Efficacy of the Patient Advocate Component in a Behavioral Intervention to Improve Treatment Adherence in the HIV Positive Population: A Systematic Review

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Abstract
Background: HIV/AIDS is a global health concern affecting as many as 39 million people worldwide. Viral spread persists secondary to patient non-compliance to antiretroviral therapy. Healthcare providers struggle to identify methods to improve adherence. Patient advocates (PAd) are being utilized as part of a behavioral intervention to improve patient compliance. PAd are highly trained in topics of HIV/AIDS disease and management to assist patients with education, motivation, and treatment adherence support. The studies reviewed here address the efficacy of the PAd component in HIV/AIDS treatment adherence. The significance of each study will be discussed and the overall quality of evidence will be evaluated using GRADE, a universal system utilized to determine quality of evidence and strength of treatment recommendations.

Method: An exhaustive search of medical literature was conducted using three different databases to identify articles addressing this research question. The search was limited to articles published since the year 2001 that addressed the PAd component alone.

Results: The search resulted in three articles suitable for this study. The three articles address the effect of the PAd component on treatment adherence and patient retention in care. Evidence from all three articles suggests that PAd significantly augment treatment adherence and encourage patients to remain in care.

Conclusion: Current evidence suggests that PAd improve HIV/AIDS treatment adherence. However, further objective research is required through randomized controlled trials that will better address the criticism of validity and study design.

Keywords: HIV/AIDS treatment adherence, patient advocate, treatment advocate, adherence counselor, ART, retention in care.

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Efficacy of the Patient Advocate Component in a Behavioral Intervention to Improve Treatment Adherence in the HIV Positive Population:

A Systematic Review

Stefanie Forrester

A course paper presented to the College of Health Professions in partial fulfillment of the requirements of the degree of Master of Science

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Biography

Stefanie Forrester is a native of California who is currently working on a Master of Science in Physician Assistant Studies at Pacific University Oregon. She intends to pursue a Master’s degree in Public Health upon completion of her current program. Stefanie graduated from Missouri State University where she earned a Bachelor of Science degree in Psychology with a minor in Sports Medicine. She is also the Founder and President of Forrester Canopy Outreach, Inc., a non-profit public benefit corporation of the State of California which she developed in honor of her father who recently lost his battle against cancer. The organization works to provide medical, educational, and nutritional resources to hospitals and orphanages in underserved communities throughout the world. Stefanie hopes to further her education and dedicate her life to helping others through her skills as a Physician Assistant and through the workings of her organization.

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To my mother who has been relentless in helping to support my dreams and whose love and devotion has enabled my success. Thank you from the bottom of my heart. I couldn’t have done this without you.

To my father who can’t be with me to share in this accomplishment but whose presence is always with me. I’ve drawn strength and guidance from you every day of this journey and you’ve given me the inspiration to reach beyond my grasp. I miss you.
ABSTRACT

Background: HIV/AIDS is a global health concern affecting as many as 39 million people worldwide. Viral spread persists secondary to patient non-compliance to antiretroviral therapy. Healthcare providers struggle to identify methods to improve adherence. Patient advocates (PAd) are being utilized as part of a behavioral intervention to improve patient compliance. PAds are highly trained in topics of HIV/AIDS disease and management to assist patients with education, motivation, and treatment adherence support. The studies reviewed here address the efficacy of the PAd component in HIV/AIDS treatment adherence. The significance of each study will be discussed and the overall quality of evidence will be evaluated using GRADE, a universal system utilized to determine quality of evidence and strength of treatment recommendations.

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INTRODUCTION

Background

The human immunodeficiency virus (HIV) is a comprehensive and progressive pathogen which attacks and depletes a portion of the immune system, rendering it unable to defend against opportunistic infections and malignancy. Infection with HIV is the precursor to acquired immunodeficiency syndrome (AIDS) and if untreated, will lead to death. According to the World Health Organization (WHO), HIV/AIDS is considered to be pandemic infecting as many as 39 million persons worldwide. To date, 20 million have already died as a result of the infection and it continues to be a major cause of morbidity and mortality throughout the world (Bartlett, 2010). Although there currently is no cure for the virus, antiretroviral therapy has managed to increase the quality of life for HIV-infected patients and prolong overall life expectancy through suppression of viral replication and the sustenance of immunologic function. The HIV/AIDS pandemic persists secondary to the shortcomings of current treatment plans which inadequately address factors such as ignorance of HIV status, illiteracy, poor education about disease awareness and cultural misogyny, ineffective counseling on treatment options and side effects, and lack of resources and supporting structures. Interventions which fail to address HIV/AIDS management with a holistic and comprehensive approach perpetuate treatment failure and subsequent viral spread.

