Psychological Distress and Adherence to Anti-retro Viral Treatment among HIV-infected Adolescents in Uganda.

by

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Dedication

I would like to dedicate this dissertation to my dear parents for they have taught me to look beyond myself and think of how to make this world a better place.

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Abstract

Psychological distress among HIV-infected adolescent has been associated with non-adherence to anti-retroviral therapy (ART), leading to increased risk for AIDS morbidity and mortality. However, data on prevalence and correlates of psychological distress in low-income countries are scarce, and efforts to establish the nature, prevalence, and presentation of psychological distress in these settings are hindered by the lack of culturally relevant assessment tools. The purpose of this study was to develop and test a measure for psychological distress among HIV-infected adolescents aged 12-19 years in Uganda, generate knowledge on the predictors of psychological distress in this population, and assess the impact of psychological distress on adherence to ART, net of mitigating psychosocial resources.

Using mixed method approaches and a sample of 511 HIV-infected adolescents, a 25-item scale, with six scales was developed and tested. The subscales were labeled as: anhedonia, depressive-anxiety, isolation, suicidal ideation, sleep problems, and somatization. Reliability of the subscales was adequate, with Cronbach's alpha ranging from 0.615 to 0.732 for the subscales, and 0.89 for entire scale. Confirmatory factor analysis indicated that the scale structure was consistent with the data with RMSEA < 1.0, and CFI and TLI > 0.90. An exploratory factor analysis supported use of a composite global psychological distress score. Psychological distress was positively associated with negative events, stigma, on-going worries, poverty-related hardships, and HIV-related concerns, and negatively associated with psychosocial resources such as spirituality, coping, satisfaction with social support. Psychosocial resources partially mediated

the effects of stressors on psychological distress. In the logistic regression analyses, psychological distress was associated with 75%, 63% and 79% increase in odds for non-adherence using self-reported missed pills, following medical regimen and visual analog scale measures, respectively, and 30% increase in the odds for non-adherence in the Structural Equation Model (SEM) analyses. In these analyses, psychosocial resources partially mediated the effect of psychological distress on non-adherence. Non-adherence was positively associated with frequency of praying privately and negatively associated with satisfaction with social support. The findings in this study underscore the need for interventions to prevent or reduce psychological distress among HIV-infected adolescents, thereby improving adherence to ART.

Chapter 1

Introduction

Overview of HIV/AIDS Epidemic in Sub-Saharan Africa

The Human Immune-deficiency Virus/Acquired Immune-Deficiency Syndrome (HIV/AIDS) epidemic remains a major public health challenge in sub-Saharan Africa: of the estimated 35.3 million people living with HIV/AIDS worldwide, 69% were living in sub-Saharan Africa in 2012 (UNAIDS, 2013b). The aggregate number of new infections worldwide declined from 3.4 (3.1 – 3.7) million infections in 2001 to 2.3 (1.9 – 2.7) million infections in 2012 (33% decline) but the incidence of HIV in sub-Saharan Africa remains high; in fact, 69.6% (1.6 million) of all new infections in 2012 occurred in sub-Saharan Africa (UNAIDS, 2013b). Given that only 12% of the global population lives in sub-Saharan Africa, these statistics indicate that this region is disproportionately over-burdened by HIV/AIDS.

The HIV/AIDS epidemic has been devastating, globally, but most especially for sub-Saharan Africa. At the macro-level, the HIV epidemic has slowed economic growth and development in Africa by depleting the human resource capital (Dixon, McDonald, & Roberts, 2002) and erasing earlier gains life expectancy (Piot, Bartos, Ghys, Walker, & Schwartländer, 2001; Topouzis & HIV/AIDS, 2003; World Health Organization, 2014). At the peak of the HIV/AIDS epidemic (in 1990s), AIDS was responsible for one in five deaths in sub-Saharan Africa; prevalence was highest among young men and women in

their most productive life, including those in the most educated and skilled sectors, as well as women of child bearing age (Danziger, 1994; Dixon et al., 2002; Piot et al., 2001). The ensuing erosion in human capacity has crippled delivery of services in sub-Saharan Africa, particularly, in the health, education, agricultural and manufacturing sectors (Case & Paxson, 2011; Dixon et al., 2002). The HIV epidemic has also transformed demographic patterns in sub-Saharan Africa as evidenced by the increased number of female- and child- headed households (Ayieko, 1997; Foster, Makufa, Drew, & Kralovec, 1997; Foster & Williamson, 2000), increased rates of household dissolution (Foster & Williamson, 2000; Hosegood, McGrath, Herbst, & Timæus, 2004; Wagner, Ryan, Huynh, Kityo, & Mugyenyi, 2011), and household poverty with AIDS affected households (Bachmann & Booysen, 2003), and expanding number of AIDS- orphaned children (Foster & Williamson, 2000; UNAIDS, 2013b).

Anti-retroviral therapy

Anti-retroviral therapy (ART) has been instrumental in reducing HIV/AIDS mortality and morbidity worldwide (Baker et al., 2008; Fielden et al., 2008; Lima et al., 2009; UNAIDS, 2013b; World Health Organization, 2003), and transforming HIV/AIDS from a death sentence into a chronic illness. Since 1996, ART has averted approximately 6.6 million deaths worldwide, including 5.5 million deaths in low- and middle-income countries (UNAIDS, 2013b). ART has also contributed to the reduction in HIV transmission, at both individual and population levels (Cardo et al., 1997; Cohen et al., 2011; Donnell et al., 2010; Smith et al., 2005). At the individual level, ART reduced mother-to-child transmission of HIV (Guay et al., 1999; Hoffman et al., 2010; Siegfried, van der Merwe, Brocklehurst, & Sint, 2011; Thorne & Newell, 2004)

and HIV transmission within discordant couples (Attia, Egger, Müller, Zwahlen, & Low, 2009; Reynolds et al., 2011). At the population level, ART mediated virologic suppression and reduced infectiousness has been associated with a decrease in HIV transmission within communities (Das et al., 2010; Montaner et al., 2010; Tanser, Bärnighausen, Grapsa, Zaidi, & Newell, 2013). By reducing mortality and morbidity, ART has played a critical role in reversing the economic impact of HIV by restoring productivity (Baker et al., 2008; Lima et al., 2009). It has also reduced strain of over-burdened health care system in sub-Saharan Africa, and continues to play a major role in curbing the increasing number of AIDS-orphaned children (Anema et al., 2011).

HIV/AIDS in Uganda

HIV/AIDS was first identified in Uganda in the early 1980s along the shores of Lake Victoria: the first case of AIDS was diagnosed in 1982. At the start of the epidemic, HIV was largely concentrated within urban and semi-urban areas, and among the wealth, especially those involved in transnational trade activities. In 1992, the HIV prevalence rate among pregnant women attending antenatal care was 18.3% in rural areas and 30% in urban areas. HIV prevalence increases with wealth: adults in the lower wealth quintiles have prevalence below the national average, while adults in the fourth and fifth wealth quintiles have prevalence above the national average (Uganda AIDS Commission, 2012).

The HIV epidemic in Uganda is generalized, and heterosexual transmission accounts for 84% of the HIV infections among adults aged 15 – 49 years (Uganda AIDS Commission, 2012). Among children aged 0 – 14 years, the transmission is largely through mother-to-child transmission (MTCT), which accounts for 14% of the overall

number of new HIV infections in Uganda: infected blood products account for additional 1% of the transmission (Uganda AIDS Commission, 2012).

Uganda has been one of two countries with remarkable HIV success stories, having succeeded in reducing the HIV prevalence rate from close to 27.5% in the early 1990s to less than 5.2% by the end of 2001 (Uganda AIDS Commission, 2012). Uganda's success in reducing prevalence has been largely attributed to implementation of behavioral changes strategies such as the ABC campaign (Abstain, Be-Faithful and use a Condom) (Cohen, 2003); Stoneburner and Low-Beer (2004). However, the high-rates of AIDS mortality prior to introduction of ART also contributed significantly to lowering HIV-prevalence in Uganda (Hogle, Green, Nantulya, Stoneburner, & Stover, 2002). Anti-retroviral therapy (ART) has been available in Uganda since 2004; these programs are largely supported by Global Fund and Presidential Emergency Plan for AIDS Relief (PEPFAR).

Currently, 1.5 million people are living with HIV in Uganda; of these, 1.4 million are adults aged 15-49 years and 190,000 are children aged 0 – 14 years. Females account for 57% of all HIV-infected persons in Uganda, and prevalence is higher among married women compared to unmarried women (Uganda AIDS Commission, 2012). The national prevalence rate of HIV among adults aged 15 – 49 years is 7.2% (UNAIDS, 2013b). In 2012, 124,000 people are newly infected with HIV (Uganda AIDS Commission, 2012).

AIDS mortality remains high in Uganda: approximately 63,000 people die of AIDS-related complications annually (Uganda AIDS Commission, 2012; UNAIDS, 2013b), and 1.1 million children have been orphaned by AIDS (UNAIDS, 2013b). Among adults aged 15 – 49 years, HIV prevalence is higher among women (7.7%)

compared to men (5.6%) (Uganda AIDS Commission, 2012). HIV prevalence increases with age, that is 2% among youth aged 15 – 19 years and 10.3% among adults aged 35-39 years: this is characteristic of a maturing epidemic (Uganda AIDS Commission, 2012).

Approximately 290,971 people were enrolled on ART in 2011, representing 52% coverage for all eligible persons (Uganda AIDS Commission, 2012). However, a national survey conducted in 2011 reported an increase in HIV prevalence, suggesting that demand for ART will increase in the future. The increase in HIV prevalence has been attributed to the government's shift towards abstinence-only prevention programs and increased population complacency towards safe sex and greater access to ART, which has reduced fear and urgency to test for HIV and increased the likelihood of engaging in risky behaviors (Uganda AIDS Commission, 2012).

The risk factors associated with increased risk for HIV infection in Uganda are varied, and include behavioral, social and structural factors. The behavioral risk factors include: multiple partnerships, inconsistent condom use, transactional sex, alcohol and substance abuse, and high burden of sexual transmitted infections, especially Herpes Simplex Virus (HSV-2) (Uganda AIDS Commission, 2012). HIV infection has also been associated with socio-economic risk factors such as poverty and wealth, economic migration, and cultural practices such as widow inheritance, polygamy, gender-based violence, and gender inequalities and norms have been associated with increased risk of HIV infection. The structural factors associated with risk infection include: inequitable access to health services, stigma and discrimination, and urban residence (Uganda AIDS Commission, 2012).

The HIV/AIDS Epidemic among Young People

Globally, young people aged 10 – 24 years have emerged as one of the most vulnerable populations to HIV/AIDS (UNAIDS, 2012; World Health Organization, 2010). Approximately 5.4 million young people were living with HIV in 2012, and young people also accounted for 41% of all new HIV infections in 2012 (UNAIDS, 2013b). The prevalence of HIV among young people varies with age and sex. Of the 5.4 million youth living with HIV in 2012, 17% were aged 10- 14 years, 22% were aged 15 – 19 years, and 61% were aged 20 – 24 years (UNAIDS, 2013b). Additionally, sex/gender disparities vary globally: in low-income countries, HIV prevalence is twice as high in females compared males, while in Europe and North America is HIV epidemic is predominately affects males, especially young men who have sex with men (YMSM) (Center for Disease Control, 2012; UNAIDS, 2013b).

Currently, 2.1 million adolescents (10 – 19 years) are living with HIV in low- and middle-income countries (UNAIDS, 2013b). In sub-Saharan Africa, HIV prevalence among young people reduced by 42% between 2001 and 2012 (UNAIDS, 2013b). Sustained progress in scaling up access to prevention of mother-to-child transmission (PMTCT) services has dramatically reduced the number of new infections among children (vertical infections), contributing to the decline in HIV prevalence among young people: the annual number of new infections among children declined by 52% worldwide between 2001 and 2012 (UNAIDS, 2013b). However, these aggregate statistics mask vast disparities in pediatric HIV infections, between low-income and high-income countries, and within low-income countries. New HIV infections among children in high-income countries are almost non-existent, while some 260,000 new infections occurred among

children in low and middle-income countries in 2012 (UNAIDS, 2013a). In sub-Saharan Africa, gross disparities in the number of new infections persist due to differences in HIV prevalence between the countries, and to marked variations in coverage for PMTCT services. For example, annual number of new infections among children declined by 50% or more in seven countries – Bostwana, Ethiopia, Ghana, Malawi, Namibia, Zambia and Zimbabwe- where coverage of PMTCT service was very high, but progress in has been slower in other countries, including Uganda (UNAIDS, 2013b), where coverage for PMTCT continues to lag behind yet prevalence is very high.

Beyond the perinatal period, young people remain vulnerable to HIV (horizontal transmission) due to a host of social, political, biological and economic factors (UNFPA, 2014; World Health Organization & Unicef, 2008), which curtail their access to comprehensive information and health services, and engender risky sexual practices that increase their vulnerability to HIV/AIDS. Among young people, the increase in HIV prevalence among young people also occurred in tandem with the rising incidence of other sexually transmitted infections (UNFPA, 2014), which heighten their risk of acquiring and transmitting HIV (Bonell, Weatherburn, & Hickson, 2000; Fleming & Wasserheit, 1999; Galvin & Cohen, 2004; Grosskurth et al., 1995). However, access to comprehensive sexual reproductive health services for young people in sub-Saharan Africa remains very limited (Kiapi-Iwa & Hart, 2004; Mbizvo & Zaidi, 2010; Shaw, 2009), further increasing young people's vulnerability to poor sexual and reproductive health outcomes, including HIV/AIDS.

In Uganda, the number of HIV-infected adolescents (10 – 19 years) remains unknown, because epidemiological data are not disaggregated by age group. However,

it's estimated that approximately 190,000 children aged 0 – 14 years age are currently living with HIV. HIV prevalence among youth (15 – 24 years) remains also high: 4.0% among females and 3.4% among males (UNAIDS, 2013b), and new HIV infections among children continue to occur, as only 72% of HIV-infected pregnant women receive ART for PMTCT (UNAIDS, 2013b). Altogether, these statistics indicate that the challenge of HIV among adolescents in Uganda will persist for a while, especially as the increasing prevalence of HIV within this population increases the risk of exposure to HIV among adolescents.

The Impact of HIV/AIDS on Adolescents

Approximately 90% of adolescents living with HIV in sub-Saharan Africa have been infected through mother-to-child transmission of HIV (Earls, Raviola, & Carlson, 2008). Prior to introduction of ART, children perinatally-infected with HIV were not expected to survive through their first decade, but the expanding coverage for anti-retroviral therapy has promoted survival of children perinatally-infected with HIV/AIDS. The growing number of perinatally-infected children maturing into adolescence and young adulthood coupled with the increasing numbers of adolescents behaviorally-infected with HIV- presents unprecedented challenges across sub-Saharan Africa. The continent was not prepared to address the evolving and diverse needs of this population. Nonetheless, fulfilling the needs of these adolescents requires an in-depth understanding of the determinants and barriers to wellbeing within this population.

HIV/AIDS affects every dimension of an adolescent's health – physical, social, emotional, and spiritual wellbeing. As Brown, Lourie and Pao (2000) noted, one of the challenges of understanding HIV in children and adolescents is determining which of the

biological, psychological, neuropsychiatric and social factors is most relevant for wellbeing at any given moment (Brown, Lourie, & Pao, 2000). In this section, we explore the developmental, neuropsychiatric and psychological challenges that impact wellbeing among HIV-infected adolescents.

Developmental challenges

Arnett (1999) describes Stanley adolescence as a period of great emotional upheaval and stress characterized by physiological changes, conflict with parents, mood disruptions, risk-taking, and identity development (Arnett, 1999). This transition from childhood to adulthood involves changes in the physical, biological, cognitive, social, and emotional domains of an adolescent's life. The adolescent experiences rapid physical growth, develops secondary sexual characteristics, cultivates a personal and sexual identity as well as intimate relationships, and begins to transition towards autonomy and independence from parents (Arnett, 1999; Paul & White, 1990; Tanner, 1962).

Perinatally-infected adolescents must negotiate the complexities of normal adolescent development such as identity development, romantic relationships and sexual activity in the context of a chronic and highly stigmatized disease, and in due consideration of issues such as disclosure, HIV transmission, and adherence to medications (Battles & Wiener, 2002; DeLaMora, Aledort, & Stavola, 2006), all of which could impair their social and psychological wellbeing. HIV infection impairs linear growth and causes delayed sexual maturation among perinatally-infected adolescents (Buchacz et al., 2003; de Martino et al., 2001; Mahoney, Donfield, Howard, Kaufman, &

Gertner, 1999; Pozo & Argente, 2002), which could further exacerbate adolescent's feelings of being different and unwell, leading to psychological distress.

Adolescent's premature cognitive and decision-making skills impact their decision-making and strategies for coping with HIV infection and its associated self-management demands. Preventive action requires an appreciation of future consequences (Friedman & Litt, 1987), but adolescent's poor estimation (or lack of estimation altogether) of their own risks and the apparent need for immediate pleasure or gratification (Arnett, 1992; Haugaard, 2000) limits their ability to make rational assessments on the consequences of their behaviors. For example, in a review on predictors of youth sexual behaviors, Diamond and Savin-Williams (2011) found that youth's ability and willingness to realistically and honestly assess their own sexual behavior, take proactive steps to plan for their sexual activity affects their use of appropriate protections (Diamond & Savin-Williams, 2011).

Peer groups are central to identity development process of an adolescent. Peers provide the adolescent with social support in form of role models, very personal social feedback, advice, comfort and companionship (Muuss, 1996). However, peer relations could promote or hinder adolescent's wellbeing, including their adherence to ART (Dodds et al., 2003). For example, perceived differences between the adolescent and peers may lead to feelings of isolation, resulting in psychological distress. Fear of rejection by peers may prompt the HIV-infected adolescent to abandon his/her medical regimen in order to fit in with peers; this is most likely to occur if the HIV self-care interferes with group activities (Dodds et al., 2003; Michaud, Suris, Thomas, Gnehm, & Cheseaux, 2010). Peer beliefs and attitudes, regarding HIV and its management create

additional sources of stress for HIV-infected adolescents. For example, stigma against HIV-infected persons remains rife in Uganda (Tsai, Bangsberg, Bwana, et al., 2013; Tsai, Bangsberg, Kegeles, et al., 2013); perceived stigma from friends creates barriers to adherence, especially if the adolescent has not disclosed their HIV status to peers, as taking ART in the presence of peers could lead to unintentional disclosure of their HIV status (Lyon & D'Angelo, 2009a; Michaud et al., 2010; Obare, van der Kwaak, & Birungi, 2012; Rao, Kekwaletswe, Hosek, Martinez, & Rodriguez, 2007). Moreover, HIV-related stigma has been associated with increased psychological distress among HIV-infected persons (Akena, Musisi, Joska, & Stein, 2012; Clark, Lindner, Armistead, & Austin, 2004; Stutterheim et al., 2009).

Neurocognitive disorders

Neurocognitive deficits are common among children and adolescents perinatally infected with HIV (McGrath et al., 2006; Msellati et al., 1993; Van Rie, Harrington, Dow, & Robertson, 2007; Wolters et al., 2005), and these range from subtle neurobehavioral abnormalities such as impaired language and motor skills, cognitive deficits, impaired visual-spatial integration, behavioral disorders, and impaired executive functions to frank encephalopathy (Chase et al., 2000; Smith et al., 2012; Van Rie et al., 2007). In a retrospective study of 86 school-age children with HIV in the United States (U.S.), Papola, Alvarez and Cohen (1994) found that 44% of the children were functioning in the below-average to average-range of intelligence and 56% demonstrated significant language impairments (Papola, Alvarez, & Cohen, 1994). In the U.S., Belman et al (1996) compared neurological outcomes in 32 HIV-infected children, 99 HIV exposed but uninfected (reverters) and 116 control children; they found that HIV-infected children

showed significantly more signs of neurological deficits, compared to HIV-exposed but uninfected children (Belman et al., 1996). In a study of 93 HIV-infected children in Uganda, Ruel et al (2012) found that HIV-infected children had worse neurological outcomes on the TOVA visual reaction times, sequential processing, simultaneous processing, planning or reasoning and global performance (Ruel et al., 2012).

Neurocognitive disorders among children and adolescents have been attributed to prenatal exposure to maternal immune dysregulation, ART, sexually transmitted infections and teratogens such as alcohol and illicit drugs, and to the postnatal neurotoxicity associated with HIV infections and abnormal immune activation (Johnson & Nath, 2009; Mekmullica et al., 2009) as well as intermittent or sub-optimal anti-retroviral therapy (Van Rie et al., 2007). Neurocognitive disorders have also been associated with environmental factors such as poverty and lack of resources, and exposure to alcohol and illicit substances (Brown et al., 2000; McDonald et al., 2013; Mellins et al., 2003). The risk factors for HIV-related neurocognitive disorders include: maternal HIV status, elevated plasma viral load, timing of HIV-infection, degree of immune suppression early in life, and route of transmission. Perinatally-infected children vertically infected with HIV (that is from parents vs. horizontal transmission from peers), and children with intra-uterine infections (versus perinatal or post-natal) were more likely to experience neurocognitive disorders (Smith et al., 2000; Van Rie et al., 2007)

Psychiatric disorders

HIV-infected children and adolescents are at increased risk for psychological disorders- due in part to the direct effects of the HIV virus on the central nervous system (CNS) structures responsible for emotional, behavioral and cognitive functions, and due to

accumulation of stressors related to coping with the medical, social and psychological demands of a life-threatening chronic illness (Wolters & Schmitt, 1994; Wolters, Brouwers, & Moss, 1995). Several studies have documented a high burden of psychiatric disorders among HIV-infected adolescents (Mellins, Brackis-Cott, Dolezal, & Abrams, 2006), compared to HIV-uninfected adolescents (Bachanas et al., 2001; Elkington et al., 2011; Gaughan et al., 2004; Mellins et al., 2009). In a longitudinal study of mental health outcomes among perinatally-exposed youth (9 – 16 years), Mellins, Brackis_cott, Leu, Elkington, Dolezal et al (2009) found that 61% of HIV-infected youth met the diagnostic criteria for a non-substance use psychiatric disorder, compared to 49% of HIV-exposed but uninfected youth (Mellins et al., 2009).

The most prevalent diagnoses among HIV-infected adolescents in this study included: anxiety (49%), behavioral disorders (25.7%), Attention Deficit Hyperactivity Disorder (ADHD: 18%), mood disorders (7.3%) and substance abuse (1.9%) (Mellins et al., 2009). In a systematic review on psychiatric disorders among HIV-infected children and adolescents, Scharko (2006) found that the pool of 328 children aged 4 – 21 years, 28% had Attention Deficit Hyperactivity Disorder (ADHD), 25% had depression and 24.3% had anxiety disorders (Scharko, 2006).

Psychiatric disorders among infected and un-infected adolescents have been associated with increased alcohol and substance abuse, sexual risk-taking, delayed health care seeking, and poor adherence to HIV care (Brown, Danovsky, Lourie, DiClemente, & Ponton, 1997; Brown et al., 2000; Murphy, Durako, et al., 2001; Pao et al., 2000; Shrier, Harris, Sternberg, & Beardslee, 2001; Stevens, Murphy, & McKnight, 2003; Tapert, Aarons, Sedlar, & Brown, 2001).

