#### BARRIERS TO ANTIRETROVIRAL THERAPY ADHERENCE FOR HIV-POSITIVE ADOLESCENTS IN SOUTH AFRICA

by

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University of Pittsburgh, 2015

#### ABSTRACT

Background: The story of HIV in South Africa has been riddled with confusion and misinformation, claiming the lives of countless people. In 2014 HIV claimed the lives of over 140,000 people across the country. While the last 10 years have seen immense growth and improvement with regards to access to antiretroviral therapies (ART), new gaps in coverage have become apparent. We have entered an era in which children born HIV-positive are able to access treatment, and are likely to live through their teen years and beyond, but it is during this adolescent period that unique barriers threaten ART adherence efforts. Objective: This paper has two aims. Aim 1: Conduct a literature review of peer reviewed publications addressing barriers to ART adherence among HIV-positive adolescents in South Africa. Aim 2: Propose a pilot research project to improve ART adherence among adolescents seeking treatment in Khayelitsha, South Africa. **Conclusion:** There remains a notable gap in the literature with regards to data that determines and analyzes the barriers that HIV-positive adolescents on ART face within the context of South Africa. This paper seeks to fill the identified gaps and aims to summarize the important themes resulting from the literature search. In addition, it highlights potential barriers to adherence and outlines a pilot program to identify and address barriers for HIV-positive adolescents in Khayelitsha. Public Health Relevance: According to UNAIDS, if we address the issues of ART adherence within the adolescent population the current HIV/AIDS climate will change for the better. Increased adherence leads to lower and undetectable viral loads; lower viral loads then leads to a decreased likelihood of transmission, both horizontally and vertically. Ultimately, if greater adherence were to be achieved, there would be fewer people living with HIV and more people enabled to live longer, healthier and more productive lives.

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#### PREFACE

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This experience has continued to shape my interests and goals as an aspiring public health professional. Throughout this ongoing adventure I have learned more than I could have ever imagined possible. I know and trust that these experiences will continue to help me to become person, advocate, confidant and friend that I need to be to best assist the communities that I will work with in the future.

#### **1.0 INTRODUCTION**

The summer of 2015 I conducted my practicum with Doctors Without Borders (MSF) in Khayelitsha, a township outside of Cape Town, South Africa. I worked closely with MSF's pediatric doctors and nurses and observed as many of their HIV-positive patients experienced virological failure due to antiretroviral treatment failure. After speaking with the clinic staff, it became apparent that they were relatively successful in managing the majority of their cases, but faced many problems with their adolescent patient population. The adolescent patients presented unique challenges with disease and medication management, and the staff was often unsure how to best address the issues at hand.

My experience with MSF refined the approach I took regarding my thesis. I knew anecdotally that adolescent patients were facing unique barriers to ART adherence, but I wanted to know what barriers the literature explicitly identified. Although the literature did identify important themes and concepts related to the topic of interest, to my chagrin, it lacked data identifying specific barriers that inhibit adherence for HIV-positive adolescents in South Africa. Considering the minimal literature uncovered from the search, I decided to take an unconventional approach towards this thesis and create a document with two overarching aims. Aim 1: Conduct a literature review of peer reviewed publications addressing barriers to ART adherence among HIV-positive adolescents in South Africa. Aim 2: Propose a pilot research

project to improve ART adherence among adolescents seeking treatment in Khayelitsha, South Africa.

#### 2.0 BACKGROUND

#### 2.1 SCOPE OF THE PROBLEM

There are currently 35 million people in the world living with HIV/AIDS. Since the beginning of the global HIV/AIDS epidemic there have been 39 million deaths attributed to HIV-related causes [1]. The global HIV prevalence in adults is 0.8%, 71% of which are people living in Sub-Saharan Africa [1], and only half of whom know their HIV-positive status [2]. In South Africa the national HIV prevalence rate is 18.8% [3]—totaling to 6.3 million people currently living with HIV/AIDs [2]—the most of any country in Sub-Saharan Africa. Within South Africa, the national prevalence rate for people aged 15-24 is 7.1% [3]. As identified in *South Africa's National Strategic Plan on HIV, STIs and TB for 2012-2016*, populations at high risk for acquiring HIV include: young women between the ages of 15-24, people living in informal settlements, young people not attending school, people of low socio-economic status, uncircumcised men, people using illegal drugs, people who frequently abuse alcohol, transgender persons, orphans and other vulnerable children and youth [4].

Antiretroviral therapy (ART) (also known as highly active antiretroviral therapy [HAART]) is a key component to curbing the spread of HIV. When adequately adhered to, ART is known to stop the progression of the virus and allow for the HIV-infected person to live a longer, more productive life [5]. The therapy is generally a regimen of at least three antiretroviral

(ARV) drugs [5]. There are more than 25 ARVs that fall into six different categories: nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), a fusion inhibitor (FI), a CCR5 antagonist, and integrase strand transfer inhibitors (INSTIs).

#### 2.2 HISTORY OF HIV AND ART IN SOUTH AFRICA

The first two diagnosed cases of AIDS in South Africa occurred December 1982 [6], in two homosexual flight stewards in their early 40s [7]. The men acquired the virus while traveling to the United States—both cases progressed rapidly and the men died shortly after their return to South Africa [7]. Throughout the 1980s the majority of AIDS diagnoses in South Africa were limited to gay men and blood transfusion recipients. Until the late 1980s, the rate of the virus present in the heterosexual population remained relatively low with only 12 cases identified in the city of Pretoria in 1986 [8, 9]. Even as the virus spread beyond the initially limited population the issue went largely unaddressed by the South African Apartheid government as AIDS was seen to be an issue only within black and gay communities [9].

In 1990 the government began to measure infection rates by collecting data from anonymous antenatal surveys. The results showed a volatile and rapid increase, suggesting that the national prevalence rate was 0.76%, which increased to 10.44% by 1995, and astonishingly to 22.4% by 2000 [9, 10]. Despite the rapidly increasing prevalence rates, the government denied the evidence and made no concerted efforts to address the issue [11]. Despite what the global and scientific community repeatedly suggested about the spread and management of the disease, South African government officials were often found reporting the opposite. For example, in

1999, President Thabo Mbeki defended a statement that HIV does not cause AIDS and any medications created to manage HIV were unnecessary [12]. He also claimed that Zidovudine, a proven effective drug used to prevent the transmission of HIV from mother to child in utero, had "toxic" side effects and was a "danger to health" [12]. As a continuation of these claims the government restricted the use of Nevirapine, a medication in the antiretroviral family, although it had been donated to the South African Government by the global community [11]. The government instituted ban on life-saving medication was ultimately seen as unconstitutional and was overturned by the High Court in July of 2002, enabling HIV-positive pregnant women to access prevention of mother to child transmission (PMTCT) services and medications [11, 13, 14].