First discovered in 1981, HIV/AIDS came to light when several cases of an aggressive form of Karposi’s sarcoma (KS), thought to be a rare form of relatively benign cancer that afflicts the elderly population, began to appear in young homosexual males in New York (AVERT, n.d.). Around the same time, physicians in both New York and
California started seeing increased incidence of the rare lung infection Pneumocystis carinii pneumonia (PCP) (AVERT, n.d.). Physicians hypothesized that KS and PCP were different manifestations of the same infectious syndrome. A report published in late 1981 by the Centers for Disease Control (CDC) alerting the public of the occurrence of PCP in five men in the Los Angeles area became credited as the beginning of the general awareness of AIDS in the USA (AVERT, n.d.). The disease was initially referred to as Karposi’s Sarcoma and Opportunistic Infections (KSOI) in the United States but later became known as gay-related immune deficiency (GRID) or the “gay cancer” due to the association with the homosexual community (AVERT, n.d.). In July 1982, manifestations consistent with the disease began appearing in heterosexual Haitians and hemophiliacs. It was subsequently renamed and officially defined by the CDC as “acquired immune deficiency syndrome” (AIDS) in September 1982 (AVERT, n.d.).

The cause of AIDS, at that point undetermined, became of heightened interest. In May 1983, doctors at the Institute Pasteur in France isolated a virus named lymphadenopathy-associated virus (LAV) which they believed to be the cause of AIDS (AVERT, n.d.). However, in April 1984, Dr. Gallo of the National Cancer Institute isolated the human t-lymphotropic virus III (HTLV-III) and proposed this to be the cause of AIDS (AVERT, n.d.). Ultimately, HAV and HTLV-III were concluded to be the same virus and it was renamed HIV by the International Committee on the Taxonomy of Viruses in May 1986 (AVERT, n.d.). Syndromes emulating HIV/AIDS soon began being reported in various regions throughout the world. By late 1986, the pandemic had spread through 85 different countries with 38,401 reported cases of HIV/AIDS in the regions of Africa, the Americas, Asia, Europe, and Oceania (AVERT, n.d.).
The introduction of antiretroviral therapy in 1986 advanced management of HIV/AIDS, but it was the phenomenon of combination therapy with highly active antiretroviral therapy (HAART) that dramatically altered the course of the disease (Bartlett, 2010). Levels of cases progressing to AIDS, AIDS-defining infections, AIDS-associated hospitalizations, and related mortality all declined between 60 to 80 percent in the first few years following the discovery and implementation of HAART (Bartlett, 2010). With the discovery of this new medication regimen, the virus could be treated and suppressed to levels adequate to prolong life and reduce the rate of transmission.

Antiretroviral therapy (ART) has revolutionized the treatment of HIV/AIDS. If taken consistently as prescribed, the medications have the ability to inhibit viral replication and suppress viremia to levels not conducive to disease progression. Viral load is directly proportional to the destruction of CD4+ lymphocytes. Therefore, suppression of the active replicating virus sustains immunologic function. A significantly problematic barrier to this outcome is patient non-compliance with medication regimen. This non-compliance can stem from a misunderstanding about the consequences associated with treatment failure, the inability to tolerate medication side effects, lack of support structures, or simply laziness on the part of the patient. Strict adherence to the ART medication dosing schedules is required in order to maintain therapeutic levels, within the plasma, sufficient to prevent viral replication. The HIV virus is extremely prone to mutation during the RNA/DNA conversion and synthesizing process. A single missed dosage can potentially lead to a mutation that renders the medication ineffective, leaving the patient with limited treatment alternatives. Increasing patient awareness and improving understanding of the disease in addition to instruction regarding ways to
manage side effects of medications will help to improve treatment adherence. (MERCK, 2009)

Despite advancements in medical treatment, HIV/AIDS continues to plague individuals and challenge healthcare providers around the world. According to the CDC’s report, based on the national prevalence in 2006, there are estimated to be more than 1 million people currently living with HIV/AIDS in the United States alone (CDC, 2010). This number is higher than ever before, showing an 11% increase from previous estimates made in 2003 (CDC, 2010). Further research is merited to identify successful prevention and treatment strategies for HIV/AIDS as a global health concern.