Psychological disorders

The term "psychological distress" is ubiquitous in the health literature, but it is seldom used as a distinct concept; rather, several researchers use it inter-changeably with psychological stress, and stress (Ridner, 2004). There is no standard definition for psychological distress. Abeloff et al (2000; p.56) describe psychological distress as the general concept of maladaptive psychological functioning in the face of stressful life events (Abeloff, Armitage, Lichter, & Niederhuber, 2000). Ridner (p. 539) defines psychological distress as 'a unique discomforting, emotional state experienced by an individual in response to a specific stressor or demand that results in harm, either temporary or permanent, to the person (Ridner, 2004). The National Comprehensive Cancer Network defines distress as a "multi-factorial unpleasant emotional experience of a psychological (cognitive, behavioral, emotional), social, and/or spiritual nature, that may interfere with the ability to cope effectively with cancer, its physical symptoms and its treatment (National Comprehensive Cancer Network, 2011).

Cohen, Janicki-Deverts and Miller (2007) describe psychological stress as an outcome of an appraisal process that "occurs when an individual perceives that environmental demands tax or exceed his or her adaptive capacity" (Cohen, Janicki-Deverts, & Miller, 2007). According to Cohen et al (2007), this definition does not include psychiatric disorders that may arise as downstream consequences of stressful exposures (Cohen et al., 2007). However, psychological stress is distinct from "stress", which originates from the experimental works of Hans Selye (1956); in this context, stress is defined as a non-specific deviation from the normal resting state; it is caused by function or damage and stimulates repair (Selye, 1955, 1956). Murray and Heulskoetter

(1983; p.374) elaborated on the prior works of Selye, describing stress as a physical and emotional state that is always present in the person as a result of living (Murray & Huelskoetter, 1983b). Further, Selye (1976) and Murray and Heulskoetter (1983) assert that stress, good or bad is always present; does not necessarily result in harm to an individual and is necessary to support life (Murray & Huelskoetter, 1983b; Selye, 1976).

The Cohen et al (2007) definition of psychological distress is most consistent with the Lazarus's transactional stress and the coping theory that grounds this study (Cohen et al., 2007). For purposes of conceptual clarity, the term psychological distress will be used to differentiate between psychological distress and stress. Similar to Cohen et al (2007), this term is used to refer to the accumulation of psychological symptomatology that may precede the development of psychiatric disorders following exposure to stressful events.

Psychological distress is often conceptualized as a multidimensional construct. Past studies generally describe psychological distress as consisting of depression, anxiety and somatic symptom and social dysfunction (Derogatis & Fitzpatrick, 2004; Goldberg & Hillier, 1979), and as noted earlier, it is a precursor to clinical depression (Cohen et al., 2007). More recent studies have expanded on these domains. For example, in a study conducted among French Quebecois people in Canada, Masseé (2000) identified six idioms of distress – demoralization and pessimism towards the future, anguish and stress, self-depreciation, social withdrawal and isolation, somatization and withdrawal onto oneself (Massé, 2000). In a U.S. study of 74 women newly diagnosed with breast cancer, Cimprich (1999) three symptom distress domains – insomnia, fatigue and loss of concentration (Cimprich, 1999).

Psychological distress among HIV-infected adolescents has received less attention, compared to psychiatric and neurocognitive disorders. However, the available data indicates a high prevalence of psychological distress among HIV-infected adolescents. In a study conducted among 24 HIV-infected youth (16-24 years) in United States (U.S.), Naar-King et al (2006) found that 54% of respondents score above the clinical cut-off for psychological distress on the Brief Symptom Index (Naar-King et al., 2006). In another study of 230 HIV-infected adolescents (13 – 19 years) in the United States, Murphy, Moscicki, Vermund, Muenz, Larry (2000), 18% and 17% of the sample scored clinical range for anxiety and depression (Murphy, Moscicki, Vermund, & Muenz, 2000a). In Uganda, two studies have assessed psychological distress among HIV-infected children and adolescents. A recent cross-study of 82 HIV-infected youth in care at the Mildmay Center found that 51% of the adolescents had psychological distress (Musisi & Kinyanda, 2009). An unpublished 2003 study found high rates of depression (41.5%), anxiety (58.5%) and suicide attempts (20%) among HIV-infected children (Musisi & Kinyanda, 2003).

The causes of psychological distress among HIV-infected adolescents are varied, and include: developmental processes as the complex challenge of developing an identity in the context of a highly stigmatized and life threatening disease (Battles & Wiener, 2002; DeLaMora et al., 2006), negative life events such as bereavement (Lester, Chesney, Cooke, Whalley, et al., 2002; Murphy et al., 2000a; Tam et al., 2008; Thorsteinsson, Sveinbjornsdottir, Dintsi, & Rooke, 2013), daily hassles of managing demanding and complex ART regimens (Lazarus & Folkman, 1984; Mukolo & Wallston, 2012), worry about parents' health (Elkington et al., 2011), uncertainty of their life (Mukolo &

Wallston, 2012), deteriorating physical health (Murphy et al., 2000a; Musisi & Kinyanda, 2009), HIV/AIDS related stigma (Lyon & D'Angelo, 2009b), and partial disclosure of HIV (Bikaako-Kajura et al., 2006; Lester, Chesney, Cooke, Whalley, et al., 2002).

Why focus on psychological distress?

Studies exploring the psychosocial determinants of adherence to ART have either focused on the stressors preceding psychological distress, or on psychiatric morbidities- the result of prolonged exposure to psychological distress. The stressors associated with psychological distress among HIV-infected adolescent are diverse, and is some cases- uncontrollable e.g. bereavement. For these reasons, it is not ways possible to prevent an adolescent's exposure to these stressors. Additionally, not all adolescents experiencing stressful events will have psychological distress. Psychiatric morbidities such as depression and anxiety require clinical management, which would be an additional burden for HIV-infected adolescent due to the increased pill burden and stigma associated with mental illness in Uganda. Moreover, similar health consequences – non-adherence, sexual risk-taking and increased risk of AIDS mortality have been observed for both psychological distress and psychiatric morbidity. This study focuses on psychological distress because it is more amenable to intervention, compared to stressors or psychiatric morbidities. Psychological distress is amenable to a diverse array of psychosocial interventions that could prevent or attenuate the impact of stressors and/or prevent escalation to psychiatric morbidities. For example, interventions could target the cognitive process involved in evaluation of a stressful event and/or the perceived availability of personal or environmental resources to cope with the stressor. Interventions could build or increase an adolescent's access to psychosocial resources

within their social support network. For example, these interventions could target structures such as households (caregivers and siblings), schools (peers and teachers), and health institutions (e.g. health providers) as sources of support for the adolescent. From a public health perspective, the focus on psychological distress provides to selectively target adolescents whose environmental demands tax or exceed their adaptive capacity to cope, and to prevent the escalation to psychiatric morbidities.

Adherence to Antiretroviral therapy among HIV-infected adolescents

What is adherence?

Anti-retroviral therapy is a life-long treatment (Gill, Hamer, Simon, Thea, & Sabin, 2005), and reaping the benefits of ART requires strict adherence to the medication regimen (Bangsberg et al., 2000; García et al., 2002; Mannheimer, Friedland, Matts, Child, & Chesney, 2002; World Health Organization, 2010).

Adherence is broadly defined as the extent to which a patient's health behaviors correspond with medical advice or recommendations (World Health Organization, 2003). There is no standard criteria for adherence to ART as each ART drug regimen has a unique adherence-resistance relationship (Bangsberg, Moss, & Deeks, 2004; Sethi, Celentano, Gange, Moore, & Gallant, 2003). Earlier drug regimens required levels of adherence greater than 95%, but classes including the protease inhibitor (PI) boosted regimens and non-nucleoside reverse transcriptase inhibitors (NNRTI) may achieve full virologic suppression at adherence levels lower than 70% (Bangsberg, 2006; King, Brun, & Kempf, 2005).

Measuring adherence

Several measures have been developed to monitor adherence to ART across diverse populations including:- self-reports of adherence, electronic monitors, un-announced pill counts, provider assessments, pharmacy refills, and biological indicators such as CD4 cell counts and HIV-RNA (viral) load (Bangsberg et al., 2001; Chesney et al., 2000; Giordano, Guzman, Clark, Charlebois, & Bangsberg, 2004; Oyugi et al., 2004). There is no perfect measure of adherence, as each measure has several limitations-including cost (electronic monitoring devices), and accuracy of estimates (pharmacy refills, pill counts, physician assessments, and self-reports) (Liu et al., 2001; Simoni et al., 2006). Self-reported adherence is the most frequently used measure in clinical practice and research, especially in resource-limited settings such as Uganda (Giordano et al., 2004).

Additionally, there is no standard cut-off for adherence on measures such as pill counts. For example, a recent review on gender effects in treatment adherence found that adherence cut- offs vary widely across studies, ranging from 80% – 100% (Puskas et al., 2011). The lack of standard criterion for defining adherence prompted Holzemer et al (1999) to conclude that "adherence is defined as measured" (Holzemer et al., 2009). However, majority of the ART regimens in Uganda and most of sub-Saharan Africa are largely based on nucleoside reverse transcriptase inhibitors (NRTI) (Ministry of Health-Uganda, 2008), which are susceptible to resistance at levels of adherence less than 95% (Bangsberg, 2006).

Rates of adherence in children and adolescents

Children and adolescents have significant difficulty adhering to their medications. A systematic review on pediatric adherence in low and middle-income countries (LMICs) found adherence estimates ranging from 49% to 100% but the differences in measuring adherence prohibited estimation of pooled estimates on adherence in this study (Vreeman et al., 2010). In sub-Saharan Africa, studies have noted marked differences in rates of adherence between adults, young people and children. In a systematic review comparing rates of adherence among adolescents and adults in sub-Saharan Africa, Nachega et al (2009) found that the percentage of adolescents (11- 19 years) achieving 100% adherence was 20.7% at 6 months, 14.3% at 12 months and 6.6% at 24 months, compared to 40.5% at 6 months, 27.9% at 12 months, and 20.6% at 24 months for adults (Nachega et al., 2009).

In Uganda, the reported rates of adherence vary across studies, and range from 72% to 100%. In a study exploring adherence among HIV-infected children and adolescents in Uganda, Nabukeera-Barungi et al (2007) found adherence levels ranging between 72% with home-based unannounced pill counts and 94.1% with a self-report measure; both rates below the required minimum (95%) for successful ART outcomes (Nabukeera-Barungi, Kalyesubula, Kekitiinwa, Byakika-Tusiime, & Musoke, 2007). A small study assessing the feasibility of electronic adherence monitoring at the Joint Clinical Research Center in Uganda found that adherence varied with the type of assessment method used- 99% of self-reports, 97% for pill counts, and 88% with electronic medication vials (Wiens et al., 2012). Similarly, in a longitudinal study exploring adherence in HIV-infected parents and their children initiating ART in a family treatment program in

Kampala, Byakika-Tusiime et al (2009) found that rates of adherence declined with increased duration of ART, and also varied with type of assessment: 98.1%, 97.8% and 100% by 3-day self-report, 30-day visual analogue scale and pill counts, respectively (Byakika-Tusiime et al., 2009). The findings from this study also indicated that adherence to ART reduces with increasing duration on ART. The findings from the above studies suggest that self-reports on adherence may lead to over-estimation of adherence. However, electronic measurements are not perfect either, as taking a pill from the medicine container does not necessary mean that the patient swallowed the medication.

Barriers to non-adherence

The barriers to adherence among HIV-infected children and adolescents have been extensively explored in prior studies conducted in low, middle and high-income countries. The global barriers to adherence include: side effects, pill burden, child's health status, appointment schedules that interfere with daily schedules, disorganized natural families, parent-child conflict, having several adults involved in pill supervision, residential instability, incomplete parental disclosure of the child's HIV status, household poverty, stigma, low caregiver education, lack of comprehension of the HIV and its management, and traveling away from home (Arrivé et al., 2012; Biadgilign, Deribew, Amberbir, & Deribe, 2009; Byakika-Tusiime et al., 2009; Dodds et al., 2003; Fassinou et al., 2004; Haberer et al., 2011; Haberer & Mellins, 2009; Lyon & D'Angelo, 2009b; Moodley, Myer, Michaels, & Cotton, 2008; Nabukeera-Barungi et al., 2007; Rao et al., 2007; Vreeman et al., 2010; Vreeman, Wiehe, Pearce, & Nyandiko, 2008).

In resource-constrained settings such as sub-Saharan Africa, household poverty and orphan-hood have also emerged as some of the most important predictors of adherence to ART among HIV-infected children and adolescents. Lack of food and money for transport to the clinic to refill their prescriptions have been associated with non-adherence to ART (Biadgilign et al., 2009; Byakika-Tusiime et al., 2009; Bygrave et al., 2012; Haberer et al., 2011; Haberer & Mellins, 2009; Mills et al., 2006; Roura et al., 2009; Tsai & Bangsberg, 2011; Tsai et al., 2011; Tsai et al., 2012; Vreeman, Wiehe, Pearce, et al., 2008). For example, in a study of 96 HIV-infected children in Zambia, Haberer et al (2011) found that the number of missed ART days increased by 8% per 100,000 kwacha ($20) income (Haberer et al., 2011).

Negative life events such as bereavement and orphan-hood have been identified as antecedents to psychological distress and non-adherence to ART among HIV-infected adolescents (Elkington et al., 2011; Kikuchi et al., 2012; Lester, Chesney, Cooke, Weiss, et al., 2002; Rotheram-Borus, Weiss, Alber, & Lester, 2005; Thorsteinsson et al., 2013). Haberer et al (2011) also found that adherence was highest among children whose primary caregiver was the mother, and improved by 23% if the child had multiple caregivers (Haberer et al., 2011). Nyandiko, Ayaya, Nabakwe et al (2006) found that one year mortality following initiation of ART was higher among orphaned children (7.1%) compared to non-orphaned children (6.6%) in western Kenya, but adherence was not significantly associated with adherence to ART (Nyandiko et al., 2006). However, a retrospective study of adherence on ART outcomes among HIV-infected children in western Kenya, Vreeman, et al (2008) found that the non-adherence to ART was higher

among orphaned children, particularly children who had lost both parents (Vreeman, Wiehe, Ayaya, Musick, & Nyandiko, 2008).

Adherence facilitators

A few studies have sought to identify the psychosocial resources that facilitate adherence among HIV-infected children and adolescents. A majority of these studies have focused on elaborating on the role of coping and social support in dealing with adversity among HIV-infected adolescents, and these are described below.

Coping

Lazarus and Folkman (1991; p.141) define coping as a dynamic process that entails deployment of cognitive and behavioral efforts to manage specific external and or internal demands that have been appraised as stressful (Lazarus & Folkman, 1991). Adolescents living with chronic illnesses are likely to use a variety of coping strategies in dealing with different aspects of a stressful situation. The type and complexity of coping strategies utilized varies with the adolescent's age (Keller & Nicolls, 1990; Knapp, Stark, Kurkjian, & Spirito, 1991; Snethen, Broome, Kelber, & Warady, 2004) and gender (Bull & Drotar, 1991; Spirito, Stark, Gil, & Tyc, 1995). For example, older adolescents are more likely to use emotion management and cognitive coping strategies such as cognitive restructuring, while younger adolescents, incapable of abstract thinking, are more likely to use emotion-focused strategies such as venting or avoidance and problem-solving coping strategies (Bull & Drotar, 1991; Snethen et al., 2004). Females are more likely to use emotion management coping

strategies, while males are more likely to use problem-solving coping strategies (Bull & Drotar, 1991). Among HIV-infected adolescents, active coping styles such as confrontation or seeking social support have been associated with positive psychological adjustment, while passive coping styles such as withdrawal or depressive reactions are related to poor psychological adjustment (Meijer, Sinnema, Bijstra, Mellenbergh, & Wolters, 2002; Murphy, Moscicki, Vermund, & Muenz, 2000b).

Specific adherence strategies such as associating drug-taking times with a daily routine, pillboxes, alarm device, reminders, visual medication schedules, carrying pills in a bag etc. (Liu et al., 2001; Machtinger & Bangsberg, 2007; Michaud et al., 2010; Murphy et al., 2003) have been associated with increased adherence to ART. (Bikaako-Kajura et al., 2006; Hosek, Harper, & Domanico, 2005; Michaud et al., 2010; Murphy et al., 2003; World Health Organization, 2003).

Social support

Social support refers to the flow of emotional concern, instrumental aid, informational and appraisal resources between people (House, 1981). It is the functional characteristic of social networks (Israel & Rounds, 1987). The association between social support and health is well documented (DiMatteo, 2004; Krause, 1987; Lee, Detels, Rotheram-Borus, & Duan, 2007; Sopeña, Evangeli, Dodge, & Melvin, 2010). Social support mitigates the potentially deleterious effects of stress (physical or psychological) on health across all levels of the life course (Krause, 1987; Murphy et al., 2000b; Sopeña et al., 2010). House (1981) hypothesizes that social support may enhance health and wellbeing either, directly by meeting basic human needs for security, social contact, approval, belonging and affection or reducing levels of perceived stress, or

indirectly enhance health and wellbeing by moderating the relationship between stress and health (stress-buffering hypothesis) (House, 1981).

Among HIV-infected adults, social support has been associated with reduced psychological distress and increased adherence to ART (Chesney, Chambers, Taylor, & Johnson, 2003; Kalichman, DiMarco, Austin, Luke, & DiFonzo, 2003; Kelly, Hartman, Graham, Kallen, & Giordano, 2014; Koopman et al., 2000; Lehavot et al., 2011; Serovich, Kimberly, Mosack, & Lewis, 2001; Takada et al., 2014; Tsai et al., 2012). Among HIV-infected youth, social support has been associated with reduced distress among HIV-infected youth (Battles & Wiener, 2002; Lam, Naar-King, & Wright, 2007; Murphy et al., 2000b), but its relationship with adherence in this population has been less consistent; a few studies found a positive association between social support and adherence (Comulada, Swendeman, Rotheram-Borus, Mattes, & Weiss, 2003), but majority have not found any association (Murphy, Wilson, Durako, Muenz, & Belzer, 2001; Naar-King et al., 2006; Nugent et al., 2010).

The lack of association between social support and adherence among adolescents has been attributed to differences in the measurement of social support, especially the type of social support assessed. For example, in a meta-analysis on the role of social support in predicting patient adherence to medical treatment, DiMatteo (2004) found that practical social support had the highest correlation to adherence to medications. Emotional social support was not associated with adherence (DiMatteo, 2004). In a small study of HIV-infected youth in the United States, Naar-King et al (2006) found that ART-specific social support was a stronger predictor of adherence to ART compared

to general social support but these relations were not statistically significant (Naar-King et al., 2006).

Additionally, the lack of association between social support and adherence among HIV-infected adolescents could also been attributed to conflicts between the functions of social support and adolescents' desire for autonomy. Instrumental support such as provision of foods and transport to the clinic (practical support) could be perceived as helpful but accompanying the adolescent to the clinic or reminding the adolescent about medication could be perceived as annoying or crippling the adolescent's desire for autonomy, thereby affecting their adherence to ART. However, formal support systems are largely non-existent in Uganda, where survival largely depends on family and kinship networks (Mills et al., 2006). For these reasons, the significance of social support may supersede adolescents' desire for autonomy.

Spirituality and religiosity

Religiosity and spirituality have been identified as important psychosocial resources for coping with illness, as religious persons are less likely to experience negative psychological states such as depression and anxiety (Cotton et al., 2012; Schapman & Inderbitzen-Nolan, 2002). Religiosity and/or spirituality have been identified as coping strategy among HIV-infected adults (Coleman & Holzemer, 1999; Cotton, Zebracki, Rosenthal, Tsevat, & Drotar, 2006; Ironson et al., 2002; Makoae et al., 2008; Nooney & Woodrum, 2002; Prado et al., 2004; Tuck, McCain, & Elswick Jr, 2001). Religious institutions also play a major role in providing health care and support to people living with HIV/AIDS (Kaldjian, Jekel, & Friedland, 1998).

However, the role of spirituality and religiosity among HIV-infected adolescents has not been fully explored. Emerging sub-Saharan Africa data indicates that religiosity may have detrimental effects on the wellbeing of HIV-infected persons, as religious beliefs have also been associated with HIV-stigma. Additionally, religious beliefs and/or religious leaders may interfere with patient's adherence to ART (Kagee & Delport, 2010). According to the Uganda Demographic Health Survey, more than 90% of the Ugandans identify as either Catholic, Protestant, Muslim or Pentecostal suggesting that religion is an important factor to consider in Uganda (Measure DHS & ICF International, 2011). Therefore, it's important to explore the role of religiosity and spirituality in coping with adversity among HIV-infected adolescents in Uganda.

Public health implications of non-adherence

The consequences of non-adherence are varied and dire. Non-adherence to ART has been associated with poor clinical health outcomes such as, increased HIV viral loads and reduced CD4 count leading to accelerated progression to AIDS and death (Bangsberg et al., 2000; García et al., 2002; Mannheimer et al., 2002). Non-adherence to ART has also been associated with development of drug resistance and transmission of ART resistant strains (Bangsberg et al., 2004; Gardner et al., 2008; Grant et al., 2002; Little et al., 2002). In resource-constrained countries such as Uganda, widespread ART resistance could compromise scale-up of ART programs management, yet less than 60% of ART eligible population has access to these lifesaving medications (Uganda AIDS Commission, 2012; UNAIDS, 2013b). The ensuing increase in AIDS-associated morbidity would increase the strain on the overburdened healthcare system and informal care giving networks (Kinfu, Dal Poz, Mercer, & Evans, 2009; Ministry of Health-

Uganda, 2008; Naicker, Plange-Rhule, Tutt, & Eastwood, 2009; Tarimo, Kohi, Outwater, & Blystad, 2009). Non-adherence also has numerous societal costs including increased costs of tertiary treatment and lost productivity, exacerbating the household poverty rampant within AIDS-affected households in sub-Saharan Africa. From a public health perspective, the findings that viral suppression is related to decreased in transmission of HIV suggests that it's important to ensure that HIV-infected persons adhere to their ART, as this will decrease risk of HIV transmission at the individual and population level.

Psychological distress and adherence among HIV-infected adolescents

As noted earlier, studies conducted in high-income countries have documented high rates of psychological distress among HIV-infected adolescents (Murphy et al., 2000b; Musisi & Kinyanda, 2003, 2009; Naar-King et al., 2006), and psychological distress has been associated with non-adherence to ART (Hosek et al., 2005; Murphy et al., 2005; Murphy, Wilson, et al., 2001; Wagner et al., 2011; Williams et al., 2006) and poor health outcomes such as rapid progression to AIDS and increased risk of mortality (Benton, 2008; Ickovics et al., 2001; Leserman, 2003, 2008; Leserman et al., 2002; Mayne, Vittinghoff, Chesney, Barrett, & Coates, 1996). Psychological distress has also been associated with increased sexual risk-taking, drug and substance abuse, and poor school performance (Foster & Williamson, 2000; Murphy et al., 2000b; Rao et al., 2007; Wagner et al., 2011).

