the five-step problem solving approach in session three, it was discovered that P1 often fell asleep before remembering to take her medication. Primary contributors to this problem were: 1) returning home late and tired from her part-time job and, 2) the remote location in which her medications were kept (on top of a tall entertainment center in the family room). During the brainstorming portion of this session, numerous ideas were generated to overcome this barrier, among which was the relocation of P1's medications to a place in which she was highly likely to encounter before falling asleep. Thus, P1's medications were moved from on top of the entertainment center to in front of the power button on the television in her bedroom. Both P1 and her guardian agreed that this would be a more effective strategy as P1 always turned her television on in order to go to sleep.

After implementation of this plan, P1's adherence increased to 91.7% and 100% for treatment weeks three and four, respectively (Figure 2). From session three until the end of treatment, P1's average adherence rate was 94.3%. Her overall adherence for the treatment phase of the study was 88.3%. Improvements in adherence rates were maintained at three month follow-up (average adherence 95%). Physician rating of adherence was 86% at both post-treatment and at follow-up.

Visual inspection

The magnitude of change and rate of change across phases were visually inspected in Figure 2 to determine if change occurred due to the intervention. In evaluating magnitude of change, changes in the mean and level of performance across phases were considered. Mean adherence increased from baseline (64.7%) to treatment (88.3%) to follow-up (95%). Level of performance declined between the end of baseline monitoring and the beginning of treatment, suggesting that the intervention did not produce a rapid shift in improving adherence. However,

as this intervention was designed to be delivered across several sessions, a rapid change in behavior from baseline to the first treatment session was not expected. When problem solving was implemented and followed through by P1 and her guardian (session three), the level of performance experienced a shift from 75% to 91.7% adherence.

Rate of change was examined by inspecting the trend and latency of change. Although adherence data from the baseline period had a generally positive trend (slope=0.23), the data were highly variable. Treatment phase data clearly illustrate a positive trend with increased stability in data points (slope=0.04). Follow-up data appear to continue the trend established during the treatment phase and a ceiling effect was seen in overall adherence by the end of the study (slope=-0.02). With regard to latency, changes in adherence data were visible after implementation of the adherence strategy agreed upon during session three. Thus, visual inspection suggests that the intervention was effective in promoting behavior change over time.

Statistical analyses

Autocorrelations from one to 10 lags were calculated to identify any serial dependency in the baseline and treatment phase study data prior to all statistical analyses. As seen in the correlogram and its corresponding table (Figure 3), associations between data points for all lags were small, suggesting that the autocorrelations did not significantly deviate from zero. This suggests that the data points could be treated as independent observations. Because P1's data were not serially dependent, conventional statistical analyses were used to examine differences between baseline, treatment, and follow-up adherence data.

Table 3 presents descriptive statistics of the CAS during the baseline, treatment, and follow-up phases of the study. As seen in Table 3, skewness and kurtosis values from the baseline and follow-up phases of the study were beyond acceptable limits, suggesting that the

data were not normally distributed. Because this basic assumption of the general linear model was not met, non-parametric statistics were used to compare differences between phases.

No statistically significant differences in adherence were found between baseline and treatment (Mann-Whitney U=19, p>.05). Treatment phase adherence and follow-up phase adherence did not significantly differ (Mann-Whitney U=8, p>.05). Baseline and follow-up adherence data also did not statistically differ (Mann-Whitney U=12.5, p>.05).

Virologic functioning

At the beginning of baseline monitoring, P1 had a viral load of 2800. When treatment was initiated, laboratory results suggested that P1's viral load had increased to 3300. At the end of treatment, Participant 1's viral load had decreased to below baseline and pre-treatment levels (2700). This decrease in viral load continued into the three-month follow-up period (viral load at follow-up = 430). Though P1's viral load decrease from 3300 at pre-treatment to 430 at follow-up was 100 short of reaching clinical significance (1 $\log_{10}$ reduction), this change represented an 87% reduction in viral load.

Knowledge of medication regimen

On the Treatment Interview Protocol completed at the end of the baseline period, P1 was able to correctly provide 100% of her prescribed antiretroviral medications, 100% of her prescribed dosing frequencies, and 100% of her prescribed dosing amounts. It must be noted, however, that this information was not recalled from memory but rather from a list of her medications that P1's caregiver had brought to clinic. Under guidelines of the Treatment Interview Protocol, use of a cheat sheet is allowed as a memory recall tool. At post-treatment, P1 did not have a cheat sheet. Despite this, she was able to recall the names of 100% of her prescribed medications, 100% of her prescribed dosing frequencies, and 75% of her prescribed dosing amounts.

Barriers to adherence

During the initial assessment, P1 reported a number of barriers to adherence over the past month including: not getting medications refilled in time (frequent problem), forgetting (almost always a problem), not remembering if dose was already taken (frequent problem), falling asleep (frequent problem), and being away from home (hardly ever a problem). In total, P1's barrier severity score at baseline was 10. At post-treatment, P1 reported no barriers to her adherence.

Parent-child conflict

P1's score on the Conflict Behavior Questionnaire (CBQ) at the beginning of treatment suggested that her response pattern was similar to that of nondistressed families (CBQ=3). Her score on the CBQ at post-treatment was two.

Caregiver report of conflict at the beginning of treatment was similar that of nondistressed families (CBQ=5). At the end of treatment, her response pattern indicated increased levels of conflict more similar to that of distressed families (CBQ=8).

Participant 2

Background information

Participant 2 was a 15-year-old biracial (African-American/Hispanic) female living with her biological mother. Caregiver reported annual family income fell between $40,000 and $49,999. Participant 2 (P2) was diagnosed with HIV at three years, 11 months and was informed of her diagnosis at this time. Her prescribed treatment regimen consisted of two NRTI's (Epivir 150 mg twice a day; Zerit 40 mg twice a day) and two tablets of one PI (Viracept 1,250 mg twice a day). According to P2, she had not taken any of her medications over the past two months. At the time of study enrollment, physician estimated adherence for the past month was 39%.

Construction of composite adherence score

P2's physician requested that Viracept be electronically monitored as this medication required the greatest number of pills to be swallowed per day (2 pills at each dosing). Adherence data as measured by MEMS, pill count, and self-report for Viracept are presented in Figure 4. As seen in Figure 4, self-report estimates were generally higher than both MEMS cap and pill count estimates. MEMS data were substantially correlated with pill counts (58%) and with self-report (57%). Pill counts and self-report estimates were strongly correlated with one another (60%). Given the substantial-to-strong correlations between MEMS cap and other adherence assessment measures, MEMS data were used as the foundation for CAS for all but one of the data points (session 3). Because pill count and self-report data for session three were more congruent with one another than with MEMS, pill count data were used for this time point only.

Treatment and adherence

Composite adherence data for P2 are presented in Figure 5. During the baseline monitoring period, P2's adherence ranged from 75% to 83.3%, with an average adherence rate of 78.5%. Physician estimate of adherence for the baseline period was 79%.

During the baseline monitoring period, "being away from home" and "falling asleep" were the most commonly reported reasons for missing a dose. These barriers were identified as targets for intervention in addition to other barriers that arose while working with P2 and her mother.

Adherence dropped from 77.8% at the end of baseline monitoring to 60% in the week following the first treatment session. In session two, P2 and her mother expressed interest in using the problem solving approach to help P2 improve her adherence to her morning medications. According to P2, she often forgot to take her morning dosings because she did not have a structured routine in place. During the brainstorming portion of the session, P2 and her mother were able to come up with numerous solutions to help overcome this barrier. The

solution rated most positively by P2 and her mother was taking her medications along with breakfast in the morning. Individual responsibilities for implementing this plan were identified including cooking breakfast in the morning and placing P2's dosings next to her meal (mother) and being willing to be woken up to take her medicine if found sleeping past 10 am (P2). Following implementation of this plan, P2's adherence increased from 60% to 86.7%.

Unfortunately, increased responsibilities coinciding with the start of the school year for both P2 and her mother led to greater day-to-day variability and decreased adherence for both morning and nighttime medications. Adherence following session four dropped to 42.1% and problem-solving was re-implemented to overcome newly arisen barriers. Because P2's mother had begun leaving very early for work and could no longer cook breakfast for P2, the previously implemented solution no longer applied to the family's circumstances. At night time, P2 often returned home late and tired from cheerleading practice and went straight to bed without remembering to take her medications. Because electronic monitoring indicated that night time doses were missed at a greater frequency than morning doses, session six focused on improving adherence to nighttime medications. Using the problem solving approach, P2 and her mother agreed to implement a plan in which P2 would take her medications upon arriving home after cheerleading practice. P2's mother agreed to be responsible for reminding P2 to take her medication. Unfortunately, this plan was not well implemented and adherence remained low for session weeks six and seven (44.4% & 50%, respectively).

P2's overall adherence for the treatment phase of the study was 57.7%. Physician estimated adherence for the treatment phase of the study was 81.5%. For the follow-up period, P2's average adherence rate was 73.2%. Physician rating of adherence for the follow-up period was 91%.

Visual inspection

Magnitude and rate of change across phases were visually inspected in Figure 5. Changes in the mean and level of performance across phases were considered in evaluating magnitude of change. Mean adherence decreased from baseline (78.5%) to treatment (57.7%) but increased at follow-up (73.2%). As with P1, P2's level of performance declined between the end of baseline monitoring and the beginning of treatment, suggesting that the first intervention session (e.g., HIV education) did not produce a rapid shift in improving adherence. When problem solving was implemented in session two, adherence improved to 86.7%, the highest adherence rate obtained thus far. However, increased barriers coinciding with the start of school led to a decrease in adherence rates for sessions four through seven, bringing down the overall adherence rate for the treatment phase of the study to below baseline levels.

Overall, adherence data from the baseline period had a slight negative trend (slope =-0.01) with relatively good stability in data points. Treatment phase data were highly variable but also had a slight negative trend (slope=-0.05). This trend was continued at follow-up (slope=-0.05). With regard to latency, a change in adherence was seen following the session which introduced problem solving (session two). Thus, visual inspection suggests that the intervention was only temporarily effective in promoting behavior change but that this behavior was not sustained over time.

Statistical analyses

Autocorrelations from one to 10 lags were calculated to identify any serial dependency in the baseline and treatment phase study data prior to all statistical analyses. As seen in the correlogram and its corresponding table (Figure 6), associations between data points were greatest at one lag but did not significantly deviate from zero, suggesting that the data points

could be treated as independent observations and conventional statistical analyses could be used to examine differences between treatment phases.

As seen in Table 3, kurtosis values from the baseline and follow-up phases of the study were beyond acceptable limits, suggesting that the data were not normally distributed and non-parametric statistics should be used to compare differences between phases.

Significant differences were found between baseline and treatment adherence rates (Mann-Whitney $U=4$, $p<.05$), suggesting that the average baseline adherence rate was significantly greater than the average treatment adherence rate. Treatment and follow-up adherence rates did not significantly differ (Mann-Whitney $U=21.5$, $p>.05$). Baseline and follow-up adherence data were significantly different (Mann-Whitney $U=4$, $p>.05$), with the average baseline rate being significantly greater than the follow-up period rate.

Virologic functioning

At the beginning of baseline monitoring, P2's viral load was 470. This number decreased to 77 by the end of the baseline period. At post-treatment, P2's viral load was 59. By the end of the follow-up period, P2 had an undetectable viral load, representing a clinically significant (1 $\log_{10}$) decrease from baseline to follow-up. According to medical records, P2 had not been undetectable for over two years prior to enrolling in the study.

Knowledge of medication regimen

On the Treatment Interview Protocol completed at the end of the baseline period, P2 was able to correctly name 100% of her prescribed antiretroviral medications. She was able to provide her prescribed dosing frequencies but not her dosing amounts. At post-treatment, P2 was able to correctly name 100% of her medications and 100% of her dosing frequencies. Though she was unable to report her dosing amounts, P2 was able to distinguish medications which required two pills per dosing from those requiring one pill per dosing.

Barriers to adherence

During the initial assessment, P2 reported a number of barriers to adherence over the past month. In total, P2's barrier severity/frequency score at baseline was 13. Barriers endorsed as being hardly ever a problem (1-2 times per month) included: not getting medications refilled in time, too busy with school, and worried others would find out about HIV. Barriers endorsed as frequent problems (1-2 times per week) included: forgetting, couldn't deal with it/needed a break, didn't think I needed medications anymore, don't remember if dose was already taken, and falling asleep. At post-treatment, P2 reported fewer barriers to adherence. Her barrier severity/frequency score at post-treatment was five.

Parent-child conflict

P2's score on the Conflict Behavior Questionnaire (CBQ) at the beginning of treatment suggested that her response pattern was similar to that of distressed families (CBQ=6). Her score on the CBQ at post-treatment was four, midway between distressed and non-distressed families.

Caregiver report of conflict at the beginning of treatment was similar that of nondistressed families (CBQ=5). At the end of treatment, her response pattern indicated increased levels of conflict more similar to that of distressed families (CBQ=8).

Participant 3

Background information

Participant 3 (P3) was a 13-year-old African-American female living with her biological father. Annual family income was between $5,000 and $9,999. P3 was diagnosed with HIV at birth and was informed of her diagnosis at age 11. Her prescribed treatment regimen consisted of two NRTI's (Viread 300 mg every morning; Epzicom 1 tablet every morning) and two PI's (Norvir 100mg every 12 hours; Lexiva 700 mg every 12 hours). Per the clinic social worker, who had been conducting pills counts prior to study enrollment, P3's average adherence was 40%.

Though physician estimate of adherence was 73% at the time of study enrollment, her physician described P3's adherence as "erratic."

Construction of composite adherence score

Per the suggestion of her physician, Lexiva was selected as the medication to be monitored electronically throughout the entire study as this medication had one of the greatest dosing frequencies. Adherence data as measured by MEMS, pill count, and self-report for Lexiva are presented in Figure 7. As seen in Figure 7, self-reported adherence was usually higher than adherence as measured by pill counts or MEMS. MEMS data were very strongly associated with pill count data (77%). Self-report was moderately correlated with MEMS (27%) and pill counts (33%).