Active research is being conducted in order to devise a method or methods to improve HIV/AIDS treatment adherence. In addition to pharmacotherapy, behavioral approaches have been studied and implemented. Several studies address the determination of a patient’s “readiness” before initiating treatment since ART therapy is a lifelong commitment. A relatively smaller number of studies have specifically addressed the patient advocate (PAd) component in the psychosocial aspect of treatment adherence. Such a PAd, highly skilled in HIV/AIDS management, provides educational awareness of the disease, discusses and answers questions regarding treatment availabilities, offers remedies for side effects, and provides supportive counseling aimed at creating a safe, welcoming, and trustworthy environment conducive to serving patients’ individualized needs. Such persons serve as advocates for patients and act as liaisons to enhance patient-provider relationships with the ultimate goal of improving treatment adherence and reducing transmission of HIV/AIDS.
Purpose of Study

The purpose of this paper is to review the literature on the efficacy of the PAd component on HIV/AIDS treatment adherence. The goals of such a strategy are to increase treatment adherence, achieve viral load suppression, sustain immunologic function, and reduce transmission of HIV/AIDS. This review will serve to assess the outcomes of each study individually, and will further serve to grade the overall quality of evidence produced by all studies combined. The evidence will be graded utilizing a universal grading system that will allow providers to fully assess the benefits and risks of adding a PAd component to HIV/AIDS treatment intervention programs.

METHOD

An extensive review of the literature was conducted using CINHAL, Medline, and EBM Multifile. All three databases were accessed through the Pacific University Library system. The keywords searched included “HIV treatment adherence” and “treatment advocates” individually and in combination. The search was limited to human subjects, the English language, and full text articles. The initial results included seven articles. Articles before 2001 were excluded as were articles not addressing the patient advocate component specifically. Ultimately, this search resulted in three studies. Aspects all three articles were included in the final systematic review.

RESULTS

The first study reviewed was conducted by Igumbor et al., (2011) who performed a retrospective study based on patient clinical records to assess the impact of a patient advocate (PAd) on retention in care, adherence to antiretroviral therapy, and treatment outcomes. The terms “adherence counselor” and “patient advocate” were used
synonymously and were defined as a professionally trained person with specific skills and knowledge in health promotion, ethics, confidentiality, HIV/AIDS disease and management, and treatment adherence support. Services provided by PAds included performance of psycho-social assessments to preemptively identify adherence barriers, administration of pre-treatment education designed to promote adherence, and coordination of support services such as home visits and follow-up appointments to suit patients’ individualized needs.

Igumbor et al., (2011) performed a two level analysis consisting of a patient-level and a site-level. The patient-level analysis was used to compare variables among patients receiving care from antiretroviral (ART) sites with PAd services with those at sites without PAd services. A total of 540 patient records targeting patients initiated to ART between July and September 2007 were selected from four ART sites within three provinces of South Africa. Selected sites were chosen based on higher enrollment rates, better data quality, and comparable proportions of patients with and without PAd services. Site contributions within respective provinces were 17%, 46%, and 37%. PAd distribution across sites was significantly different. The main outcomes addressed in the patient-level analysis included PAd impact on treatment pickup rates, patient retention status, and viral load.

Results from the patient-level analysis concluded that a significantly higher proportion of patients with PAd exposure were able to sustain viral loads less than 400 copies/mL at 6 months follow up (70%, p = 0.001) when compared to patients without PAd support (Igumbor et al, 2011). However, there were also more patients who had been exposed to PAd with viral loads greater than 400 copies/mL at six months follow
up (51%, $p = 0.001$). With regard to suppression of viral load, data concluded that the proportion of patients with unsuppressed viral loads at six months follow-up was higher among those without PAd support (42%) when compared to those with PAd exposure (24%, $p > 0.001$). Medication pick-up rate and pharmacy refill data was used to measure adherence to ART. Authors reported that 78% of participants attained a 95% pick-up rate (commonly cited global requirement for optimum adherence to ART) while 22% did not. Half of the 22% who failed to attain the 95% pick-up rate and 17% of those who did achieve it experienced virologic failure (incomplete viral load suppression or virologic rebound after complete suppression). The pick-up rate was significantly higher among patients with viral loads less than 400 copies/mL. Overall, a significantly higher proportion of patients with PAd exposure (89%) attained a treatment pick-up rate of over 95% when compared to patients without PAd exposure (67% $p = 0.021$).

Authors addressed and analyzed multiple confounding variables in this level of the study. It was found that patients who lived more than 40 km from the health clinics were less likely to have had PAd exposure and PAds were more likely to be allocated to patients who lived in impoverished or low-income housing (Igumbor et al, 2011). Patients with PAds were more likely to have disclosed their HIV status and be receiving clinic-based counseling. Average treatment duration was nine months. Majority of subjects were female (64%), ranged between 25 and 39 years of age (59%), had records of PAds or adherence supporter utilization (56%), and lived within a 9 km radius of the health clinic (58%). Twenty-five percent (n = 125) of subjects were not exposed to any PAd service or clinic-based adherence counseling.
The site-level analysis compared patient outcomes at sites offering PAd services with those that did not offer PAd services. Patient records were obtained from 26 sites, 12 with PAd services and 14 without PAd services (Igumbor et al, 2011). Sites were included if patient records included viral load results. Sites where patients initiated ART before PAd services commenced were excluded. Patient records were used to assess virologic failure and retention in care (Igumbor et al, 2011).