Psychological distress may impact adherence to ART through various mechanisms. Psychological distress is closely associated with feelings of helplessness and loss of self-esteem due to perceived inability to cope with situations that demand effective response (Cohen and Wills, 1985); these may impair self-care behaviors among

distressed persons. Additionally, the behavioral changes e.g. substance and drug abuse that may occur as adaptations or coping responses to psychological distress may impact adherence to ART. Psychological distress may cause disruptions in the neuroendocrine system, resulting in marked changes in health-related behaviors (e.g. alcohol and substance abuse) or other failures in self-care (Cohen and Wills, 1985). Beyond these direct pathways, psychological distress may cause changes in the immune system, thereby reducing the efficacy of ART mediated immune responses; this may result in increased disease progression and risk for mortality (Cohen et al., 2007; Leserman, 2003, 2008). Disease progression and morbidity may also create barriers to ART adherence, particularly if they reduce ART optimism. Further, psychological distress or its related feelings of helplessness and loss of self-esteem may compromise an adolescent's ability to mobilize psychosocial resources, which prevent or attenuate appraisal of an event or stimuli as stressful. For example, social support from significant others can provide the necessary resources to cope with a stressful event and/or bolster an adolescent's ability to cope with the demands imposed by the stressful event and medication regimen.

Justification for this study

Data, descriptive and epidemiological, are necessary to inform local policies and support decision-making on issues affecting the health and well-being of HIV-infected adolescents in Ugandan and other countries in sub-Saharan Africa. Approximately 69% of HIV-infected adolescents live in sub-Saharan Africa (UNAIDS, 2013b) but little is known about the psychosocial circumstances of HIV-infected adolescents in Uganda and other countries in sub-Saharan Africa. Majority of the descriptive and epidemiological

data that inform our understanding of the determinants of wellbeing among HIV-infected adolescents comes from studies conducted in United States and other high-income countries. However, the differences in the social patterning of the HIV-epidemic in sub-Saharan Africa and United States creates systematic differences in the psychosocial vulnerabilities and challenges experiences by adolescents in these diverse settings, raising questions about the contextual relevance of these factors for HIV-infected adolescents in sub-Saharan Africa.

Majority of the adolescents in the United States and Europe acquire HIV primarily through behavioral exposure – unprotected sexual intercourse and injection drug use (IDU) and this population is predominantly young men who have sex with men (YMSM). On the other hand, more than 90% of HIV-infections among adolescents in sub-Saharan Africa are due to mother-to-child transmission of HIV (MTCT). Moreover, the high prevalence of substance and drug abuse among behaviorally infected adolescents compared to perinatally-infected adolescents increases their vulnerability to poor health outcomes, as it creates barriers to enrolling in, adherence to, and sustaining HIV-care, and also increases the risk of re-infection through unprotected sexual intercourse. Additionally, the differences in duration of living with HIV and the prevalence of behavioral risk-factors also create selective risks and vulnerabilities between these populations, which differentially affect the health and wellbeing of these adolescent sub-populations. For example, the burden of neuropsychiatric disorders is higher among perinatally-infected adolescents compared to behaviorally infected adolescents (Mellins et al., 2009), due to impact of the HIV-virus on the neurological system during the intra-utero development and the subsequent assaults of the HIV-virus on various body systems

throughout infancy and childhood. Arguably, the psychological profiles between these populations would be different, as perinatally-infected adolescents are more likely to have come to terms with their HIV-status and adapted the necessary coping strategies at a time when behaviorally-infected adolescents are still struggling to cope with their HIV diagnosis.

The social and economic differences between the global north and global south also create unique vulnerabilities for these adolescent sub-populations. The high rates of orphan-hood (UNAIDS, 2013) among perinatally-infected adolescents creates structural barriers that heighten these adolescent's vulnerability to poor health outcomes. The lack of formal social support services in most of sub-Saharan Africa further compounds the challenges of HIV-infected adolescents in this context, as they have to depend on over-burdened kinship networks for social support. Majority of the HIV-infected adolescents in United States are young men who have sex with men (CDC, 2013); these adolescents face the double burden of stigma against their sexuality and HIV status.

Additionally, the available data from both low- and high-income countries are constrained by the small sample sizes and huge variability in demographics, mechanisms of HIV transmission and methods of psychiatric assessment among study participants. Majority of these studies combine children and adolescents, precluding any assessment of developmental factors that are relevant to the adolescent population. These studies also highlight a multiplicity of factors across various levels of an adolescent's ecological environment, yet the scarcity of material and human resources in sub-Saharan Africa demands prioritization and targeted investments in interventions and policies that would ameliorate or mitigate the most important predictors.

The lack of locally validated measures of psychological distress for HIV-infected adolescents in Uganda and other countries in countries sub-Saharan Africa further constrains efforts to accrue descriptive and epidemiological data on these adolescents. There are several measures of psychological distress, but none of these measures is specifically developed for African youth, and even fewer have been validated among African youth. However, majority of these existing measures have been developed and validated among non-African adult populations, and do not incorporate developmental aspects such as peer and family relations, school, alcohol and substance abuse, all of which affect adolescent's psychological wellbeing. This raises uncertainty about the reliability and validity of these tools in non-western setting, as the presentation of mental health constructs varies across cultures (Betancourt, Speelman, Onyango, & Bolton, 2009; Derluyn, Broekaert, Schuyten, & Temmerman, 2004; Harms, Kizza, Sebunnya, & Jack, 2009; Okello & Musisi, 2006; Okello & Ekblad, 2006).

The limitations of the current data -the differences between behaviorally and perinatally-infected adolescent populations that limit generalization of available data to HIV-infected adolescents in sub-Saharan Africa, coupled with the sample size constrains in present studies highlight the need to identify the contextually relevance predictors of health and wellbeing among HIV-infected adolescents in Uganda and other countries in sub-Saharan Africa. There is also a need for large scale studies that can enable simultaneous assessment of varied psychosocial predictors and evaluation of the relative importance of each predictor. Lastly, differences in cultural expression of psychological symptomatology highlight the need for studies to develop and test local measures of

psychological wellbeing for adolescents in sub-Saharan Africa, irrespective of their HIV status.

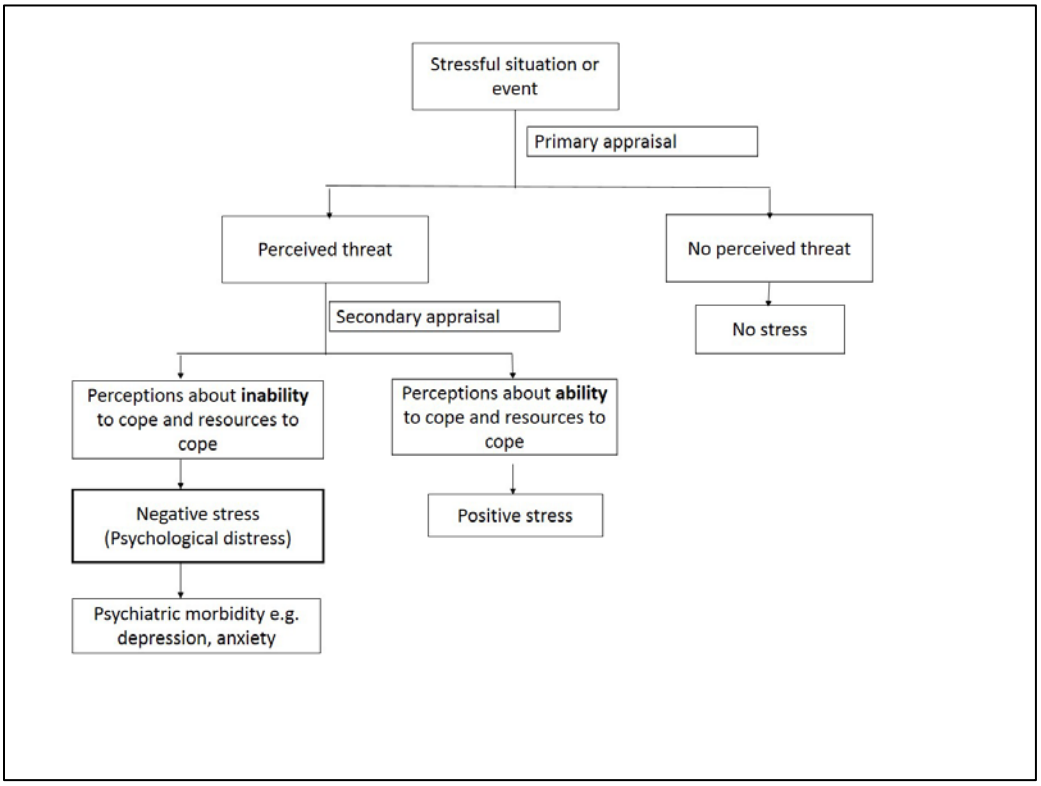
Overview of the study

Theoretical background

This thesis is grounded in Lazarus's Transactional Model of Stress and Coping. Lazarus and colleagues (Lazarus 1966; Lazarus and Folkman, 1984) assert that the way people cope with stressor is crucial to their physical, social and psychological wellbeing. Stressors are demands made by the internal or external environmental that upset balance, thus affecting physical and psychological wellbeing, and require action to restore balance (Lazarus & Cohen, 1977). One of the core constituents of the TMSC is appraisal (Antonovsky, 1979; Lazarus, 1996), that is, the meaning and significance of a stressor to the individual (threatening vs. non-threatening in primary appraisal), and controllability

and resources available to mitigate the stressor (secondary appraisal). Additionally, the relationship between stress and coping is reciprocal: it depends on the person's appraisal of the stressor, and is mediated by the social and cultural resources available at his or her disposal to combat the stressor (Antonovsky, 1979; Cohen & McKay, 1984; Lazarus & Cohen, 1977). There are two important assumptions that underlie this model: first, the model asserts that an individual's subjective perception of the stimuli is more important that the any objective assessment of the stimuli, and this perception is represented by the appraisal processes – both primary and secondary appraisal processes in the model; secondly, the model posits that that not all stress is bad; some positive stress in necessary human beings, and argument is consistent with earlier works on stress by Selye (Selye, 1976, 1979) and Murray and Huelskoetter (1983) (Murray & Huelskoetter, 1983a).

Figure 1.1: The Transactional Model of Stress and Coping

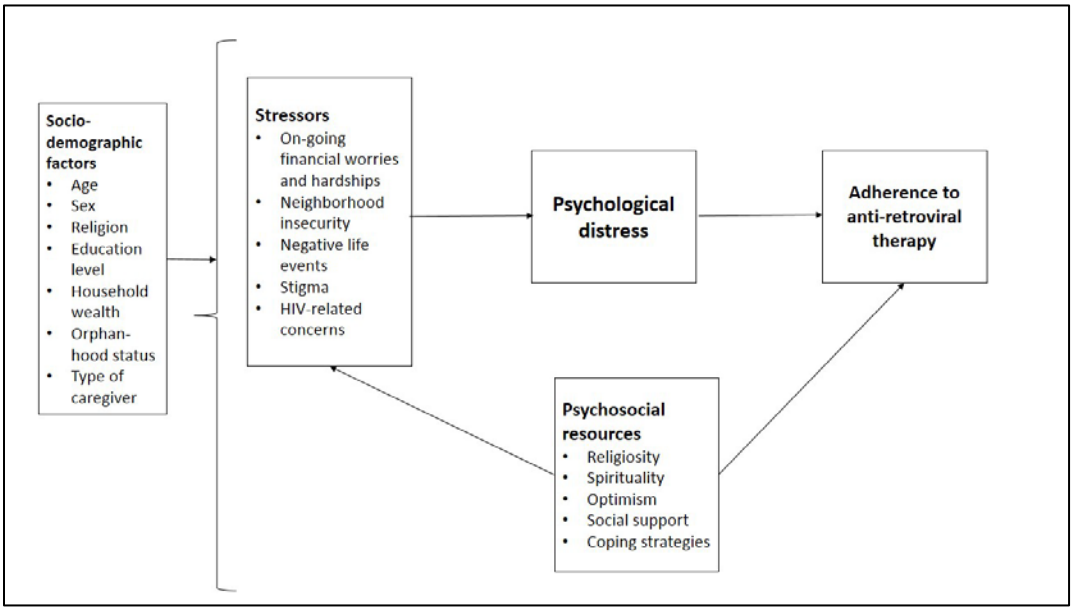


The processes of the TMSC are depicted in Figure 1.1. When a person experiences a stressful stimuli, s/he will evaluate this stimuli based on the perceived significance and controllability of this stimuli (primary appraisal). There are two possible outcomes of this primary appraisal process - threat or non-threat. If the stimuli is not perceived as a threat, there will be no stress, but if the stimuli is perceived as a stressor, then the person will conduct a secondary appraisal to determine if they have the ability and resources to cope with this stimuli. The outcome of the secondary appraisal process is either positive stress (‘eustress”), which can lead to personal growth, or negative stress (“distress”). Prolonged down exposure to stressors may lead to psychiatric morbidities such as depression and anxiety. One of the major limitations of this model is the inability

to assess the appraisal processes that determine how a stimulus is perceived. These processes are largely intrinsic and therefore inaccessible to anyone beyond the individual.

The conceptual framework (Figure 1.2) depicts the operationalization of Transactional Model of Stress and Coping in this study. Consistent with the Lazarus and Cohen's Transactional Model of Stress and Coping, this conceptual framework asserts that stressors such as bereavement, poor quality of life and stigma are antecedents to psychological distress (Johnson & Nath, 2009; Lyon & D'Angelo, 2009a; McKnight, Huebner, & Suldo, 2002; Murphy et al., 2000a; Musisi & Kinyanda, 2009; Thorsteinsson et al., 2013), which in turn leads to poor adherence to ART (Murphy, Wilson, et al., 2001; Naar-King et al., 2006; Nugent et al., 2010). Additionally, psychosocial resources mediate the relationship between stressor and psychological distress (Brown et al., 2000; Murphy et al., 2000a; Thorsteinsson et al., 2013), and also mediate the relationship between psychological distress and adherence to ART (Murphy, Wilson, et al., 2001; Naar-King et al., 2006; Nugent et al., 2010).

Figure 1.2: The Conceptual Framework



Study goals and objectives

The purpose of this study was to develop and validate a new screening instrument for psychological distress among HIV-affected youth (age 12-19 years) in Uganda, examine the predictors of psychological distress in this cohort, and to assess the impact of psychological distress on adherence to HIV care, net of mitigating factors such as the adolescent' psychosocial resources.

Study aims and hypotheses

Aims

Aim 1: Develop a local measure of psychological distress for Ugandan adolescents living with HIV/AIDS.

Aim 2: Identify psychosocial determinants of psychological distress among perinatally-infected adolescents, and assess the mediating role of psychosocial resources;

*Aim 3**:*** Examine the relationship between psychological distress and adherence to ART, net of personal and psychological factors, and evaluate the mediating role of psychosocial resources.

Hypotheses

Hypothesis 1: Increasing levels of psychological distress will have a measurable negative affect on adherence to ART.

*Hypothesis 2**:*** Psychosocial resources such as social support, coping strategies, spirituality/religiosity etc. will measurably impact psychological distress, but also measurably mediate the impact of psychological distress on adherence to ART

Methods

The study was conducted in two phases: the first phase involved developing a local psychological distress measure for HIV-infected among adolescents in Uganda, while the second phase collected data on personal factors, stressors, psychological distress, stressors, psychological resources and adherence to HIV care among 464 HIV-infected adolescents, aged 12 – 19 years. The entire research study was conducted at the Joint Clinical Research Center, Kampala, Uganda.

The results of these analyses are presented as three distinct but inter-related chapters. Chapter 2 describes the process of developing and testing a measure of psychological distress; chapter 3 explores the predictors of psychological distress and the mediating role of psychosocial resources; and chapter 4 examines the relation between psychological distress and adherence to ART. This thesis concludes with a brief

summary, discussion of limitation to the present work and consequent needed future research.

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Chapter 2

Development of the psychosocial distress measure for HIV-infected adolescents in Uganda

Introduction

Psychological distress is a commonly used construct in the medical and mental (Ridner, 2004) distress is defined and measured. For example, Abeloff et al (p.56) describe psychological distress as the general concept of maladaptive psychological functioning in the face of stressful life events (Abeloff et al., 2004). The National Comprehensive Cancer Network defines distress as a "multi-factorial unpleasant emotional experience of a psychological (cognitive, behavioral, emotional), social, and/or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms and its treatment (National Comprehensive Cancer Network, 2011). Cohen, Janicki-Deverts and Miller (2007) describe psychological stress as an outcome of an appraisal process that "occurs when an individual perceives that environmental demands tax or exceed his or her adaptive capacity" (Cohen, Janicki-Deverts, & Miller, 2007). All these applicants use different terminology that have conceptually distinct meaning in the stress and coping literature to describe a phenomenon similar to the Lazarus et al description of psychological distress (Cohen et al., 2007), which is adapted in this paper. Lastly, psychological distress is often conceptualized as a multidimensional construct generally consisting of depressive, anxiety and somatic symptoms and social dysfunction (Derogatis & Fitzpatrick, 2004; Goldberg & Hillier, 1979), and as a precursor to clinical depression (National Comprehensive Cancer Network, 2011).

Psychological distress impacts health and wellbeing (DeLongis, Folkman, & Lazarus, 1988; Lazarus & Folkman, 1984). Among HIV-infected adolescents, mental disorders, including psychological distress, have been associated with poor health outcomes including increased progression to AIDS, non-adherence to HIV care, increased sexual risk-taking, drug and substance abuse, and poor school performance (Leserman, 2003; Murphy, Moscicki, Vermund, & Muenz, 2000; Rao, Kekwaletswe, Hosek, Martinez, & Rodriguez, 2007; Wagner et al., 2011). Data on the causes of psychological distress among HIV-infected children and adolescents are largely based on studies conducted in high-income countries (HICs); the documented causes are varied, and include orphan-hood and bereavement, HIV-related stigma, poverty, HIV-related morbidities, parental illness, medication adherence and stressful life events (Battles & Wiener, 2002; Brown & Lourie, 2000; Cluver, Gardner, & Operario, 2007; Murphy et al., 2000; Orban et al., 2010; Petersen et al., 2010; Rousseau, 2009; Sopeña, Evangeli, Dodge, & Melvin, 2010).

Studies conducted in high-income countries have documented a high burden of psychological symptomatology among HIV-infected adolescents (Benton & Ifeagwu, 2008; Mellins et al., 2009; Mellins & Malee, 2013; Murphy et al., 2000; Orban et al., 2010; Scharko, 2006). Less is known about the burden of psychological distress among adolescents in low-income countries, despite the high burden of HIV in sub-Saharan Africa (UNAIDS, 2013). For example, in a small cross-sectional study of 82 HIV-infected adolescents in care, 51% of the participants had psychological distress (Musisi & Kinyanda, 2009). In Rwanda, Stulac (2011) (Sara, 2011) found significantly high levels of major depression (94%), suicidal ideation (66%), anxiety (31%), and conduct disorders (28%) among HIV-infected young people. Similarly, an unpublished study conducted in 2003 found high rates of depression (41.5%), anxiety (58.5%) and suicide attempts (20%) among HIV-infected children (Musisi & Kinyanda, 2003).

Efforts to understand the association between psychological symptomatology and medical illness in Low-income countries (LICs) are hindered by the lack of culturally relevant assessment tools (World Health Organization, 2013), a characteristics of the most commonly utilized measures of psychological distress- the General Health questionnaire (GHQ) (Goldberg & Hillier, 1979), the Patient Health Questionnaire (PHQ) (Kroenke, Spitzer, & Williams, 2001), the Beck Depression Index (BDI) (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961), the Brief Symptom Inventory (BSI) (Derogatis & Melisaratos, 1983), the Symptom Check List (SCL-90-R) (Derogatis & Cleary, 1977), the Short Mood and Feeling Questionnaire (SMFQ) (Ancold & Stephen, 1995), the Child Behavior Checklist (CBCL) (Achenbach & Edelbrock, 1983), and the Kessler-10 (K-10) (Kessler et al., 2003). None of these measures were specifically developed for African youth, and even fewer have been validated among African youth. A majority of these existing measures have been developed and validated among adult populations, and do not incorporate developmental aspects of adolescent psychological wellbeing. The extent to which these instruments can reliably and/or validly assess psychological distress among adolescents in Africa is unclear, as the presentation of psychological symptomatology varies between cultures (Betancourt, Speelman, Onyango, & Bolton, 2009; Derluyn, Broekaert, Schuyten, & Temmerman, 2004; Harms, Kizza, Sebunnya, & Jack, 2009; Okello & Musisi, 2006; Okello & Ekblad, 2006; Organization, 2003). Given the disproportionate burden of HIV/AIDS in Africa, including the largest cohort of young persons infected and affected by HIV/AIDS (UNAIDS, 2013), there is a need to develop culturally and developmentally relevant measures of psychological distress for African adolescents.

This paper is grounded in Lazarus's Transactional Model of Stress and Coping (TMSC). Lazarus and colleagues (Lazarus 1966; Lazarus and Folkman, 1984) assert that the way people

cope with stressor is crucial to their physical, social and psychological wellbeing, Stressors are demands made by the internal or external environmental that upset balance, thus affecting physical and psychological wellbeing, and require action to restore balance (Lazarus & Cohen, 1977). Additionally, the relation between stress and coping is reciprocal: it depends on the person's appraisal of the stressor and is mediated by the social and cultural resources available at his or her disposal to combat the stressor (Antonovsky, 1979; Cohen & McKay, 1984; Lazarus & Cohen, 1977).

The purpose of this study was to develop and test a measure of psychological distress for HIV-infected adolescents in Uganda, where more than 190,000 children less than 14 years are living with HIV (UNAIDS, 2013). This paper describes the process of developing and testing a measure of psychological distress among Ugandan HIV-infected adolescents, 12- 19 years, by elaborating the procedures used to develop the psychological distress measure, and then describing the processes used to assess the psychometric properties of the developed measure.

Methods

Setting

The study was conducted among HIV-infected adolescents at the Joint Clinical Research Center (JCRC) in Kampala, Uganda. The JCRC is a not-for-profit organization established in 1991 and provides HIV care to approximately 10,000 patients, of which approximately 2,500 are children and adolescents.

Study population and procedures

Adolescents, aged 12 - 19 years and currently enrolled in HIV care at the JCRC during February – September 2013 were recruited to participate in this study. A total of 507 adolescents participated in the study. Forty seven (47) adolescents participated in the scale

development phase (in-depth interviews (10), focus group discussions (27), cognitive interviews (6), and 464 in the scale assessment phase. Participants were recruited during their scheduled clinic visits, by the principal investigator and three (3) research assistants who had received training on interviewing and research ethics. Potential respondents were approached in the clinic waiting room; initial inquiries focused on ascertaining the adolescent's disclosure, followed by a discussion of the study purpose and participants' rights. Adolescents expressing interest in the study, and their caregivers (if present) were invited to the interview rooms adjustment to the clinic were informed consent was sought; if the caregiver was absent, the necessary arrangements were made with the adolescent to obtain caregiver consent. Permission to conduct this study was provided by the Institutional Review Board at the JCRC, the University of Michigan Ethics Review Board, and Uganda National Council for Science and Technology Ethics Review Board.

Study approach

The study was conducted over a period of nine months (February - September, 2013). The scale development phase focused on developing culturally and developmentally meaningful measure of psychological distress, utilizing the principles of scale development described by Krause, 2002 (Krause, 2002) and DeVellis (2011) (DeVellis, 2011). This was followed by the scale testing phase, which focused on assessing the psychometric properties of the measure.