Given the very strong correlation between MEMS cap and other pill counts data, MEMS was used as the foundation for CAS for all but one of the data points (session five). At this time, P3 was hospitalized for 1.5 days and had her medication administered to her by hospital nurses. Because the hospital required that P3's medications come from their own supplies while hospitalized, MEMS and pill count (which are based off of P3's personal medication supply) could not be used. Self-report was used for session five data. This data, however, was only slightly greater than MEMS and pill count estimates.

Treatment and adherence

Composite adherence data for P3 are presented in Figure 8. During the baseline monitoring period, adherence was 100% for the first two weeks of monitoring. Adherence then dropped by 40% for week three. Suggesting that the effects of being monitored were less powerful. After four weeks of monitoring, adherence became less erratic. This coincided with increased parent involvement and awareness of changes in adherence rates from week two to week three. Overall

adherence for the baseline monitoring period was 86%. Physician estimate for the baseline period was 90%.

Because P3 often reported 100% adherence rates that were not supported by MEMS and pill count data, very few reasons for missing a dose were listed on baseline self-report adherence sheets. Discussions with P3 and her father about general reasons for missing a dose revealed that forgetting and falling asleep were the most commonly, though rarely, encountered barriers to adherence.

Following session one, which focused on HIV education and improved knowledge of the medical regimen, adherence improved to 100%. Session two focused on using problem solving to identify methods to ensure that P3 took her evening medications before falling asleep. Solutions agreed upon by both P3 and her father included having P3's father place all of her medications in a pill box (minus Lexiva which continued to be monitored by MEMS) and having her father verify with P3 that she had taken her medication by 11 pm by checking her pill box for any remaining doses. Adherence remained high following sessions two and three (92.9% and 93.8%, respectively). During session four, which focused on family communication, P3's father expressed interest in having P3 assume more responsibility for her treatment regimen. Specifically, he requested that P3 be in charge of pre-filling her pill box every week and that she assume more responsibility for making sure her morning medications were taken. P3 expressed interest in assuming more responsibility as she felt her father sometimes nagged her about taking her medicine. Because this often led to increased conflict, both P3 and her father agreed to shift responsibility for filling out pill boxes to P3. As part of the agreement, P3's father also promised not to nag P3 for the next week about taking her medicine. Following implementation of this plan, P3's adherence experienced a slight decrease (87.5%). Further decreases in adherence were

seen during week five (83.3%). During session six, this trend was brought to the attention of P3 and her father. P3's father vowed to resume responsibility to P3 taking her medication by reimplementing the adherence plan agreed upon in session two. Despite this, adherence continued to decline. Disruptions in family routines during sessions six and seven coincided with the Thanksgiving holiday and increased work hours for P3's father. P3's overall adherence for the treatment portion of the study was 86.2%. Physician rating for the treatment phase of the study was 80%.

During the follow-up period, P3 maintained an average adherence rate of 92.5%. Physician rating of adherence for this time period was 92%.

Visual inspection

The magnitude of change and rate of change across phases were visually inspected in Figure 8 to determine if change occurred due to the intervention. In evaluating magnitude of change, changes in the mean and level of performance across phases were considered. Mean adherence remained constant from baseline to treatment (86% to 86.2%) but improved to 92.5% at follow-up. Level of performance increased between the end of baseline monitoring and the beginning of treatment, suggesting that session one produced a rapid shift in improving adherence.

Rate of change was examined by inspecting the trend and latency of change. Adherence data from the baseline period had a neutral trend (slope = 0), with increased stabilization of data points following week four. Treatment phase data illustrate a slight negative trend (slope = -0.05) over time. Follow-up data illustrate a very slight positive trend (slope = 0.03). With regard to latency, adherence improved following session one but gradually declined over time. Thus, visual inspection suggests that the intervention had slight effectiveness in promoting sustainable behavior change.

Statistical analyses

Autocorrelations from one to 12 lags were calculated to identify any serial dependency in the baseline and treatment phase study data prior to all statistical analyses. As seen in the correlogram and its corresponding table (Figure 9), associations between data points for all lags were small, suggesting that the autocorrelations did not significantly deviate from zero and that the data points could be treated as independent observations.

Table 3 presents descriptive statistics of the CAS during the baseline, treatment, and follow-up phases of the study. As seen in Table 3, kurtosis values from the baseline period and skewness and kurtosis values from the follow-up period were beyond acceptable limits, suggesting that the data were not normally distributed. As such, non-parametric statistics were used to compare differences between phases.

No statistically significant differences in adherence were found between baseline and treatment (Mann-Whitney $U=35$, $p>.05$). Treatment adherence and follow-up adherence did not significantly differ (Mann-Whitney $U=8.5$, $p>.05$). Baseline and follow-up adherence data also did not statistically differ (Mann-Whitney $U=12$, $p>.05$).

Virologic functioning

P3 had a viral load of 48 at the beginning of baseline monitoring. When treatment was initiated, laboratory results suggested that P3's viral load had increased to 220. At the end of treatment, Participant 3's viral load had decreased to below pre-treatment levels (68), representing a 31% decrease in viral load. At follow-up, P3's viral load increased to 820. Though an increase was noted in viral load from post-treatment to follow-up, this increase did not represent a clinically significant change.

Knowledge of medication regimen

On the Treatment Interview Protocol completed at the end of the baseline period, P3 was able to correctly provide 100% of her prescribed antiretroviral medications, 100% of her prescribed dosing frequencies, and 0% of her prescribed dosing amounts. Knowledge of medication name, dosing frequency, or dosing amount did not change from pre- to post-treatment.

Barriers to adherence

During the initial assessment, P3's barrier severity score was six, with forgetting, not having help remembering, being busy, not remembering if dose was already taken, and needing to take a break being the most commonly reported barriers. Although P3 reported a fewer number of overall barriers at post-treatment, the barriers endorsed (i.e., forgetting, not remembering if dose was taken, and falling asleep) were endorsed as being a problem with greater frequency (barrier severity score= 6).

Parent-child conflict

P3's score on the Conflict Behavior Questionnaire (CBQ) at the beginning of treatment suggested that her response pattern was similar to that of distressed families (CBQ=9). Though her score on the CBQ at post-treatment decreased to six, this level of conflict remained more similar to distressed families than nondistressed families.

Caregiver report of conflict at the beginning of treatment was similar that of nondistressed families (CBQ=4). However, at the end of treatment, parent report of conflict had increased to be more similar to that of distressed families (CBQ=11). This may have been due to increased opportunities for conflict as P3 and her father were spending more time together as a result of the intervention.

Participant 4

Background information

Participant 4 (P4) was a 17-year-old Caucasian male who had been living in the legal custody of his older sister for the past six years. Annual family income was reported to fall between $50,000 to $59,999. P4 was diagnosed with HIV at birth and was informed of his diagnosis at age seven. His prescribed treatment regimen consisted of two NRTI's (Viread 300 mg once a day; Epzicom 1 tablet once a day) and two PI's (Norvir 100mg once a day; Reyataz 300 mg once a day), all of which were taken in the morning. P4 had a history of poor adherence to his medical regimen, with particular problems adhering to dosings during the summer break and on weekends. Physician estimate of adherence for the month prior to enrolling in the study was 24%.

Construction of composite adherence score

Based on physician recommendation, Reyataz was selected as the medication to be electronically monitored. Adherence data as measured by MEMS and self-report for Reyataz are presented in Figure 10. Pill count estimates could not be reliably obtained for P4 as part of his medications were kept at school and part were kept at home. As an additional complication, unknown refill amounts were distributed to the school and P4 at unknown times by the clinic social worker, further complicating pill count adherence computations. The barriers encountered in obtaining reliable pill counts did not affect MEMS measurements as two MEMS caps were used (one at school, one at home) to track P4's adherence. As seen in Figure 10, self-report estimates were generally higher than MEMS estimates though they were strongly correlated with one another (70%). MEMS data were used as the foundation for CAS for all data points.

Treatment and adherence

Composite adherence data for P4 are presented in Figure 11. During the baseline monitoring period, P4's adherence ranged from 57.1% to 87.5%, with an average adherence rate of 65.3%. Physician estimate of adherence for the baseline period was 80%.

During the baseline monitoring period, "being away from home" and "running out of medication" were the most commonly reported reasons for missing a dose during the weekend. These barriers were identified as targets for intervention.

Adherence dropped from 71.4% at the end of baseline monitoring to 33.3% in the week following the first treatment session. In session 2, the five-step problem solving approach was used to improve P4's adherence to his weekend dosings. According to P4, primary reasons for missed doses included: 1) not being reminded to take his medications, and 2) the remote location in which his medications were kept (in a kitchen cabinet that contained no other items). During the brainstorming portion of this session, numerous ideas were generated to overcome this barrier, among which was the relocation of P4's medications to a place in which he was highly likely to encounter them in the morning. In P4's case, this meant relocating his medications from the kitchen cabinet to a cabinet containing cereal boxes. Both P4 and his guardian agreed that this would be a more effective strategy as P4 always ate cereal in the morning. P4's guardian agreed to check in with P4 on weekends to make sure he took his medication. To help P4's guardian remember to do this, she set an alarm on her mobile phone.

Immediately following implementation of this plan, P4's adherence rate improved to 100%. P4's adherence following session 3 was 85.7% (6 out of 7 doses taken according to MEMS). This estimate was lower than P4's self-report of 100% adherence due to P4's claim that he "pocketed" a dose over the weekend to avoid having to bring the MEMS cap to his friend's house. However, because this could not be verified by pill count, MEMS data were used.

Following session four, P4 ran out of medications at home was unable to take his weekend doses, dropping his adherence down to 71.4%. Though P4's guardian was able to obtain more medicine by session five, this session coincided with the Thanksgiving holiday and P4 did not take his medications as regularly as he had been doing so when he had a routine in place. Session six focused on implementing the problem solving approach in order to help P4 overcome the barrier of running out of medication. When providing her perception of the problem, P4's guardian reported that P4 often waited until he was out of medication in order to notify her. This usually happened on a weekend, a time in which P4's guardian was unable to reach the clinic social worker to arrange more pills to be delivered, thereby leading to P4 to miss 29% of his weekly doses. Following the brainstorming and evaluation portion of the session, P4 agreed to notify his guardian whenever he had less than three pills left of his medication. This number was chosen as it would provide P4 with enough medication to make it through the weekend and would give his guardian five days in which to obtain additional supplies before the next weekend. To help remind P4 of this plan, a sticker containing the agreed upon plan and the name and number of the social worker was attached to his medication vial. Immediately following this session, adherence improved to 100%. Unfortunately, this was not maintained for session seven due to forgetting doses. Overall, P4's average adherence for the treatment portion of the session was 74.4%. Physician rating of adherence for the treatment period was 86%.

P4's follow-up period adherence was characterized by high levels of instability. Just prior to the beginning of the follow-up monitoring period, P4 and his family (six individuals in total) were displaced from their home by a fire that destroyed all of their possessions. Throughout the follow-up monitoring period, P4 and his family lived in hotel rooms and with family friends.

Lacking a stable daily routine, P4's adherence during the follow-up period dropped to 60.7%. Physician rating of adherence for the follow-up period was 73%.

Visual inspection

Magnitude and rate of change across phases were visually inspected in Figure 11. Changes in the mean and level of performance across phases were considered in evaluating magnitude of change. Mean adherence increased from baseline (65.3%) to treatment (74.4%) but decreased at follow-up (60.7%). As with P1and P2, P4's level of performance declined between the end of baseline monitoring and the beginning of treatment, suggesting that the first intervention session (e.g., HIV education) did not produce a rapid shift in improving adherence. When problem solving was implemented in session two, adherence improved to 100%, the highest adherence rate obtained up to that point. However, running out of medication and the disruptions in normal routine due to the Thanksgiving holiday led to a decrease in adherence rates for sessions four and five. These disruptions lowered the overall treatment adherence rate to 74.4%, though this was still above P4's baseline average.

Overall, adherence data from the baseline period had a very slight negative trend (slope =-0.01). Treatment phase data had a slight positive trend (slope=0.03). This trend was not continued at follow-up (slope=-0.01). With regard to latency, improvements in adherence were seen immediately following sessions two and six, which had a major focus on problem solving. Overall, visual inspection suggests that the intervention was modestly effective in promoting behavior change but that this behavior was not sustained over time.

Statistical analyses

Autocorrelations from one to 11 lags were calculated to identify any serial dependency in the baseline and treatment phase study data prior to all statistical analyses. As seen in the correlogram and its corresponding table (Figure 12), associations between data points did not

significantly deviate from zero, suggesting that the data points could be treated as independent observations.

As seen in Table 3, the kurtosis value from the baseline phase of the study was beyond acceptable limits. Thus, non-parametric statistics were used to compare differences between phases.

No significant differences were found between baseline and treatment adherence rates (Mann-Whitney U=34, p>.05), suggesting that the average baseline adherence rate was not significantly greater than the average treatment adherence rate. Treatment and follow-up adherence rates did not significantly differ (Mann-Whitney U=19, p>.05). Baseline and follow-up adherence data also did not significantly differ (Mann-Whitney U=19, p>.05).

Virologic functioning

At the beginning of baseline monitoring, P4's viral load was 56,000. By the end of the baseline monitoring period, his viral load had increased to 77,000. Unfortunately, this trend continued despite improved adherence. At post-treatment, P4's viral load was 190,000. Laboratory tests conducted at post-treatment indicated that P4 had developed high levels of resistance to all of his prescribed antiretroviral medications. By the end of the follow-up period, P4's viral load was 80,000. This change was not clinically significant.

Knowledge of medication regimen

On the Treatment Interview Protocol completed at the end of the baseline period, P4 was able to correctly name 100% of his prescribed antiretroviral medications and 100% of his dosing frequencies. He was unable to correctly provide any of his dosing amounts. No changes in medication name, dosing frequencies, or dosing amounts were seen at post-treatment.

Barriers to adherence

P4 reported a number of barriers to adherence during the initial assessment. Forgetting, not having family members help remind him, not remembering if dose was taken, falling asleep, and being away from home were identified as frequent problems (1-2 times per week). Not getting medications refilled in time was identified as a less frequent problem (1-2 times per month). In total, P4's barrier severity score was 11 at pre-treatment. At post-treatment, P4 reported a fewer number of barriers to adherence (barrier severity score = 2).

Parent-child conflict

P4's score on the Conflict Behavior Questionnaire (CBQ) at the beginning of treatment suggested that his response pattern was similar to that of nondistressed families (CBQ=2). His score on the CBQ at post-treatment remained at two.