Igumbor et al., (2011) reviewed a total of 3,097 patient records from various sites throughout South Africa to determine the impact of PAd exposure on rate of virologic failure, 1,139 from clinics with PAd services and 1,958 from clinics without PAd services. The median time patients maintained suppressed viral loads at clinics with PAd services was 235 days while the median time for patients at clinics without PAd services was 199 days. The authors concluded that viral load suppression was more likely to be achieved at sites with PAd services compared to sites without PAd services (p = 0.001). In reference to the impact of PAd exposure on retention in care, median values were 561 days for patients in clinics offering PAd services and 455 days in clinics without PAd services. Authors concluded that a significantly higher proportion of patients at sites with PAd services remained in care for longer duration when compared with patients treated at sites without PAd services (Igumbor et al, 2011).

The next study reviewed was conducted by Mutchler et al. (2011) who performed a qualitative process evaluation using community-based participatory research (CBPR) to assess the effect of treatment advocates (TA) on improving engagement in care, ART initiation, and ART adherence. The study addressed the following questions: 1). How does a TA help engage patients living with HIV/AIDS in care? 2). How does a TA help
patients living with HIV/AIDS improve adherence? A TA was defined as a person who would work to empower HIV/AIDS patients through education and client-centered counseling regarding HIV pathogenesis, testing, treatment options and ART initiation, treatment adherence, complications with comorbid health conditions, side effects of medications, diagnostic interpretation, nutrition, and who would advocate on behalf of patients with providers helping to provide referrals to ancillary treatment and support services.

The study was conducted through semi-structure qualitative interviews that were used to explore a TA’s influence on treatment and care (Mutchler et al., 2011). Participants were recruited from the AIDS Project Los Angeles Organization. Recruitment was through study fliers and eligibility screening. Fliers were distributed to all clients with TAs at the time of the study and the first 25 who responded were interviewed. Eligible clients spoke English or Spanish and were at least 18 years of age. In addition, researchers interviewed two TAs, and four of the managing providers to supplement client perspectives. Qualitative analysis was conducted using the Atlas software. Content analysis was conducted using inductive and deductive techniques. Trained coders identified recurring themes throughout the interviews and graded the evidence using the following system (Mutchler et al, 2010):

- Almost all (theme emerged in almost every interview, n = 27-31)
- Most (theme emerged in majority, n = 20-26)
- About half (theme emerged in ~50%, n = 13-19)
- Some (theme emerged in a substantial minority, n = 6-12)
- A few (theme emerged in a small number, n = 1-5)
The patient demographic analysis of the study showed that 92% of the participants were male, with the average age being 42.9 years, the majority of whom were African-American ethnicity (60%) (Mutchler et al., 2011). Mutchler et al. (2011) found that almost all participants (n = 27-31) mentioned that TAs helped them to understand treatments by providing comprehensive education about HIV and treatment. The participants sought out TAs to confirm and validate treatment information and felt that TAs influenced patients’ engagement in HIV medical care and decisions to initiate ART. About half of the participants (n = 13-19) mentioned that TAs provided education about the importance of adherence, provided positive reinforcement, and worked with clients to determine appropriate strategies for supporting adherence. Most participants (n = 20-26) mentioned that TAs offered services within a holistic care model and were able to make well-informed recommendations and referrals regarding care and treatment. Most participants (n = 20-26) mentioned that TAs provided a bridge to providers acting as patient advocates and matching clients with appropriate providers that fit their needs, personality, and insurance requirements. The authors concluded that through holistic care, client-provider liaison, client advocacy, and self-empowerment encouragement, TAs contributed to client engagement in care, use of ART, and treatment adherence. TAs were seen as particularly valuable because they empowered clients to better advocate for their own care and were found to provide a critical component in quality of care (Mutchler et al., 2011).