Scale development

Repeat in-depth interviews and focus group discussions

In-depth interviews (IDIs) were conducted with a convenience sample of 10 HIV-infected adolescents (5 males and 5 females), to explore adolescents' understanding of

psychological symptomatology and the terms frequently used to describe such conditions. The interviews were conducted in English, Luganda or both, depending on the respondent's language preference and proficiency. Respondents were asked to describe what "good" and "bad" mental health means to them, including the causes and manifestation of these conditions. Given the lack of semantic equivalency for the term "mental health" in Luganda (Harms et al., 2009; Okello & Ekblad, 2006), the local language used in this study, the term "ebilowoozo" was used to initiate discussions among Luganda respondents, a term that roughly corresponds to "thought process" in English. These data were analyzed to identify themes relevant to psychological distress symptomatology and the local terms commonly used to describe to describe distinct symptoms.

Subsequently, three focus group discussions (FGDs) were conducted with purposively selected sample of 27 HIV-infected adolescents, to test the validity and reproducibility of common meanings attached to terms found through the IDIs and identify any further elaboration of terms and definitions. Participants were selected to capture the diversity in age, sex and schooling status (currently in school or out of school). The size of each group (males only (9), females only (10), and mixed sex- males (4) and females (5)) depended on the number of respondents available at the start of the discussion. The FGDs were moderated by the principal investigator, assisted by a JCRC pediatric counselor. All participants were fairly proficient in English but questions were presented in both English and Luganda, and participants were asked to use the language they found most comfortable expressing their opinions. No participants took part in both the IDIs and FGDs.

The discussions also utilized the funnel approach (Morgan, 1998): data from earlier FGDs was used to revise the FGD guide for subsequent discussions. To set the stage for discussion, each respondent was asked to describe one thing that makes them happy and another

that makes them unhappy. Using a Smiley Faces rating scale (**see Figure 2.1**), participants were asked to provide a term that best describes each emotion, describe how the hypothetical person feels, why a person would feel that way and what could help the person feel better. FGDs were audio-taped and transcribed; content analysis was used to confirm the local terms and phrases that were used to describe psychological distress symptomatology, and these were sorted into related symptomatology groups.

Item selection

The results of IDIs and FGDs were subsequently used to develop a battery of items for a psychological distress scale. Items from several published measures of psychological distress – Kessler-10, BDI, PHQ, BSI and GHQ- were used whenever possible, and two criteria guided the item selection: first, the item corresponded to themes of psychological distress identified in the in-depth interviews and FGDs, and secondly, the items had good cultural fit, as determined by cultural references or terminology used. For example, items referring to infrastructure or events that are uncommon in Uganda e.g. trains or subways were omitted or adapted as were items using colloquial English terms that had no direct consonance in the local language e.g. feeling down, blue, blocked, open spaces etc. In these two illustrative cases, the replaced phrasing was "I was not able to feel happy" and "I could not get going". Items related to the somatic symptoms of depression and anxiety were largely included in the pool based on prior empirical support for somatization as a construct of psychological distress (Cimprich, 1999; Derogatis & Fitzpatrick, 2004; Goldberg & Hillier, 1979; Massé, 2000). Due to overlap in items across measures of psychological distress, only one such item representing a distinct construct was selected into the item pool.

Using these criteria, a total of 67 items were identified from existing scales. These items were grouped into candidate subscales of depression, anxiety, social difficulties, anger, optimism/hopelessness, loneliness, happiness/sadness, self-perception, irritability, and somatization. Conceptually equivalent items were removed from the pool and three additional questions were written to capture substance and drug abuse; this had been identified in the FGDs as a component of psychological symptomatology but had not been included in previously published scales. This process resulted in an item pool of 52 items, describing psychological distress symptomatology over the past week. Consistent with previous measures of psychological distress, responses were measured on a five-point scale - never, almost never, sometimes, often, and most of the time.

Translation

All questions were independently translated into Luganda by two translators – a certified translator at the JCRC and a translator at Makerere University Language Institute. These translations were subsequently reviewed by a 3- person committee including the principal investigator, a nurse and a pediatric counselor at the JCRC, in order to assess how well they captured the conceptual basis of the items, and to discern whether the Luganda terms used in the translations could be understood by non- native Luganda speakers, given the diversity in ethnicity and cognitive capabilities of the adolescent population at the JCRC. During this review, the team noted that the translated version from the Language Institute often consisted of terms that are not commonly used, and which would be difficult for adolescents to understand. The final wording of these items was usually taken from the JCRC translation. If there was difficulty finding semantically equivalent terms that could be easily understood by adolescents, multiple terms that captured the conceptual basis of the item were included in the translation. For example,

"dizziness" was translated into "Kantolooze" or "kamunguluze", and "suddenly scared for no reason" was translated into "Okwekanga" or "Okutya awatali ne'kitiisa". Discrepancies between the original and translated versions, and between translated versions were examined. Final choices on the most appropriate translation were based on consensus within the team, and on a few occasions, through consultations with other pediatric providers within JCRC.

Expert panel review

Following translation of the final 52 items, the scale was reviewed by an expert panel consisting of five bi-lingual Ugandan health providers (four psychiatrists, and a pediatric HIV specialist) and two psychologists based at the University of Michigan. Two of the Ugandan psychiatrists had extensive experience working with HIV-infected children, the other two Ugandan psychiatrists had extensive experience working with children and adolescents experiencing trauma in Uganda; the two University of Michigan psychologists had extensive experience working with HIV-infected youth in the USA and sub-Saharan Africa. Each panelist reviewed the items independently, and was asked to evaluate the developmental, cultural and conceptual appropriateness of each item. Panelists were also asked to assess the conceptual breadth of the items pool as an aggregate measure of psychological distress in adolescents, the accuracy of the translations (for local clinicians) and ability of adolescents to understand the terms used, and any suggestions on additional domains and/or items that could be added to the item pool.

Overall, the panelists agreed that the scale items covered the breadth of psychological distress, with several noting that this is a relatively new field and the literature is not as expansive as other psychiatric manifestations of mental health. They noted that several items had been translated literally yet a contextual approach to the translation would be more effective.

Panelist also noted that constructs such as “feeling scared” and “feeling fearful” and “feeling nervous” and “feeling anxious” cannot be differentiated in Luganda, so they should be eliminated from the measure to avoid redundancy.

Of particular concern were the items “thinking that you are watched or talked about my others” and “thoughts about ending your life” which were thought to tap into paranoia and suicidal ideation, rather than distress. One panelist noted that the measure tapped into highly specified psychiatric conditions including depression, anxiety, psychosis, and disruptive behavior, and recommended focusing more narrowly on psychological distress. However, these items- “thoughts of ending your life” and “thinking that you are watched or talked about by others” - were not removed from the scale because they were consistently associated with psychological distress in both the IDIs and the FGDs, and a prior exploratory study conducted within this population**.**

The panelists suggested adding questions to capture domains related to drug and substance abuse, school and body image challenges. The scales was revised accordingly. Suggested alternatives to item wording were incorporated into the measure. Items without linguistic differentiation- lacking unique words in Luganda- were removed. The final scale was comprised of 48 items.

Cognitive interviews

Following the panel’s revisions to the scale, cognitive interviews were conducted with 6 adolescents (3 females and 3 males) to undertake a final assessment of the item wording, respondents’ understanding of the scale items, adequacy of translated items, and identify questions that could potentially elicit respondent discomfort. Four interviews were conducted in English and two in Luganda. Paraphrasing, a technique to assess understanding of items, was the

most frequently to assess respondent's understanding of scale items. Respondents had difficulty with the think aloud technique, a commonly used technique in cognitive interviewing. Interviews lasted approximately 30 minutes, and respondents did not report discomfort with any scale item.

Difficulty in understanding was identified for select items. For example, one respondent interpreted "nervousness or shakiness inside" as losing balance or feeling like your 'insides" or stomach are twisting or upset. The item "pains in heart or chest" was interpreted as a heart attack and heart break; "suddenly scared for no reason" was associated with cowardliness, while "spells of terror or panic" was associated with witchcraft and sorcery. To address these issues, either the English or Luganda translations were revised, depending on the source of the misconceptions. For example, the English item "pains in heart or chest" was revised into "physical pains in heart or chest" to differentiate it from a heart break and the term "spells of terror or panic" was revised into "occasional feelings of terror or panic".

Pilot testing

The psychological distress items were then subjected to pilot testing to assess the preliminary psychometric properties of the scale, and identify potential areas of revision of the scale, prior to large scale testing. The pilot tested sample consisted of 98 adolescents, ages 12 – 19 years who were recruited during their scheduled clinic visits. Interviews were conducted following the doctor visits, or during scheduled interview appointments. Data were collected using a paper questionnaire administered by the principal investigator, a pediatric counselor and nurse: interviews were conducted at the clinic and lasted approximately 25 minutes. Additional data on respondent's age, sex, and level of education were collected. The data were entered into Excel and exported to SPSS (version 21) for analysis.

Evaluation at scale

Participants

The scale testing was part of a larger study exploring the relationship between psychological distress and adherence to HIV care among HIV-infected adolescents in Uganda. A convenience sample of 464 respondents, aged 12 – 19 years, was recruited during subject scheduled clinic visits. A quota sampling strategy was used to ensure adequate representation of males and females across all ages. Study eligibility was limited to adolescents, 12 – 19 years, on ART, aware of their HIV status, and without any known cognitive limitations. Adolescents who had participated in the IDIs, FGDs and other pilot study activities were excluded from the study. Additionally, adolescents presenting to the clinic with severe illness were not interviewed at that visit. Attempts were made to interview these participants at a later date.

Procedure

The minimum sample size for evaluation was based on considerations for the broader study outcomes- exploring the relationship between psychological distress and adherence, and was determined to be 460, using Optimal Design Software (version 3.0) (Spybrook, Raudenbush, Liu, & Congdon, 2006) to obtain the minimum sample size at alpha (α) = 0.05, power = 0.80 and medium design effect (d = 0.5) (Cohen, 1992). The adequacy of the determined sample size for testing the psychometric properties of the psychological distress scale was deemed adequate based on the recommendation of at least 5 cases per item. Data were collected May and September 2013 in face-to-face interviews, using questionnaires programmed onto Personal Digital Assistant (PDA) devices. This mode of data collection was chosen primarily, to reduce missing data and also reduce costs and errors related to data entry.

The psychological distress scale was embedded within a larger study questionnaire consisting of 315 questions distributed over six (6) sections: (1) demographics (e.g. age, sex, education, religion, orphan-hood status, type of caregiver, self-rated health and overall happiness; (2) stressors (e.g. negative life events, concerns and hardships, and quality of HIV, stigma); (3) psychological distress measure of 45 items described above; (4) personal resources- coping resources, social support, optimism, spirituality; (5) measures of adherence to HIV care; and (6) alcohol and substance abuse. Interviews lasted between 60 – 75 minutes, including the scheduled breaks in the questionnaire. Participants were given a drink and snack during the interview.

Three additional measures were included in the questionnaire to evaluate the construct validity of the psychological distress scale: (1) quality of life assessed using a 39-item locally adapted Functional Assessment of Human Immunodeficiency Virus Infection (FAHI) (Cella & Bonomi, 1994) assessing emotional, physical, social, family and functional concerns and relationship with doctor; (2) life satisfaction assessed using the question– "taking all things together, would you say you are- very happy, fairly happy, not very happy or not at all happy?"; and (3) self-rated health assessed using the question- "all in all, how would you describe your state of health these days- very good, good, fair or poor?".

Data Analysis

Univariate analyses were computed for data from the pilot (96 respondents) and scale testing (464 respondents) such as measures of central tendency- frequencies, standard deviation, and range. Exploratory factor analysis (EFA), using principal components analysis (PCA) and Promax rotation was used to identify the underlying factors (subscales). Subscales were used if with Eigen values were greater than greater than one, and the minimum item loading score was

0.4 (Institute for Digital Research and Education). PCA was chosen to maximize common variance in the data, while the Promax was chosen based on the theoretical assumption that psychological constructs are correlated. Reliability analyses (Cronbach's alpha) were conducted to assess the internal consistency of the extracted subscales and the entire scale. Inter-item correlations, means, standard deviations, and ranges were also computed.

The suitability of the data for factor analysis was evaluated using the Kaiser-Meyer_Olkin (KMO) measure of sampling adequacy and Bartlett's test of sphericity of the correlation matrix. The KMO assesses sampling adequacy by comparing the magnitude of the observed correlation coefficients in relation to the magnitude of the partial correlation coefficient: the recommended cut off for sampling adequacy is 0.6. Bartlett's test of sphericity of the correlation matrix is used to test the hypothesis that the correlation matrix is an identity matrix (all the diagonal terms are one and all the off diagonal terms are zero); a p-value less than 0.05 is required to reject the null hypothesis. The correlation matrix was inspected for presence of coefficients greater than 0.4, which may have indicated potential collinearity among scale items.

The above analyses were replicated in the scale testing sample, where the following additional analyses were also conducted. The rotated factor solution was revised to remove cross-loading items, and the remaining scale items were re-analyzed to confirm the scale factor structure. Reliability analyses to assess the internal consistency (Cronbach's alpha) of each subscale and the entire scale were examine to determine of the suggested minimum criterion for a new scale is 0.70 (Nunnally & Bernstein, 1978) was met. The average subscale scores, and a composite scale score (summation of the averaged sub-scale scores) were computed as well as correlations between subscales, and between each sub-scale and composite score. An exploratory

factor analysis with principal components and varimax rotation using the average subscale scores as an item, was conducted to assess the viability of the composite of scale score.

Construct validity of scale was assessed through examination of correlations with other measures of wellbeing, and with confirmatory factor analysis. The scale scores – subscale scores and composite score- correlations with FAHI score, overall happiness score, and self-rated health score were examined. Confirmatory factor analysis was used to assess the fit of the derived scale structure to the data, and assessed through the model fit indices- chi-square, RMSEA (< 0.1), TLI and CFI (> 0.9).

Results

Pilot testing

The initial pilot sample as majority female (58%; n = 57) and the average age of participants was 15.5 years (SD = 1.6). Half of respondents were enrolled in secondary school, and only 5% (5) were currently out of school. The mean item score was 1.995 (SD = 1.1); inter-item correlations ranged from 0.272 to 0.622, and averaged 0.184. The KMO measure of sampling adequacy was 0.692 and the Bartlett's test of sphericity of the correlation matrix was significant; chi-square = 140 (*df* = 666); p < 0.001, indicating the sample size was adequate for factor analysis, Prior to factor analysis, three items on drugs and substance abuse were removed due to very low response to these items. An EFA of remaining 45 items revealed an 11 factors with Eigen value greater than 1.0 and explaining 64.9% of the variance. Using 0.4 minimum factor loading as a threshold for cut off eliminated "feeling no interest in things"; "the idea that you should be punished for you sins"; "feeling weak in parts of your body"; and "felt depressed". The total scale reliability (45 items) was high: Cronbach's alpha = .891.

Since the KMO measure of sample adequacy (recommended cut off of 0.6) indicated that the sample size was just adequate for these analyses, and given the lack of clear cut theoretical consistency within subscales, the results of these analyses were deemed to be inconclusive. However, these results were used to refine the scale further. Three items on tobacco, alcohol and substance abuse were removed the scale due to low item mean scores and concerns about under-reporting on these items. Based on field notes indicating difficulty in changing directionality in positively worded items such as "didn't have fun at school", several items were reversed to ensure uniformity in the direction of all scale items, thereby reducing cognitive demands on respondents. The final scale of 45 items along with item translations are presented in **Table 2.1.**

Scale testing

Demographic characteristics of respondents are presented in **Table 2.2.** The majority of the participants were female (53.4%), and the average age was 15.6 (SD = 2.4). Few participants were currently out of school (6.4%) and 5.4% did not have any education. The KMO measure of sampling adequacy was 0.93, and Bartlett's test of sphericity was statistically significant: chi-square = 6718.04 (df = 990); $p < 0.001$, suggesting that the sample was adequate for factor analysis. The rotated factor solution revealed 10 factors, explaining 53.3% of the total variance. There was significant overlap across items factors and several items with factor loadings less than 0.4. Removal of low loading and overlapping scale items reduced the scale from 45 to 25 items. The exploratory factor analysis was repeated and three (3) additional items with factor loadings less than 0.4 were removed. The final solution revealed six factors, which were labeled anhedonia, depressive-anxiety, isolation, suicidal ideation, sleep problems, and somatization. These six factors explained 50.5% of the variance. The factor structure of the final scale is presented in **Table 2.3.**

Inter-item correlations of the measure ranged from 0.018 to 0.483 with a mean inter-item correlation of r = 0.237. The average and range inter-item correlations of the subscales were as follows: anhedonia, r = 0.313 (0.240 – 0.379); depressive-anxiety, r = 0.348 (0.224 -0.421); isolation, r = 0.369 (0.326 – 0.421); suicidal ideation, r = 0.303 (0.322- 0.498), sleep problems, r = 0.389 (0.309 – 0.483); and somatic, r = 0.285 (0.241 – 0.348).

A descriptive summary of the total scale score (Global psychological distress score) and sub-scales and the internal reliability of each total scale and sub-scales is presented in **Table 2.4**. The standardized Cronbach's alpha (α) for the subscales were for anhedonia, α = 0.732 (6 items); depressive-anxiety, α = 0.724 (5 items); isolation, α = 0.635 (3 items); suicidal ideation, α = 0.633 (4 items); sleep problems, α = 0.732 (3 items); and somatic symptoms, α = 0.615 (4 items). The Cronbach's alpha of the combined (25 items) was 0.89.

Table 2.5 presents the correlations between the Global psychological distress score and each sub-scale scores. The global psychological distress score correlated with the subscales scores as follows: anhedonia (r = 0.77), depressive-anxiety (r = 0.80), isolation (r = 0.72), suicidal ideation (r = 0.70), sleep problems (r = 0.73) and somatic (r = 0.66). Correlations among subscales ranged from 0.27 (somatic and isolation) to 0.58 (anhedonia and depressive-anxiety).

The results of the convergent validity analyses are presented in Table 2.6. As anticipated, a statistically significant positive correlation was observed between the psychological distress scale and FAHI quality of life scale (r = 0.5483; p < .001), and between the psychological distress scale and each FAHI sub-scale:- emotional concerns (r = 0.4396; p < .001), social concerns (r = 0.3014; p < .001), functional concerns (r = 0.4110; p < .001), physical concerns (r = 0.5803; p < .001), relations with providers (r = -0.1832; p < .001), and additional concerns, (r = 0.1514; p < .001).

Additionally, the scale was negatively correlated with overall happiness ($r = -0.3054$; $p < .001$), and self-rated health ($r = -0.2478$; $p < .001$). Results of the confirmatory factor analysis assessing fit of the scale structure to the data indicated adequate model fit, with chi-square (260 degrees of freedom) of 470.772 ($p < 0.000$), RMSEA = 0.042 (CI: 0.036 – 0.048), CFI = 0.922, and TLI = 0.910.

Lastly, results of the exploratory factor analysis using subscales scores to assess the viability of composite score revealed a one dimensional scale explaining 52.5% of the total variance. This confirmed the utility of using a composite score of global psychological distress. The item loadings of these EFA derived scales ranged from 0.654 to 0.804: depressive-anxiety, 0.804; anhedonia, 0.781; isolation, 0.710; suicide, 0.708); sleep disturbance, 0.687; and somatic symptoms, 0.654.

Discussion

Using a mixed method approach, we have developed a 25-item psychological distress scale for adolescents in Uganda with good psychometric properties. This scale has six scales- anhedonia, depressive-anxiety, isolation, suicidal ideation, sleep problems, and somatization. Analysis indicated that the subscales had adequate fit with internal reliability of the subscales ranging between 0.615 and 0.732, and reliability of the entire scale at 0.89. The results of the confirmatory factor analyses indicated the scale structure adequately fits the data. And exploratory factor analysis of the sub-scales, revealed a one-dimensional factor, thus supporting the use of a composite global psychological distress score.

With the exception of the suicidal ideation sub-scale, which has not been documented in prior distress measures, the results of this study are consistent with published measures of psychological distress, which also incorporate the subscales – depressive- anxiety and anhedonia

(Derogatis & Melisaratos, 1983), social isolation and somatization (Massé, 2000) and sleep disturbances (Cimprich, 1999). The findings on suicidal ideation are consistent with findings from a studies conducted among HIV-infected adolescents in Uganda. In a small study conducted among 82 HIV-infected adolescents aged 10 – 18 years, Musisi and Kinyanda (2009) found that 17.1% of respondents had attempted suicide within the past 12 months (Musisi & Kinyanda, 2009). Similarly, in an unpublished qualitative study conducted among HIV-infected adolescents at the JCRC (12 – 19 years), several respondents reported considering suicide following diagnostic disclosure of their HIV status (Mutumba et al, unpublished). Suicide is one of leading causes of death among young people aged 10 – 24 years worldwide (World Health Organization, 2014). A systematic review of studies conducted among youth living in seven African countries, including Uganda, Page et al (2011) found that 25% of boys and 26.3% of girls has seriously considered suicide; these were higher than rates of suicidal ideation among youth in high-income countries (Page & West, 2011). A study conducted among children and adolescents (3 – 19 years) in western Uganda found that the life time prevalence of suicidal ideation in this population was 6.1% (Kinyanda, Kizza, Levin, Ndyanabangi, & Abbo, 2011). The risk factors for suicidal ideation among adolescents worldwide include: psychiatric illness, especially major depressive disorder; alcohol and substance abuse; cognitive factors such as deficits in problem-solving skills, low-self-esteem, hopelessness; major negative life events such as personal bereavement; socio-economic disadvantage; and biological factors such as abnormal serotonergic function (Fleischmann, Bertolote, Belfer, & Beautrais, 2005; LaFromboise & Howard-Pitney, 1995; Mc Manama, Kimberly, & Berzin, 2012; Page & West, 2011; World Health Organization, 2014). Therefore, the prominence of suicide in both the adolescents'

narratives (in-depth interviews and FGDs) and as a domain of this psychological distress measure, underscores its clinical relevance in this population.

While the procedures used to develop this scale are consistent with steps routinely recommended and utilized in prior studies of scale development, including several conducted in Africa (Betancourt et al., 2011; Betancourt, Speelman, et al., 2009; Ertl et al., 2011), the study procedures also differed from prior studies in several notable ways. First, we utilized in-depth interviews followed by focus group discussions to identify psychological distress symptomatology, but we did not give weight to a symptom tally during analysis of data from IDIs and FGDs, an approach favored by Betancourt et al (Betancourt et al., 2011; Betancourt, Speelman, et al., 2009). While the symptom tally has value for circumscribed outcomes, in IDIs and FGDs were judged as more suitable for the breadth of psychological distress symptomatology explored in this study. Secondly, adolescents' caregivers were not involved in identifying distress symptomatology; while their input could have enriched discussions on psychological distress symptomatology, the study sought to utilize adolescent's experience with psychological distress and also identify the terminology used to describe these symptoms. However, involvement of clinicians- pediatric HIV consultants, a nurse and counselor with extensive experience working with this population compensated for this inadequacy.

Lastly, this study could not include a "gold standard" to ascertain the reference criterion for the developed measure, or attempt to cross-validate adolescent's reports. The literature of psychological distress is not as well developed as other mental disorders such as depression, and there is no gold standard for psychological distress. Prior scale development studies (Betancourt et al., 2012; Ertl et al., 2011) have relied on structured diagnostic interviews, and or clinical judgment of locally trained psychiatrists to establish reference criterion for developed scales.