The first ART regimen was approved by the United States Food and Drug Administration (FDA) by the end of 1995 and made available to the American public shortly thereafter [15, 16]. In contrast, widespread implementation of ART programs in South Africa did not occur until April 1<sup>st</sup>, 2004 [11], all while PMTCT programs and ARV campaigns were well underway in neighboring country, Botswana, by 1999 and 2001, respectively. Chigwedere et al. [17] conducted a study in efforts to estimate the benefits lost due to South Africa's delay in implementing widespread ART programs. The results suggested that more than 330,000 lives (approximately 2.2 million person-years) were lost due to the lack of ART implementation.

Despite the complicated history in South Africa in the fight against HIV, the past five years have been largely defined by growth and success. With the election of President Jacob Zuma in 2009 and the appointment of Dr. Aaron Motsoaledi as South Africa's Minister of Health, new attention and urgency was given to the HIV situation in South Africa [11]. After Dr. Motsoaledi acknowledged that the past 10 years were spent "pedaling backwards", the president

declared World AIDS Day 2009 as, "the day on which we start to turn the tide in the battle against AIDS" [11, 18]. The effects of this new charge were seen shortly thereafter; the rate of adults on ART rapidly increased from 4.9% in 2004 to 55% in 2010 [11, 19]. Simultaneously, with the increase of coverage and continual monitoring, segments of the population that did not have adequate access to care have been identified. On World AIDS Day 2011, South Africa released their third National Strategic Plan (NSP) for the years 2012 – 2016 which included a new and emphasized focus on under-reached populations such as sex workers, men who have sex with men, and adolescents [4, 11].

#### 2.3 ART AND TREATMENT FAILURE

Antiretroviral treatment failure is defined as an HIV-positive patient who is experiencing virological failure, which can occur due to poor medication adherence, drug resistance, poor medication absorption, inadequate dosing, and drug interactions [20]. A person's virological state is measured through a viral load blood test. If the results shows that a person's blood contains anywhere from 1,000 to 5,000 copies of the HIV virus per milliliter, they are said to be experiencing virologic failure [21]. High adherence, defined as taking the prescribed medication 95% or more of the time, is necessary for a greater chance of virological suppression; a state when the virus is controlled within an individual's system [22]. If a person is able to achieve longstanding suppression, their immune system can restore functionality and will likely avoid the progression of HIV to AIDS [23, 24].

Based on the National Institute of Health's AIDS info [25], there are three stages of HIV infection: 1) acute infection 2) chronic infection and 3) AIDS. Acute infection, the earliest stage,

is when the virus multiplies rapidly and destroys the immune system's CD4 cells. The chronic infection stage is asymptomatic and is when the virus continues to multiply in the body, although at a much slower rate than in the acute phase. Without regular treatment, the virus usually advances to the AIDS stage in 10 to 12 years. AIDS is diagnosed when a person has a CD4 count of less than 200 cells/cubic millimeter and/or they have one or more opportunistic infections (i.e. pneumonia, tuberculosis). Without treatment, a person with AIDS will generally live three years following their diagnosis.

#### 2.4 TREATMENT FAILURE IN ADOLESCENTS

Adherence to an ART regimen is key if an HIV-positive individual is to live a long, productive life. Adherence issues are, however, present in both adult and adolescent populations. A combination of factors, including but not limited to, the relationships between the patient and the provider, medication issues, psychological status, and structural issues can impede adherence efforts [26]. Adolescents face a unique set of challenges with ART and management. In a paper reviewing the literature to identify ART management challenges for perinatally HIV-infected adolescents, authors Agwu and Fairlie [26] identified barriers including: diverse presentation of HIV and its symptoms, ART usage in a setting of rapid physical growth and development, nonadherence, resistance, long-term treatment management, and difficult transition from pediatric care to adult care.

Adolescents, according to the World Health Organization [27], are young people between the ages of 10 and 19 years. It is reported that in both high and low income countries, adolescents have a lower rate of ART adherence than HIV-positive adults [28-31]. Many HIV-positive perinatally infected adolescents display an array of delays, including delayed onset of puberty [32], decreased levels of school functioning [33, 34] and behavioral problems [35]. Additionally, many HIV-positive adolescents face family disruptions, often including loss of a parent or primary caregiver [36]. These challenges can hinder an HIV-positive adolescent's ability to properly adhere to an ART regimen.

Pediatric and adolescent treatment failure is often a neglected and under-recognized issue within the realm of HIV treatment [37], possibly because adolescents face such unique circumstances when compared to their pediatric and adult counterparts [26]. This lack of recognition poses a severe threat given that 2.1 million adolescents are HIV-positive worldwide [38]. According to the UNAIDS 2014 report on *HIV prevention, treatment, care and support for adolescents and youth*, it is critically important to address the issues surrounding adolescent and youth HIV because this group has the, "opportunity to end the AIDS epidemic through leadership and behavioral and social changes which would have an impact on new HIV infections, AIDS-related deaths and the way the world responds to HIV and AIDS" [39].

#### **3.0 LITERATURE SEARCH**

In efforts to assess the barriers to ART adherence that adolescents face specifically in South Africa, a search of the current literature was conducted.

#### 3.1 METHODS

#### 3.1.1 Search Strategy

Under the guidance of a Health Systems Librarian at the University of Pittsburgh, I created a search strategy to best extract relevant articles on the topic of interest. The terms used to create this search were variations of the following: antiretroviral therapy, medication adherence, HIV/AIDS, adolescents and South Africa (See Appendix A). The initial PubMed search resulted in 120 articles, with none excluded based on date or language. This PubMed search was adjusted for both PsycINFO and Global Health databases, which resulted in an additional 87 articles. After removing the duplicate articles, the result was 192 unique articles.

## 3.1.2 Data Extraction and Management

The title and abstracts were extracted from each of the 192 articles. Two independent reviewers read the title and abstracts for each article and decided to keep or pass the article based on established inclusion and exclusion criteria. For an article to be included in the analysis it had to include the following topics:

Population of Interest:	Adolescents; including any papers that have a target population within the specified 10-19 age range. Include any papers that deal with pediatrics but do not specify age.
Location:	South Africa
Condition:	HIV/AIDS
Medication:	Antiretroviral Therapy
Behavioral Component:	Medication Adherence
Specified Date:	Include publications from all dates <sup>1</sup>

**Figure 1. Inclusion/Exclusion Criteria** 

<sup>&</sup>lt;sup>1</sup> Oldest article dates back to 2003. Based on complex history of ART in South Africa, decided to not initially exclude.

The reviewers were not blinded to the names of the authors or journals. Following the initial independent sorting, the reviewers agreed to include nine of the papers, exclude 163, and due to disagreeing results, discuss 20. The discussion included an in depth look at the title and abstract to determine if the paper met the inclusion criteria. Following the discussion, the reviewers decided to include nine of the 20 papers that were initially disagreed upon, resulting in a total of 18 papers that were read and analyzed for potential barriers to adherence.