The final study reviewed was conducted by Scheid (2007) and was funded by the Local Regional HIV/AIDS Consortium serving 12 counties in North Carolina to assess the impact of specialized adherence counselors on treatment adherence. Three
adherence counselors were hired to participate in the study. Each of the counselors spent time learning the newest information about HIV medications and adherence and met with the evaluator once a month for a year to develop strategies to improve adherence. Recruitment was by referral from doctors, nurses, and case managers who were made aware of the study and provided with specific referral forms. Fifty-three clients were referred during the first year of the program. Upon referral, participants completed an intake interview with one of the adherence counselors. The counselor assessed living situation, treatment history, social support status, comorbidities, substance abuse, mental health illness, and any other pertinent medical history. Patients currently on ART provided a five day medication recall history to determine potential barriers to adherence. Three-month progress notes were completed to assess adherence measured by three components: client self-report, clinician assessment, and lab work. All three components had to concur in adherence at the time of the three-month progress report for improvement to be noted. Clients were discharged from the program once they had been fully compliant with all three concurring components, two three-month progress notes, and no missed medication doses.

The author reported that 53 clients were referred for participation and 11 were lost to follow up after the initial intake assessment. Of the 42 clients who continued with the adherence counseling, five never initiated ART, five died, and two relocated out of the area. A total of thirty clients initiated ART and received adherence counseling for at least one year. Data analysis showed that 57% (n = 17) of study participants showed improved adherence at six-month follow-up and 33% (n = 10) were discharged as adherent at one year. Seventeen percent (n = 5) were non-adherent at the six-month
follow up and 10% (n = 3) remained non-adherent at one year. Four clients discontinued ART between the six-month follow-up and one year secondary to comorbidities and lab abnormalities. Conclusions made by the evaluator suggested that adherence counseling is effective and does lead to improved adherence but recommends long term follow up and continued patient education to fully address non-adherence (Scheid, 2007).

DISCUSSION

The three studies were evaluated on the basis of their design and validity, their outcomes, and their limitations.

Design plays a critical role in the credibility of a research study. The design utilized must be objective and free from bias in order to yield high quality evidence. Control groups must be utilized for comparison to accurately assess efficacy of an intervention. Randomized controlled trials are objective studies that provide high quality evidence through random allocation of subjects and blinding of participants/researchers that exclude interfering variables and avoid forms of bias. By creating controlled environments, researchers can more accurately determine a cause and effect relationship between the variables under investigation. In observational studies, researchers have no control over assignment of subjects into treatment groups; rather they compare existing cohorts exposed to a particular treatment or intervention to those without exposure and draw inferences about the treatment/intervention effects. While these studies observe much larger treatment groups and their results have more generalization, they fail to exclude confounding variables which could potentially influence treatment outcomes posing a threat to the study’s validity. Additionally, observational studies are subject to many forms of bias contributing to poor quality of evidence.
Validity is another component used to determine credibility of outcomes and is often addressed when discussing limitations of studies. Validity is threatened by the presence of random variation, bias, and confounding variables. Random variation is avoided by using large samples to eliminate outcomes due to chance. Bias occurs when there is systematic error in sample selection, measurement, or analysis and is avoided through randomization and blinding procedures and through maximizing follow up of all subjects. Confounding variables are extraneous factors not controlled for within the study that could potentially alter or have significant effects on outcomes. Finally, generalization of study outcomes can also threaten study validity, that is, how well the outcomes can be generalized to the patient population under investigation. Population characteristics, sample size, and patient demographics are factors used to assess generalization. Large diverse samples with balanced numbers of sex, ethnicity, age, etc., will yield outcomes that are highly generalizable and thus more valid.

The studies included in this review were performed by researchers whose goal was to assess the effect of PAd on treatment adherence. In other words, whether augmenting a treatment plan for HIV/AIDS patients with a PAd counselor will significantly improve antiretroviral medication adherence and encourage patients to remain in care. Each study’s design, outcomes, and associated limitations will be discussed here in detail. For the purpose of consistency, the term patient advocate (PAd) will be utilized to represent the intervention under investigation except within discussion of each study.

Igumbor et al., (2011) utilized a study with an observational design known as a historical cohort analysis. This approach allowed the researchers to identify two separate
cohorts of subjects who shared a common health condition, HIV/AIDS, but who differed in exposure to PAd services. The study was conducted in retrospect using existing medical records of patients initiated to antiretroviral therapy between July and September 2007. Data was extracted and analyzed on both the patient level and the site level to observe for improvements in treatment adherence and retention in care when exposed to PAd services. The primary outcomes addressed on the patient level included effect of PAd services on treatment pick-up rate, patient retention status, and viral load. The primary outcomes addressed on the site level included impact of PAd services on rate of virologic failure and patient retention in care.