These practices, while helpful in ensuring comparability across contexts, may contradict the rationale behind developing locally relevant scales, as such standards based on Eurocentric concepts of mental health and majority have not been locally validated. The use of local psychiatrists is not infallible as psychiatric training in Africa is based on concepts of western medicine. Betancourt et al (Betancourt, Bass, et al., 2009; Betancourt et al., 2011) and Mels et al (Mels, Derluyn, Broekaert, & Rosseel, 2010) have each utilized parent/caregiver reports to establish reference criterion but these are also not without limitations, as parent/caregiver and youth reports vary in agreement, across different mental disorders (Duhig, Renk, Epstein, & Phares, 2000; Weisz, Sigman, Weiss, & Mosk, 1993). Current findings indicate that the proposed measure has adequate construct validity; additional evidence on the predictive properties of this measure is provided in chapter 3 and Chapter 4.

While the results of these analyses indicate that the underlying factor structure of the measure adequately fits the population- RMSEA = 0.042, CFI = 0.922 and TLI = 0.910, caution should be exercised interpreting these results since these analyses are conducted on the population from which the tested factor structure was derived. Further investigations to assess the validity, true test-retest reliability, and relational properties of the scale with clinical diagnosis within diverse populations is warranted.

There are several limitations to this study. The study population consisted of adolescents drawn from one HIV treatment center, located in an urban area, and response rates were not evaluated; the experiences of these respondents may systematically from adolescents in other health centers, and also from adolescents who did not participate in the study. However, the fact that the center draws clients from all over the country, and that final sample is more than 75% of the adolescent population at JCRC may attenuate any potential

selection bias in the sample population. Despite these limitations, the study has several noteworthy attributes including the use of extensive qualitative methods to establish the target populations experiences and understanding of psychological distress, development of a measure that can be used among adolescents of diverse ethnic background and cognitive capabilities, and a large sample size (464 participants). The potential contribution to improving the quality of adolescent HIV care in the country provides justification for future use and refinement of this proposed measure.

Conclusion

The psychological distress measure developed in this study provides a mechanisms for integrating psychological care and HIV care. The tool enable clinicians and researchers to screen for psychological distress among HIV-infected adolescents in Uganda, thus facilitating early recognition, referral and monitoring of adolescents in the context of their daily care. The measure also health providers and researchers with information to tailor their clinical care and develop psychosocial interventions in accordance with the adolescent's psychological needs. For example, within the clinical setting, adolescents scoring high on suicidal ideation should be referred to psychiatric services, while adolescents scoring high on isolation could be referred to social support groups, where available. This measure could be self-administered within a clinical and research setting. Within the clinical setting, this measure could serve as starting point for discussions about the adolescent's psychological wellbeing, particularly, if administered by the health provider, and it could provide a mechanism for monitoring the adolescent's wellbeing in the course of their routine HIV care. Lastly, the measure providers researchers with a tool to accrue the much needed data on the burden and breadth of psychological distress symptomatology among HIV-infected adolescents, and enables both, the examination of how

different psychological symptomatology impact adolescents' well-being, and prioritization of scales to develop for diagnostic purposes.

Additional research is needed to establish the cut-off points for this measure. A score two standard deviations above the mean in the study population could serve as a preliminary cut-off point for differentiating between adolescents with or without psychological distress. While these cut-offs may be adequate, future research is needed to establish reference criterion and test-retest reliabilities for the scale and its subscales, and also investigate the validity of the derived factor structure across diverse populations. Lastly, there is a need for future research on how tobacco, alcohol and substance abuse could be incorporated into measures of psychological distress, given the prominence of themes related alcohol and substance abuse within adolescent's narratives.

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Appendices

Figure 2.1. Smiley faces rating scale

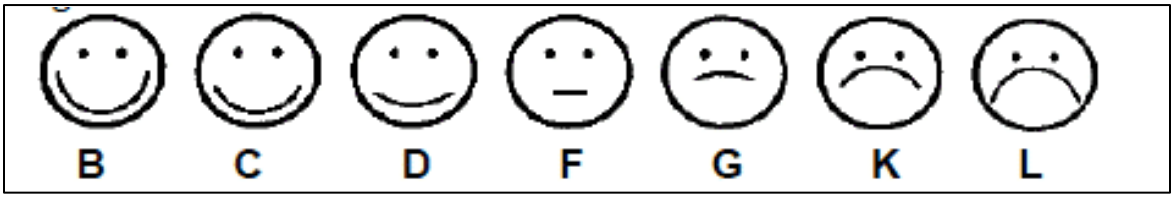

Table 2:1: List of scale items and corresponding translations

Please indicate how often you have felt this way DURING THE LAST WEEK Muwiiki eyise, mbulira emirundi emeeka gyowuride…….	
1.	Faintness or dizziness Okuwulira nga agenda okuzilika or Kantolooze/ kamunguluze
2.	Nervousness or shakiness inside Entiisa oba Okujugumira n'okukankana
3.	Physical pains in the heart or chest Obulumi mu Kifuba oba mu Mutima
4.	Thoughts of ending your life Ebirowoozo eby'okwetta
5.	Suddenly scared for no reason Okwekanga oba okutya awatali ne'kitiisa
6.	Feeling no interest in things Obutabawo na kikunyumira
7.	Trouble getting your breath Okuziyira oba obutasa bulungi
8.	Numbness or tingling in parts of your body Okuwulira amasannyalaze ng'agakuba mu bitundu ebimu eby'omubiri gwo oba okuwulira obuntu obukufumita oba okusanyalala
9.	Feeling hopeless about the future Okugwaamu essuubi
10.	Feeling fearful Okufuna entiisa oba okuwulira okutya mumutima
11.	I felt lonely Nawulira nga mpubaadde
12.	I felt something bad might happen Nalowooza nti nja kufuna ekizibu oba nga'nsubira waliwo ekibi ekigenda okubawo oba okugwawo
13.	I felt depressed Nafuna Ennyiike.
14.	Felt worry Nawulira nga Nelaliikirira
15.	Felt uneasy, troubled or uncomfortable Nawulira nga sirina mirembe
16.	Had trouble remembering things Nalina Obuzibu okujjukira
17.	Feeling easily annoyed or short-tempered Nawulira nga'kwatibwa obusungu amangu oba nga'nyyiga mangu oba nga'nvako waya manguu
18.	Didn't feel like eating

	Nali ssaagala kulya
19.	I felt worthless Nawulira nga sikyalina mugaso
20.	I felt like the children I know were not friendly or that they didn't want to be with me Nawulira nga silina mukwano ne'baana bannange, oba nti tebaagala kubeera nange
21.	Found difficulty getting started on my schoolwork Kyanzibuwalira okutandika okukola homework wange
22.	Did not have fun at school Nawulira nga'sikyanyumirwa ku somero
23.	I wasn't able to feel happy; even when my family and friends tried to make me feel better Saalina sanyu; newakubadde nga ab'Olunganda n'Emikwano bagezaako okunsanyusa
24.	Felt like I hated myself Nga'mpulira nga nekyaye kyaye
25.	Felt like I did not want to be with other people Nawulira nga'saagala okubeera nabantu abalala
26.	Felt bad about the way I look Nawulira bbuubi kungeeri gye'nfanaanamu
27.	Nausea or upset stomach Okusindukirirwa emeeme oba Olubuto okwekyanga /okulumaluma
28.	Feeling tense Okubulwa obuwerero oba okuwulira nga'toli mukakamu
29.	Occasional feelings of terror or panic Okutya okwamanyi oba okupapa
30.	Feeling so restless that you could not sit still Okuwulira nga toterede nga tosobola na'kukakana
31.	Feeling weak in parts of your body Okugwamu amaanyi mu bitundu ebimu ebyo'mubiri gwo
32.	Thinking that you are watched or talked about by others Okulowooza nti abantu bakugeya oba bakulondola
33.	Trouble falling asleep Okubulwa otulo oba obizibu okufuna otulo
34.	Felt that you had too many thoughts Wawulira nga'alina ebiroowozo bbingi
35.	The idea that you should be punished for your sins Okwerumiriza nti osaana kubonerezabwa Okulowooza nti olina okubonerezabwa olye'bibi byabwe
36.	Feeling that people are unfriendly or dislike you Okuwulira nti abantu tebanjagala
37.	I could not get going

	Nakalubirirwa mubulikimu
38.	I felt lonely Nawulira nga nsigadde bwomu
39.	My sleep was restless Nateganyizibwa mutolo
40.	I felt everything I did was an effort Nawulira nga bulikyenkola kyintwalira ekiseera okutandika
41.	I was bothered by things that don't usually bother me Natawanyizibwa ebintu ebitatera kuntawanya
42.	I had trouble keeping my mind on what I was doing Nafuna obuzibu okussa mwoyo ku byenkola
43.	I felt happy Nawulira e' ssanyu
44.	I thought my life has been a failure Nawulira nga alemedwa mubulamu
45.	Felt that I was just as good as other children Nawulira nga'nninga abaana abalala/ okwegerageranya

Table 2:2: Descriptive statistics of respondents socio-demographic

Variable	Percent (frequency) / Mean (SD)
Age	M = 15.6 (SD = 2.44)
Sex	
Males	46.6 (217)
Females	53.4 (249)
Religion	
Protestant	25.9 (121)
Catholic	37.3 (174)
Muslim	16.7 (78)
Pentecostal	7.1 (33)
Other e.g. SDA	12.8 (60)
Education level	
None	5.4 (25)
Primary	37.8 (176)
Secondary	49.6 (231)
Tertiary	7.3 (34)
Type of school	
Day	69.7 (280)
Boarding	30.4 (122)
Orphan-hood	
Both parents alive	32.6 (152)
Paternal orphan-hood	26.4 (123)
Maternal orphan-hood	19.5 (91)
Double orphan-hood	21.5 (100)

Table 2:3: Results of exploratory factor analysis for a psychological distress scale using data collected from 462 HIV-infected adolescents in Uganda

Items	1	2	3	4	5	6
Anhedonia						
1. I had trouble keeping my mind on what I was doing	.867					
2. Found difficulty getting started on my school work	.629					
3. I felt everything I did was an effort	.588					
4. Feeling no interest in things	.525					
5. Numbness or tingling in parts of your body	.498					
6. Felt uneasy, troubled or uncomfortable	.428					
Depressive- anxiety						
7. Feeling easily annoyed or irritated		.818				
8. I felt depressed		.641				
9. Felt you had too many thoughts		.561				
10. I felt something bad might happen		.478				
11. Thinking you are watched or being talked about		.467				
Isolation						
12. I felt like the children I know were not friendly or that they didn't want to be with me			.795			
13. Feeling that people are unfriendly or dislike you			.772			
14. I felt lonely			.433			
Suicidal ideation						
15. The idea that you should be punished for your sins				.758		
16. Felt worthless				.675		
17. Thoughts about ending your life				.650		
18. I thought my life had been a failure				.525		
Sleep problems						
19. My sleep was restless					.753	
20. Trouble falling asleep					.715	
21. Suddenly scared for no reason					.515	
Somatization						
22. Nausea or upset stomach						.900
23. Physical pains in heart or chest						.632
24. Faintness or dizziness						.505
25. Didn't feel like eating						.455

Table 2:4: Descriptive summary of the subscales and their corresponding internal reliability (Cronbach's alpha) of the global distress measure and its subscales

	Mean (SD)	Min	Max	Number of items	Cronbach's alpha
Global psychological distress	0.97 (0.59)	0	2.89	25	0.89
Anhedonia	1.12 (0.77)	0	3.33	6	0.73
Depressive-anxiety	1.20 (0.87)	0	4.0	5	0.72
Isolation	0.86 (0.85)	0	4.0	3	0.64
Suicide	0.59 (0.67)	0	3.0	4	0.63
Sleep	0.69 (0.81)	0	4.0	3	0.65
Somatic	0.99 (0.78)	0	3.5	4	0.62

Table 2:5: Correlations between global psychological distress score and sub-scales

	Global psychological distress	Anhedonia	Depressive-anxiety	Isolation	Suicidal ideation	Sleep problems
Anhedonia	0.834***					
Depressive-anxiety	0.819***	0.583***				
isolation	0.644***	0.459***	0.505***			
suicide	0.673***	0.445***	0.470***	0.481***		
Sleep problems	0.683***	0.453***	0.468***	0.378**	0.429***	
Somatization	0.654***	0.420***	0.441***	0.281**	0.322**	0.449***

Table 2:6: Convergent validity of the psychological distress scale – composite score and sub-scale with measures of wellbeing – quality of life, self-rated happiness and self-rated health

Index	Quality of life (FAHI)	Overall happiness	Self-rated health status
Global psychological distress	0.543***	-0.300***	-0.248***
Anhedonia	0.383***	-0.229***	-0.201***
Depressive- anxiety	0.513***	-0.269***	-0.189***
Isolation	0.335***	-0.187**	-0.154***
Suicidal ideation	0.474***	-0.293***	-0.178***
Sleep problems	0.321***	-0.228***	-0.105
Somatization	0.363***	-0.139**	-0.241***
***p < .001; **p < .05			

Chapter 3

Predictors of psychological distress among HIV-infected adolescents in Uganda

Introduction

Approximately 1.7 million adolescents aged 10-19 years are living with the Human Infection Virus (HIV) in sub-Saharan Africa (UNAIDS, 2013a). The HIV epidemic has been linked to the increased prevalence of psychological symptomatology among HIV-infected children and adolescents (Benton & Ifeagwu, 2008; Mellins & Malee, 2013), which in turn, have been associated with risky health behaviors including non-adherence to anti-retroviral treatment (ART) leading to poor immunological outcomes (Hosek, Harper, & Domanico, 2005; Murphy et al., 2005; Murphy et al., 2001; Naar-King et al., 2006; Williams et al., 2006) and increased mortality (Benton, 2008; Ickovics et al., 2001; Leserman, 2003; Leserman et al., 2002; Mayne, Vittinghoff, Chesney, Barrett, & Coates, 1996).

Neuropsychiatric disorders such as depression, substance abuse and conduct disorders are common among HIV-infected adolescents (Lee, Chabra, Oberdefer,, 2011; Mellins and Malee, 2013; Mellins, Brackis-Cott, Leu, et al, 2009; Malee, Williams, Montepiedra et al, 2009; Williams, storm, Montepiedra et al 2006; Menon, 2007; Puthanakit et al, 2012), and psychiatric disorders, especially depression and conduct disorders, have been associated with poor adherence to ART among HIV-infected adolescents (Mellins, Tassipolous et al, 2011; Williams,

Storm, Montepiedra et al, 2006; Mellins, Brackis-Cott, Dolezal et al, 2004; Malee, Williams, Montepiedra, McCabe et al, 2011; Hosek, Harper and Domanico, 2005; Nichols et al, 2012).

Psychological distress is also common among HIV-infected adolescents in both low-income and high-income countries (Bomba et al., 2010; Louthrenoo, Oberdorfer, & Sirisanthana, 2013; Menon, Glazebrook, Campain, & Ngoma, 2007; Murphy, Moscicki, Vermund, & Muenz, 2000; Musisi & Kinyanda, 2009; Naar-King et al., 2006), and has also been associated with poor adherence to ART (Naar-King et al 2006; Murphy et al, 2001; Chandwani et al, 2012; Lowenthal et al, 2012). The predictors of psychological distress among HIV-infected adolescents include: negative life events such as bereavement, daily hassles of managing demanding and complex ART regimens, HIV status disclosure or non-disclosure, uncertainty about life, deteriorating physical health, HIV-related stigma and discrimination, the HIV status of caregiver, and the availability and quality of social support networks (Battles & Wiener, 2002; Bikaako-Kajura et al., 2006; DeLaMora, Aledort, & Stavola, 2006; Elkington et al., 2011; Lyon, McCarter, & D'Angelo, 2009; Mukolo & Wallston, 2012; Musisi & Kinyanda, 2009).

Little is known about the prevalence and correlates of psychological distress among HIV-infected adolescents in sub-Saharan Africa, where the burden of HIV remains disproportionately high (UNAIDS, 2013b). For example, only two studies have assessed the psychological wellbeing of HIV-infected adolescents in Uganda. A recent small cross-study of 82 HIV-infected youth in care found that 51% of the adolescents had psychological distress (Musisi & Kinyanda, 2009). An unpublished 2003 study found high rates of depression (41.5%), anxiety (58.5%) and suicide attempts (20%) among HIV-infected children (Musisi & Kinyanda, 2003). These findings are consistent with study reports from high-income countries (Murphy et al., 2001; Naar-King et al., 2006). In Zambia, Menon et al (2012) found that HIV-infected youth

in Zambia (29%) were twice more likely to score outside the normal cut-off of the Child Behavioral checklist compared to HIV-positive youth in the UK (16.5%). Additionally, significant uncertainty remains regarding the important predictors of psychological distress among HIV-infected adolescents in sub-Saharan Africa has majority of these studies have been conducted among behaviorally infected and young gay youth, yet majority of adolescents in sub-Saharan Africa are perinatally-infected. Further, most of these studies exploring predictors of psychological distress are constrained by small sample size, which precludes the simultaneous assessments on the multiplicity of factors associated with psychological distress, in order to identify the most important predictors. Further, only a few studies have explored the psychosocial resources, and majority of these studies have focused on social support and coping strategies. Psychological resources such as optimism and spirituality/religiosity and coping strategies has received less attention, despite their ubiquity in the literature on psychological distress among HIV-infected adults and children living with other chronic illnesses. Moreover, the role of the role of social support remains unclear (Lam, Naar-King, & Wright, 2007; Murphy et al., 2000; Naar-King et al., 2006; Thorsteinsson, Sveinbjornsdottir, Dintsi, & Rooke, 2013).

Therefore, the goal of this study was to expand understanding of the risk and protective factors for psychological distress among HIV-infected adolescents. This study focuses on psychological distress, a precursor to psychiatric disorders, to enable assessment of how an accumulation of psychological symptomatology across the varied health domains – physical, emotional, social and spiritual could impact adolescent's health. Using a sample of 464 HIV-infected adolescents at the Joint Clinical Research Center in Kampala, this study explores the relationship between specific measurable stressors, psychosocial resources and psychological

distress. Additionally, this study explores the mediating role of these psychosocial resources on stressors.

Theoretical background

This study is grounded in Lazarus and Folkman (1984) Transactional Model of Stress and Coping (TMSC). The TMSC provides a meaningful framework to understand to explore predictors of psychological distress among HIV-infected adolescents. Lazarus and colleagues (Lazarus 1966; Lazarus and Folkman, 1984) hypothesis that the way people cope with stressor is crucial to their physical, social and psychological wellbeing. The TMSC asserts that psychological distress is a direct response to stressors, and psychosocial resources mediate the relationship between stress and psychological distress (Lazarus & Cohen, 1977), and highlights three important concepts- stressors, coping efforts and psychosocial resources. Stressors are defined as "demands made by the internal or external environment that upset balance, thus affecting physical and psychological well-being, and requiring action (coping efforts) to restore balance". Coping efforts are conceptualized as the actual strategies used to manage the emotional and/or physiological effects of stressors; deficits in these actions result in psychological distress. Finally, psychosocial resources defined as described as the psychological, social and cultural assets at a person's disposal that are deployed to reduce or eliminate the stressor. The impact of a stressor on physical and psychological wellbeing is mediated by these psychological, social and cultural resources at a person's disposal (Cohen & McKay, 1984; Folkman, 1984; Lazarus & Cohen, 1977). Therefore, available psychosocial resources enhance or complement coping efforts.

Therefore, when an individual experiences a stressful stimuli, it will be evaluated based on the perceived significance and controllability of this stimuli. There are two possible outcomes

of this appraisal process - threat or non-threat. If the stimuli is not perceived as a threat, there will be no stress. If the stimuli is perceived as a stressor, then the individual will conduct a secondary appraisal to determine if they have the ability and resources to cope with this stimuli. The outcomes of this secondary appraisal process are either positive stress (‘eustress”), which can lead to personal growth or negative stress (“distress”). Prolonged down exposure to stressors may lead to psychiatric morbidities such as depression and anxiety. Consistent with the TMSC, this study hypothesizes that stressors such as bereavement, poor quality of life and stigma are antecedents to psychological distress (Johnson & Nath, 2009; Lyon & D'Angelo, 2009; McKnight, Huebner, & Suldo, 2002; Murphy et al., 2000; Musisi & Kinyanda, 2009; Thorsteinsson et al., 2013).

Methods

Setting

This study was conducted among adolescents seeking HIV care at the Joint Clinical Research Center (JCRC) in Kampala, Uganda. The JCRC, is a not-for-profit organization established in 1991; the center provides HIV care to out to approximately 2500 children and adolescents. These data were collected as part of a larger study exploring the relationship between psychological distress and adherence to antiretroviral medications (ART).

Study population

A convenient sample of 464 adolescents aged 12 – 19 years was recruited to take part in this study. Eligibility was limited to adolescents who were aware of their HIV status and without any known cognitive limitations.

Procedures

The survey was conducted between May and September 2013. The minimum sample size for study was based on considerations for the primary purpose of this study – to examine the relationship between psychological distress and adherence to HIV care, and was determined to be 460, using Optimal Design Software, version 3.0 (Spybrook, Raudenbush, Liu, & Congdon, 2006) with alpha (α) set at 0.05, power = 0.80 and medium design effect (d = 0.5) (Cohen, 1992). A quota sampling strategy was employed to ensure adequate representation of males and females across all ages.

Adolescents were recruited during their scheduled clinic visits by a team of three interviewers (university graduates with social sciences training), each of whom were trained in interviewing skills and research ethics. Potential respondents were approached in the clinic waiting room; initial inquiries focused on ascertaining the adolescent's disclosure, followed by a discussion of the study purpose and participant's rights. Adolescent expressing interest in the study, and their caregivers (if present) were invited to the interview rooms adjustment to the clinic were informed consent was sought; of the caregiver was absent, the necessary arrangements were made with the adolescent to obtain caregiver consent. To ensure coordination within the research team, a list of scheduled clinic visits was generated from the JCRC patient care database and made available to the research team. Adolescents presenting to the clinic with severe illness were not interviewed at that visit; attempts were made to interview these participants at a later date.

Questionnaires were administered in face-to-face interviews using Personal Digital Assistant (PDA) devices. Interviews were either conducted following the respondent's clinic visit, as respondents awaited laboratory results, or during scheduled visits for interviews. The interview language was Luganda or English, depending on the participant's language preference

and proficiency. Response cards in Luganda and English – providing visual analogs for potential responses (e.g. likely, somewhat likely or very likely), were provided. The questionnaire included 5 major sections: socio-demographic characteristics, stressors, psychological distress, psychosocial resources, and measures of adherence to HIV care. The entire questionnaire included 315 items: the interviews lasted between 60 – 75 minutes, including the scheduled breaks in the interview. Respondents were provided with a snack during the interviews.

Ethics statement

Permission to conduct this study was sought from the Institutional Review Board at the Joint Clinical Research Center, the University of Michigan Ethics Review Board, and Uganda National Council for Science and Technology Ethics Review Board.

Measurement

Psychological distress

Psychological distress was assessed with a local measure developed and validated in a pilot study preceding this study; a detailed description of the measure is provided in chapter 1. Briefly, ten (10) in-depth interviews and three focus group discussions were conducted to explore understanding and language of psychological distress among HIV-infected Ugandan adolescents at the JCRC. Emerging themes on distress symptomology were mapped onto published measures and models of psychological distress, and relevant items were extracted to create a pool of 67-items assessing frequency of distress symptomatology in the past week, using a 5-point scale- never, almost never, sometimes, often, and most of the time.