Caregiver report of conflict at baseline and post-treatment were similar that of nondistressed families (CBQ=2 for both assessments).

Treatment Satisfaction

Out of a possible range of eight to thirty-two points, with eight being very dissatisfied and thirty-two being very satisfied, adolescent average rating of the program was 30.25 (range=26-32). Parent-reported program satisfaction was also very high (average rating=31; range=29-32).

Table 3-1. Descriptive statistics of CAS data for all participants

Participant 1

Phase	N	Mean	SD	Range	Median	Skewness	Kurtosis
Baseline	4	64.7	45	0-100	72.25	-1.60	2.66
Treatment	7	88.3	11.37	71.4-100	91.7	-0.61	-1.78
Follow-up	4	95	10	80-100	90	-2.00	4.00

Participant 2

Phase	N	Mean	SD	Range	Median	Skewness	Kurtosis
Baseline	4	78.5	3.47	75-83.3	77.9	1.03	2.09
Treatment	7	57.7	16.68	42.1-86.7	50	1.03	-0.15
Follow-up	4	73.2	9.14	66.7-86.7	69.6	1.86	3.56

Participant 3

Phase	N	Mean	SD	Range	Median	Skewness	Kurtosis
Baseline	10	86	11.4	60-100	85.2	-1.12	2.60
Treatment	7	86.2	10.4	71.4-100	87.5	-0.29	-1.15
Follow-up	4	92.5	15.0	70-100	100	-2.00	4.00

Participant 4

Phase	N	Mean	SD	Range	Median	Skewness	Kurtosis
Baseline	7	65.3	11.25	51.7-87.5	60	1.54	2.13
Treatment	8	74.4	23.49	33.3-100	71.4	-0.65	0.33
Follow-up	4	60.7	13.68	42.9-71.4	64.3	-0.85	-1.29

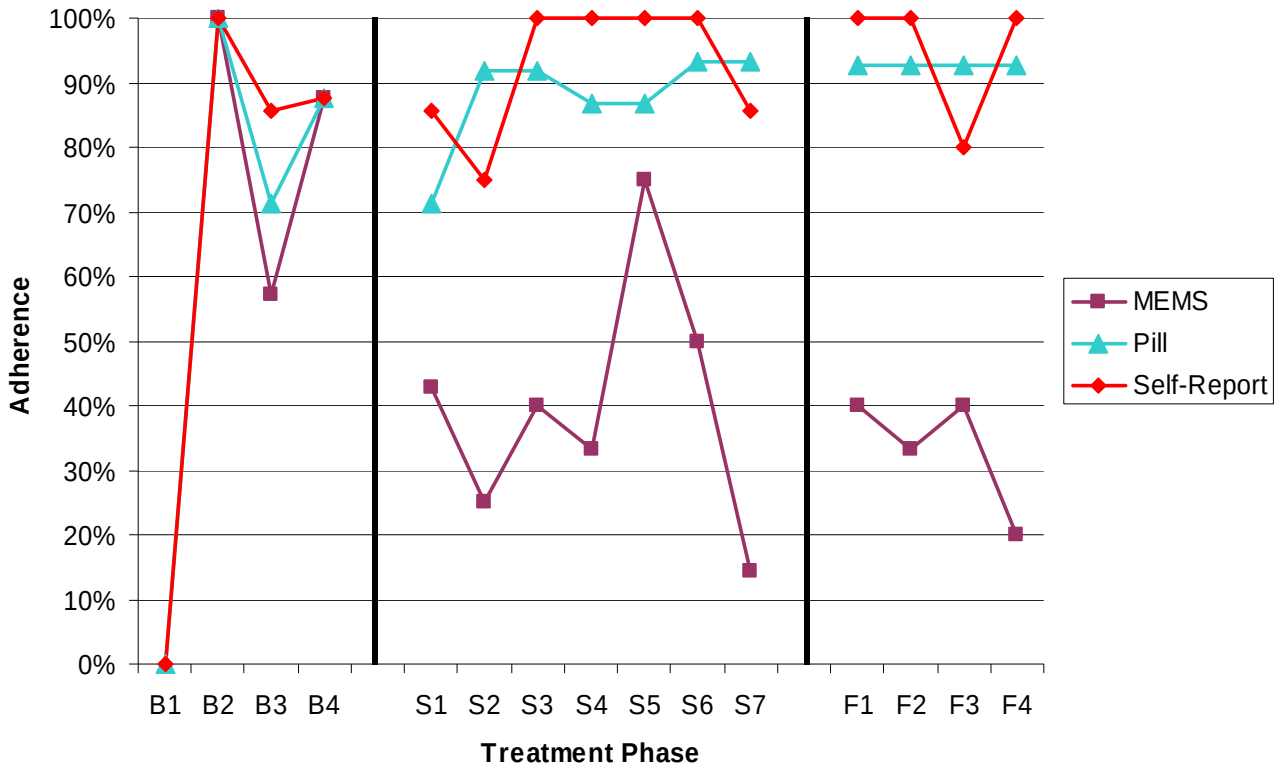


Figure 3-1. Comparison of individual adherence measures for Participant 1

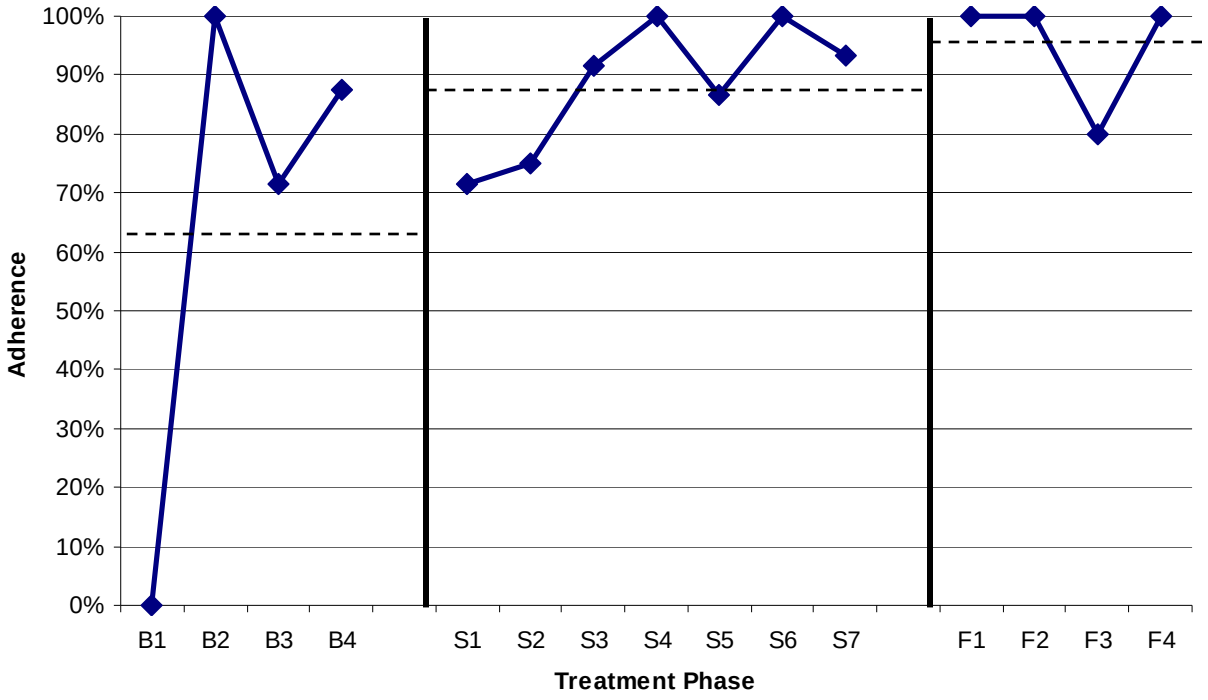
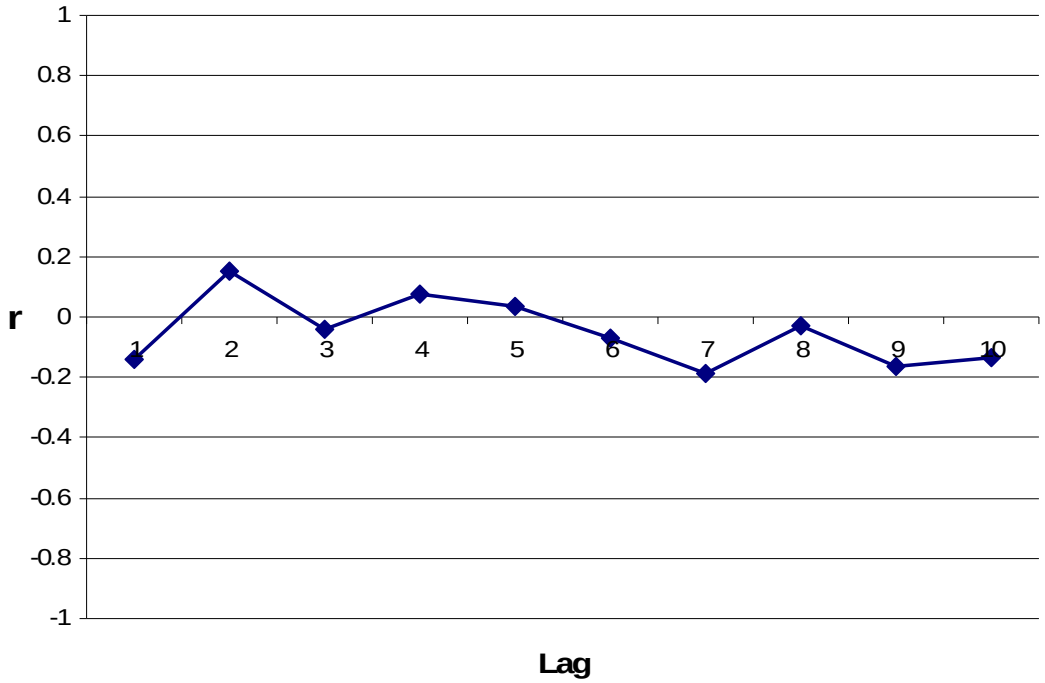


Figure 3-2. Composite Adherence for Participant 1



Time lag k	ACF(k)	p
1	-0.17	0.29
2	0.29	0.18
3	-0.03	0.46
4	0.05	0.43
5	-0.01	0.49
6	-0.07	0.41
7	-0.21	0.25
8	-0.06	0.42
9	-0.16	0.30
10	-0.14	0.33

Figure 3-3. Participant 1's correlogram as a function of time lag indicating independence of adherence data points