In the patient-level analysis, PAd services were found to have a positive effect on treatment pick-up rate with a significantly higher proportion of patients (89%, \( p = 0.021 \)) attaining a rate of over 95%, consistent with the globally cited value required for optimum adherence to ART (Igumbor et al., 2011). This was compared to the 67% of those patients who attained a rate of 95% without ever being exposed to patient advocate services. In addition, those patients with PAd exposure were significantly more likely to have achieved virologic suppression with viral loads less than 400 copies/mL at 6 months. However, the authors concluded that PAd services did not significantly impact retention in care. Surprisingly, there appears to be no specified basis for this conclusion. It was found that 82% of all subjects remained in care throughout the study time frame, 12% were lost to follow up, 4% transferred or relocated out of the area, and 3% died. With respect to the site level analysis, patients at sites with PAd services were found to remain in care for longer periods of time and were less likely to have unsuppressed viral
loads consistent with virologic failure when compared to those in care at sites without PAd services.

The evidence acquired from this study strongly suggests that PAd services positively impact HIV treatment adherence. However, there are several limitations. Firstly, this was an observational study performed retrospectively which means it was subject to several forms of bias. For example, the researchers were unable to control for frequency of PAd exposure in this study, therefore, those participants who saw a PAd once were grouped with those who had frequent visits with a PAd (Igumbor et al., 2011). Additionally, subjects were exposed to various PAds without uniform training and thus could have received a variety of different services. These are examples of systematic error in the form of measurement bias which compromise the validity of the associated outcomes. Furthermore, in both the patient level and site-level analyses, authors indicated that patient records were chosen from sites with higher enrollment rates, better quality records, and comparable distributions of patients with and without PA exposure. In an attempt to obtain high quality data, the authors likely chose records from better quality institutions thus creating an error in the process of gathering the sample called selection bias leading to inaccuracy of results. On a positive note, the authors addressed a variety of confounders in the patient-level analysis. By identifying these confounders, it shows the authors were considering alternate variables that could have been contributing to study outcomes. This adds validity to the associated evidence. Another strength of this study was found in the large sample size eliminating outcomes secondary to chance and in the generalization of its results. Patient records were selected from four clinics among three separate provinces in South Africa, therefore, results could be generalized to
a larger patient population than if the cohort came from one specific clinic within a single province. However, since the cohort was limited to clinics in South Africa, the results cannot be generalized to HIV/AIDS patients globally. In addition, the majority of the participants in the patient-level analysis were found to be female (64%), were between the ages of 25 and 39 (59%), were supported by a PA (56%), lived within a 9 km radius of the health facility (58%), and were exposed to clinic-based adherence counseling (66%) (Igumbor et al., 2011). This further reduces the generalization to a specific subset within the HIV/AIDS patient population making the evidence less applicable to all HIV-infected patients.

The second article authored by Mutchler et al., (2011) was an observational study that utilized a qualitative process evaluation with community-based participatory research. Information was gathered by interviewing twenty-five HIV/AIDS patients currently receiving treatment from a single clinic in Los Angeles. Patient interviews were supplemented with information obtained from interviews with TAs and providers from the same clinic. This approach enabled the researchers to understand how and why TAs improved treatment adherence and retention in care rather than solely focusing on if they had an effect. Qualitative analyses utilize a smaller sample size in order to obtain qualitative information which is analyzed in a holistic and contextual manner. Researchers utilized a coding system to systematically identify and extract recurrent themes from all of the interviews enabling them to make reliable and consistent interpretations and reduce errors in content validity.

The outcomes of this study supported the use of TAs in HIV/AIDS management. The evidence produced by this study stemmed from a compilation of recurrent themes
plucked from patient and provider interviews. Majority opinion elicited from study participants and participating providers/TAs suggested that TAs helped clients in a holistic manner to more thoroughly understand the treatment process, available options, and provided comprehensive education on the pathogenesis of HIV and on the benefits and consequences of treatment adherence (Mutchler et al., 2011). Overall, evidence showed that clients, TAs, and providers agreed that TAs are a critical component in HIV management contributing to client engagement in care, initiation to ART, and treatment adherence through providing a holistic approach to care, enhancing patient-provider relationships through patient advocacy, and promoting self-empowerment (Mutchler et al., 2011).