The scale was translated into Luganda (the local language used in this study) by two independent translators, and reviewed by a team consisting of the principal investigator, a counselor and pediatric nurse at the JCRC to identify and resolve inconsistencies. The scale was

reviewed by an expert panel consisting of four psychiatrists and pediatric HIV specialist in Uganda, and two psychologists at the University of Michigan, to assess its conceptual breadth, developmental and cultural appropriateness (for the Ugandan experts) and face validity. Cognitive interviews (6) were conducted with adolescents to assess question wording, adequacy of translations and identify difficult or uncomfortable items.

The scale was piloted among 98 HIV-infected adolescents (12- 19 years) at the JCRC to determine the psychometric properties of the scale. Final refinements to the scale were conducted prior to the present analyses: using exploratory factor analysis, the scale was reduced to 25 items and six (6) subscales labeled as anhedonia, depressive-anxiety, isolation, sleep problems, suicidal ideation and somatic symptoms. Construct validity of the measure was assessed through correlations with other measures of well-being and confirmatory factor analysis was used to assess the fit of the model to the data. Internal consistency of the subscales ranged between, r = 0.615 and r = 0.758; internal consistency of the entire scale was r = 0.89. Additionally, exploratory factor analysis of sub-scale indicated one-dimensional factor, supporting the use of a composite scale score. The composite global psychological distress score was computed as the mean of all items.

Socio-demographics Measures

Socio-demographics assessed included self-reported age, sex, religion, level of education, orphan-hood and type of caregiver.

Religion was assessed using five categories that represent the dominant faiths in Uganda – Catholic, Protestant, Muslim, Pentecostal and other (e.g. Seventh Day Adventist (SDA), Mormons).

Education was measured as the level of last level of education attended: - primary school, secondary school, tertiary institutions or no education.

Orphan-hood was operationalized as: non-orphan-hood (both parents living), maternal orphan-hood (mother deceased), paternal orphan-hood (father deceased) and double-orphaned (both parents deceased).

Type of caregiver was assessed as the self-reported relationship between the respondent and their primary caregiver, categorized as: biological parents, aunt or uncle, grandparents, sibling, and other such as foster parents.

A *household wealth index* was computed from a list of 21 household assets adapted from the Uganda Demographic and Health Survey (UDHS; 2011) (Measure DHS, 2012). Consistent with the prior studies (Filmer & Pritchett, 2001; Measure DHS & ICF International, 2011), principal component analysis was used to derive indicator weights for each household asset; a household wealth index for each respondent was computed as a sum of the product of each household item and derived weight used as quartiles. Given that majority of adolescents in Uganda are perinatally infected, this study did not adjust for mode for transmission.

Stressors

The stressors assessed included: neighborhood insecurity, life concerns and worries, hardships, negative life events, stigma, and HIV concerns.

Neighborhood insecurity was assessed using an eight items on neighborhood issues such as safety at night, safety during day, easy to get to know people, presence of street lighting and quality of housing; responses were recorded on a yes/no scale. A neighborhood insecurity score was computed as the mean score of these items.

On-going worries were assessed using a 12 items evaluating ongoing concerns about health, getting enough to eat, performing well in school, taking medications, being teased, parent's job, trouble at home, and fear of getting pregnant or getting someone pregnant; responses were measured on a three-point scale- not worried, somewhat worried and very worried. The worries score was computed as the mean score of these items.

Hardships were assessed using five items on recurring difficulties experienced in past 12 months, such as going without enough food to eat, not having enough medications, having no job or source of money, lacking money to come to the clinic, and feeling unsafe from crime at home; responses were measured on a four-point scale- never, rarely, sometimes and often. The hardships score was computed as the mean score of these items.

Major negative life events were assessed using a modified 9-item index from the South African Stress and Health (SASH) study (Herman et al., 2009) evaluating exposure to acute traumatic life events in the past 12 months e.g. serious illness or injury, personal attacks, bereavement, break up of a close relationship etc. Responses were measured on a yes/no scale. The negative life events score was computed as the mean of these items.

HIV concerns were assessed using the modified Functional Assessment of Human Immunodeficiency Virus Infection (FAHI) quality of life instrument (Cella, McCain, Peterman, Mo, & Wolen, 1996), a 46-item scale assessing concerns in the physical, social, family, emotional and functional health domains, and relationships with doctors. Responses were measured on a five-point scale- not at all, a little bit, somewhat, quite a bit and very much. The HIV concerns score was computed as the mean score of these items.

Stigma was assessed using an adapted 21-item Berger HIV stigma scale (Berger, Ferrans, & Lashley, 2001); responses were measured on a four-point scale – strongly disagree, disagree, agree and strongly agree. The stigma score was computed as the mean score of these items.

Psychosocial resources

The psychosocial resources assessed included; spirituality and religiosity, optimism, social support, overall satisfaction with social support, and coping strategies.

Spirituality was assessed using the seven-item Brief RCOPE Spirituality subscale; responses were measured on a 4-point scale – not at all, somewhat, quite a bit and a great deal (Pargament, Feuille, & Burdzy, 2011). The spirituality score was computed as the mean of all items.

Religiosity was assessed using two items: "How often do you pray privately in places other than a church or mosque…more than once a day, Once a day, a few times a week, once a week, a few times a month, once a month, less than once a month, a few times a year, and never" and "How often do you go to religious services -more than once a week, every week or more often, once or twice a month, every month or so, and once or twice a year".

Optimism was measured using 7-item scale adapted from the national Longitudinal Study of Adolescent Health (ADDHealth) (UNC Carolina Population Center Project, 2014). These items assessed beliefs that the respondent- will live to age 35, will graduate from school, be rich, get married, have children, receive cure for HIV etc. The optimism score was computed as mean of these items.

Social support was measured using the Social Support Questionnaire (SSQ) (Sarason, Sarason, Shearin, & Pierce, 1987), which assessed access for the four typologies of social

support (emotional, instrumental, informational, appraisal), and overall satisfaction with social support. Responses were measured on a 5-point scale; none of the time, a little of the time, some of the time, most of the time and all of the time. The social support score was computed as the mean of these items.

Coping strategies were assessed using a locally adapted Adolescent Coping Orientation for Problem Experiences scale (ACOPE) (Patterson & McCubbin, 1987): responses were measured on a 5-point scale (not at all, sometimes, a lot of the time and almost all the time). The overall coping score was computed as the mean of these items.

Data analysis

Univariate analyses (e.g. frequencies, mean, median, mode, and standard deviations etc.) and graphical tools (e.g. histograms, box-plots, stem and leaf plots and scatter plots) were used to examine the distribution of variables- dependent and independent. Bivariate analyses – correlations, two-sample t-tests, analysis of variance (ANOVA) and chi-square tests of independence were used to examine the relationship (strength and direction) between each predictor variable and indictors of distress (the global index score and each subscale). Posthoc comparisons, using the Bonferroni correction were conducted to identify statistically significant mean differences in psychological distress indictors across the socio-demographic characteristics (Cohen, Cohen, West, & Aiken, 2003).

Hypothesis testing

Zero-order regressions were conducted to assess the relationship between each predictor variable and indicators of psychological distress; only statistically significant variables or variables with theoretical relevance (even if lacking statistical significance), were included in subsequent analysis. Sequential stepwise regression analyses were conducted to assess the

relationship of each predictor and groups of predictors (stressors and psychosocial resources) with psychological distress. First, all socio-demographic variables were entered into the model, followed by a series of analyses, where one, two and then three stressor variables where added to the model; finally, all stressor variables were added as a block to the model. For each step, the unique and joint effects (noted by change in direction and strength of coefficients) of each independent variable and group effect (stressors combined) on psychological distress was assessed. A similar process was used to evaluate the unique and joint effects of psychosocial resources on psychological distress, and assess their mediating roles on stressor variables. Consistent with the Kenny and Baron mediation method was assessed as changes in magnitude of beta coefficients of the stressor variables when psychosocial resources where added to the model (Baron & Kenny, 1986).

Finally, model fit was assessed using the percentage of variance explained by the model (R^2). Variance inflation factors (VIF) were computed to detect multi-collinearity among predictor variables (values greater than 10 are considered indicate multi-collinearity). Residuals plots and scatter plots were used to identify potential outliers and influential variables; Cook's distance (Cook's D), the scaled change in fitted values, was also computed for influential outliers. Potential violations of the assumptions of linear regression were also evaluated. Linearity between the predictor variables and psychological distress was assessed using plots of observed versus predicted values and plots of residuals versus predicted values. Independence of errors was assessed using an autocorrelation plot of the residuals; constant variance of the errors (homoscedasticity) was assessed using plots of the residuals versus predicted values; and normality was assessed using a normal probability plot of the residuals.

Results

The socio-demographic characteristics of respondents are presented in Table **3.1.** The majority of respondents were female (53.4%; n = 249), and the mean age of the sample was 15.6 years (SD = 2.44), with comparable representation across the 12 – 19 age range, except for a smaller proportion of 16 and 17 year olds, for unknown reasons. Almost 95% of the sample had some education, and majority of the school going respondents were currently enrolled in secondary school (69.6%; n = 280). Sixty-seven percent (67.4%; n = 312) of respondents were orphaned: of these, two-thirds had lost one parent and one- third had lost both parents.

A descriptive summary of the outcome variables (psychological distress) and predictor variables (stressors and psychosocial resources) is presented in Table 3.2. The mean and standard deviation of the psychological distress indicators were as follows: global psychological distress, M = 0.97 (0.59); anhedonia, M = 1.23 (0.77); anxiety/depression, M = 1.20 (0.87); isolation, M = 0.86 (0.85); suicidal ideation, M = 0.59 (0.67); sleep problems, M = 0.69 (0.81); and somatization, M = 0.99 (0.78). The average number of major negative life events in this sample was 2.25 (SD = 1.8). More than half of respondents reported attending religious services once or twice a month, while the majority of respondents prayed privately in places other than the church or mosque a few times a month. Fifty-six percent (259) of respondents reported attending religious services at least once or twice a month. The majority (53.9% [251]) of the respondents rated their health as good, and more than half of the respondents (50.4% [233]) were not satisfied with their social support.

Analyses using global psychological distress score

Results of the regression analyses are presented in Table 3.3. In the zero-order regression analyses, all stressor variables- neighborhood insecurity, worries, hardships, major negative life

events, HIV concerns and stigma- were significantly associated with global psychological distress (hence forth, global distress). After controlling for respondents' socio-demographics, global distress remained significantly associated with worries ($\beta = 0.179$, $t(462) = 3.69$; $p < .001$), major negative life events ($\beta = 0.221$, $t(462) = 5.55$; $p < .001$), HIV concerns ($\beta = 0.323$, $t(462) = 7.40$; $p < .001$), and stigma ($\beta = 0.155$, $t(462) = 3.99$; $p < .001$). Neighborhood insecurity and hardships were not significantly associated with global distress, after controlling for respondents' socio-demographics characteristics. Among the socio-demographic variables, only religion- Pentecostalism was significantly associated with global distress ($\beta = 0.081$, $t(462) = 2.08$; $p < .05$). All other socio-demographic variables were not significantly associated with distress in this model. The combined model of socio-demographics and stressors explained 43.2% the variance in global distress.

All psychosocial resources were significantly associated with lower levels of global distress in the zero- order regression analyses. Results of the subscale analyses were similar with the exception that frequency of praying privately was not significantly associated with suicidal ideation and sleep problems. In the model controlling for respondents' socio-demographic characteristics, respondent's frequency of praying privately was positively associated with increased psychological distress ($\beta = 0.124$, $t(462) = 3.07$; $p < .05$), while spirituality ($\beta = -0.173$, $t(462) = -4.25$; $p < .001$), coping ($\beta = -0.298$, $t(462) = -6.79$; $p < .001$), and satisfaction with social support ($\beta = -0.221$, $t(462) = -4.82$; $p < .001$) were negatively associated with global psychological distress. Social support and optimism were not significantly associated with global distress. The combined model with socio-demographic factors and psychosocial resources explained 28.2% of the variance in global psychological distress.

The regression model with socio-demographic variables, stressors, and psychosocial resources on global psychological distress explained 49.2% of the total variance in global psychological distress. Among the socio-demographic variables, global distress remained significantly associated with Pentecostalism ($\beta = 0.086$, $t(462) = 2.32$; $p < 0.05$), and marginally associated with paternal orphan-hood ($\beta = -0.083$, $t(462) = -1.95$; $p < .10$). All other socio-demographic variables were not significantly associated with global distress. Among the stressors, global distress was significantly associated with worries ($\beta = 0.118$, $t(462) = 2.52$; $p < 0.05$), negative life events ($\beta = 0.209$, $t(462) = 5.50$; $p < 0.001$), HIV concerns ($\beta = 0.299$, $t(462) = 7.08$; $p < 0.001$), and stigma ($\beta = 0.089$, $t(462) = 2.36$; $p < 0.05$). Among psychosocial resources, global distress was significantly associated with frequency of praying privately ($\beta = 0.079$, $t(462) = 2.26$; $p < .05$), spirituality ($\beta = -0.083$, $t(462) = -2.40$; $p < .05$), satisfaction with social support ($\beta = -0.169$, $t(462) = -4.28$; $p < .001$), and coping ($\beta = -0.160$, $t(462) = -4.15$; $p < .001$). Global distress was not significantly associated with optimism and social support. When psychosocial resources where added to the model, there was a slight attenuation in the beta coefficients of all stressors variables indicating psychosocial resources partially mediate the relationship between stressors and psychological distress.

Analyses using psychological distress sub-scales

Using the procedures used to identify the predictors of global psychological distress, the sub-scale analyses examined the socio-demographic, stressor, and psychosocial factors associated with the psychological distress sub-scales- anhedonia, anxiety/depression, isolation, suicidal ideation, sleep problems, and somatization. Only statistically significant results that differed from the findings with the global psychological distress measure are reported below.

In the regression models with stressors and socio-demographic variables only, age was significantly associated with anxiety ($\beta = 0.115$, $t(462) = 2.10$; $p < .05$). Sleep problems were marginally associated with neighborhood insecurity ($\beta = 0.083$, $t(462) = 1.82$; $p < .10$) but were not significantly associated with worries and stigma. Sex was significantly associated with somatization ($\beta = 0.139$, $t(462) = 3.30$; $p < .001$), but worries were not significantly associated with somatization.

In the regression models with psychosocial resources and socio-demographic variables only, the results of the subscale analyses were similar to findings with the global distress analyses with the following exceptions: frequency of praying privately was not significantly associated with suicidal ideation and sleep problems. Optimism was negatively associated with anhedonia ($\beta = -0.133$ $t(462) = -3.06$; $p < .05$) and isolation ($\beta = -0.094$, $t(462) = -2.01$; $p < .05$). Social support was significantly associated with isolation ($\beta = -0.163$, $t(462) = -3.28$; $p < .001$) and was marginally associated with depressive-anxiety ($\beta = -0.082$, $t(464) = -1.72$); $p < .10$). Satisfaction with social support was not significantly associated with satisfaction with suicidal ideation. Spirituality was not significantly associated with somatization.

In the final sub-scale regression analyses with socio-demographic variables, stressors nad psychosocial resources only, the results of the anxiety/depressive sub-scale were similar to findings with the global psychological distress score. Anhedonia was significantly associated with optimism ($\beta = -0.131$, $t(462) = -3.00$; $p < .05$), and was marginally associated with major negative life events ($\beta = -0.085$, $t(462) = 1.90$; $p < .10$) and coping ($\beta = -0.081$, $t(462) = -1.77$; $p < .10$). Isolation was marginally associated with optimism ($\beta = -0.088$, $t(462) = -1.94$; $p < .10$), and significantly associated with social support ($\beta = -0.132$, $t(462) = -2.77$; $p < .05$) and coping ($\beta = -0.102$, $t(462) = -2.17$; $p < .05$). Isolation was not significantly associated worries, with

frequency of praying privately, spirituality, and satisfaction with social support. Suicidal ideation was not significantly associated with frequency of praying privately, spirituality, optimism, stigma, and satisfaction with social support. Sleep problems were only associated with negative life events ($\beta = 0.172$, $t(462) = 3.59$; $p < .001$) and HIV concerns ($\beta = 0.196$, $t(462) = 3.69$; $p < .001$), but sleep problems were not significantly associated with stigma. Among the psychosocial resources, sleep problems were not frequency of praying privately, spirituality optimism and social support. Lastly, somatization was significantly associated with respondents' sex ($\beta = 0.139$, $t(462) = 3.32$; $p < .001$) and double orphan-hood ($\beta = -.131$, $t(462) = -2.10$; $p < .05$), and was not significantly associated with spirituality.

Discussion

The purpose of this study was to identify the psychosocial predictors of psychological distress among HIV-infected adolescents in Uganda, and assess the mediating role of psychosocial resources. The results affirmed prior reports that HIV-infected adolescents encounter a diverse array of stressors including: negative events such as bereavement, stigma, on-going worries, poverty-related hardships, and HIV-related concerns. Similar to prior studies (Gau, Stice, Rohde, & Seeley, 2012; Johnson, Whisman, Corley, Hewitt, & Rhee, 2012; McKnight et al., 2002; Murphy et al., 2000; Musisi & Kinyanda, 2009; Tanney, Naar-King, & MacDonnel, 2012; Thorsteinsson et al., 2013), these stressors were associated with increasing levels of psychological distress. Psychosocial resources were independently associated with higher psychological distress, and partially mediated the effects of stressors on psychological distress, implying that these resources accounted for some but not all of the differences in the relationship between stressors and psychological distress. Overall, these findings are consistent with the Transactional Model of Stress and Coping (Lazarus & Folkman, 1991), and with

findings from prior studies that have explored the relationship between psychosocial resources (e.g. coping) and psychological distress among HIV-infected youth (Brown & Lourie, 2000; Murphy et al., 2000; Thorsteinsson et al., 2013).

The relationship between spirituality/religiosity and psychological distress among HIV-infected adolescents has not been widely explored even though prior studies have found positive associations between spirituality and psychological wellbeing among HIV-infected adults and adolescents living with chronic illness such as asthma (Cotton et al., 2012; Makoae et al., 2008; Nooney & Woodrum, 2002; Schapman & Inderbitzen-Nolan, 2002). The negative association between spirituality and psychological distress suggests the potential salutogenic effects of spirituality on adolescents' psychological wellbeing, thereby contributing to the scanty literature on the relationship between spirituality and psychological wellbeing among HIV-infected adolescents. The salience of spirituality as resource for coping with adversity is not surprising given that more than 90% of Ugandans identify as religious, and religious institutions play an important role in providing health care and support to people living with HIV/AIDS (Kaldjian, Jekel, & Friedland, 1998). However, caution should be exercised in interpreting the relationship between religiosity and psychological wellbeing. In this study, frequency of praying privately and Pentecostalism were associated with increased psychological distress, suggesting that religiosity may be detrimental to the wellbeing of HIV-infected adolescents in Uganda. The findings on religiosity echoes reports from prior studies conducted among HIV-infected persons in sub-Saharan Africa, where religion, especially Pentecostalism, was associated with increased psychological distress due to moralizing and/or discriminatory attitudes with religious congregations (Otolok-Tanga, Atuyambe, Murphey, Ringheim, & Woldehanna, 2007; Pargament et al., 2004; Varas-Díaz, Neilands, Malavé Rivera, & Betancourt, 2010). For example, in a study

conducted among HIV-infected adults in South Africa, Kagee and Delport (2010) noted that Pentecostal religious beliefs were associated with HIV-stigma, which could lead to increased psychological distress among study participants. Additionally, religious beliefs interfere with patient's adherence to ART, leading to increased psychological distress as the person's health deteriorates (Kagee & Delport, 2010).

The relationship between social support and health has been widely explored in the literature (see Cohen and Wills, 1985 for review). Within the Transaction Stress and Coping Model (TMSC), social support may intervene between the stressful event and psychological distress by attenuating or preventing appraisal of an event or stimuli as stressful due to the perception that significant others can provide the necessary resources to cope with the event and/or bolster one's ability to cope with the imposed demands. Social support may also alleviate the impact of a stressor by providing a solution to the problem or by reducing the perceived significance of the stressor. Social support could impact health through emotional induced effects on the neuroendocrine or immune system functioning, or through influence on health-related behaviors (Cohen & Wills, 1985). In this study, social support was not significantly associated with global psychological distress, satisfaction with social support was significantly associated with lower psychological distress. However, in the sub-scale analyses, social support was significantly associated with isolation.

The general lack of association between social support and psychological distress in this study is consistent with findings from previous studies conducted among HIV-infected youth in the U.S (Murphy et al., 2000), and adolescents recently diagnosed with cancer (Neville, 1998). The lack of support for social support in adolescent studies could be attributed to several factors: (1) these findings may reflect the difficulty of HIV-infected adolescents to mobilize social

support: HIV/AIDS is a highly stigmatized disease and seeking social support may require disclosure of HIV status thereby exposing them to stigma and discrimination from significant others; (2) social support may also conflict with adolescent's desire for autonomy as the adolescent may feel that social support, particularly from caregivers interferes with their independence. The association between social support and isolation may suggest adolescent's inability to mobilize social support due to fear of stigma and discrimination. On the other hand, satisfaction with social support was significantly associated with lower psychological distress on both the global distress score and subscales. This finding is consistent with the broader literature on social support, which argues that satisfaction with social support is more important than the quantity of social support (Barrera Jr, 1986; Compas, Slavin, Wagner, & Vannatta, 1986; Sarason et al., 1987). The importance of satisfaction with social support as a predictor of psychological distress among adolescents is also documented in a study conducted among AIDS-orphaned children in Kenya (Okawa et al., 2011).

Prior studies have documented high levels of suicidal ideation among youth in sub-Saharan Africa (Lamis & Lester, 2012; Page & West, 2011). For example, in a systematic review of studies conducted among youth living in seven African countries, including Uganda, Page et al (2011) found that 25% of boys and 26.3% of girls has seriously considered suicide; these were higher than rates of suicidal ideation among youth in high-income countries (Page & West, 2011). The proportion of adolescents with a suicide plan increased with cumulative psychosocial challenges, form 32.9% among respondents with one psychosocial indicator to 41.9% among adolescents with two psychosocial indicators (Page & West, 2011). The levels of suicidal reported in this review mirror findings from a study conducted among HIV-infected youth in Uganda: 24% of adolescents in this study had attempted suicide (Musisi & Kinyanda,

2009). However, data on predictors of suicidal ideation among African youth remain scarce. The predictors of suicide ideation in this study are consistent with Page et al (2011) systematic review: suicidal ideation was significantly associated with worries, HIV concerns and negative life events. In this study, all stressor variables assessed were significantly associated with suicidal ideation and psychosocial resources did not mediate the impact of these stressors on suicidal ideation, suggesting that suicidal ideation is a result of stressful events that the adolescent may perceive as too stressful or uncontrollable.