**Figure 2. Literature Review Flow Chart** 

Both readers read the articles independently and extracted corresponding information regarding adolescent ART adherence (see Appendix B). Following the inclusion criteria guidelines two articles remained that directly measured adherence in HIV-positive adolescents in South Africa. Five others were identified as not directly measuring adherence as an outcome variable, but still discussed important themes surrounding HIV-positive adolescents in care in South Africa, and were therefore kept. Because of the relatively small number of articles that met the inclusion criteria (n=2), I conducted a thematic review of all the relevant articles.

Theme Identified	Paper Cited (n=6)		
Clinic Experiences	Hornschuh et al. (2014) Pienaar and Visser (2012)		
Mental Health	Petersen et al. (2010) Li et al. (2010)		
Social Support	Bhana et al. (2014) Snyder et al. (2014) Pienaar and Visser (2012) Hornschuh et al. (2014)		

**Figure 3. Thematic Review** 

The themes were identified and extracted by one reader and are discussed in the results section. Themes were chosen for thematic review if they were identified in two or more papers. The results section outlines the findings from the thematic review (n=6) and the literature review (n=2). The thematic review includes one article from the literature review, as it contained important themes relevant to the results. Additionally, the literature review summarizes the findings from the two articles extracted from the literature search that directly measure adherence. The discussion section gives context as to other studies that identify these themes as potential compounding variables that can directly or indirectly effect adherence to antiretroviral therapy.

#### 3.2 **RESULTS**

#### 3.2.1 Thematic Review

#### **3.2.1.1 Clinic Experiences**

The literature search resulted in two papers that discuss the importance of the clinic experience to HIV-positive adolescent patients. One study, conducted by Hornschuh et al. [40], examined in-clinic experiences of 18 HIV-positive young adults (aged 15 to 25 years old) in Soweto, a township community in Johannesburg. According to respondents, it was very important that the providers demonstrate nonjudgmental attitudes and ensure complete confidentiality. When staff embodied these characteristics, patients felt most at ease and trusted the care being provided. Patients expressed that when nurses treated them as individuals and with respect, they were more likely to see the nurses as "friends" or "mothers". They were also more likely to speak candidly and discuss difficult topics with them. In fact, participants admitted they would rather talk to a clinic worker instead of their own mother about sensitive topics such as sex, condom use, romantic relationships, medication difficulties, and drug abuse. Familiarity and consistency with the clinic staff was important to patients, as patients wanted the staff to know them on an individual level. Patients expressed concern with the thought of having to transfer clinics due to the phasing out process from a pediatric clinic and into an adult clinic. They fear this transition may jeopardize confidentiality, that they may feel stigmatized, and that medication availability may be less consistent.

A study conducted by Pienaar and Visser [41] examined the disease-management efforts of six HIV-positive adolescents (aged 12-18 years) in Pretoria. The respondents from this study identified lack of communication and impersonal interactions with providers as the most prominent barriers to proper disease management [41]. The findings from these two papers suggest that experiences within the clinic do affect adolescents' perception of care.

#### **3.2.1.2 Mental Health**

Petersen et al. [42] conducted a qualitative investigation to examine the psychosocial challenges and protective influences for coping among 25 HIV-positive adolescents in Durban. The major psychosocial challenges found were: dealing with the loss of one or both parents, embracing their HIV status, perceived and felt stigma, and disclosure issues. The coping factors identified were: the availability of HIV information, the ability to create goals and dreams for the future, as well has having positive family and peer support. All of these factors play a role in emotional and mental well-being of the adolescent.

Li et al. [43] conducted four focus groups with 26 total participants (10 – 15 years) to identify the needs of adolescents on ART in Cape Town. Results from this study suggest that participants embrace both positive and negative outlooks on life. Respondents stated that HIV is painful, both physically and emotionally—their status causes them to feel fearful, angry, and causes some of them to contemplate suicide. Being HIV-positive was found to drive participants to isolate themselves and retract from friends and activities they enjoy. This isolation is due to fear and potential stigma that could occur if their status were made known to friends and community members. Conversely, adolescents were able to maintain a positive mindset when they reported having strong support from their family and friends.

#### **3.2.1.3 Social Support**

#### Family/Caregiver Support

Bhana et al. [36] evaluated the VUKA Family Program—a pilot program that used a familybased psychosocial intervention in KwaZulu-Natal. In this evaluation, 33 patients (10-14 years) received the intervention and were compared with a control group. The results suggest that certain aspects of familial and peer support may improve ART adherence in adolescents. The VUKA Family Program not only created a support group for adolescent patients, but also created a system for parents and caregivers to learn how to best help their child, resulting in improved caregiver-child support. With improved support, adolescents were seen to have higher rates of adherence. And while many of the adolescents claimed primary responsibility for taking their medication, caregivers began to provide much-needed backup assistance.

#### Peer Support

The Hlanganani Program, a support group for recently diagnosed 16-24 year olds in Cape Town (n=109), was evaluated by Snyder et al. [44]. Results show that participants were initially unaware of how to access support and different services from their community, especially given the fear of stigma. Following the three-session support group, participants exchanged cell phone numbers with one another and expressed interest in more group sessions. Following the completion of the program, both rates of disclosure and self-reported feelings of support improved for the participating adolescents. The program helped increase participants self-efficacy in accessing their surrounding social network and support systems. With increased access of said network, rates of perceived support increased.

#### Clinician Support

As previously mentioned, from the Pienaar and Visser paper [41], the experiences that adolescents have in health care facilities and with health care workers do affect them and have the potential to affect their efforts regarding disease management. Aside from traditional functions, the clinic also serves to provide a social network for many HIV-positive adolescents. As Hornschuh et al. [45] reported, when good interactions occur in the clinic setting, adolescents are much more likely to trust the clinic workers and heed their instruction. The increase of positive interactions aids in creating a strong network for adolescents within the clinic setting and decreases the likelihood of loss to follow-up.

#### 3.2.2 Literature Review Results

#### 3.2.2.1 The VUKA Family Program [36]

The aforementioned Bhana et al. paper [36] evaluated The VUKA Family Program to determine the effect that a family-based psychosocial intervention can have on HIV-positive adolescents with regards to adherence, mental health, self-concept, HIV knowledge, treatment knowledge, youth-caregiver communication and perceived stigma. The program used evidence based interventions (CHAMP and CHAMP+) [42] to target HIV-positive adolescents (10-14 years) in KwaZulu-Natal. The VUKA intervention was delivered to 65 adolescents through 10 sessions that lasted over a three-month period. Sessions were conducted by community lay-counselors and utilized a culturally-adapted cartoon story line within the support-group setting.

Adherence was measured using a derivative from the Pediatric AIDS Clinical Trials Group [46, 47], on a single item scale, and by qualitative process evaluation measures. Comparing participants enrolled in the VUKA group to the control group, the adolescents in the program showed significant improvements in self-reported ART adherence. Looking at self-reported adherence between groups, using a multivariate analysis to measure the change between the comparison and control groups, improvement was calculated to demonstrate a p value of .05 at a significance level of .05. Additionally, the qualitative evaluation reported repeating themes of improved adherence. One caregiver was quoted saying:

"I'm very happy because he didn't want to take his medication and now [after coming to VUKA Family Program] he takes it on time, with no difficulties. I think it's also because he can see other children, he can see that he's not the only one, there are many others..." [Caregiver response from Bhana et al. focus group][36]

Based on these findings, it can be concluded that elements of the VUKA Family Program yielded improved self-reported rates of adherence in HIV-positive adolescents living in KwaZulu-Natal.