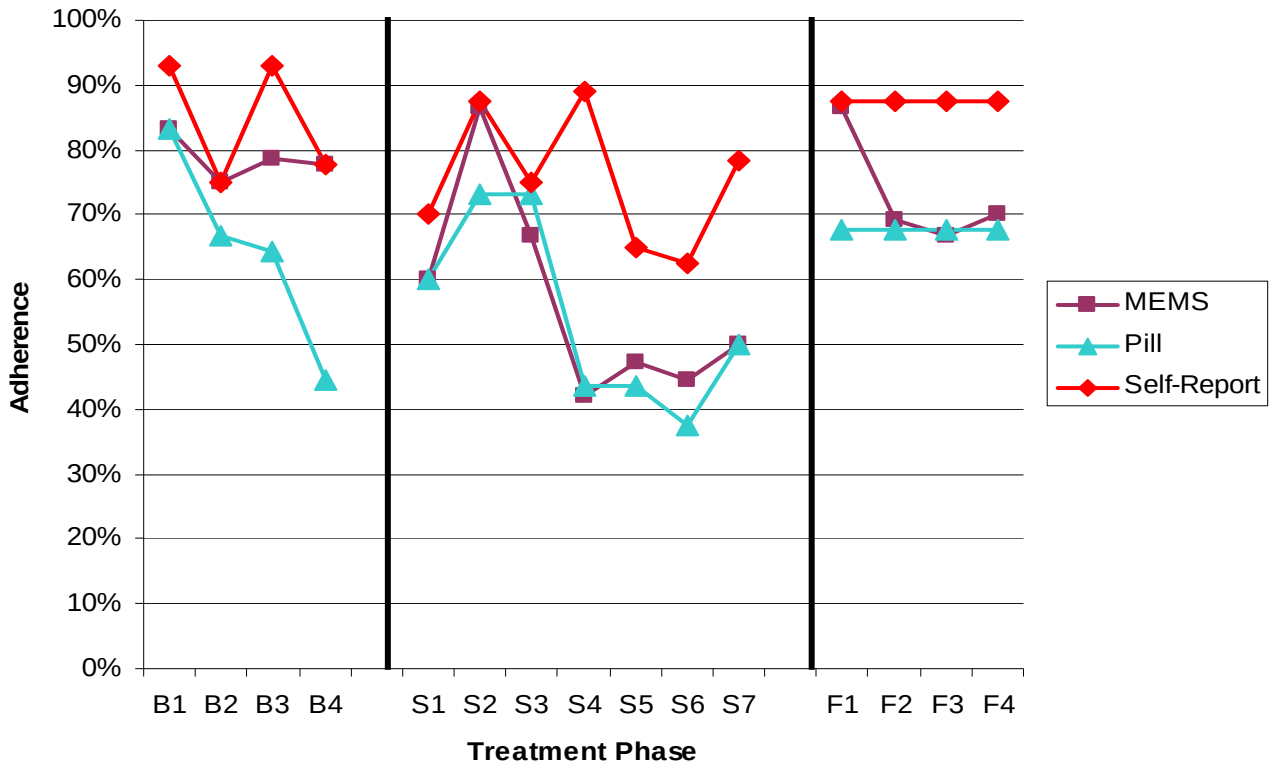
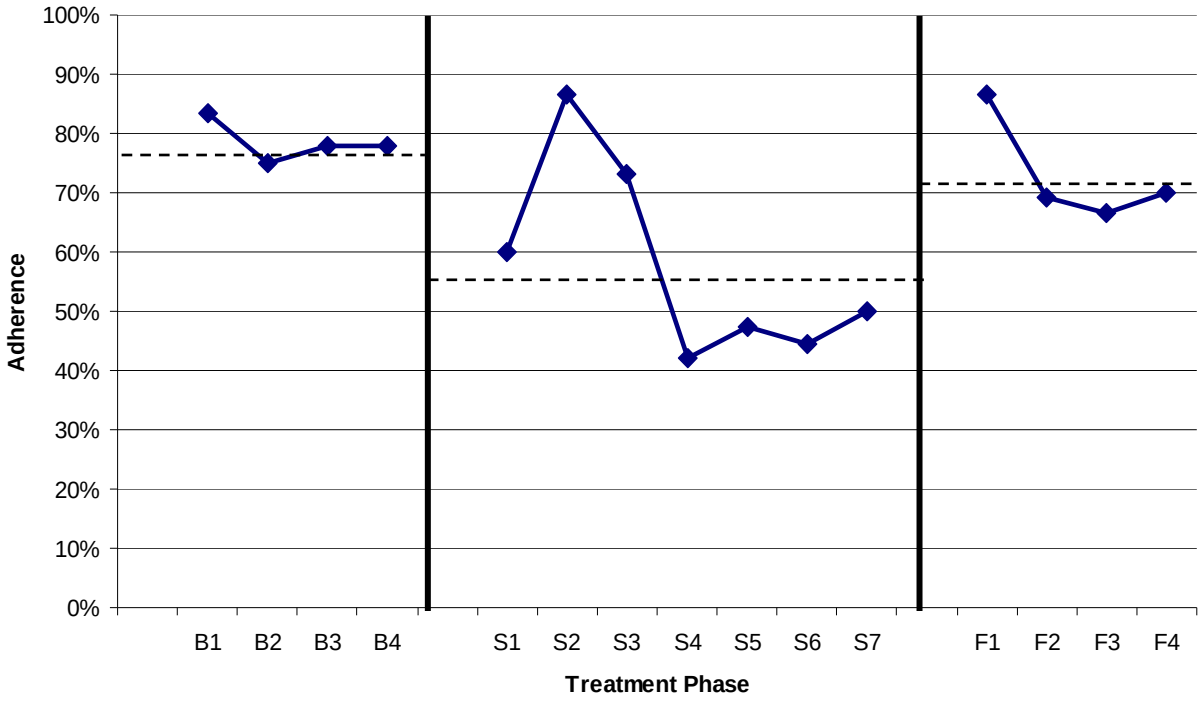
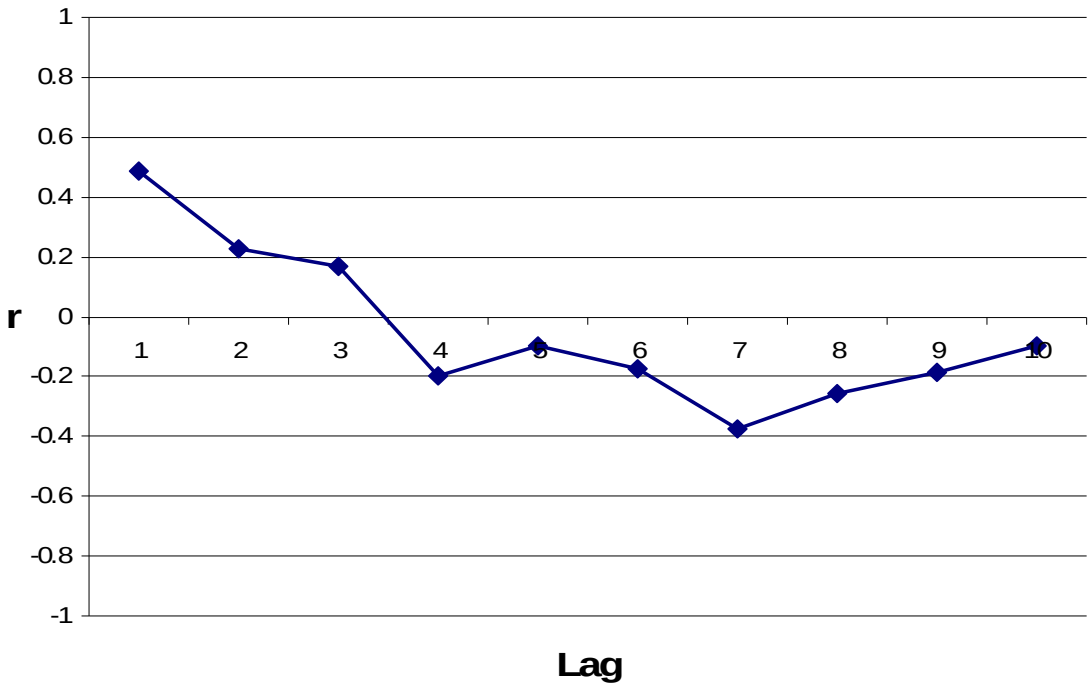


Figure 3-4. Comparison of individual adherence measures for Participant 2



- - - - = Mean adherence rate for treatment phase

Figure 3-5. Composite adherence for Participant 2



Time lag k	ACF(k)	p
1	0.49	0.07
2	0.22	0.24
3	0.17	0.29
4	-0.20	0.27
5	-0.10	0.38
6	-0.18	0.29
7	-0.37	0.12
8	-0.26	0.21
9	-0.19	0.27
10	-0.10	0.36

Figure 3-6. Participant 2's correlogram as a function of time lag indicating independence of adherence data points

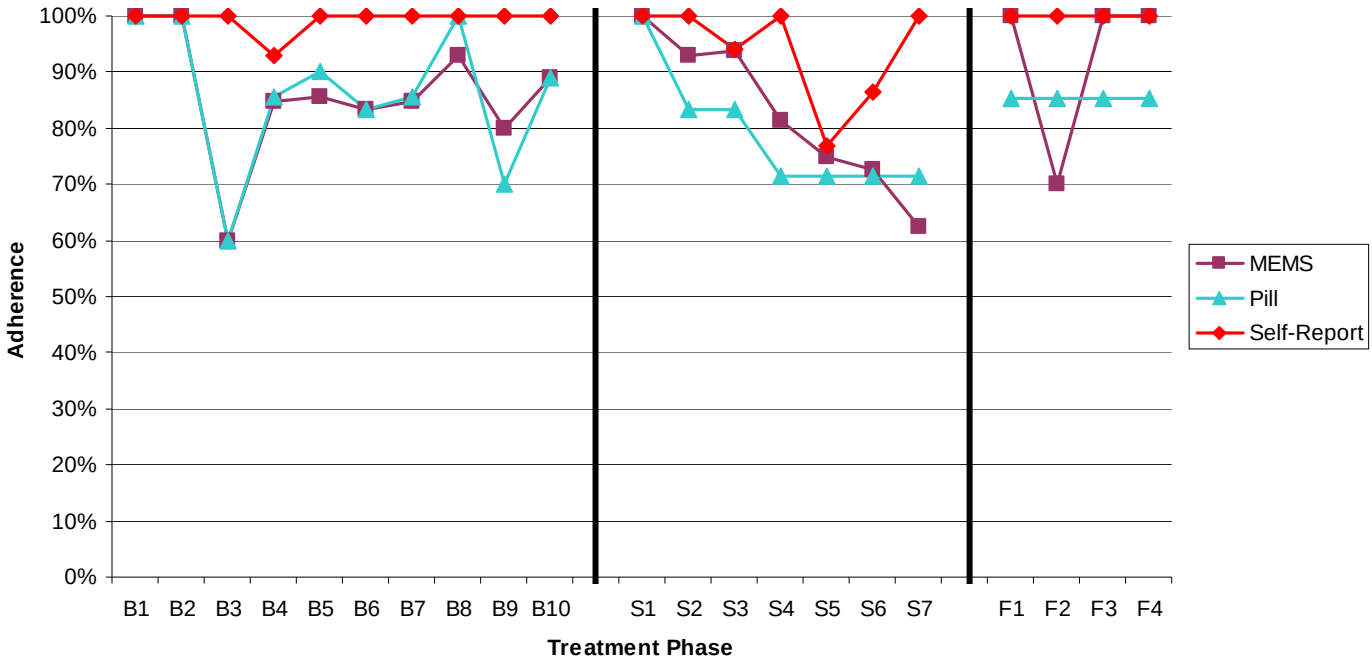
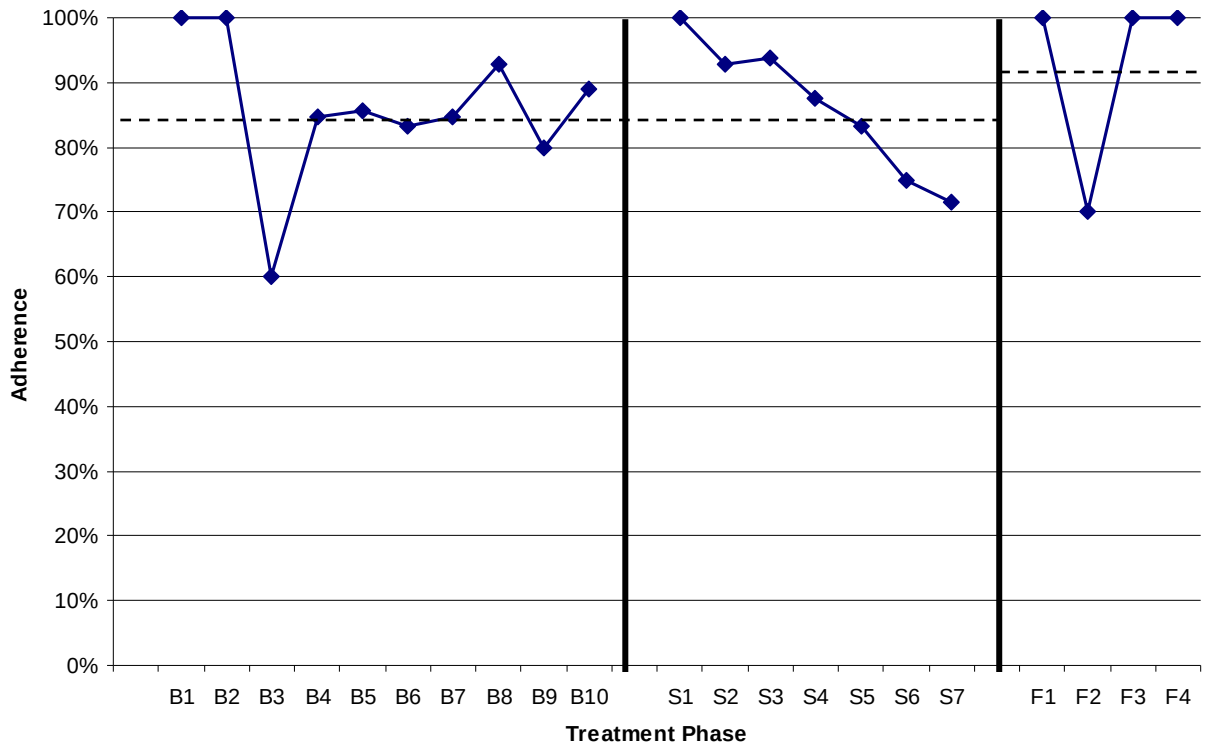
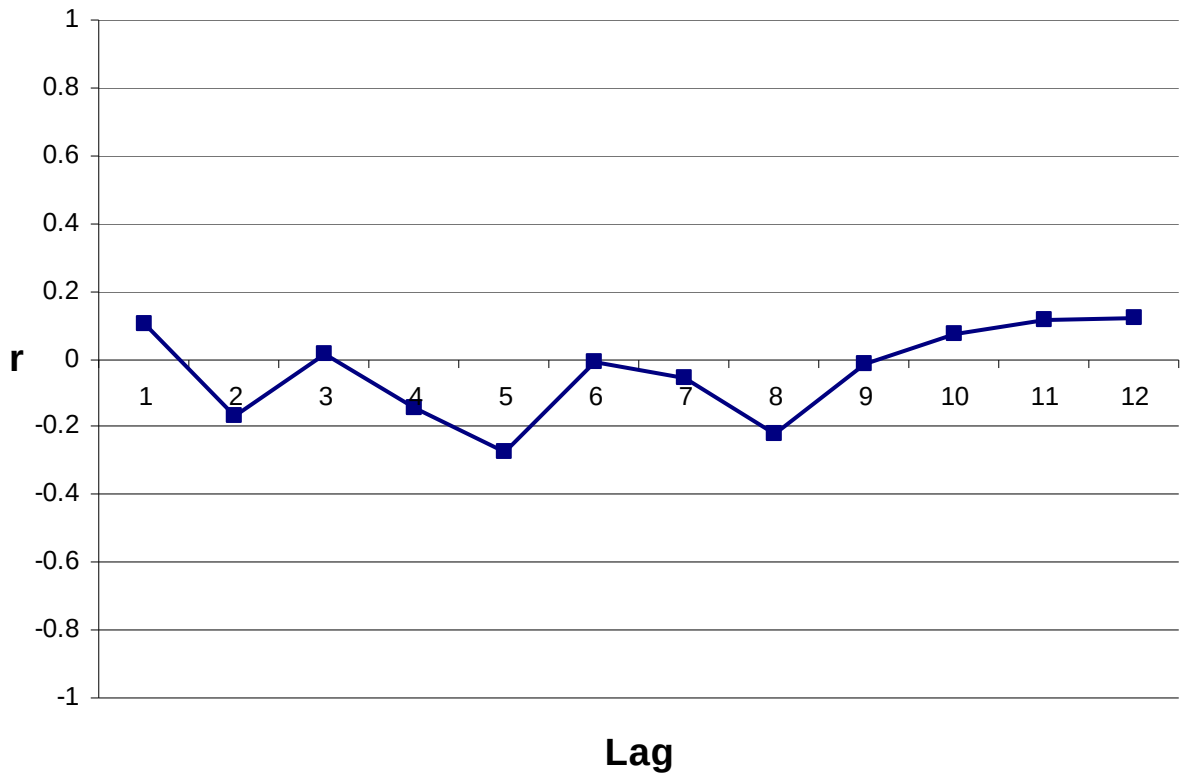


Figure 3-7. Comparison of individual adherence measures for Participant 3



- - - - = Mean adherence rate for treatment phase

Figure 3-8. Composite adherence for Participant 3



Time lag k	ACF(k)	p
1	0.11	0.33
2	-0.17	0.25
3	0.02	0.48
4	-0.15	0.28
5	-0.27	0.14
6	-0.01	0.49
7	-0.06	0.41
8	-0.22	0.18
9	-0.02	0.47
10	0.08	0.38
11	0.12	0.32
12	0.12	0.31