The limitations to this study were endless. The qualitative design provided insight as to how and why participants felt that TAs were advantageous but it failed to produce quantitative and objective measurements defining the efficacy of TAs on treatment adherence. In other words, the evidence was purely subjective and based on general opinion. As a type of observational design, this study lacked a control group and random allocation of participants and thus could only establish an association between TAs and HIV/AIDS treatment adherence. Furthermore, the study was subject to many forms of bias creating systematic error which works to invalidate study outcomes. Authors claimed that the TAs and providers who provided supplemental interviews were hand-selected due to their direct association with the study participants and worked at the same clinic in Los Angeles, a form of selection bias. Researchers admitted that, despite guarantees that all information elicited was confidential and would not affect placement in programs, participants could have felt pressured to give positive feedback on TAs (Mutchler et al.,
Additionally, coders were not blinded leading to a potential source of personal bias consistent with measurement error. Lastly, while the holistic and qualitative approach of the study design helped to limit confounding variables, the authors failed to identify any of these variables within their results further compromising study validity. The outcomes of this study have poor generalization. The sample was taken from one clinic in Los Angeles, therefore, the results cannot be generalized to the overall HIV/AIDS patient population. Outcomes reflected only the opinions of patients already enrolled in a treatment program excluding opinions of those not in care. Further limiting the generalization of the outcomes was the fact that researchers only included participants who spoke English or Spanish and were at least 18 years of age (Mutchler et al., 2011). The many limitations found in this study exemplify why observational studies consistently produce low quality evidence.

The final study was an observational study in which a solo researcher conducted an experiment within a community to assess the effectiveness of adherence counselors on HIV/AIDS treatment adherence. The article provided very limited information on the details of the study. Two nurses and a case manager were hired and trained as adherence counselors in HIV medicine (Scheid, 2007). Referral forms were developed and distributed among healthcare providers in the community for subject recruitment. Referred subjects took part in an initial intake interview with an adherence counselor at which time barriers to adherence were identified and plans or strategies to promote adherence were created. Patients presented for three-month follow ups and adherence status were judged based on three pre-defined factors: self-report of adherence to
medication, physician confirmation and appraisal, and improvements in lab values used to track HIV progression (Scheid, 2007).

The author concluded that evidence attained from this study showed that adherence counselors favorably effect HIV treatment adherence claiming that 57% showed improvement at 6 months and 33% were discharged fully adherent at one year (Scheid, 2007). The author’s claim is erroneous. The observational design of this study is very weak and reveals many forms of bias. Firstly, adherence was measured by one unmasked researcher using subjective self-report from the patient as one of the components to track adherence yielding two forms of potential measurement bias and systematic error. Eleven patients were lost to follow up after the initial intake evaluation, five patients died, five never initiated ART, and two patients transferred or relocated during the course of the study, all contributing to analysis bias, another source of systematic error (Scheid, 2007). More importantly, secondary to the small sample size of patients who actually received the intervention with the adherence counselors combined with the lack of a control group with which to measure the intervention against, outcomes resulting to chance cannot be excluded. Furthermore, the author failed to list any confounding variables such as substance abuse, psychosocial issues, mental health issues, comorbidity complications, pregnancy, etc., which could have significant impact on study outcomes. Lastly, minimal information was given on the source of the sample and population demographics were excluded in the results section. Subjects were recruited based on referrals from healthcare providers throughout a community. While this method of sampling is more representative of a true HIV-infected patient population, limiting subjects to a specific community prevents outcomes from being generalized to
HIV/AIDS patients in other communities, states, countries, or geographical regions. These various limitations diminish the quality and compromise validity of the study results.

All three of the articles discussed above provide evidence that there is a place for PAbs in HIV/AIDS management programs. However, further studies with more objective and experimental design need to be conducted to decipher their efficacy and how best to utilize such a construct. Secondary to the fact that all three studies were of observational design, the evidence attained is of low quality. Observational studies provide insight into a phenomenon and can potentially avoid ethical dilemmas drawing associations and making inferences about a cause and an effect. However, none of the three studies rise to the level of establishing a causal effect. Therefore, more studies must be conducted that are controlled experiments with an independent variable utilizing methods of randomization, blinding of participants/researchers, and which avoid systematic error due to bias in order to produce valid outcomes and resultant high quality evidence.

Patients depend on their healthcare providers to allocate the best treatment suited to their individual needs. This entails comparing the benefits of a treatment against the risks, costs, and burdens (GRADE, 2011). Treatment recommendations and/or guidelines are designed to suit the average patient who exhibits the classical manifestations of a disease. Providers must be able decipher between standard guidelines and alternative options when presented with atypical presentations such that they can incorporate patient values and preferences into treatment recommendations.
In an attempt to ease this burden on providers, a group of researchers developed a grading system called “Grading of Recommendations Assessment, Development and Evaluation” (GRADE, 2011). GRADE defines a systematic approach to grade quality of evidence and strength of recommendations. The quality of evidence is graded based on the design of the study and on the precision and accuracy of the results.

Evidence is graded as high, moderate, low, or very low. A grade of “high” means that further research is unlikely to change the effect, ”moderate” suggests that further research will have an impact on the effect, “low” quality claims that further research could have an impact and will likely change the estimate of effect, and “very low” suggests that any estimate of effect is very uncertain (GRADE, 2011).