# 3.2.2.2 Associations Between HIV-Disclosure and Adherence to Antiretroviral Treatment [28]

Cluver et al. [28] conducted a cross-sectional study to measure the association between HIVstatus disclosure and ART adherence amongst adolescents in South Africa's Eastern Cape Province. The study included 684 adolescents aged 10-19 years who were already in an ART program. An adolescent is considered to be disclosed to if they have been informed that they are HIV-positive and have an understanding of HIV and ART [48, 49]. Structured interviews and focus groups were used for the qualitative and quantitative measurements. Adherence was measured using self-reported measures that were adapted from a similar study conducted in Botswana [50], as well through the Patient Medication Adherence Questionnaire [51]. The results suggested that adolescent knowledge of HIV-positive status is associated with higher adherence (OR 2.18; 95% CI 1.47-3.24), and there is an even stronger correlation between adherence levels and being disclosed to before the age of 12 (OR 2.65; 95% CI 1.34-5.22). Based on the results of this study, there is reason to believe that a relationship exists between adherence to ART and disclosure status for HIV-positive adolescents in the Eastern Cape.

#### 3.3 DISCUSSION

The following discussion brings context to the findings identified above by placing them within the context of current literature. It aims to bring to light how the themes and concepts discovered do play an important role in ART adherence efforts for adolescents

#### 3.3.1 Health Care

Perceptions of health care and quality of care provided can alter adherence efforts for HIVpositive patients. Roberts [52] conducted a study in the United States to determine if there was a correlation between adult HIV-positive patients, satisfaction with their physician, and ART adherence. Results showed an apparent association between the perceived relationship and levels of adherence—good patient-provider relationships strengthened adherence and poor relationships hurt adherence. In fact, the literature demonstrates that there are specific factors within the patient-provider relationship that can affect adherence [53]. These factors include the patientprofessional relationship [54, 55], communication, and characteristics of the health professional (i.e. experiences with ARV treatment, attitudes towards the client [56]). Additionally, the literature shows that the same holds true for adolescent patients [57]. When a positive patientprovider relationship is present, there is a greater likelihood for information to be conveyed accurately and received completely. Conversely, poor patient-provider relationships can result in poor communication where the message is not accurately or clearly received, which may result in lower rates of patient compliance, adherence, and loss to follow up [58].

Pediatricians and adult physicians are often unprepared to identify and address the needs of their adolescent patients. Hence, there needs to be greater emphasis on adolescent-friendly health services. This includes facilities that are physically accessible, open at convenient times, require no appointment, offer free services, provide referrals for other needed services, and are staffed with clinicians who break down cultural, generational and gender-specific barriers [59]. In efforts to properly address the emerging health concerns of the world's adolescent population, UNICEF released the 2011 *State of the World's Children* report [59], which identifies and addresses the unique challenges that adolescents pose in the health care setting.

The results from this search demonstrate that patients value aspects of health care services such as relationships with providers, consistency, and open communication. These aspects of care are important to adolescents, and without taking them into consideration we cannot begin to address the issue of ART adherence.

#### 3.3.2 Mental Health

Many HIV-positive individuals have experienced severe trauma and suffer from severe depression [60]. If an HIV-positive individual has a mental disorder, especially is the case for depression [61, 62] or have experienced trauma [63], they are less likely to have adequate ART adherence and more likely to experience treatment failure [64]. This is often is the case for HIV-

positive adolescents, as many of them have lost one or both parents or primary caregivers. According to UNICEF [65], 2.5 million children lost one or both of their parents due to AIDS in 2012. A study conducted by Rotheram-Borus et al. [66] found that adolescents in the United States bereaving the loss of a parent due to HIV-related causes had more emotional distress, more contact with the criminal justice system, increased reports of depressive symptoms, and increased instances of risky sexual behaviors when compared to non-bereaving adolescents of HIV-positive parents.

The literature suggests that an individual's ability to adhere to an ART regimen can be directly affected by their mental state. Additionally, as is the case with adolescents, HIV can negatively impact the mental health status of an individual. It therefore can be suggested that there is likely a correlation between the mental state of adolescents in South Africa and their ability to properly adhere to an ART regimen.

#### 3.3.3 Social Support

Studies strongly suggest that there is a relationship between levels of social support and ART adherence among populations, such as, pregnant mothers in South Africa [67], newly diagnosed young adults in the United States [67], and adults in South Africa [68]. Social support has been identified to improve a patient's mental health status and is known to help improve ART adherence [61, 69]. The themes uncovered from the literature search demonstrate that among HIV-positive adolescents in South Africa, social support may come by way of caregivers, friends, or clinicians. Support may also come in the form of disclosing ones HIV-status to friends, family members or teachers. However, disclosing to friends or family can be a complicated process due to the high levels of HIV-related stigma and fear of potential shame [42,

43, 70]. When an adolescent is able to disclose their status to members within the community, there tends to be greater sense of support felt by the patient [44] and a lessened perception of stigma [36]. This decreased perception of stigma is linked to improved measures of mental health and adherence [71]. Additionally, patient support groups can aid in decreasing felt shame and stigma [72].

#### 3.3.4 Disclosure

Disclosure of HIV status is seen to have a positive correlation with adherence—as was observed in Cluver et al. [28], reported by the WHO [70], and found in a similar study conducted in Uganda [73]. Disclosure is of extreme importance and has implications for long-term ART adherence. It is not only important for the patient to know the name of the condition they have (HIV), but it is also important for them to have an understanding of HIV and ART [28]. In response to the data demonstrating the connection between disclosure and ART adherence, the WHO has created a recommended process for the disclosure of HIV-positive children [70]. This process takes into consideration the sensitive, and at times traumatic, nature of the disclosure process and has created recommendations to make it as effective as possible.

#### 3.4 STRENGTHS AND LIMITATIONS

There are several limitations from this literature search worth noting. There were only two readers for the initial phases of the literature search, which could have introduced certain selection biases. Additionally, based on the guidance of the Health Systems Librarian, only three databases were used to gather data, which may have excluded relevant papers published elsewhere. Lastly, the thematic review was solely based on the discretion of one reader, which may have allowed for inclusion and exclusion bias.

The strengths of this literature review should be mentioned. The extensive assistance from a qualified librarian ensured that the search terms were formulated to extract the most relevant papers. The exclusion phase did rely on two independent readers that were strict with their inclusion criteria and also discussed papers that were disagreed upon. Any papers that were continually disagreed upon or were unclear as to whether they met the criteria, were kept and read by each reader.