These study findings highlight several opportunities to improve the psychological wellbeing of HIV-infected adolescents in Uganda, and other low-income countries. At the individual level, the findings suggest the importance of equipping HIV-infected adolescents with the skills and psychosocial resources to navigate the diverse array of stressors they may encounter, in order to prevent or reduce psychological distress. Of particular importance are skills that could modify appraisal process that determine adolescent's evaluations of stressful stimuli. Resilience, life skills trainings, and interventions using cognitive based therapy techniques to influence adolescents' feelings or thoughts regarding stressful stimuli may be helpful. Additionally, its interventions that promote psychosocial resources such as coping strategies, spirituality, building and maintaining social networks as well as evaluation social support may also be useful in reducing psychological distress among HIV-infected adolescents. Resilience or life skills training interventions are effective in reducing psychological distress among HIV-infected youth (Bhana et al., 2013; Naar-King, Parsons, Murphy, Kolmodin, & Harris, 2010) and un-infected (Kerrigan et al., 2011; Parker et al., 2011). However, few such interventions have been tested or validated for adolescents in Uganda and low-income countries; therefore, the efficacy of these interventions in these settings in unknown.

At the inter-personal level, these study findings highlight the need to address stigma against HIV-infected persons. HIV-related stigma remains rampant within households and schools, the ecological spaces of most significance to adolescent wellbeing. In an exploratory study conducted among 28 adolescents at the JCRC, household disclosure of the adolescent's HIV status was low and several respondents reported low acts of stigma enacted by both teachers and students in school. Majority of these adolescents had not disclosed their HIV status to peers or school authorities at school due to fear of stigmatization. The low rates of disclosure within households and schools reinforces adolescents' feelings of isolation, and limits their ability to seek social support and even adherence to their HIV care. For these reasons, it is important to eliminate stigma within these ecological spaces. At the household level, these findings underscore the needs to eliminate poverty, particularly among AIDS-affected households.

The findings psychosocial resources only account for some but not all of the difference in the relationship between stressors explored in this study and psychological distress suggests that there are other contextually important psychosocial resources that were not explored in this study but are important to eliminating psychological distress among HIV-infected adolescents. Therefore, there is a need for additional research- both qualitative and quantitative- to identify these additional psychological resources. This study explored a minority of psychosocial resources, largely at the intra-personal level; future research should explore the potential role of family, peers and health facility attributes.

These study findings also have varied clinical implications: first, they highlight the need for incorporate psychosocial assessments within HIV care to facilitate identification at increased risk of psychological distress. The positive association between HIV-related concerns and psychological distress particularly highlights the need to create opportunities for HIV-infected

adolescents to discuss any concerns pertaining to their wellbeing. Social support groups, particularly, peer support groups and access to psychosocial counseling services within HIV care facilities could provide such avenues for adolescents to discuss such concerns.

The findings should be interpreted within the limitations of this study. First, the cross-sectional study design limits inferences about causality. In this study, the relationship between stressors, psychosocial resources and distress is conceptualized as linear. However, this relationship could be reciprocal. Additionally, the study population is drawn from an urban HIV treatment center, which could limit generalizability of these to adolescents in other settings, but this potential selection bias may be minimal as the JCRC draws patients from all regions of the country and the considerably large study sample size. Despite these limitations, the findings in this study increase our understanding of the risk and protective factors for psychological distress among HIV-infected adolescents in Uganda, and could be extended to adolescents living in other sub-Saharan Africa.

Conclusion

Studies exploring the predictors of psychological distress among HIV-infected adolescents in low-income countries are scarce. The purpose of this study was to explore the risk and protective factors for psychological distress among HIV-infected adolescents in Uganda. Consistent with the study hypotheses, stressors, especially, negative life events, HIV-related concerns, worries and stigma were significantly associated with increasing levels of psychological distress, while psychosocial resources reduced levels of psychological distress, and partially mediated the effects of worries and stigma on global distress. This study is an important step towards increasing understanding of risk and protective factors for psychological distress among HIV-infected adolescents in low-income countries, and underscores the need for

interventions to address HIV-related stigma and household poverty, and equip or enhance adolescents' psychosocial resources to cope with adversity. These study findings potentially pave way for additional research to document the prevalence of distress in this population, and evaluation research to identify effective interventions that would address the needs of this population. The findings also highlight the need for additional research to identify contextually relevant psychosocial resources for HIV-infected adolescents in sub-Saharan Africa, and elaborate on the relationship between and psychological wellbeing among HIV-infected adolescents in Uganda and other countries in sub-Saharan Africa.

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Variable	Percent (frequency) / Mean (SD)	Variable	Percent (frequency)
Age	M = 15.58 (SD = 2.44)	Education level	
		None	5.36 (25)
		Primary	37.77 (176)
12 & 13	26.82 (125)	Secondary	49.57 (231)
14 & 15	24.25 (113)	Tertiary	7.30 (34)
16 & 17	14.59 (68)		
18 & 19	34.33 (160)		
Sex		Orphan-hood	
Males	46.57 (217)	Both parents alive	32.62 (152)
Females	53.43 (249)	Mother alive	26.39 (123)
Household wealth index score	M = 2.78 (SD = 0.94)	Only father alive	19.53 (91)
		Both parents deceased	21.46 (100)
Religion		Relation to caregiver	
Protestant	25.97 (121)	Biological parents	57.73 (269)
Catholic	37.34 (174)	Aunt or uncle	18.24 (85)
Muslim	16.74 (78)	Grandparents	11.59 (54)
Pentecostal	7.08 (33)	Other e.g. foster parents	12.45 (58)
Other e.g. SDA	12.89 (60)		

Table 3:1: Socio-demographic characteristics of the study sample

Table 3:2: Descriptive summary of outcome and predictor variables- stressors and psychosocial resources

Variable	Mean (SD) or Percentage (N)	Median	Range	Internal consistency (alpha)
Psychological distress				
Global distress score	0.97 (0.59)	0.92	0 – 2.89	0.89
Anhedonia	1.23 (0.77)	1.67	0 – 3	0.73
Anxiety	1.20 (0.87)	1.20	0 - 4	0.72
Isolation	0.86 (0.85)	0.67	0 - 4	0.64
Suicidal ideation	0.59 (0.67)	0.50	0 – 3	0.63
Sleep problems	0.69 (0.81)	0.67	0 - 4	0.65
Somatic	0.99 (0.78)	1.0	0 – 3.5	0.62
Stressors				
Neighborhood insecurity	0.19 (0.17)	0.13	0 - 1	0.46
Worries	0.59 (0.39)	0.58	0 – 1.7	0.75
Hardships	1.82 (0.72)	1.8	1-4	0.72
Major negative Life events	0.25 (0.18)	0.22	0 – 0.9	0.53
HIV concerns	1.72 (0.34)	1.67	0 - 3	0.81
Stigma	2.56 (0.36)	2.52	1.24 – 3.76	0.78
Psychosocial resources				
Spirituality	1.63 (0.28)	1.7	1 - 2.9	0.44
Frequency of praying privately	5.51 (1.7)	6.0	1 - 8	n/a
Optimism	1.33 (0.38)	1.43	0 – 1.7	0.75
Social support	2.64 (0.71)	2.73	0 - 4	0.87
Coping	1.69 (0.26)	1.7	1 - 2.7	0.70
	Percentage (N)			
Frequency of attending religious services				
More than once a week	4.5% (21)			
Every week or more often	12.9% (60)			
Once or twice a month	56.1% (259)			
Every month or so	15.6% (72)			
Once or twice a year	10.8% (50)			
Satisfaction with social support				
No	50.4% (233)			
Yes	49.6% (229)			

Table 3:3: Unstandardized Regression Coefficients on Predictors of Psychological Distress among HIV-infected adolescents (12 – 19 years), seeking HIV care at the Joint Clinical Research Center in Kampala, Uganda (N = 464)

Variables	Demographics only	Stressors only	Psychosocial resources only	Demographics & stressors	Demographic & psychosocial resources	Demographics, stressors & psychosocial resources
Socio-demographics						
Age	0.028 (0.02)*			0.005 (0.1)	0.001 (0.01)	0.009 (0.01)
Sex	0.091 (0.06)*			0.068 (0.04)	0.083 (0.05)	0.083 (0.04)*
Household wealth						
First quartile						
Second quartile	-0.045 (0.08)			-0.019 (0.06)	-0.057 (0.07)	-0.035 (0.06)
Third quartile	-0.067 (0.09)			0.127 (0.07)	-0.040 (0.07)	0.098 (0.07)
Fourth quartile	-0.181 (0.09)**			0.116 (0.08)	-0.063 (0.08)	0.114 (0.08)
Religion						
Protestant						
Catholics	0.152 (0.07)**			0.061 (0.06)	0.129 (0.06)**	0.060 (0.05)
Muslims	0.119 (0.09)			0.022 (0.07)	0.094 (0.08)	0.023 (0.06)
Pentecostal	0.342 (0.12)**			0.190 (0.09)**	0.317 (0.10)**	0.201 (0.09)**
Other	-0.013 (0.09)			-0.019 (0.07)	0.018 (0.08)	0.005 (0.07)
Education level						
None						
Primary	-0.352 (0.14)**			-0.138 (0.11)	-0.189 (0.12)	-0.079 (0.10)
Secondary	-0.272 (0.13)**			-0.143 (0.10)	-0.091 (0.14)	0.055 (0.09)
Tertiary	-0.308 (0.16)*			-0.113 (0.13)	-0.097 (0.15)	-0.005 (0.12)
Orphan-hood						
None						
Paternal orphan	0.057 (0.07)			-0.007 (0.06)	-0.147 (0.07)**	-0.113 (0.06)
Maternal orphan	0.022 (0.08)			-0.143 (0.10)	-0.059 (0.07)	-0.044 (0.06)
Double orphan	-0.056 (0.09)			-0.113 (0.13)	-0.217 (0.08)**	-0.136 (0.07)*
Type of caregiver						
Parents						
Aunt/uncle	0.033 (0.09)			0.024 (0.07)	0.025 (0.08)	0.033 (0.07)
Grandparents	0.186 (0.09)*			-0.001 (0.08)	0.119 (0.09)	-0.004 (0.08)
Siblings	-0.024 (0.11)			-0.127 (0.09)	-0.069 (0.09)	0.132 (0.08)

Other	0.063 (0.15)			0.060 (0.12)	0.038 (0.13)	0.039 (0.11)
Stressors						
Neighborhood insecurity		0.122 (0.13)		0.173 (0.14)		0.118 (0.13)
Ongoing worries and concerns		0.239 (0.07)***		0.271 (0.07)***		0.178 (0.07)**
Hardships		0.023 (0.04)		0.049 (0.04)		0.027 (0.04)
Negative life events		0.714 (0.13)***		0.713 (0.13)***		0.675 (0.12)***
HIV-related concerns		0.599 (0.06)***		0.559 (0.08)***		0.519 (0.07)***
Stigma		0.279 (0.06)***		0.256 (0.06)***		0.147 (0.063)**
Psychosocial resources						
Frequency of praying privately			0.044 (0.01)***		0.044 (0.01)**	0.027 (0.01)**
Spirituality			-0.378 (0.09)***		-0.371 (0.09)***	-0.179 (0.08)**
Optimism			-0.096 (0.07)		-0.104 (0.07)	-0.098 (0.06)*
Social support			-0.053 (0.04)*		-0.054 (0.04)	-0.016 (0.03)
Overall satisfaction with social support Not satisfied Satisfied			 -0.266 (0.05)***		 -0.264 (0.06)	 -0.202 (0.05)***
Coping strategies			-0.676 (0.10)***		-0.705 (0.11)***	-0.379 (0.09)***
Adjusted R^2	0.053	0.427	0.262	0.432	0.282	0.495

Table 3:4: Standardized Regression Coefficients on Predictors of Psychological Distress among HIV-infected adolescents (12 – 19 years) seeking care at the Joint Clinical Research Center in Kampala, Uganda (N = 464).

Variables	Demographics only β(t)	Stressors only β(t)	Psychosocial resources only β(t)	Demographics & stressors β(t)	Demographic & psychosocial resources	Demographics, stressors & psychosocial resources
Socio-demographics						
Age	0.115*			0.022	-0.003	-0.036
Sex	0.078*			0.056	0.069*	0.061*
Household wealth						
First quartile (ref)						
Second quartile	-0.033			-0.014	-0.042	-0.025
Third quartile	-0.048			0.092*	-0.029	0.071
Fourth quartile	-0.132**			0.085	-0.046	0.083
Religion						
Protestant (ref)						
Catholics	0.124**			0.049	0.105	0.049
Muslims	0.075			0.014	0.059	0.014
Pentecostal	0.148***			0.081**	0.135***	0.086**
Other	-0.007			-0.011	0.010	0.003
Education level						
None (ref)						
Primary	-0.287**			-0.112	-0.154	-0.064
Secondary	-0.229**			-0.119	-0.077	-0.046
Tertiary	-0.135*			-0.049	-0.042	-0.002
Orphan-hood						
None (ref)						
Paternal orphan	0.042			-0.005	-0.108**	-0.083*
Maternal orphan	0.015			0.001	-0.039	-0.029
Double orphan	-0.038			-0.026	-0.149**	-0.094*
Type of caregiver						
Parents (ref)						

Aunt/uncle	0.021			0.016	0.016	0.022
Grandparents	0.100*			-0.001	0.062	-0.002
Siblings	-0.011			-0.059	-0.033	-0.062
Other	0.020			0.019	0.012	0.013
Stressors						
Neighborhood insecurity		0.034		0.048		0.033
Ongoing worries and concerns		0.158***		0.179***		0.118**
Hardships		0.028		0.058		0.032
Negative life events		0.221***		0.221***		0.209***
HIV-related concerns		0.346***		0.323***		0.299***
Stigma		0.169***		0.155***		0.089**
Psychosocial resources						
Frequency of praying privately			0.126**		0.125**	0.078**
Spirituality			-0.176***		-0.173***	-0.083**
Optimism			-0.062		-0.067	-0.063*
Social support			-0.063		-0.064	-0.018
Overall satisfaction with social support Not satisfied (ref) Satisfied			-0.223***		-0.222***	-0.169***
Coping strategies			-0.285***		-0.297***	-0.160***
Adjusted R^2	0.053	0.427	0.262	0.432	0.282	0.495

Chapter 4

Exploring the Relationship between Psychological Distress and Non-adherence to Anti-retro Viral Treatment among HIV-infected adolescents in Uganda

Introduction

Antiretroviral treatment (ART) has dramatically reduced HIV and AIDS related mortality and morbidity (Baker et al., 2008; Lima et al., 2009; UNAIDS, 2013), transforming HIV/AIDS from a death sentence into a chronic illness. ART also reduces the risk of both acquisition and transmission of HIV (Das et al., 2010; Kelesidis & Landovitz, 2011; UNAIDS, 2013; Volmink, Siegfried, van der Merwe, & Brocklehurst, 2007), making it a vital component of HIV prevention strategies. Currently, 1.3 million adults (> 15 years) and 190,000 children (0-14 years) are living with HIV/AIDS in Uganda (UNAIDS, 2012; UNGASS, 2012). The annual number of AIDS-related deaths in Uganda has been reduced from an estimated 110,000 deaths per year prior to availability of ART in (2003) to 63,000 deaths in 2013, a 42.7% decline in mortality (UNAIDS, 2013). Despite the progress, AIDS mortality persists because fewer than 50% of adults eligible for ART have access to treatment (UNAIDS, 2013).

Efforts to expand access to ART, particularly among young people (10 – 24 years), there is increasing concern about low rates of ART adherence among children and adolescents in low- and middle-income countries, which threaten to erode progress in expanding access to ART. Rates of adherence among adolescents in both low- and high income countries typically range from 49% - 100%, depending on the method of assessment (Simoni et al., 2007; Steele & Grauer, 2003; Vreeman, Wiehe, Pearce, & Nyandiko, 2008). In Uganda, Nabukeera-Barungi et al (2007)

found adherence levels ranging between 72% with home-based unannounced pill counts and 94.1% with a self-report measure (Nabukeera-Barungi, Kalyesubula, Kekitiinwa, Byakika-Tusiime, & Musoke, 2007); both of these rates are below the required minimum (95%) for successful ART outcomes.

Non-adherence to ART has been associated with drug resistance (Liu et al., 2006) (Bangsberg et al., 2000; Sethi, Celentano, Gange, Moore, & Gallant, 2003), transmission of drug-resistant virus (Grant et al., 2002; Little et al., 2002; Nazziwa et al., 2013; Wensing et al., 2005), and poor clinical health outcomes, including, increased viral loads, reduced CD4 count, and accelerated progression to AIDS and death (Bangsberg, Hecht, Charlebois, Chesney, & Moss, 2001; Bangsberg et al., 2000; García et al., 2002; Mannheimer, Friedland, Matts, Child, & Chesney, 2002). The consequences of non-adherence are a major concern for clinicians and public health practitioners involved with HIV/AIDS prevention and care, as they threaten to derail current gains in both the prevention and management of HIV/AIDS (Bangsberg, 2008; Bangsberg, Kroetz, & Deeks, 2007). Specific adherence strategies such as associating drug-taking times with a daily routine, pillboxes, alarm devices, phone reminders, visual medication schedules, carrying pills in a bag etc. (Liu et al., 2001; Machtinger & Bangsberg, 2007; Michaud, Suris, Thomas, Gnehm, & Cheseaux, 2010; Murphy et al., 2003) have been associated with increased adherence to ART (Bikaako-Kajura et al., 2006; Hosek, Harper, & Domanico, 2005; Michaud et al., 2010; Murphy et al., 2003; World Health Organization, 2003)

A few studies have explored barriers and facilitators to adherence among adolescents in low- and middle-income countries (LMICs). The documented barriers to adherence include: *patient factors* e.g. age, gender, HIV status disclosure, mental health status, knowledge and attitudes towards HIV and its treatment, social support, parent-child conflict; *treatment related*

factors e.g. pill burden, complexity of regimen - dosing and food instructions and medication side effects; *disease characteristics* e.g. duration and stage of HIV infection, presence of co-morbidities, and HIV-symptomatology; psycho*social/familial factors* e.g. household income, caregiver education level, stigma, caregiver emotional wellbeing, and caregiver permanence; and *clinical setting* e.g. convenience of scheduling appointment, availability of transport and perceived confidentiality of services (Bikaako-Kajura et al., 2006; Mills et al., 2006; Vreeman et al., 2009; Vreeman et al., 2008).

Despite the mounting evidence on a high burden of psychological distress among HIV-infected adolescents in both low-income (Musisi & Kinyanda, 2003, 2009) and high-income countries (Murphy, Moscicki, Vermund, & Muenz, 2000; Naar-King et al., 2006), none of the present studies have explored the relationship between psychological distress and adherence among HIV-infected adolescents. Yet, studies conducted in high-income countries documented negative associations between psychological distress and adherence to ART among HIV-infected adolescents (Murphy et al., 2005; Naar-King et al., 2006; Nugent et al., 2010).

Only a few studies have examined the factors that mitigate the impact of psychological distress on adherence to ART among HIV-infected adolescents, and majority of these studies have focused on exploring the role of social support and coping. Active coping styles such as confrontation or seeking social support have been associated with positive psychological adjustment, while passive coping styles such as withdrawal or depressive reactions have been associated with increased psychological distress (Meijer, Sinnema, Bijstra, Mellenbergh, & Wolters, 2002; Murphy et al., 2000). Specific adherence strategies such as associating drug-taking times with a daily routine, pillboxes, alarm device, reminders, visual medication schedules, and carrying pills in a bag, have been associated with increased adherence to ART.

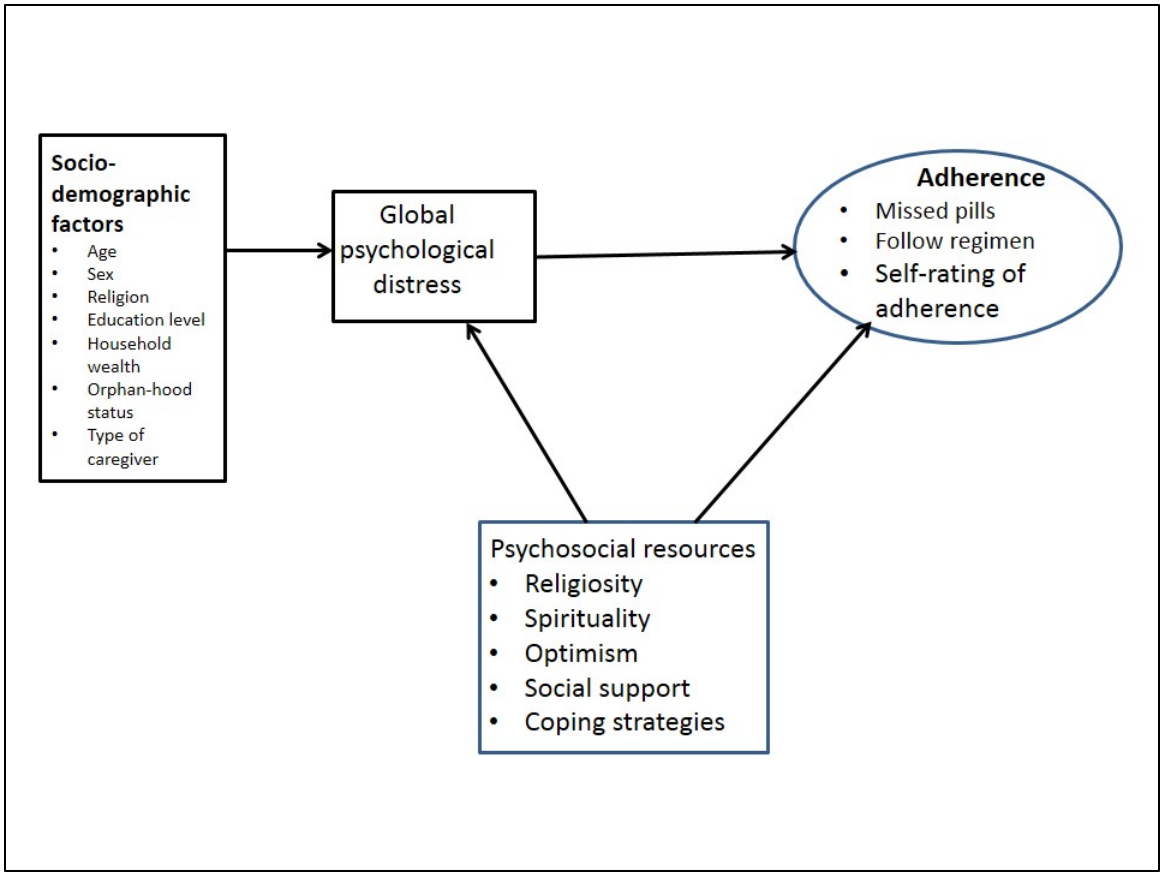
(Bikaako-Kajura et al., 2006; Hosek et al., 2005; Michaud et al., 2010; Murphy et al., 2003; World Health Organization, 2003). Social support has been associated with reduced distress among HIV-infected youth (Battles & Wiener, 2002; Lam, Naar-King, & Wright, 2007; Murphy et al., 2000), but its relationship with adherence in this population has been less consistent as a few studies have found a positive association between social support and adherence (Comulada, Swendeman, Rotheram-Borus, Mattes, & Weiss, 2003), but the majority have not found any association (Murphy, Wilson, Durako, Muenz, & Belzer, 2001; Naar-King et al., 2006; Nugent et al., 2010).