Figure 3-9. Participant 3's correlogram as a function of time lag indicating independence of adherence data points

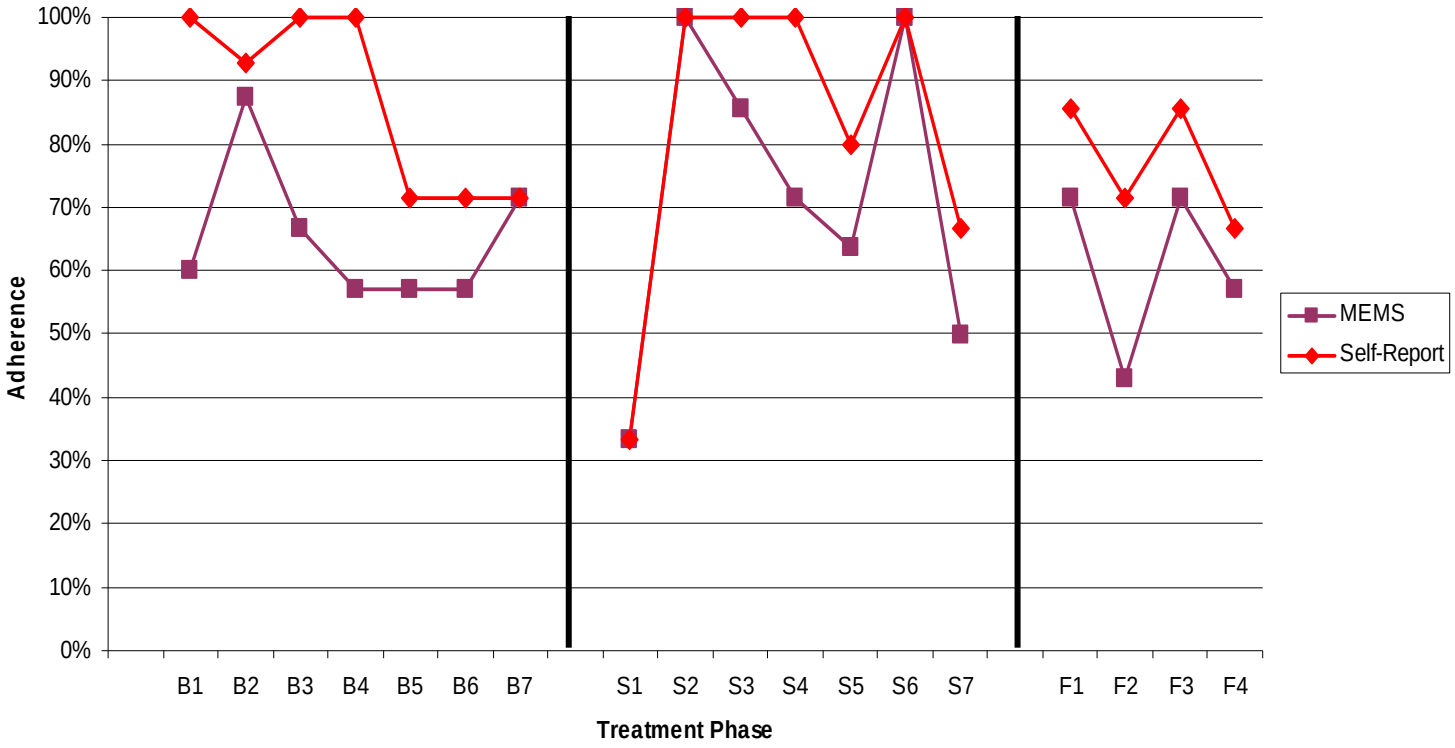


Figure 3-10. Comparison of individual adherence measures for Participant 4

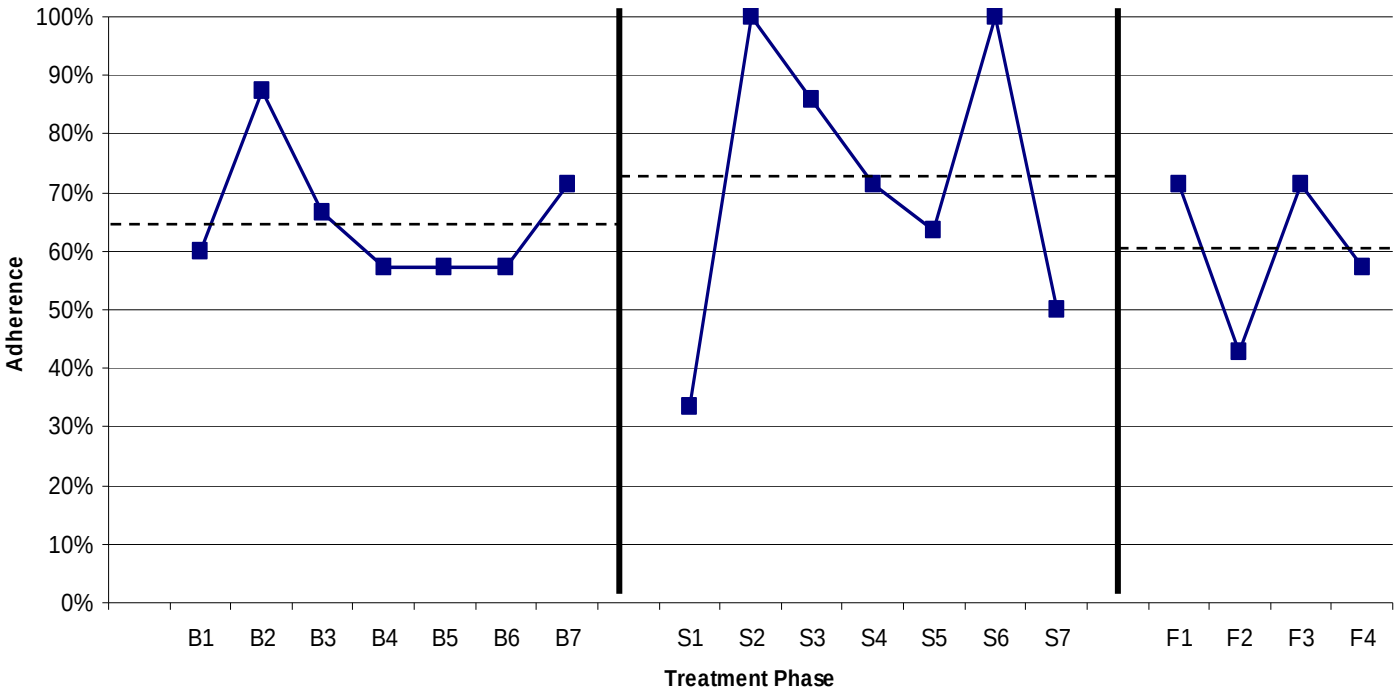
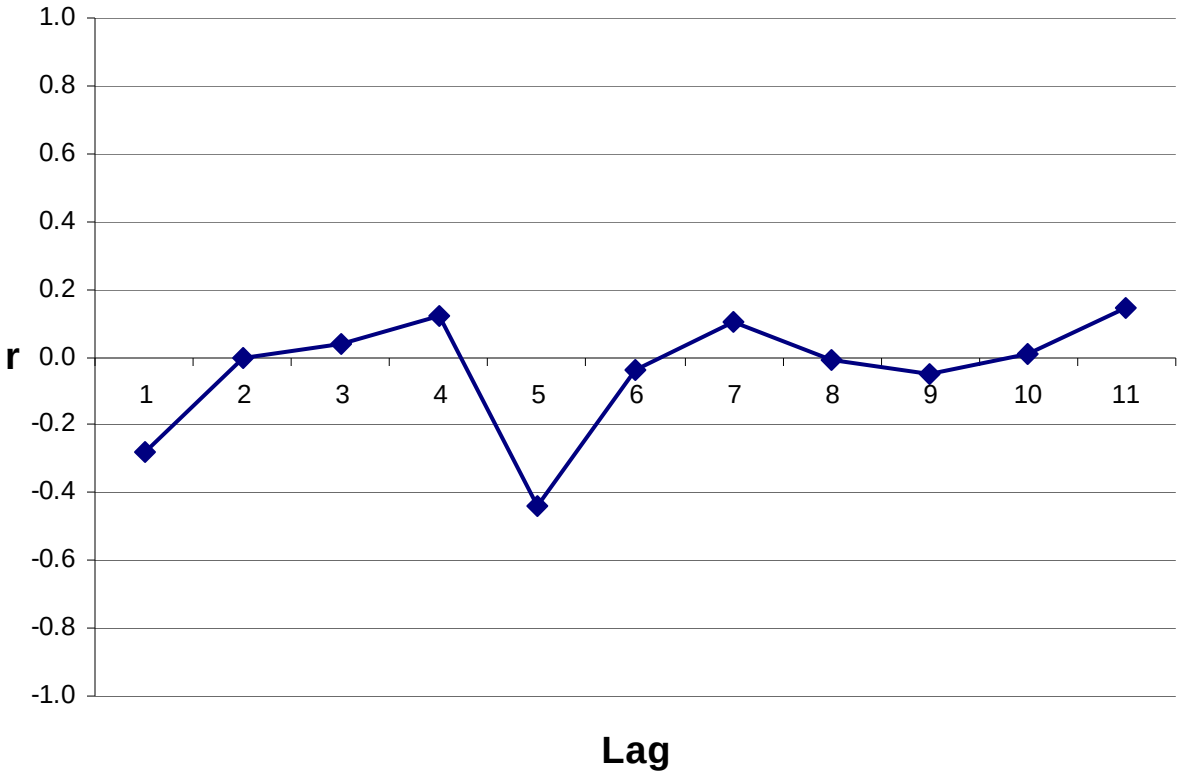


Figure 3-11. Composite adherence for Participant 4



Time lag k	ACF(k)	p
1	-0.28	0.16
2	0.00	0.50
3	0.04	0.44
4	0.12	0.33
5	-0.44	0.06
6	-0.04	0.45
7	0.10	0.36
8	-0.01	0.49
9	-0.05	0.43
10	0.01	0.49
11	0.14	0.30

Figure 3-12. Participant 4's correlogram as a function of time lag indicating independence of adherence data points

CHAPTER 4
DISCUSSION

The purpose of the current study was to examine the effect of an intervention to improve antiretroviral medication adherence among adolescents with HIV. The current study expanded upon the limited extant literature through the use of a multi-method adherence approach, the inclusion of laboratory data at each assessment, and its exclusive focus on adolescents, a population known to have problems with adherence.

All four adolescents who received the intervention had a history of poor compliance to their treatment regimen prior to enrolling in the study. When compared to pre-enrollment adherence information as reported by either the medical team, the patient, pre-study enrollment pill counts, or pharmacy records, all participants demonstrated improved adherence by the end of treatment. However, because improvements in adherence varied across treatment phases and across participants, it is difficult to draw conclusions regarding the overall effectiveness of the treatment program. Closer examination of individual treatment components and changes in adolescent adherence may be helpful in identifying possible active treatment components.

Possible Active Treatment Variables

Several aspects of the treatment must be considered as potentially influencing adherence levels among participating adolescents. As part of this study, adherence was closely monitored through the use of electronic monitoring caps, pill counts, weekly self-report, and weekly home visits. This in-depth level of monitoring is significantly greater than what is typically employed in standard clinical care and raises the possibility that being monitored may have contributed to increased rates of adherence.

Within the greater intervention literature, researchers have questioned the extent to which monitoring, specifically, electronic monitoring, may affect patient pill taking behavior. Findings

in the HIV literature regarding a monitoring intervention effect are mixed and limited only to adult populations. While one research study documented a monitoring intervention effect that waned over a 40-day period (Deschamps, Van Wijngaerden, Denhaerynck, Vandamme, & De Geest, 2006), others have found that electronic monitoring without consequences has not been found to alter adherence in patients with HIV (Wagner & Ghosh-Dastidar, 2002).

During the baseline monitoring period of this study, adherence data were discretely obtained and no consequences were implemented so that the effect of being monitored on patient adherence could be minimized. Despite this, it is still possible that being monitored may have impacted adherence. Taking patient history and baseline monitoring data for P1 and P2 into account, some evidence exists for monitoring alone as an active treatment component. Prior to enrolling in the study, P1 had not had her medications refilled in over three months while P2 openly admitted to being completely non-adherent for a two-month period. However, during the baseline monitoring period, both P1 and P2 had adherence rates greater than what would be expected given their history.

Changes in physician estimate of adherence from pre- to post-baseline monitoring may also provide support for monitoring-alone as an adherence improving strategy. Assuming that monitoring had no effect on adherence, it would be expected that physician rating of adherence, if accurate, would remain the same at both the beginning and end of this period. However, across all participants, physician rating of adherence increased by an average of 40 percentage points, suggesting that physicians perceived adherence to improve during the baseline monitoring period. This change occurred despite that fact that physicians were aware that the intervention program had not yet been delivered.

Though monitoring was intended as an assessment tool in the current study, it is likely that monitoring contributed to some extent to improved medication adherence by increasing adolescent awareness. In order to obtain a better understanding of how monitoring-alone may impact adolescent treatment adherence, the inclusion of a monitoring-only comparison group is needed in future treatment designs.

Caregiver involvement is another potential mechanism of change. Prior to enrolling in the study, caregivers of participating adolescents appeared to be less involved in their child's treatment regimen. As part of the program, caregivers and teens met on a weekly basis with the intervention team to discuss the teen's adherence. It is possible that these weekly meetings led to greater caregiver awareness and involvement in the teen's treatment regimen. Among two of the families enrolled in this study (P3 and P4), caregivers spontaneously began keeping their own pill counts to obtain a better understanding of their child's adherence. Increased awareness of problems with adherence may have led to additional involvement. This may have provided additional support for the adolescent to take their medication. Because greater medication knowledge has been associated with higher rates of adherence among children and adolescents with HIV (Martin et al., 2007), the first session of the treatment program was designed to improve patient knowledge of their illness, their medication regimen, and the importance of adherence. It was expected that such an improved understanding would provide adolescents with additional motivation to adhere to their regimen. Unfortunately, data suggest that among the three oldest adolescents in the study, adherence rates decreased rather than increased following this session. Though this drop in adherence may be due to extraneous factors, it is also possible that the educational component may have played a role. Adolescents often hear about the importance and consequences of being non-adherent at every medical appointment. They also

likely hear this information on a regular basis from their family when they miss doses. Though this information is given with good intentions, adolescents may consider this to be a form of lecturing and may react negatively. Drops in adherence following the educational session raises the possibility that the educational component in this treatment may have had unintended consequences. Obtaining adolescent feedback on educational approaches to improve adherence may provide valuable information on the efficacy of this approach in future interventions. Comparison of an education-only approach to a more practical medication management approach (such as problem solving-only or education + problem solving) may help to clarify the effect of education on adolescent adherence.