#### 3.5 **RECOMMENDATIONS**

The lack of relevant literature clearly demonstrates the need for more data in order to better understand the barriers that HIV-positive adolescents in South Africa face. Despite the lack of literature, there remains important themes and concepts that provide insight into the struggles of HIV-positive adolescents in care. I suggest that the data uncovered from this literature search be used to serve as the formative framework for the creation of a pilot program.

#### 4.0 PROGRAM PLAN

#### 4.1 INTRODUCTION

Findings from the literature search suggest that there is a range of barriers that hinder South African adolescents' ability to fully adhere to an antiretroviral therapy (ART) regimen. This proposal outlines the development and pilot testing of a program that aims to further identify the barriers adolescents in this setting face, as well as to actively address these barriers by ways of video-making activities. The three aims of the project are as follows:

Aim 1: Identify the top three barriers to ART adherence that HIV-positive adolescents self-report

Aim 2: Create a pilot program that addresses the identified barriers

**Aim 3:** Pilot test the program to identify if the adolescents involved were seen to have improved ART adherence, and whether this pilot can be scaled up to reach other similar communities

The program will be conducted under the umbrella of Doctors Without Borders (MSF) pediatric and adolescent treatment failure clinic [37]. This pilot uses a multi-faceted approach to improve self-efficacy, knowledge and social-support for HIV-positive adolescents on antiretroviral therapy in Khayelitsha, a large township outside of Cape Town, South Africa. Increased ART adherence will result from the creation and implementation of a video series for adolescents who are currently enrolled and receiving treatment at the treatment failure clinic.

#### 4.2 CONTEXT

The national HIV prevalence rate in South Africa is 18.8% [3]. Additionally, the national prevalence rate for people aged 15 - 24 is 7.1% [3]. The Western Cape Province is known to have the lowest prevalence rate in South Africa, at 16.9% [74], and of those who are infected in the Western Cape, 44.1% of them are under the age of 24 [74]. While the Western Cape does have the lowest prevalence rate, there appears to be a large area where there is an apparent need for intervention.

Khayelitsha, a township community located about 20 kilometers outside of the metropolitan center of Cape Town, is home to more than 400,000 people [75] and has an HIV prevalence rate of 33.1% [76]. Khayelitsha is a mixture of both formal and informal settlements—55% of the population lives in what is considered to be an informal settlement or dwelling [77]. An informal settlement, as defined by the South African Census is, "an unplanned settlement on land which has been surveyed or proclaimed as residential, consisting mainly of informal dwellings (shacks)." The definition for an informal dwelling is, "a makeshift structure not erected according to approved architectural plans"[78]. Only 62% of households in Khayelitsha have access to piped water in their home or yard, and 74% of households have a monthly income of 3,200 South African Rand or less (equivalent to about \$238USD) [77]. Within the community, 99% of people are defined as black South African, and the majority of the population is under the age of 30. Additionally, only 36% of people living in Khayelitsha 20

years or older have completed grade 12 or higher [77]. Khayelitsha is a community of migrants – 72% of the adult population above the age of 20 were born in the Eastern Cape Province [77, 79], many of whom migrated for economic purposes [80].

Khayelitsha is known to have very high rates of violence, which greatly affects the residents. Violence in this area is cited to be a constraint to self-employment, is a source of anxiety, and inhibits people from moving around at night [79]. Two of three young adults in Khayelitsha report having seen someone being hurt in their community, one in nine reported being the victim of a physical assault, and one in eight reported being a victim of armed robbery [79].

#### 4.3 TARGET POPULATION

The target population for this intervention is HIV-positive adolescents (10-19 years old) currently attending MSF's treatment failure clinic in Khayelitsha. The clinic has two general groups of patients: 1) those who have an unsuppressed viral load, are failing treatment, and are currently seeking clinical care; and 2) those who are virologically suppressed and are enrolled in a family or teen support club [37, 81]. There are 144 HIV-positive pediatric patients enrolled in MSF's treatment failure clinic [81]. While the data is unavailable about the stratification of ages within this group, based on MSF's findings, it is known that 42% of the patient population falls within the age range 10-15 [37]. If remaining ages are equally distributed, this means that there are about 87 adolescent patients in the clinic. No data is available for the exact number of adolescent patients that are suppressed and have been transferred to a teen or family support club, but based on a report from MSF [81], it can be inferred that about 35 suppressed patients

are enrolled in a teen support club. Therefore, for the purposes of this pilot program plan, the target population consists of 35 suppressed adolescents enrolled in a support club and 52 non-suppressed adolescents currently seeking care. While we do fully recognize that this is a convenience sample—and given the relationship that we have with MSF and the relationship that MSF has with the target population—it is reasonable to best determine the future impact of this program we pilot this program with a readily accessible population.

#### 4.4 PROGRAM APPROACH

In order to best engage the adolescent community, we will employ a stakeholder-engaged approach and call upon the support and relationships that many of the adolescents have with the MSF clinic staff. We will work closely with staff to gain entrée with patients and caregivers of this community in order to build their trust so that they are more likely and willing to participate in the pilot program.

#### The Ithemba Pilot Project

**Problem Statement:** Antiretroviral Therapy (ART) has changed the lives for people living with HIV, allowing them to live longer, more productive lives. However, strict adherence (measured as taking the medication 95% or more of the time) is key for suppression and to avoid medication resistance. HIV-positive adolescents living in South Africa face many different kinds of barriers that discourage and inhibit them from being adherent to their prescribed ART regimen including misinformation, lack of support, and stigma.

Inputs	Out	Outputs		Outcomes Impact		
	Activities	Participation		Short	Medium	Long
<ul> <li>A relationship with MSF and the ability to work with their patients</li> <li>52 adolescents who are currently failing treatment and are seeking treatment</li> <li>35 adolescents who were failing treatment and are not suppressed and enrolled in teen or family clubs</li> </ul>	Suppressed adolescents who are currently enrolled in a "Teen Club" or "Family Club" create a movie series to help adolescents who have not suppressed	<ul> <li>HIV positive teens from MSF's treatment failure clinic – both those who are currently suppressed and those who are not</li> <li>Primary care givers to adolescents enrolled in the clinic</li> </ul>		<ul> <li>(12 Months)</li> <li>3 focus groups are held with the teen club participants to identify barriers and themes for the film</li> <li>Patients participate in the Ithemba Pilot Project activities – i.e. create script for the short-films, film, edit, etc.</li> <li>Baseline assessments are completed for both suppressed and non-suppressed patients</li> <li>Hire Project Manager, Project Assistant and Creative Director</li> <li>Hold once-weekly Club meetings</li> <li>Complete one 10-minute movie</li> </ul>	<ul> <li>(24 Months)</li> <li>Two more 10-minute movie to be shown in clinic appointments completed</li> <li>Movie series is shown at clinic appointments</li> <li>Increase in number of virologically suppressed adolescents</li> <li>Self-reported measures of ART adherence increase in by in both suppressed adolescents</li> <li>Chart review reports affirm improved ART adherence</li> </ul>	<ul> <li>(36 Months)</li> <li>Continued increase of number of suppressed adolescent patients</li> <li>Self-reported measures of adherence continue to increase</li> <li>Chart review affirm reported measures of adherence on a virological level</li> <li>Patients report greater felt caregiver and peer support</li> <li>Majority of in-clinic patients are shown the video series</li> <li>Evaluation is done to determine impact and scalability</li> </ul>
Assumptions			]	External Factors		
<ul> <li>Lack of adherence is due to a lack of understanding about the barriers that HIV positive adolescents in Khayelitsha face. With a video series that identifies these barriers as well as provides a manageable "solution" to them, ART adherence will increase for the unsuppressed patients</li> <li>Through the video series, the caregivers will gain a better understanding to the difficulties</li> </ul>				Stigma     Unsupportive family     Lack of disclosure     Previous negative e     Erequent travel/min	/caregivers xperiences in clinic settings ration	
<ul> <li>that their child can face and will be more able to support them</li> <li>HIV-positive adolescents that are currently suppressed and take part in the Ithemba Project have a greater responsibility, sense of accountability and are now role models and therefore have a greater incentive to continue to adhere</li> </ul>				- includit adverning		