Randomized control trials produce high quality evidence due to randomization and blinding of participants. The body of evidence can be downgraded secondary to study limitations to include inconsistency of results, indirectness of evidence, imprecision, and bias. Observational studies typically produce low quality evidence because they lack random allocation and are subject to bias (Hannan, 2008). Observational studies can be upgraded if the magnitude of treatment effect is large, if there is a dose response gradient, or if all plausible confounders are well controlled.

The GRADE system classifies treatment recommendations as strong if the benefit of treatment significantly outweighs the associated risks or harm, costs, and burdens. The recommendations are graded as “weak” if there is a fine balance between the benefits and the downfalls of the treatment. Using this system, providers can make better informed decisions before allocating treatments.
Appendix A is a table illustrating the systematic grading of the three articles included in the paper. The studies were evaluated for two primary outcomes: (1) PAd impact on HIV treatment adherence and (2) PAd impact on retention in care. The first five vertical columns in the table after “starting grade” labeled with subheadings “study quality”, “consistency”, “directness”, “precision”, and “publication bias” are measures used to downgrade high quality evidence provided by randomized controlled trials and were non-applicable to these studies. The remaining three vertical columns with subheadings “magnitude of effect,” “dose-gradient,” and “confounders” are measures used to upgrade low evidence provided by observational studies. Only two of the studies, Igumbor et al. (2011) and Mutchler et al. (2011), addressed the retention in care outcome. Both were observational studies. Therefore, the quality of evidence assigned to that outcome was low. Evidence from both studies strongly suggested that PAd exposure had positively influenced retention in care. Neither study provided evidence to support the question of high magnitude of effect and dose-gradient in non-applicable circumstances. The evidence was upgraded by one point under the confounder column because the positive impact of PAs on retention in care derived from the small sample sizes in both studies could potentially have a much larger effect when a more representative sample of the HIV/AIDS population is evaluated. This upgraded the evidence from low to moderate when suggesting that PAd exposure has a significantly positive impact on HIV/AIDS patient retention in care. All three studies, Igumbor et al. (2011), Mutchler et al. (2011), and Scheid (2007), were found to suggest that exposure to PAds enhances HIV/AIDS treatment adherence. Since all three studies were observational studies, the evidence was low and the measures to downgrade evidence were not applicable. Dose-gradient was not
applicable to these studies and evidence did not show a high magnitude of effect. The evidence was again upgraded by one point in the confounder column secondary to the small sample sizes in each study. When a larger and more representative sample is evaluated in future studies, the positive correlation between exposure to PAd and HIV/AIDS treatment adherence could show significantly higher results. Overall, both outcomes yielded moderate quality of evidence. Therefore, the overall quality of evidence is moderate which confirms previously stated opinion that further research is merited to assess efficacy of the PAd component on HIV/AIDS treatment adherence and will likely impact and possibly change the presented estimate of effect.

In conclusion, the observational studies reviewed in this paper have succeeded in hypothesizing that incorporating a PAd component into behavioral interventions will enhance HIV/AIDS treatment adherence. However, further experimental studies need to be performed with randomization blinding procedures to avoid bias and to retain validity of study findings. The objectivity of these studies will better produce high quality evidence which can be used to strongly recommend that PAds are vital components in HIV/AIDS treatment management and further suggest that their incorporation into interventional programs will significantly improve treatment adherence helping to promote virologic suppression, enhance immunologic function, and reduce transmission of HIV/AIDS.
REFERENCES


APPENDIX
Table 1: GRADE Table

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Outcome</th>
<th>Quantity and type of evidence</th>
<th>Findings</th>
<th>Starting grade</th>
<th>Decrease GRADE</th>
<th>Increase GRADE</th>
<th>Grade of Evidence for Outcome</th>
<th>Overall GRADE of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Advocate vs No Patient Advocate</td>
<td>Engagement in care/retention in care/ART initiation</td>
<td>2 Obs studies</td>
<td>Increased engagement/retention in care</td>
<td>Low</td>
<td>0</td>
<td>0</td>
<td>0 0 +1</td>
<td>Moderate</td>
</tr>
<tr>
<td>Treatment adherence</td>
<td>3 Obs studies</td>
<td>Improved treatment adherence to ART</td>
<td>Low</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0 0 +1</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

Patient Advocate vs No Patient Advocate

Engagement in care/retention in care/ART initiation

Increased engagement/retention in care

Low

Decrease GRADE

Consistency

Directness

Precision

Publication Bias

Large Magnitude

Dose-Response

Confounders

Increase GRADE

Grade of Evidence for Outcome

Overall GRADE of Evidence

Moderate

Moderate