A major component of the intervention program was the use of problem solving to help adolescents and their caregivers overcome commonly experienced barriers to adherence. Using a structured approach, it was expected that caregivers and teens would be able to move beyond failed attempts to improve adherence and arrive at innovative and effective solutions. Adherence improved for all adolescents following the implementation of a plan agreed upon during problem solving. Successful solutions generally involved finding a way in which the medication regimen could be incorporated into the adolescent's daily routine rather than getting the adolescent's routine to bend to the demands of the treatment regimen. Such practical medication management approaches have been associated with improvements in adherence among adults (Rueda et al., 2006). In the case of P1 and P4, this meant physically moving their medications to a place in which the adolescent would likely come across their medication while engaging in their regular routine. Unfortunately, the long-term effectiveness of the plans implemented were limited by the extent to which adolescent routines maintained stability.

As seen in the data for P2, P3, and P4, changes in the adolescent's routine, upon which previously implemented plans were based, led to decreases in adherence. For P2, this change occurred with the commencement of school, demanding after school activities, and increased parent work responsibilities. For P3 and P4, school breaks/holidays and a destructive home fire (P4) interfered with their normal routines. When such changes occurred, participants tended to deviate from their previously established plans and adherence decreased. These patterns are consistent with prior research showing that changes in daily routine are associated with decreases in adherence among adolescents (Murphy et al., 2003) and highlight a critical area for intervention. Within the immediate context of the intervention, problem solving should be tailored to help adolescents plan ahead for how to handle expected changes in routine so that the extent to which such changes negatively impact adherence are minimized. Additionally, to maximize the likelihood that behavior changes are maintained over time, interventions should focus on helping caregivers and adolescents internalize the problem solving framework so that they can implement this approach on their own after the conclusion of the intervention.

Unlike prior research documenting an association between lower socioeconomic status (SES) and poorer adherence rates in individuals with HIV (for a review, see Mehta, Moore, & Graham, 1997), no clear relationship between these two variables were seen in the current study. In the current sample, caregiver report of annual family income varied widely. Of all participating adolescents, P1 (who had an annual family income ranging from $20,000 to $29,999) demonstrated the greatest improvement in adherence throughout the course of the study. Conversely P4, whose annual family income was the highest and fell within the $50,000 to $59,999 range, did not demonstrate such improvements in adherence. Prior research documenting the link between lower SES and poorer adherence has cited a lack of resources

(e.g., reliable transportation to attend medical appointments, adequate medical insurance to afford medications) as a primary contributor to the SES/adherence relationship. In the current study, the impact of such barriers may have been minimized through the delivery of sessions within the home and the provision of no-cost medication coverage through state-sponsored insurance programs offered to all children and adolescents with HIV. Given the limited research on adherence in adolescents with HIV, further research is needed to better elucidate any existing relationship between SES and adherence in this population.

Changes in Viral Load, Barriers to Adherence, Medication Knowledge, and Family Conflict

In addition to examining the impact of the intervention on adolescent adherence, the study also aimed to reduce patient viral load. Overall, reductions in viral load were seen for three out of the four participants in the study. P1 and P2's viral load decreased from pre- to post-treatment, with further decreases seen at follow-up. P3 experienced a decline in viral load from pre- to post-treatment but experienced an increase in viral load at follow-up despite a 92.5% adherence rate. Though adherence is a predictor of viral load, research has demonstrated that fully adherent patients do not always achieve or maintain viral load suppression (Williams et al., 2006). This may be due to individual variability in medication resistance and patient immune functioning (such as illness). Conversely, patients with less than optimal adherence (below 95%) may achieve an undetectable viral load if their particular viral strain remains sensitive to their treatment regimen.

Prior development of resistance and current immune functioning may impact the extent to which improved adherence leads to changes in viral load. Medication resistance may have played a role in P4's viral load throughout treatment. Despite improved adherence rates, P4's viral load continued to increase throughout the intervention. This may have been due to high levels of

medication resistance and suppressed immune functioning. Though recent testing indicated that P4's virus was highly resistant to all of his prescribed regimens, it must be noted P4's improved adherence still fell well below the optimal adherence level of 95%. Thus, it is possible that a combination of less than optimal adherence, immune suppression, and high medication resistance may have played a role in P4's increasing viral load throughout the study.

A third aim of the current study was to reduce the severity of reported adolescent barriers to adhering to their medication regimen. Overall, every participant reported a reduction in their barriers to adherence. Prior to beginning treatment, adolescents reported experiencing a number of different barriers, with "forgetting," "not remembering if dose was taken," "not getting refills in time," "falling asleep," and "being away from home" being the most commonly reported. These results are consistent with research documenting that non-adherent adolescents tend to experience "barrier clusters" rather than one single barrier to adherence (Rudy, Murphy, Harris, Muenz, & Ellen, 2009). As such, past attempts to improve adherence using a single strategy may not have adequately addressed the numerous barriers adolescents experience. Through the use of problem solving, these barrier clusters were disentangled and addressed individually. At post-treatment, the overall number of barriers reported and the severity with which these barriers interfered with adherence were reduced.

Despite reductions in barriers to adherence, adolescent knowledge of their medication regimen did not appear to improve from pre- to post-treatment. This may have been due to the high level of knowledge already possessed at the beginning of the study. All adolescents were able to accurately name their medications and their dosing schedule. Though participants were unable to provide specific dosing amounts, they were able to identify how many pills were

required for each dose. Thus, adolescents appeared to possess sufficient knowledge of their medication regimen in order to adhere appropriately.

Future research may benefit from a broader assessment of adolescent HIV knowledge including knowledge of the immunologic and virologic benefits of adherence, the consequences of poor adherence, different routes of transmission, the types (and limited number of) treatment options, etc. In addition to allowing for a more thorough assessment of adolescent knowledge from pre-to post-treatment, such an assessment would provide valuable information that can be used to tailor the delivery of any HIV educational component.

A final aim of the current study was to examine changes in family conflict. Three out of the four adolescents reported a decrease in conflict from pre- to post-treatment. One participant (P4) reported very low levels of conflict at pre-treatment that were unchanged at post-treatment. Though teens reported either no change or a decline in conflict, three caregivers reported an increase in conflict from pre- to post-treatment. One caregiver reported no change (P4's guardian). Caregiver report of increased conflict may have been related to increases in caregiver involvement with regard to the adolescent's treatment regimen. As part of the intervention, adults met with their teen on a weekly basis to discuss their adherence. This may have provided increased opportunities for conflict. However, given that only caregiver, and not teen, report of conflict increased over time, this hypothesis is unlikely.

Another possibility is that the intervention had a differential impact on caregiver and teen perception of conflict. As part of the intervention, maladaptive patterns of communication were immediately interrupted by the therapist, who assisted in helping families communicate their thoughts, opinions, and feelings in a more effective manner. Overall, participating caregivers were more likely to engage in negative communication strategies than teenagers. This often

occurred in the form of a lecture or interrupting/talking over the adolescent. Intervening when caregivers engaged in these negative forms of communication may have been viewed positively by the adolescent, as they were spared being lectured or nagged and may have gained additional opportunities to express themselves. This may have led to perceptions of decreased conflict over time. Caregivers, on the other hand, may have perceived this aspect of the intervention differently. Although they were guided in expressing thoughts previously communicated in the form of nagging or lecturing in a manner in which the adolescent would be more responsive, caregivers may have felt that this aspect of the intervention limited the extent to which they were able to express themselves. This may have led to caregiver perceptions of increased conflict.

Another possibility is that changes in family conflict levels, as measured by the Conflict Behavior Questionnaire, were unrelated to the study. Instead, these changes might have been reflective of the natural ebb and flow of conflict levels that occur within a caregiver-adolescent relationship over time (Robin & Foster, 1989). Because the current study employed a global measure of family conflict, it is difficult to determine to what extent conflict levels were associated with the adolescent's adherence or with other factors. Use of a specific adherence conflict measure may help to clarify this issue in future research. Although a family conflict measure specific to HIV-related care does not currently exist to our knowledge, disease-specific family conflict measures developed among other populations, such as the Diabetes Family Conflict Scale (Rubin, Young-Hyman, & Peyrot, 1989) may help guide the development of a similar measure for use with individuals with HIV.

Utility of Multi-Method Adherence Assessment

The use of a multi-method adherence approach was helpful in obtaining a comprehensive evaluation of the adolescent's medication taking behavior. MEMS provided valuable information regarding adherence patterns that otherwise would not have been detected with pill count or by

self-report, which is subject to social desirability. MEMS data helped guide the intervention to target problematic trends in medication taking. In the case of P4, this meant focusing on developing strategies to improve adherence to weekend doses and developing a plan to order refills in a timely manner. For P2, this meant better regulating her summer break routine to improve morning medication adherence.

Though overall MEMS were considered a valuable addition to the study, the use of MEMS had its drawbacks. By nature of its programming, MEMS caps did not record any vial opening of less than five seconds duration or any opening within a 15-minute time-frame of another opening. These unchangeable program features may have led to an underestimation of adherence. This was likely the case for P1 who reported that she often forgot to keep her bottle open for more than five seconds. MEMS may have also underestimated adherence by interfering with previously established adherence strategies such as pill boxes and the pocketing of doses. Due to the cumbersome size of the MEMS cap, patients may have opted to remove their doses from the bottle ahead of time to avoid having to carry their bottles with them. This occurred several times with P4, who preferred to transport his medications discretely when staying with friends on the weekend, possibly leading to an underestimation of adherence.

An additional barrier to the use of MEMS relates to the reliability of the data. MEMS data can be compromised by caps malfunctioning or being lost. Though all participants were instructed in proper MEMS care, MEMS were sometimes dropped onto hard surfaces (as with P1). In the current study, approximately 23.8% of MEMS observations were discarded due to suspected validity issues. However, fewer substitutions were made in this study compared to Liu et al. (2001), who discarded approximately 40% of all MEMS observations in construction of his widely used composite adherence score.

Because of the aforementioned limitations with MEMS, pill counts were used as a back-up adherence assessment strategy. Though pill count estimated adherence was inexpensive and generally easy to compute, barriers encountered with this method included working with patients who had more than one supply of the same medication and unexpected increases, rather than decreases, in pill count. While these issues were generally resolved by helping patients consolidate their different sources of pills and referring to pharmacy refill data, numerous factors affected the ability to calculate pill counts with P4. Fortunately, all of P4's MEMS data were considered to be valid thereby preventing the need to rely on self-report in the absence of MEMS and pill count data.

Self-report data collected also had strengths and weaknesses. A primary reason for the inclusion of self-report was that these data were generally very easy and inexpensive to obtain. Additionally, because participants were asked to provide a reason for each missed dose, self-report data provided valuable information on barriers to adherence that would not otherwise have been obtained if only MEMS and pill counts were used. This information played a crucial role in informing the intervention. However, self-report data were considered a last-resort strategy in calculating a composite adherence score due to its tendency to consistently provide higher rates of adherence than MEMS or pill count estimates.

As discussed above, the use of a multi-method adherence approach provided many benefits to the design of treatment. An additional advantage to the use of this approach was the elimination of missing data through the construction of a composite adherence score. High correlations between MEMS, pill counts, and self-report data, along with prior research on the use of a multi-method adherence approach (Liu et al., 2001), supported the use of this substitution approach in constructing a composite adherence score.

Limitations

Although the current study is a promising and innovative attempt to improve adherence among adolescents with a longstanding history of less than optimal adherence to their HIV treatment regimen, several limitations prohibit the extent to which definitive conclusions can be drawn regarding the effectiveness of the intervention. A few limitations have been discussed in context of the discussion above. The following are additional limitations and suggestions for further investigation.

First, by nature of the single-case experimental design, which lacks a control group and randomization to treatment, it is not possible to confidently conclude that the changes observed in adolescent adherence were due to the intervention or were a result of extraneous variables. Given the small sample size, it is not possible to determine if the treatment or response pattern obtained can be generalized to the greater population of adolescents with HIV, including those adolescents who were behaviorally-infected. Unfortunately, given the small number of adolescents with HIV who also have problems with adherence and are living in any one area, the feasibility of conducting a randomized clinical trial with sufficient statistical power and generalizability is somewhat limited unless multi-site collaborations are established.

An additional limitation with regard to the study design was a deviation from the non-concurrent multiple baseline design. Because of a scheduling conflict, one participant began the intervention out of sequence. Thus, instead of having participants with four, six, eight, and 10-week baseline periods, two participants had a four-week baseline and no participant had an eight-week baseline. This deviation from the multiple baseline design limited the extent to which changes in adherence could be compared across participants.

A third limitation relates to the collection of data through the delivery of the intervention via alternating home and telephone sessions. Though this design was chosen in order to

minimize treatment burden experienced by families, the extent to which adherence could be accurately assessed during telephone session weeks was somewhat limited. Because the intervention was guided by adherence data obtained, and the only adherence data collected during telephone sessions was adolescent self-report, data collected during telephone sessions was often an over-report of adherence. Thus, actual slips in adherence were often not detected until MEMS data were downloaded at the following home session. By this time, up to two weeks may have passed and opportunities for early intervention were lost. In the current study, MEMS data were collected via a single personal laptop computer brought to each participant's home during home treatment sessions. In a study with greater levels of financial support, it may be possible to equip each participant with a laptop, MEMS transponder, and the proper computer software to enable them to upload their MEMS data each week. This would allow researchers to more quickly detect slips in adherence and may allow for more immediate intervention.