Figure 4. Pilot Program Logic Model

# 4.4.1 Aim 1: Identify the top three barriers to ART adherence that HIV-positive adolescents self-report

Considering the lack of data available identifying the barriers that HIV-positive adolescents in South Africa face, and accounting for the unique context that a setting such as Khayelitsha presents, the first aim of the pilot program is to identify barriers that are most relevant for the adolescents living in this community. This will be accomplished by way of focus groups: three focus groups will be conducted with 5-7 adolescents from the support clubs. The aim of the barriers they faced before they were fully adherent to their ART regimen and what helped them to overcome said barriers. All of the focus groups will be audio recorded and then coded and analyzed in the ATLAS.ti software system. The results will be analyzed to determine the top three barriers identified by the adolescents; these three barriers will then be the themes for the movies that will be created.

#### 4.4.2 Aim 2: Create a pilot program that addresses the three identified barriers

A new club, called the *Ithemba Club* (Xhosa for hope), will be established for adolescents from MSF's treatment failure clinic who have achieved suppression and no longer need to seek regular care. The primary function of the *Ithemba Club* is to create three short films to be shown in the clinic to those who are currently not suppressed to aid in their adherence efforts. The filmmaking process will occur in the once-weekly club meetings, held in the clinics meeting rooms, under the supervision of the program's Creative Director. The club members will be asked to work

together to create a script for the each of the films, with the goal of addressing how the identified barriers manifest themselves in their own lives and some practical problem solving skills that can be used to overcome these barriers. The club members will also be responsible for recording and editing the film. The videos will be shown to the patients during their regular clinic appointments. This activity has three aims:

- Aim 2a: Provide the non-suppressed adolescents with a tool that can help them to identify and address barriers that are interfering with their adherence efforts. The ability to identify barriers and solutions is in line with the evidence based intervention, Managed Problem Solving (MAPS), which is known to help HIV-positive adults achieve higher rates of adherence and maintain an undetectable viral load [82]. We believe that a video is a good platform for this pilot because a previous study, conducted with HIV-positive adults in Soweto, South Africa [83], demonstrated that after viewing HIV management related videos patients were more likely to have improved understanding and knowledge of HIV and ART, which is a key factor for adequate adherence to be achieved. A different program, that used a story line based intervention with a relatable main character, demonstrated that an intervention using a multimedia approach could help improve adherence, treatment knowledge, and parent-child communication ability for HIV-positive adolescents in South Africa [36].
- <u>Aim 2b</u>: Provide the non-suppressed adolescents with a vision of their community, and provide peer-support by presenting other people their age experiencing similar difficult situations. Peer Support is recognized by the CDC as an evidence-based intervention and best practice for HIV prevention [82]. A study in Paris, France

measured significant improvement in HIV-positive adolescent ART adherence, decreased negative perceptions of treatment as well as a higher number of patients with an undetectable viral load after being a member of a peer-support group [84].

• <u>Aim 2c</u>: Encourage suppressed adolescents to fight medication fatigue and help them to continue adhering to their medication by providing them with a platform to discuss the difficulties they face, ideas on how to counteract difficulties, and training them to play a peer-supporter role to non-suppressed adolescents. Research shows that a peer-support approach can not only provide support for the patient, but also for the supporter, as shown in studies with chronically ill patients [85]. Within the realm of HIV, a qualitative investigation was conducted to identify the impact that peer-support has on the supporters. The findings suggested that being a peer-supporter created a greater sense of social acceptance, reciprocal support, as well as greater personal growth and empowerment [86].

#### 4.4.3 Aim 3: Pilot test the program to determine the program's impact on adherence

In efforts to determine whether this pilot program would be a feasible intervention in helping improve the adherence efforts for HIV-positive adolescents in South Africa, as well as to determine the scalability of this approach, four different data collection tools that will be used:

- 1. Baseline questionnaire
- 2. Follow-up questionnaire
- 3. Biologic data
- 4. Participant questionnaire

#### Baseline and Follow-Up Questionnaires

These two questionnaires will be conducted at the onset and throughout the implementation of the pilot. The primary objective of this pilot is to determine ART adherence for adolescents who currently, or have previously, sought care from MSF's treatment failure clinic; and to determine how participation in the pilot affects levels of adherence. This study has two sides to it – we wish to examine how active participation (i.e. assisting in the movie creation) in the pilot affects adherence, as well as how being a "consumer" (i.e. patients in the clinic who watch the movie) of the project affects adherence.

Data will then be gathered to identify how the project negatively or positively affects the following: 1) Perception of care 2) Mental health 3) Measures of support 4) Caregiver support 5) Treatment knowledge 6) Perceived stigma. The following are the data collection objectives for the project accompanied by their validated measures.

Study Objective	Validated Measurement Used <sup>2</sup>	
Level of ART	Pediatric AID Clinical Trials	
Adherence	Group[87]	
Paraantian of Cara	Attitudes toward HIV Health Care	
Perception of Care	Provider scale (AHHCP) [88]	
Vouth Montal Haalth	Strengths and Difficulties	
I outil Mental Health	Questionnaire[89]	
Measures of Social	Social Support Survey[00]	
Support	Social Support Survey[90]	
Caregiver Support	Family Support Scale [91]	
Youth HIV Treatment	HIV Treatment Knowledge Scale[02]	
Knowledge	niv freatment knowledge Scale[92]	
Perceived Stigma	HIV Stigma Scale[93]	

Figure 5. Validated Evaluation Measures

<sup>&</sup>lt;sup>2</sup> Adapted from Bhana et al. [5]

#### Biologic Data

The biologic data consists of the results from bloods tests that measure a patients' viral load and CD4 count. Based on the South African guidelines [94], adolescents who are not suppressed are recommended to send their blood for testing every two months, and adolescents who are suppressed are recommended to send their blood in for testing every six months. In order to best compare the groups (those receiving the intervention vs. those not) we have decided to take the blood test of those involved in the pilot once every two months. The results from the tests are put into the patients' medical chart and will be retrieved on a monthly basis by the Project Assistant. Collecting the biologic data is an important component to determine the biological impact that this program is having on the participants as well as to assess the validity of the self-reported adherence questionnaire.