An additional limitation of the study design relates to the timing of the initiation of treatment. According to study criteria, treatment was initiated after two data points in which adherence was not improving were obtained. Once the decision was made to initiate treatment, the patient was scheduled for an in-clinic appointment. Due to the busy nature of the medical clinic, same-day appointments were not possible. All patients had to be scheduled at least one week in advance. As a result, the baseline monitoring period continued for one additional week after treatment initiation criteria had been met. For three out of the four adolescents, adherence improved during this week. These improvements may have been reflective of the general trend for adherence to improve just prior to having a medical appointment (Farmer, 1999). Thus, temporal social demands may have played a role in improvements in adherence.

Because of the high expense associated with MEMS, the current study was limited to only having one medication per participant electronically monitored. Though many studies have employed a one MEMS cap per person approach in the HIV literature as a money-saving strategy, this limits the extent to which differential adherence across medications can be monitored. In the current study, pill counts were used to examine potential differences in adherence across medications. Overall, similar adherence rates were noted across medications with dosing schedules the same as the medication that was monitored with a MEMS cap. Because the medication selected for electronic monitoring was often the one with the more demanding dosing schedule, it was expected that medications with less demanding schedules would have greater levels of adherence. Pill count data for other medications appear to support this hypothesis.

Strengths

Despite the aforementioned limitations, the study possessed several strengths that may help guide the development of future research. Through its exclusive focus on adolescents, the current study addressed a critical gap in the research literature. Because adolescence is a time in which lifelong positive and risky health behaviors are established (Holmbeck, 2002), interventions targeting adolescents who have poor adherence to their HIV regimen may have direct implications for improvements in patient quality of life and longevity.

As previously discussed, the use of a multi-method adherence approach significantly enhanced data collection. This approach allowed for the collection of a wealth of information that would not have been otherwise obtained had the single-method approaches used in prior studies been employed. In addition to minimizing missing data, MEMS, pill count, and self-report provided valuable information regarding adherence patterns and reasons for non-adherence. These data allowed for a more individualized treatment approach.

An additional strength of the current study is the use of problem solving to tailor the intervention to address the unique barriers to adherence experienced by the adolescent and their family. Through use of this individualized approach, parents and teens were able to generate innovative strategies to help them overcome longstanding barriers. This individualized approach may have contributed to the high level of program satisfaction reported by all participants and the absence of participant attrition. Given that participants were enrolled in the study for at least six months, the lack of attrition is a significant strength of the current study.

The study's innovative design, which allowed for the delivery of treatment across home, clinic, and telephone settings, is also a strength. Compared to costly prior multisystemic therapy (MST) approaches which have employed two to three home visits per week across several months (Cunningham et al., 2006; Ellis et al., 2006), the current study was less intrusive to study participants and required fewer resources on behalf of the intervention team. Given that improvements in adherence were observed among all study participants to varying degrees, it is possible that interventions utilizing alternating weekly home and telephone sessions may be a more cost-effective alternative to MST approaches. Further research is needed, however, to determine how the current treatment approach would compare to MST or a no-treatment control group.

The study's high level of integration within the clinical setting is also a significant strength. Compared to prior intervention research which has interfered with the delivery of clinical services (Rogers et al., 2001), the current intervention was designed to be minimally obtrusive yet effective in data collection. The strong collaborative relationship existing between psychology and the medical team provided a strong foundation upon which the study was designed and allowed for the collection of laboratory data and physician rating of adherence at

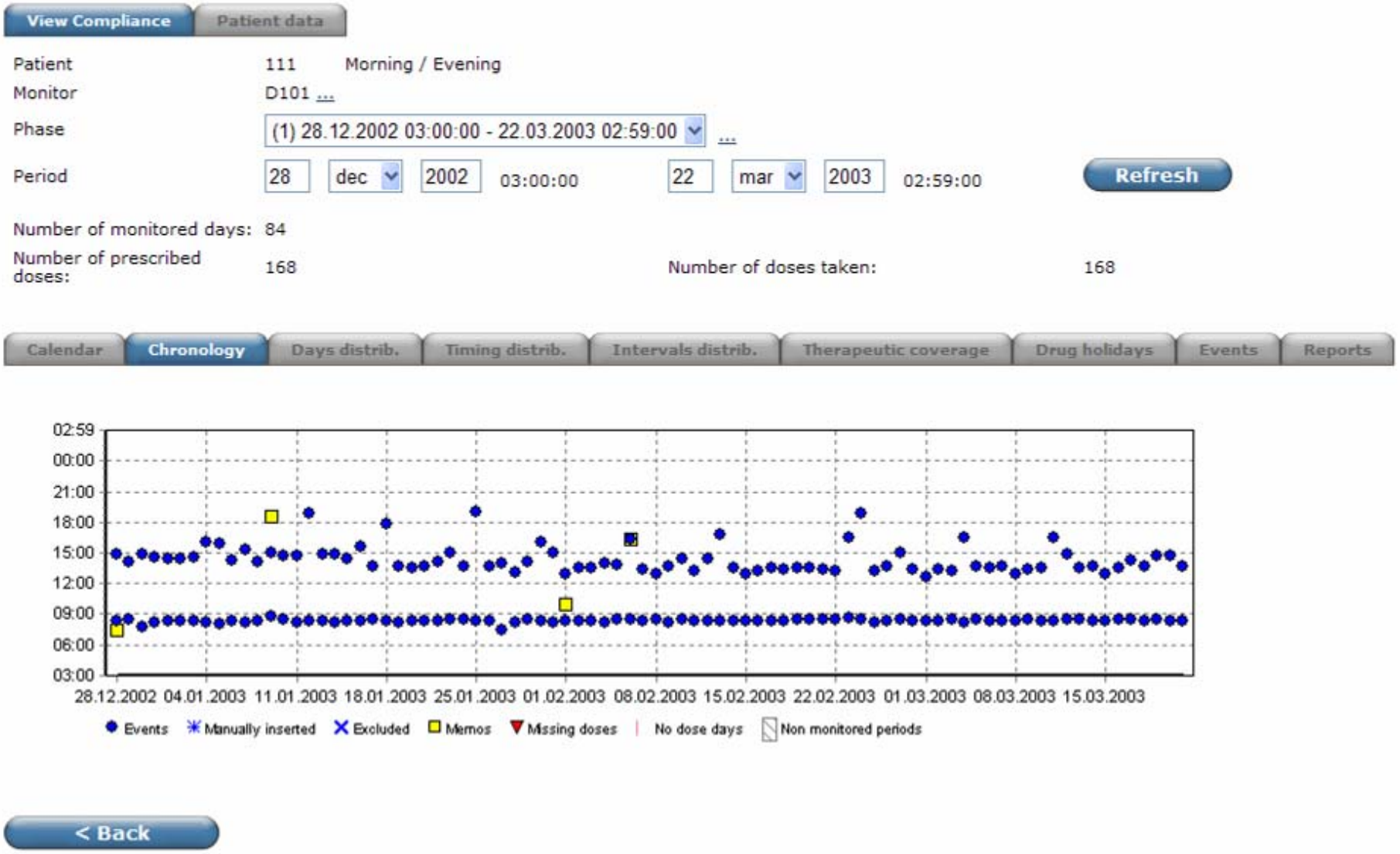
each major assessment. Given that no known intervention study for children and adolescents has been able to collect and observe changes in viral load and physician rating of adherence over time, the inclusion of these data in the current study is a significant strength.

Conclusions and Future Directions

The current study is a promising beginning to what is hoped to be a growing area of research. Limitations of the current study, as well as with prior research, are reflective of the general challenges researchers experience when working with adolescents with HIV. Helping the adolescent find ways to integrate their medical regimen within their regular routine appears to be an effective adherence improving strategy. However, this is only effective as long as the adolescent's routine remains stable. Using problem solving to proactively plan for changes in routine may help to minimize declines in adherence.

Despite the many challenges associated with intervention research among adolescents with HIV, it is important that invention research with this population continue. Multi-site research collaborations are greatly needed to allow for the design of randomized clinical trials to more clearly investigate treatment outcome. Multi-method adherence assessment approaches, along with data on patient physiological functioning, should also be included in future research as these data provide valuable information that can guide treatment design and inform the interpretation of treatment outcome data.

APPENDIX A
SAMPLE GRAPH OF PATIENT ADHERENCE FROM POWERVIEW SOFTWARE



APPENDIX B
HIV MYTHS HANDOUT

"HIV, the human immunodeficiency virus, is the virus that causes AIDS. For many reasons, AIDS is a disease that is commonly misunderstood and, as a result, unduly feared."[1]

In order to combat this fear, knowledge concerning the virus is the BEST weapon! Following are ten of the most common myths about HIV/AIDS and the reality of these misconceptions

Myth #1: "Women with HIV can't have children without infecting them with the virus."

Reality: This used to be true, but not anymore. Women living with HIV can and do have families. While certain steps and precautions have to be taken, women can now have the families they always dreamed about!

Myth #2: "People with HIV can get 'rid of' the virus if they take all of their medication like they are supposed to."

Reality: Current treatments for HIV are better than ever, but the bottom line is there these treatments only help prolong life, not cure the disease itself. When the treatments work, there is so little of the virus in the blood that blood tests can't detect it. Even though blood tests will say the virus is "undetectable," the virus is still there, hiding in a sleep-like state in your body. People whose HIV is in this state must continue taking their medicine to stay well.

Myth #3: "People with HIV do not need to take their medications when they do not feel sick."

Reality: Even when people with HIV are feeling great, HIV is making billions of copies of itself everyday and attacking their immune system. When they finally start to feel sick, HIV has already damaged their immune system and nothing can fully bring it back to normal.

<u>Myth #4</u>: "You can tell if someone has HIV just by looking at them."

<u>Reality</u>: Have you heard the old saying, "looks can be deceiving?" A person with HIV may not show any symptoms for up to 10 years. Since HIV affects each person differently, many people with HIV can look and feel healthy for years and not even know they are infected! Without knowing, that person may be practicing unsafe sex and may be spreading the virus to others.

<u>Myth #5</u>: "HIV can be spread by kissing or hugging someone who is HIV positive."

<u>Reality</u>: "Though there are other means of transmission, there are four main ways HIV spreads:

1. Through unprotected sexual contact
2. Through blood transfusion
3. By sharing needles through injection drug use
4. From mother to child

You can't contract HIV by kissing or hugging someone.

For more information, visit: http://www.cdc.gov/hiv/resources/brochures/livingwithhiv.htm

APPENDIX C
PICTORIAL REPRESENTATION OF MEDICATION REGIMEN

MY REGIMEN

ZERIT

EPIVIR

VIRACEPT

VIRACEPT

ZERIT

EPIVIR

VIRACEPT

VIRACEPT

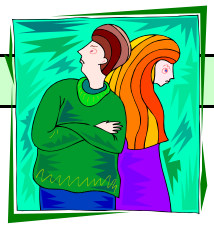
APPENDIX D
PROBLEM SOLVING HANDOUT

Problem Solving Techniques

Problem solving consists of five steps:

(1) defining the problem, (2) generating different solutions, (3) making a decision, (4) planning to use the solution, and (5) making changes over time. These five steps can be used whenever disagreements over managing medical care occur.

Step One – Defining the Problem



There are <u>three goals</u> when defining a problem:

1) Each family member should express clearly to the others his/her view about the issue.
2) Each family member should understand and be able to explain the others' view(s).
3) The topic being discussed should be simple rather than complex.

<u>Remember</u>: Differences of opinion are normal and healthy, not necessarily a sign of rebellion!

All family members should take turns defining the problem as they see it. Each person then checks how much the others understand what was just said by having family members repeat it back in their own words. If the family member's explanation does not match up with what the person was trying to say, the person should explain the definition again more clearly. Here are some tips:

- Be specific.
- Try to be brief.
- Avoid angry language, accusations, or blaming others.
- Describe behaviors, feelings, and situations, not personality characteristics of individuals.
- Only discuss the problem at hand. Do not bring up the past or other issues.
- Start with "I" rather than "you" (e.g., I feel angry…).

- ***Example:***

CHRIS: My problem is that I want to be able to look after my own medicines. I feel like a baby because I haven't been allowed to keep my medicine in my bathroom or remember to take them on my own.

MRS. SMITH: So, what you are trying to say is that it bothers you when you have little control over your medicine. You feel like keeping your meds in your bathroom and remembering on your own to take them would make you feel more responsible.

CHRIS: Yes, that's it.

Step Two – Set A Goal

Setting a goal involves stating what you would like to happen, or the end result that you want to work towards. Family members may need to discuss the goal and write it down in clear, achievable terms.

Example:

CHRIS: I want my mom to trust that I can take my meds without constantly reminding me.

MRS. SMITH: I agree. I want to trust that Chris to take his meds without me nagging him.

Step Three – Listing Different Solutions

The goal here is to think of as many ideas as possible for ways to fix the problem defined in Step One. When coming up with different solutions, don't worry about how good the ideas are until later in the discussion. Be sure to suggest creative and extreme ideas too; anything goes! Family members should take turns suggesting ideas and one family member should write down all of the ideas. Try to list at least 4-5 solutions for each problem.

Example:

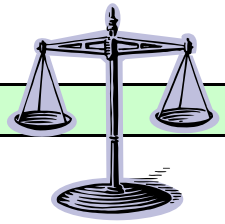
MRS. SMITH: Maybe you could keep your morning meds in your bathroom, but I will still remind you when to take them before you go to school.

CHRIS: You could put my meds in a place where I can get to them on my own without them being in my bathroom. Maybe the kitchen would be a good place.

MRS. SMITH: Maybe during the week when you're busy with school, I could keep the meds and remind you when to use them, but you could try doing it on your own on the weekends.

CHRIS: You could stop telling me when to take my medicine, but I could mark on a calendar when I've taken them, so you will know.

Step Four –Making a Decision



When making a decision, there are <u>three goals</u>:

1) Discuss the good and bad points of each idea together as a group.
2) Have each person rate each idea as good or bad overall.
3) Agree on the best solution and put it in place.

Each family member should take turns pointing out the good and bad points of the solution for himself/herself and for the rest of the family. Consider both potential short-term and long-term effects of the solution, and then rate the solution (give it either a plus or minus) based on how good the idea is, not who came up with it. When all of the solutions have been discussed and rated by each family member, see if everyone rated any of the ideas a "plus". If there is agreement by all family members on one or more ideas, select one or combine several ideas to use. If there is no agreement, begin to discuss a compromise.

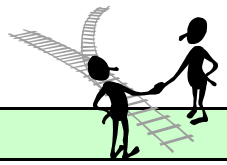
Example:

CHRIS: I rate the first solution as minus because I think that I would still feel like a baby if you have to keep reminding me to take my medicine. The second solution is a plus because I don't really need to keep my meds in my bathroom, just in a place where I can get to them myself without you having to get them for me. The third solution is a minus because I still will have to keep the old routine five out of seven days a week, and that

doesn't give me much of a chance to show that I can be responsible. The fourth solution is a plus because I have more control over when I take the medicine, and I don't mind marking it on a calendar to let you know that I did. Maybe then you will start to see that I am dependable.

MRS. SMITH: I don't like the first solution very much because it makes me uneasy knowing that you have the medication in your bathroom. I will rate the first solution as a minus. I will rate the second solution as a plus because I don't mind keeping the inhalers in a location where you can get to them. I know how much you want to show me that you are responsible and I think it will help if you can get to the medicines on your own. I will rate the third solution as a plus because I think two days a week is a good place to take care of your own medicines. I will rate the fourth solution as a plus because at least I will know whether you have taken your medicines or not and it will help me build confidence in you.

CHRIS: It looks like we've both rated the second and fourth solution as "plus." Let's try using those two solutions.



Step Five – Planning to Use the Solution

When planning to use a solution, your goals are to:

(1) Consider the details that are necessary to put the solution into place
(2) Try to predict difficulties that may come up when the solution is used.

Identify the behaviors that <u>each family member</u> needs to do in order to show that he/she is following through with the solution. Assign specific tasks to particular family members. Try to come up with ways to keep track of whether each family member is following through with their part of the solution. Plan for how the family will deal with any problems that come up.

Example:

Chris and Mrs. Smith agree that keeping the medication in the cabinet in the kitchen is a good place where both can get to them. Mrs. Smith will place them in the cabinet and check once a week to make sure that they are still there. They agree that Chris will record the time that he takes his medicines on a chart on the refrigerator. When Mrs. Smith checks on the medications and notices that they are still in the cabinet, she will record this on the chart too.

Step Six – Making Changes Over Time

If it seems that the first solution didn't work well, go back and examine step-by-step where the problems may have occurred. Avoid blaming any particular family member for the solution's failure. Start from Step One or Step Two of the problem solving process and go through the steps again. Continue this process until all family members are happy with another possible solution to try again.

Problem-Solving Worksheet

Problem to be solved: _____

_____

_____

_____

Solutions		
	Family member 1	Family member 2
1.		
2.		
3.		
4.		
5.		

Agreed-upon solution:_____

_____

_____

_____

_____

Responsibilities for each family member (list name & responsibilities):

Measurements/checks (note who, when, & how):

Date to re-evaluate how well the solution is working: _____

Signatures:

APPENDIX E
COMMUNICATION HANDOUT

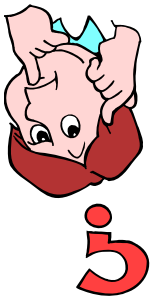
Parents can do a great deal to help and support their youth with their medical care! There are three main ways to do so: ***instructional help, informational help, and emotional support***.

Instructional help is a hands-on way of helping your youth to manage his or her medical care. Some examples of instructional help include:

- Helping your child to find a way to simplify his or her medication management.
- Keeping track of the doctor appointments and being sure that your child has enough medication refills.
- Making sure that your child takes his or her medication when he or she goes away for the evening or a weekend.
- Making sure your child takes his or her medication at the right times.

Informational help is a way to educate your youth about his or her medical condition. This should always be done in a positive or neutral manner to avoid parent-child conflict. Some <u>examples</u> of informational help include:

- Providing your child with reading material on their medical condition.
- Keeping a list of questions that you or your child may have to ask your child's physician.
- Encouraging family discussions on your child's health condition and its treatment.



Emotional support is a way of helping your child to feel good both about himself or herself and his or her medical care. Some <u>ways</u> to provide your child with emotional support include:

- Praising your child often for adhering to their treatment plan.
- Avoiding treating your child differently because of his or her illness.
- Taking an active interest in your child's life, learning about his or her likes and dislikes.

Positive Communication Between Parents and Youth

Why is communication between parents and youth important?

Adolescence is a time of rapid change, with youth seeking more independence from their parents. Parents sometimes face new issues that need to be discussed with their children rather than decided by the parents alone. The ***way*** parents and youth communicate with each other can affect the quality of their relationship.

Positive Communication

Positive communication helps parents and youth communicate effectively and avoid unnecessary conflicts. Telling one another how you feel is a very useful way to communicate. It is best to use statements that do not blame others when discussing how you feel about a problem or difficult situation. These statements are called "I" statements because they focus on how the speaker is feeling rather than on what the listener is doing wrong.

"I" statements often take the form of "I feel ____ when _____ happens."

For example, "I feel worried when you forget to take your medicine."

List an example for you and your family:

_____

Roadblocks to communication

One of the first steps of positive communication is to remove all of the obstacles, or roadblocks. These roadblocks are statements that hurt people and make them feel defensive, instead of making them want to change their behavior.

Here is a list of some common roadblocks to communication, as well as some positive ways to stay away from these roadblocks:

Roadblocks	**Positive Talk**
• Commands & orders	• Discuss possible solutions
• Threats	• Compromise
• Interrupting	• Listen and summarize
• Accusing, blaming, or shaming	• Use “I” statements
• Sarcasm	• Use a neutral tone of voice

COMMUNICATION WORKSHEET

Family Name _____ Week of _____
to _____ (Dates)

Communication Behavior to Target:

Day	Roadblock	Positive Communication Change

APPENDIX F
FAMILY ROLES HANDOUT

Family Roles

Parent:

- Provide support and encouragement to children and spouse/partner
- Create an environment where children can develop skills (physical, emotional, educational, and social)
- Provide basic needs for children (food, housing, clothing, safety)
- Discipline children for not following household rules
- Help with daily chores
- Follow household rules

What are some that are specific to your home:

_____
_____
_____
_____

Child/Teens:

- Follow household rules set by parent(s)
- Help with daily chores
- Not worry about getting basic needs met (food, housing, clothing, safety)
- Provide support and encouragement to other family members

What are some that are specific to your home:

_____
_____
_____
_____

Medication

Parent:

Child/Teen:

APPENDIX G
DEVELOPMENTAL CHANGES AND ADHERENCE HANDOUT

The Need for Parental Involvement

With school-aged children, parents often wonder how much involvement they need to have in their child's treatment regimen. It is likely that parents will need to maintain at least some degree of involvement in their child's treatment, and finding the appropriate level of involvement that works best for you and your child will be key.

♦ Children Can Forget

Adults have better memories than children do. Adults also are used to dealing with everyday tasks and duties. One of the main reasons why parents need to maintain a certain degree of involvement in their child's treatment is that children simply forget about taking their medicine.

♦ Youth May Not Understand

When explaining a treatment plan to families, doctors often use words or phrases that youth may not understand. The steps involved in properly taking medicine also can be long and complex. Children often rely upon parents to learn the procedure and then teach it to them later. Additionally, it is not uncommon for youth to require repeated instruction by parents.

♦ Parents May Be More Assertive

Doctors, nurses, or others in positions of power can easily intimidate youth. Children may be too frightened to ask questions or too embarrassed to admit that they do not understand something. Often, adolescents expect their parents to speak up in these situations.

♦ Parental Involvement May Be Required

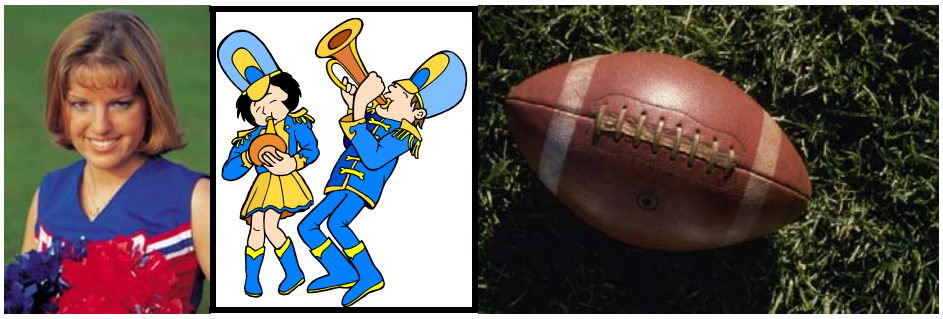
There are some aspects of children's treatment plans that youth cannot handle on their own. Parental involvement often is required in these cases. For example, issues related to health insurance paperwork, purchasing prescriptions, and transportation to and from doctor's appointments all call for some degree of parental involvement.

♦ Parents Normally Set the Rules

Parents almost always hold positions as heads of the household. As part of that position, they normally create the household rules and routines that children are expected to follow. Youth are accustomed to having parents provide structure in many areas of their lives and will expect parents mistake send the message that treatment adherence is not important.

♦ Youth May Have Many Commitments

As youth become more independent, they naturally begin to take on extra activities outside of the home (for example, sports, after-school jobs, dating). As the number of these activities increases, many young adolescents find that they have less time to give to their medical care and sometimes simply forget to take their medicine at all.



♦ Adolescents May Be Too Bold

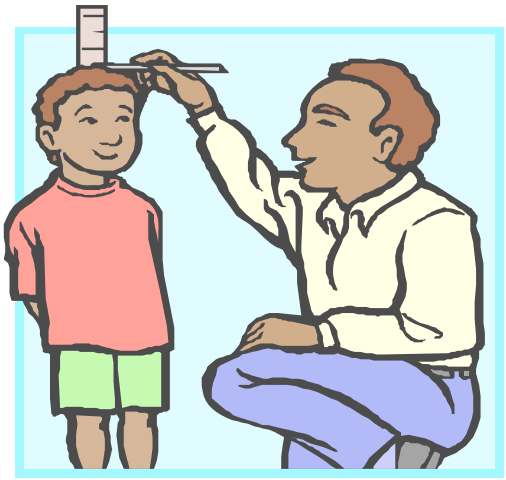
Many adolescents have an attitude that they are not at risk and that nothing bad will ever happen to them. They have difficulty seeing the possible negative consequences of their actions, particularly if these negative outcomes are far off in the future. Sometimes youth underestimate their need for medicine. Something bad may not happen right after they accidentally forget to take a dose, so some youth will fall into the habit of skipping doses often. Parents sometimes respond to this problem by nagging their children to take their medicine. Thus, medical care, particularly remembering medications, can become an area of great conflict.

♦ Parents Can Act as Coaches

Deciding how much parental involvement is needed for your individual child will likely be based upon a number of factors. Parents need to consider the child's age, the severity of his or her medical condition, the difficulty of the treatment plan, and any prior successes or failures with independence. Additionally, parents need to maintain proper expectations concerning what their child can be expected to handle. Parents are best viewed as the ***coaches*** of a medical care team, with level of involvement changing as needed.

♦ Greater Freedom May Lead to Misunderstandings

Some parents have difficulty accepting their child's new sense of independence and worry more about their child's health. Sometimes youth overestimate the amount of responsibility that they can handle. Misunderstandings about parental involvement in treatment can result. Some parents demand too much involvement, and some youth demand too much freedom. Striking a compromise would be the ideal situation.



Setting

Realistic Expectations

for Children

♦ Pre-Adolescents and Young Adolescents (Ages 9 through 12)

This age is the perfect time for teaching children about how to cope with medical regimens. As children develop, they learn to imagine situations they have not truly experienced. At this point, children can begin to consider "what if…" situations. Because youth at this stage of development place a lot of value on their personal abilities, their ability to learn new things and develop the skills required to take care of themselves is important. So, parents can begin to teach young adolescents how to manage their own medical care. Yet, youth at this stage still require a great deal of parental supervision, so parents should begin slowly.

Here are some examples of reasonable expectations for children in this age range:

- **Parents should expect that children require a great deal of PARENTAL SUPERVISION. They often will forget to take medicine on their own.**

- **Parents should expect that they may have to SET LIMITS with their children.**

- **Parents should expect to need A LOT OF PATIENCE when teaching their children how to manage their medicine. Children will have problems following complex medication routines the way that adults can.**

- **Although giving youth chances to be more active in their health care is helpful in their development, it is *most realistic* that decisions be *shared* between parents and youth.**

♦ Later Adolescents (Ages 13 through 18):

Most adolescents within this age range are beginning to think abstractly and consider different ideas and possibilities. As they get older, adolescents become increasingly independent of parents and are held responsible for parts of their own lives. Adolescence provides many chances for children to prepare for what they have to do as adults.

For example, children in this age range begin to develop the ability to manage their own medical care with less supervision by their parents. Initially however, they may need to rely upon parents to help them learn how to plan in advance for occasional troubles in routine. Younger adolescents may welcome parental advice.

As children grow into late adolescence, they develop a stronger sense of their independence and identity. At this stage, many adolescents welcome being put "in charge" of their own medical treatment. They tend to appreciate when parents ask their opinions and allow them a large role in the decision-making process. However, children may react negatively to parents who repeatedly remind them or offer advice without being asked for it. What a parent views as helpful, an adolescent may see as either nagging or a sign that the parent doesn't trust the adolescent.

Here are some examples of reasonable expectations for older adolescents:

- **Parents should expect that adolescents may want to MANAGE THEIR HEALTH ON THEIR OWN. Some adolescents view parental involvement as a clue that the adolescent is not trusted. Be prepared to discuss independence issues and give responsibility to youth when appropriate.**

- **Parents should expect that youth WILL ARGUE. Issues of "fairness" often are at the center of many parent-adolescent arguments. Be prepared to problem solve the fairest/most reasonable solution.**

- **Parents should expect that PEER PRESSURE will be a major factor in their children's lives. For many adolescents, the opinions and values of friends begin to be more important than those of family. Be ready to come across issues regarding what is or is not "cool" when addressing your youth's medical care management.**

The adolescent years are a time of increased peer pressure and feelings of self-consciousness. As such, youth tend to avoid anything that they believe will make their friends and classmates view them negatively. Sometimes, children do not like to take their medication in front of others because they are embarrassed or do not want to answer questions about why they need to take medicine. Other times, peer pressure can lead to adolescents picking up bad habits, like smoking or drinking, which can interfere with their medications.

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