#### Participant Assessment

The aim of this questionnaire is to ensure that the pilot is catering well to the target population, as to give us an idea if this is a program that can be scaled to reach other communities. This assessment will be conducted on two levels: firstly, for those who participated in the movie-making project, and secondly, for those in the clinics who are watching the movies.

The following are sample questions participants will be asked:

- To the movie-making participants:
  - What did you enjoy about making the movie?
  - What didn't you enjoy about making the movie?
  - Do you think that the topics addressed in the movies were relevant to patients in the clinic?
  - What issues, if any, do you wish the movies addressed?

- To the in-clinic patients watching the movie:
  - Were the movies relevant to your life?
  - o Did you learn any good problem-solving skills from the movie? If so, what?
  - Are there topics that you wish were covered in the movies?
  - Were there any changes you would make to the movies to make them better?

### 4.4.4 Timeline

Month	Activities
	Project Manager creates and tests evaluation material (i.e. baseline and follow-
	up questionnaire, virological reporting sheet)
	• Project manager hires and trains assisting personnel (Project Assistant, Creative
	Director, Data Analyst)
	<ul> <li>Nurses are trained on administering data collection tools - including</li> </ul>
1-5	questionnaire and biologic chart data
	• Conduct three focus groups, analyze data and determine top three barriers to
	adherence identified
	Collect baseline data
	• Begin activities of the <i>Ithemba Club</i> –adolescents meet once a week to create
	(write, product, edit, etc.) short films addressing barriers to adherence
	Complete three short-films
6-18	<ul> <li>Begin showing films in clinic appointments</li> </ul>
	<ul> <li>Complete participant assessments for those who participated in making the</li> </ul>
	films
	<ul> <li>Continue to screen movie series in clinic appointments</li> </ul>
10-36	Complete midpoint evaluation
17-30	• Complete participant assessment for those who viewed short films in the clinic
	Complete final evaluation

Figure 6. Pilot Program Timeline

### 4.4.5 Budget

The following numbers were assessed using an estimation of the standard salaries for individuals working in similar positions living in South Africa<sup>3</sup>. All numbers were converted from the South African Rand to the US Dollar (based on the exchange rate of 1USD = 13.94 Rand).

Supplies	Personnel	Percent Full-Time Effort	Total Costs (USD)
-	Project Manger Annual Salary:	25.43% FTE (Over 36 months)	\$16,480.38
-	Project Assistant Annual Salary: \$18,000*	3.99% FTE (Over 36 months)	\$2,154.81
-	Creative Director Annual Salary: \$16,800*	7.50% FTE (Over 12 months)	\$1,260.00
-	Data Analyst (1) Annual Salary: \$24,000*	1.68% FTE (Twice during project)	\$403.85
Printer (\$500/printer)	-	-	\$500
Paper for Printer (20 cases) (\$25/case)	-	-	\$500
Ink for Printer (10) \$90/case	-	-	\$900
Laptops (2) \$400/laptop	-	-	\$400
Audio Recording Device (1)	-	-	\$30
ATLAS.ti Software (1)	-	-	\$1,300
Misc. Supplies Pens, pencils, envelopes, etc.	-	-	\$200
Total Personnel Costs	\$20,299.04		
Total Supplies Costs	\$3,830.00		
Total Costs	\$24,129.04		

## Table 1. Pilot Program Budget

<sup>&</sup>lt;sup>3</sup> Numbers determined based on information from www.mywage.co.za. Part of the Wage Indicator Foundation

#### 4.4.6 Conclusion

Based on prior research [36, 82-84] we fully believe this intervention has the ability to improve adherence levels for HIV-positive adolescents attending MSF's treatment failure clinic in Khayelitsha, South Africa. This pilot will help us to determine if this approach is a feasible way to reach this population, improve adherence, and determine if this program can be scaled to reach other communities throughout the region. This pilot program fills a gap in the literature and is an innovated applied research approach. With this implementation of this pilot we will be able to better understand the daily struggles that HIV-positive adolescents face with regards to their adherence efforts all while addressing and aiming to overcome the identified barriers.

## APPENDIX A: SEARCH STRATEGY FOR PUBMED, PSYCINFO AND GLOBAL

## HEALTH DATABASES

Base Term	Search Term
Antiretroviral Therapy	PubMed ("Anti-HIV Agents/therapeutic use"[Mesh]) OR ("Antiretroviral Therapy, Highly Active"[Mesh]) OR Antiretroviral therapy[tiab] OR HAART[tiab] OR ART[tiab] OR ARV[tiab] OR ARVs[tiab] OR "Anti-HIV Agent"[tiab] OR "Anti-HIV Agents"[tiab] OR "HIV treatment"[tiab] OR "HIV treatments"[tiab] OR Antiretroviral therapy[ot] OR HAART[ot] OR ART[ot] OR ARV[ot] OR ARVs[ot] OR "Anti-HIV Agent"[ot] OR "Anti-HIV Agents"[ot] OR "HIV treatment"[ot] OR "zidovudine"[MeSH Terms] OR Zidovudine[tiab] OR AZT[tiab] OR Zidovudine[ot] OR AZT[ot]
	<b>PsycINFO</b> (exp zidovudine/ or exp antiviral drugs/ or exp aids/ or exp hiv/ or Antiretroviral therapy.ti,ab,hw. or HAART.ti,ab,hw. or ART.ti,ab,hw. or ARV.ti,ab,hw. or ARVs.ti,ab,hw. or "Anti-HIV Agent".ti,ab,hw. or "Anti-HIV Agents".ti,ab,hw. or "HIV treatment".ti,ab,hw. or "HIV treatments".ti,ab. or Zidovudine.ti,ab,hw. or AZT.ti,ab,hw.)
	<b>Global Health</b> (exp zidovudine/ or exp aids/ or exp hiv/ or Antiretroviral therapy.ti,ab,hw. or HAART.ti,ab,hw. or ART.ti,ab,hw. or ARV.ti,ab,hw. or ARVs.ti,ab,hw. or "Anti-HIV Agent".ti,ab,hw. or "Anti- HIV Agents".ti,ab,hw. or "HIV treatment".ti,ab,hw. or "HIV treatments".ti,ab,hw. or Zidovudine.ti,ab,hw. or AZT.ti,ab,hw. or exp antiviral agents/ or exp treatment/ or exp antiretroviral agents or exp highly active antiretroviral therapy/ or exp multiple drug therapy/ or exp combination therapy/ or exp proteinase inhibitors/ or exp medical treatment)
Medication Adherence	<b>PubMed</b> (Medication adherence[Mesh] OR patient compliance [Mesh] OR patient acceptance of health care[Mesh]) OR (medication adherence[ot] OR medication nonadherence[ot] OR medication noncompliance[ot] OR medication non-compliance[ot] OR patient compliance[ot] OR treatment refusal[ot] OR patient acceptance of health care[ot] OR medication compliance[ot] OR retention[ot] OR loss to follow up[ot] OR "adolescent adherence" OR (medication adherence[tiab]) OR (adherence[All Fields] AND medication[tiab]) OR adherence OR medication nonadherence[tiab] OR medication noncompliance[tiab] OR medication non-compliance[tiab] OR patient compliance[tiab] OR treatment refusal[tiab] OR patient acceptance of health care[tiab] OR treatment failure OR medication compliance[tiab] OR retention[tiab] OR loss to follow up[tiab]
	<b>PsycINFO</b> (exp treatment compliance/ or exp intervention/ or exp client attitudes/ or patients.mp. or medication adherence.hw,ti,ab. or medication nonadherence.hw,ti,ab. or medication noncompliance.hw,ti,ab. or medication non-compliance.hw,ti,ab. or patient compliance.hw,ti,ab. or treatment refusal.hw,ti,ab. or patient acceptance of health care.hw,ti,ab. or medication compliance.hw,ti,ab. or retention.hw,ti,ab. or loss to follow up.hw,ti,ab. or "adolescent

	adherence".af. or (adherence.af. and medication.ti,ab.) or adherence.af. or exp treatment outcomes/ or ("treatment" and "failure").af. or "treatment failure".af.)
	Global Health
	(exp intervention/ or patients.mp. or medication adherence.hw,ti,ab. or medication nonadherence.hw,ti,ab. or medication noncompliance.hw,ti,ab. or medication non- compliance.hw,ti,ab. or patient compliance.hw,ti,ab. or treatment refusal.hw,ti,ab. or patient acceptance of health care.hw,ti,ab. or medication compliance.hw,ti,ab. or retention.hw,ti,ab. or loss to follow up.hw,ti,ab. or "adolescent adherence".af. or (adherence.af. and medication.ti,ab.) or adherence.af. or ("treatment" and "failure").af. or "treatment failure".af. OR exp patient compliance)
	PubMed
HIV/AIDS	(HIV[tiab] OR HIV[ot]) OR (HIV/AIDS) OR (AIDS[mesh] OR AIDS[tiab] OR AIDS[ot]) OR (human immunodeficiency virus[mesh] OR human immunodeficiency virus[tiab] OR human immunodeficiency virus[ot]) OR (acquired immunodeficiency syndrome[tiab] OR acquired immunodeficiency syndrome[ot]) OR (HIV-2[tiab] OR HIV- 2[ot]) OR (HIV-1[tiab] OR HIV- 1[ot]) OR (HIV infections [Mesh])
	<b>PsycINFO</b> (HIV.hw,ti,ab. or exp HIV/ or AIDS.ti,ab,hw. or human immunodeficiency virus.ti,ab,hw. or acquired immunodeficiency syndrome.ti,ab,hw. or HIV-2.ti,ab,hw. or HIV-1.ti,ab,hw.)
	Global Health
	(HIV.ti,ab,hw. or exp HIV/ or AIDS.ti,ab,hw. or human immunodeficiency virus.ti,ab,hw. or acquired immunodeficiency syndrome.ti,ab,hw. or HIV-2.ti,ab,hw. or HIV-1.ti,ab,hw.)
Adolescent	PubMed (youth[ot] OR youth[tiab] OR youths[ot] OR youths[tiab]) OR (teen[ot] OR teen[tiab] OR teens[ot] OR teens[tiab]) OR (adolescent[tiab] OR adolescent[ot] OR "adolescent"[MeSH Terms] OR adolescents[tiab] OR adolescents[ot]
	PeveINFO
	(exp adolescent attitudes/ or adolescent.mp. or youth.ti,ab,hw. or youths.hw,ti,ab. or teen.hw,ti,ab. or teens.hw,ti,ab. or adolescent.ti,ab,hw. or adolescents.ti,ab,hw.)
	<b>Global Health</b> (exp adolescents/ or adolescent.mp. or youth.hw,ti,ab. or youths.hw,ti,ab. or teen.hw,ti,ab. or teens.hw,ti,ab. or adolescent.hw,ti,ab. or adolescents.hw,ti,ab.)
	PubMed
South Africa	South Africa[tiab] OR South Africa[ot]
	<b>PsycINFO</b> "South Africa".mp.
	Global Health "South Africa".mp.

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## APPENDIX B: EXAMPLE INITIAL SORTING GUIDE - PSYCINFO

Keep/Pass	Pass – Reasoning	Article Info (n=47)	Abstract	
[Readers fill in their decision following reading the article information and abstract]	[If readers decide to pass, they present their reaoning]	Amirfar, S., et al. (2006). "Modeling the Impact of a Partially Effective HIV Vaccine on HIV Infection and Death Among Women and Infants in South Africa." JAIDS Journal of Acquired Immune Deficiency Syndromes 43(2): 219-225.	Objective: To assess the potential impact over 10 years of a partially effective HIV vaccine in a cohort of 15-year-old adolescent girls in South Africa in terms of HIV infections and deaths prevented in mothers and infants. Methods: A computer simulation was constructed using a population of all 15-year-old adolescent girls in South Africa followed for 10 years	
		Armistead, L., et al. (2014). "Preliminary results from a family-based HIV prevention intervention for South African youth." Health Psychology 33(7): 668-676.	Objectives: Approximately 5.6 million South Africans are living with human immunodeficiency virus (HIV; UNAIDS, 2010). Prevalence among Black adolescents and young adults is particularly alarming. This pilot study of an HIV preventive intervention targeting South African youth contributes to the growing body of research on culturally competent family-based interventions. Method: A total of 99 parent-child dyads were enrolled in an experimental repeated measures study, using a wait-list control group	
		Balfour, L., et al. (2013). "HIV prevention in action on the football field: The Whizzkids United program in South Africa." AIDS and Behavior 17(6): 2045-2052.	The Africaid Trust is a grassroots South African non-profit organization that engages youth in HIV prevention by harnessing the popularity of football (i.e. soccer). WhizzKids United, the organization's primary program, operates a 12-week program in elementary schools in Pietermaritzburg, South Africa, which aims to impart knowledge and life skills critical to HIV prevention. The goal of this research was to compare elementary school youth who received the program to youth who	

## APPENDIX C: EXAMPLE READING GUIDE FOR ARTICLES

Article info	Is it a study?	What barriers are addressed?	Keep/Pass	Notes	Citations to consider
Hornschuh, S., et al. (2014). "Experiences of HIV-positive adolescents and young adults in care in Soweto, South Africa." Journal of HIV/AIDS & Social Services 13(4): 420-435.					
Li, R., et al. (2010). "Positive futures: A qualitative study on the needs of adolescents on antiretroviral therapy in South Africa." AIDS Care 22(6): 751-758.					

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