The role of spirituality/religiosity and optimism in reducing psychological distress or adhering to ART has not been among HIV-infected adolescents, yet studies conducted among HIV-infected adults have identified spirituality/religiosity (Coleman & Holzemer, 1999; Cotton, Zebracki, Rosenthal, Tsevat, & Drotar, 2006; Ironson et al., 2002; Makoae et al., 2008; Nooney & Woodrum, 2002; Prado et al., 2004; Szaflarski, 2013; Tuck, McCain, & Elswick Jr, 2001) and optimism (Mukolo & Wallston, 2012). In a study of 115 HIV-infected youth (14-23 years) in the U.S., Lightfoot and Healy found that youth who scored high on career planning reported less distress and were more likely to use positive planning (Lightfoot & Healy, 2001). In a study of 124 HIV-infected adults in the U.S., Mokolo and Wallston found a positive association between dispositional optimism and psychological wellbeing.

Developing effective HIV treatment and prevention programs in low-income countries requires understanding of the contextual barriers and facilitators of adherence in these settings. This study seeks to expand on the current literature on correlates of adherence to ART among adolescents in LMICs. Capitalizing on a large cohort of adolescents in care, the present study

examines the relationship between psychological distress, psychosocial resources and adherence to ART, net of other factors commonly examined in prior studies.

Figure 4.1. Conceptual framework



The conceptual framework of this paper is presented in figure 4.1. Consistent with the literature, this conceptual framework asserts that psychological distress leads to lower ART adherence (Murphy et al., 2005; Naar-King et al., 2006; Nugent et al., 2010), and psychosocial resources mediate the relationship between psychological distress and adherence (Battles & Wiener, 2002; Lam et al., 2007; Murphy et al., 2000).

Methods

Study Setting and population

This study was conducted among adolescents seeking HIV care at the Joint Clinical Research Center (JCRC) in Kampala, Uganda. The JCRC, is a not-for-profit organization established in 1991, providing HIV/AIDS care to one of the largest HIV-infected client populations in Africa, including approximately 2500 children and adolescents.

Study Population and Recruitment Strategy

All adolescents between the ages of 12 and 19 years, and enrolled in care at the JCRC between February and September, 2013 were approached to participants in this study, excluding adolescents who were unaware of their HIV status and those with known cognitive limitations. The minimum sample size for this study was determined to be 460, using Optimal Design Software, version 3.0 (Spybrook, Raudenbush, Liu, & Congdon, 2006) the minimum sample size at alpha (α) = 0.05, power = 0.80 and medium design effect (d = 0.5) (Cohen, 1992). A quota sampling strategy was adopted to ensure adequate representation of males and females across all ages.

Respondents were recruited during their scheduled clinic visits by a team of three (3) interviewers (university graduates with social sciences training), each of whom received training in interviewing skills and research ethics. Potential respondents were approached in the clinic waiting room. The initial interaction focused on establishing the adolescent's disclosure status, following which, the respondents were informed about the study purpose, procedures, and participant's rights. Adolescents expressing interest in the study, and their caregivers (if present) were invited to the interview room adjustment to the clinic, where the research assistants sought informed consent and conducted the interview. If the caregiver was absent, the necessary

arrangements were made with the adolescent to obtain caregiver written consent through a scheduled appointment at the caregiver's convenience; interviews were conducted at a later date after consent at been secured. To ensure coordination within the research team, a list of scheduled clinic visits was generated from the JCRC patient care database and made available to the research team. Adolescents presenting to the clinic with severe illness were not interviewed at that visit; attempts were made to interview these participants at a later date.

Procedures

Questionnaires were administered in face-to-face interviews using Personal Digital Assistant (PDA) devices. Interviews were either conducted following the respondent's clinic visit, as respondents awaited laboratory results, or during scheduled visits for interviews. The interview language was Luganda or English, depending on the participant's language preference and proficiency. Response cards in Luganda and English – providing visual analogs for potential responses (e.g. likely, somewhat likely or very likely), were provided to participants during the interview. The questionnaire included 5 major sections: socio-demographic characteristics, stressors, psychological distress, personal resources, and measures of adherence to HIV care. The entire questionnaire included 315 items: the interviews lasted between 60 – 75 minutes, including scheduled breaks in the interview. Respondents were provided with a snack during the interviews.

Permission to conduct this study was provided by the Institutional Review Board at the Joint Clinical Research Center, the University of Michigan Ethics Review Board, and Uganda National Council for Science and Technology Ethics Review Board.

Measurement

Adherence

Adherence, the primary study outcome, was measured using the self-report AACTG Adherence Scale (Chesney, Ickovics et al 2000). Three indicators of adherence were computed from the AACTG questionnaire as follows:

(1) Average adherence (missed pills): Respondents were asked to number of missed pills over the past three days for each of their prescribed ARV medication. Adherence was calculated as follows:

$$1 - \left(\frac{\text{Total number of missed pills in past 3 days}}{\text{Number of prescribed pills for 3 days}}\right) * 100$$

(2) Categorical self-reported adherence to regimen ("regimen") was assessed using a single item – "How closely did you follow your specific schedule over the past 3 days? Responses were measured on an ordinal scale – "would you say never, some of the time, about half the time, most of the time, and all of the time".

(3) Visual analogue Scale self-rated adherence ("rating") assessed using the question "On a scale of 0 to 10, how would you rate your adherence to your ART?"

Similar to prior studies, adherence was defined as taking at least 95% of the prescribed doses (Fogarty et al., 2002; Paterson et al., 2000). To facilitate comparison of findings on missed doses to prior studies and also enable a common statistical approach across the indicators, a binary measure of adherence for each indicator was computed, using the 95% cut-off to categorize respondents as either adherent or non-adherent.

Barriers to adherence

Barriers to adherence were also assessed using the AACTG Adherence Scale. The frequent reasons for missing medications within the previous year were assessed with a 15-item checklist with sample items such as: away from home, was busy, simply forgot, had too many pills to take, to avoid side effects, not want others to notice, change in daily routine, felt like drug was toxic, was sick, felt depressed etc. Responses recorded on a 4-point scale (never, rarely, sometimes, and often) and examined separately for each item.

Psychological distress

Psychological distress was assessed using a 25-item measure developed for this study. A detailed description of the measure is provided in Chapter 2. Briefly, ten (10) in-depth interviews and three focus group discussions were conducted to explore understanding and language of psychological distress among HIV-infected adolescents at the JCRC. Emerging themes on distress symptomology were mapped onto published measures of psychological distress, and relevant items were extracted to create a pool of 67-items assessing frequency of distress symptomatology in the past week, using a 5-point scale- never, almost never, sometimes, often, and most of the time. The scale was translated into Luganda (the local language used in this study) by two independent translators, and reviewed by a team consisting of the principal investigator, a counselor and pediatric nurse at the JCRC to identify and resolve inconsistencies.

The scale was subsequently reviewed by an expert panel consisting of four psychiatrists and a pediatric HIV specialist in Uganda, and two psychologists at the University of Michigan, to assess its conceptual breadth, developmental and cultural appropriateness (for the Ugandan experts) and face validity. Cognitive interviews (6) were conducted with adolescents to assess question wording, adequacy of translations and identify difficulty or uncomfortable items. The

scale was piloted among 98 HIV-infected adolescents aged 12- 19 years and seeking HIV care at the JCRC to determine the preliminary factor structure and psychometric properties of the scale.

Final refinements to the scale were conducted prior to the present analyses: using exploratory factor analysis, the scale was reduced to 25 items corresponding to six (6) subscales labeled as anhedonia, depressive-anxiety, isolation, sleep problems, suicidal ideation and somatic symptoms. Construct validity of the measure was assessed through correlations with other measures of well-being and confirmatory factor analysis was used to assess the fit of the model to the data. Internal consistency of the subscales ranged between, $r = 0.615$ and $r = 0.758$; internal consistency of the entire scale was $r = 0.89$. Additionally, exploratory factor analysis of the sub-scale scores resulted in one-dimensional factor, supporting the use of a composite global psychological distress score. The global psychological distress score was computed as an average of the item scores. The present analyses focus on exploring the relationship between global distress and adherence to ART.

Psychosocial resources

The psychological resources assessed included spirituality and religiosity, optimism, social support, satisfaction with social support, receipt of support for adherence and coping strategies. In these analyses, each psychosocial resource was used as mediator of the relationship between psychological distress and adherence. A descriptive summary of each psychosocial resource, including the range and internal reliability (Cronbach's alpha) of the scale, where applicable, is presented in table 4.2.

Spirituality was assessed using in two ways: (1) using the 7-item Brief RCOPE Spirituality subscale (Pargament, Feuille, & Burdzy, 2011): spirituality score was computed as the mean of items in the scale; (2) using the item "How often do you pray privately in places

other than a church or mosque? -more than once a day, once a day, a few times a week, once a week, a few times a month, once a month, less than once a month, a few times a year, or never". The spirituality score was computed as the means of these items.

Religiosity was assessed using two items: (1) respondent's religious affiliation- protestant, Catholic, Muslim, Pentecostal, and other e.g. Seventh Day Adventist (SDA) and Mormons; (2) and using the question- "How often do you go to religious services -more than once a week, every week or more often, once or twice a month, every month or so, and once or twice a year".

Optimism was measured using 7-item scale adapted from the national Longitudinal Study of Adolescent Health (ADDHealth) (UNC Carolina Population Center Project, 2014). These items assessed beliefs that the respondent- will live to age 35, will graduate from school, be rich, get married, have children, receive cure for HIV etc. The optimism score was computed as mean of these items.

General social support was measured using the Social Support Questionnaire (SSQ) (Sarason, Sarason, Shearin, & Pierce, 1987), which assessed access for the four typologies of social support (emotional, instrumental, informational, appraisal), and along with respondent's satisfaction with the social support. The social support score was computed as mean of all items in the scale

Coping strategies were assessed using a locally adapted Adolescent Coping Orientation for Problem Experiences scale (ACOPE), which assesses adolescent coping strategies (Patterson & McCubbin, 1987). Responses are measured on a 5-point scale, and a composite score was computed as the average of all items.

Socio-demographics

Socio-demographics were assessed using self-reported data on age, sex, religion, level of education, orphan-hood, and type of caregiver.

Religion was assessed using five categories that represent the dominant faiths in Uganda –Protestant, Catholic, Muslim, Pentecostal and other e.g. SDA, Mormons etc. The reference group was Protestants.

Education was measured as the level of current level of education attended: - primary school, secondary school, tertiary institutions or no education. The reference group was respondents without any education.

Orphan-hood was operationalized as: non-orphan-hood (both parents living), maternal orphan-hood (mother deceased), paternal orphan-hood (father deceased) and double-orphaned (both parents deceased). The reference group was the non-orphaned respondents.

Type of caregiver was assessed as the self-reported relationship of respondent with their primary caregiver, categorized as: biological parents, aunt or uncle, grandparents, sibling, and other e.g. foster parents. The reference group was respondents with a biological parent as the primary caregiver.

A *household wealth index* was computed from a list of 21 household assets adapted from the Uganda Demographic and Health Survey (Measure DHS, 2012), using procedures documented in prior studies (Filmer & Pritchett, 2001; Measure DHS, 2012). Each household asset was assigned a weight generated through principal component analysis; the resulting asset scores were then standardized using a mean equal to zero and standard deviation equal to one. The standardized scores were used to generate five wealth quintiles: lowest, second, middle,

fourth and highest wealth quintiles. The reference group was respondents in the lowest wealth quintile.

Data analysis

Univariate analyses

Measures of central tendency e.g. mean and standard deviations, median, and frequencies were computed to examine the distribution of variables- dependent and independent variables, including the barriers to adherence. Bivariate analyses –correlations, t-tests, analysis of variance (ANOVA) and chi-squares were conducted to examine the relationship (strength and direction) between each predictor variables and measured indicators of ART adherence.

Logistic regression

Logistic regressions were conducted to examine the relationship between psychological distress and each binary indicator of adherence- missed pills, following regimen and self-rating of adherence. The first model examined the zero-order association between global psychological distress and adherence. This was followed by model 2 exploring the relationship between psychological distress and each indicator of adherence, net of socio-demographic variables. Model 3 explored the mediating effects of psychological resources on distress, net of the socio-demographic variables. The results of these analyses are presented in Table 3.

Structural equation modeling (SEM)

Subsequently, structural equation modeling, with STATA (version 13) was used to explore the predictors of adherence, using a latent adherence variable that combined all three measured indicators of self-reported adherence, that is, missed number of pills, following regimen schedule and self-rated adherence. This model hypothesized that net of respondent's

socio-demographic characteristics, psychological distress was significantly associated non-adherence to ART, and psychosocial resources mediated the relationship between psychological distress and non-adherence to ART.

As mentioned earlier, the three indicator measures of adherence – missed pills, following regimen and self-rated adherence (based on the continuous measures) were combined to create a latent measure of adherence, which was used in these analyses. All other variables – global psychological distress, psychosocial resources and socio-demographics- were added to the model was manifest variables. A series of models were fitted to the data to, starting with the unadjusted model exploring the relationship between global psychological distress and adherence, and followed by addition of socio-demographic variables to the model, and finally, psychosocial resources to assess their mediational effects. Model fit was evaluated using the chi-square, root mean square error of approximation (RMSEA), comparative fit index (CFI) and Tucker-Lewis Index (TLI): these are the most widely used indicators of model fit in confirmatory factor analysis. Interpretation of these indicators is as follows: a non-significant chi-square is the ideal but the chi-square is not a robust indicator of model fit, as it is highly sensitive to minor misfit in large samples, and is often significant in large samples (Filmer & Pritchett, 2001; Hooper, Coughlan, & Mullen, 2008). However, the RMSEA, CFI and TLI are not sensitive to sample size. The RMSEA value suggests adequate fit when it's close to or less values less than 0.06. CFI and TLI values greater than 0.90 indicate satisfactory fit, while values close to or greater than 0.95 indicate good fit (Hooper et al., 2008; Hu & Bentler, 1998).

Alternative models, using psychosocial resources as latent variables were also explored but these models were unsuccessful- either failing to converge or having poor fit to the data. Additional analyses also explored the use of psychological distress as a latent variable; while the

model fit was adequate, the models using psychological distress as a manifest variable had a much better fit to the data.

Results

Univariate analyses

A descriptive summary of the socio-demographic characteristics are presented in Table 4.1. The majority of respondents were female (53.4%; n = 249), and the mean age of the sample was 15.6 years (SD = 2.44). More than 94% (439) of respondents were currently attending school; of these, 69.6% (280) were enrolled in secondary school. More than two thirds of respondents were orphaned: 68.2% had lost one parent and 21.5% (n =100) had lost both parents.

Prevalence of adherence

Respondents were categorized as adherent vs. non-adherent using a 95% cut-off. The proportions of adherence varied across the three self-reported measures of adherence: 81.7% (n = 378) of respondents were adherent based on the number of missed pills in the past 3 days; 41.4% (n = 65) of respondents had adherent to their specific regimen in their past 3 days; and 58.8%; n = 273) of respondents were adherent based on visual analog scale.

Barriers to adherence

The distribution of reported barriers to adherence across the sample is shown in Figure 4.1. The most frequently reported barriers to adherence included: forgetting (54.5%; n = 250), being away from home (48.2%; n = 221), difficulty taking pills at the specified times (48.2%; n = 221), and falling asleep through dose time (42.7%; n = 196). Too many pills (26.8%; n = 123), medication side effects (26.4%; n = 121), and felt the drugs were toxic or harmful (21.4%; n = 98) were the least reported barriers to adherence.

Logistic regression analyses of adherence

The results of the logistic regression analyses on predictors of non-adherence using the three self-reported measures of adherence, that is, missed number of pills in the past 3 days, following the medical regimen in the past 3 days, and the visual analog scale, are presented in Table 4.3.

Missed pills in the past 3 days: In the unadjusted model, a unit increase in psychological distress was associated with a 108% increase in the odds of missing pills over the past 3 days (OR = 2.08 [95% CI: 1.37 – 3.16]). After controlling for respondents' socio-demographic characteristics, a unit psychological distress was associated with a 129% unit increase in the odds of missing pills over the past 3 days (OR = 2.29 [95% CI: 1.47 – 3.59]). In the final model adjusting for respondents' socio-demographic characteristics and psychosocial resources, a unit increase in psychological distress was associated with a 75% increase in the odds of missing pills over the past 3 days (OR = 1.75 [95% CI: 1.04 – 2.95]).

The reduction in odds of non-adherence when psychosocial resources were added to the model suggested that psychosocial resources partially mediated the relationship between psychological distress and non-adherence to ART. Among the psychosocial resources, only satisfaction with social support was significantly associated with non-adherence to ART: a unit increase in satisfaction with social support was associated with a 58% reduction in the odds of missing pills over the past 3 days (OR = 0.42 [95% CI: 0.22 – 2.07]). Frequency of praying privately, frequency of attending religious services, spirituality, optimism, general social support, adherence support, and coping strategies were not significantly associated with non-adherence.

Following the specific regimen schedule: In the unadjusted model, a unit increase in psychological distress was associated with 134% increase in the odds of non-adherence to the regimen schedule in the past 3 days (OR = 2.34 [95% CI: 1.66 – 3.29]). After adjusting for respondents' socio-demographic characteristics, a unit increase in psychological distress was associated with a 129% unit increase in the odds of non-adherence to the regimen schedule over the past 3 days (OR = 2.29 [95% CI: 1.59 – 3.29]). In the final model adjusting for respondents' socio-demographic characteristics and psychosocial resources, a unit increase in psychological distress was associated with a 63% increase in the odds of non-adherence to the regimen schedule over the past 3 days (OR = 1.63 [95% CI: 1.08 – 2.46]). The reduction in odds of non-adherence, from 2.29 to 1.63, when psychosocial resources were added to the model suggested that psychosocial resources partially mediated the relationship between psychological distress and non-adherence to the medical regimen over the past 3 days.

Among the psychosocial resources, non-adherence to the medical regimen was significantly associated with frequency of praying privately and frequency of attending religious services, and satisfaction with social support. A unit increase in frequency of praying privately was associated with a 22% increase in the odds of non-adherence to the regimen schedule (OR = 1.22 [95% CI: 1.07 – 1.39]), while a unit increase in frequency of attending religious services was associated with a 38% increase in the odds of non-adherence to following the specific regimen (OR = 1.38 [95% CI: 1.09 – 1.74]). On the other hand, a unit increase in satisfaction with social support was also associated with a 58% reduction in the odds of non-adherence to the regimen schedule (OR = 0.42 [95% CI: 0.26 – 0.67]). Spirituality, optimism, general social support, adherence support, and coping strategies were not significantly associated with non-adherence.

Self-rated adherence to ART: In the unadjusted model, a unit increase in psychological distress was associated with a 119% increase in the odds of non-adherence to ART (OR = 2.19 [95% CI: 1.56 – 3.08]). After adjusting for respondents' socio-demographic characteristics and psychosocial resources, a unit increase in psychological distress was associated with a 113% increase in the odds of non-adherence to ART. In the final model adjusting for respondents' socio-demographic characteristics and psychosocial resources, a unit increase in psychological distress was associated with a 79% increase in the odds of non-adherence to ART. Similar to prior analyses, psychosocial resources also mediated the relationship between psychological distress and non-adherence to ART. Among the psychosocial resources, only frequency of praying privately and satisfaction with social support were significantly associated with non-adherence to ART: a unit increase in frequency of praying privately was associated with a 15% increase in the odds of non-adherence (OR = 1.15 [95% CI: 1.19 – 2.69]), while a unit increase in satisfaction with social support was associated with a 31% decrease in the odds of non-adherence. Spirituality, optimism, general social support, adherence support, and coping strategies were not significantly associated with non-adherence.

SEM analyses

The results of the structural equation modeling analyses are presented as two figures. Figures 4.3 shows the unadjusted model relationship between psychological distress and the latent adherence variable. Figure 4.4 depicts the relationship between psychological distress and the latent adherence variable, when respondent's socio-demographic characteristics and psychosocial resources are added to the model. In this model, psychosocial resources mediate the relationship between psychological distress and adherence to the ART.

Psychological distress: The overall fit of the unadjusted model to the data was excellent: chi-square = 0.408, RMSEA = 0.000, CFI = 1.0 and TLI = 1.0. In the unadjusted model, a unit in psychological distress was associated with a 44% increase in the odds for non-adherence (OR = 1.44 [95% CI: 1.29 – 1.59]; p < .001). The fit of the adjusted model to the data was also excellent Chi-square = 30.66; p = 0.678; RMSEA = 0.000; CFI and TLI = 1.0. In this model, a unit increase in psychological distress was associated with a 31% increase in the odds for non-adherence, net of respondents' socio-demographic characteristics and psychosocial resources (OR = 1.30 [95% CI: 1.15 – 1.49]; p < .001). In the decrease in the odds ratio when psychosocial resources were added to the model indicates the psychosocial resources partially mediated the relationship between psychological distress and non-adherence to ART.

Socio-demographics: A unit increase in age was associated with a 6% increase in the odds for psychological distress (OR = 1.06 [95% CI: 0.96 – 1.17]), and 6% increase in the odds for non-adherence, but these relationships were not statistically significant. Female sex was marginally associated with 8% increase in the odds for psychological distress (OR = 1.08 [95% CI: 0.99 – 1.17]; p < .10), and 3% reduction in the odds for non-adherence, but the relationship between sex and non-adherence was not statistically significant. Household wealth was not significantly associated with psychological distress but was significantly was associated with a 17% reduction in the odds for non-adherence (OR = 0.83 [95% CI: 0.73 – 0.95]; p < .05). Orphan-hood, level of education, type of caregiver, household wealth, and religion were not significantly associated with psychological distress and non-adherence to ART.

Psychosocial resources: A unit in spirituality was significantly associated with 16% reduction in the odds for psychological distress (OR = 0.84 [95% CI: 0.78 – 0.91]; p < .001), and 5% reduction in the odds of non-adherence (OR = 0.95 [95% CI: 0.84 – 1.06]), but the relationship

between spirituality and adherence was not statistically significant. A unit increase in optimism was associated with 7% reduction in the odds for psychological distress (OR = 0.93 [95% CI: 0.86 – 1.02]) and 6% reduction in the odds for non-adherence (OR = 0.93 [95% CI: 0.83 – 1.05]), but neither relationship was statistically significant. A unit increase in social support was significantly associated with a 9% reduction in the odds for psychological distress (OR = 0.91 [95% CI: 0.83 – 0.99]; $p < .05$) and 9% reduction in the odds for non-adherence (OR = 0.91 [95% CI: 0.96 – 1.25]), but the relationship between social support and adherence was not statistically significant. A unit increase in coping strategies was significantly associated with a 24% reduction in the odds for psychological distress (OR = 0.76 [95% CI: 0.70 – 0.83]; $p < .001$) and 1% reduction in the odds for non-adherence (OR = 0.99 [95% CI: 0.88 – 1.13]); the relationship between coping strategies and adherence was not statistically significant. A unit increase in satisfaction with social support was associated with a 23% reduction in the odds for psychological distress (OR = 0.77 [95% CI: 0.71 – 0.84]) and a 22% reduction in the odds for non-adherence (OR = 0.78 [95% CI: 0.68 – 0.89]); both of these associations were statistically significant ($p < .001$). Lastly, support with adherence was significantly associated with 11% reduction in the odds for psychological distress (OR = 0.89 [95% CI: 1.03 – 1.22]; $p < .05$) and 1% reduction in the odds for non-adherence to ART (OR = 0.99 [95% CI: 0.87 – 1.12]), but the relationship between adherence support and non-adherence was not statistically significant.

Discussion

The purpose of this study was to explore the relationship between psychological distress and adherence to ART among HIV-infected adolescents at the Joint Clinical Research Center in in Uganda. The prevalence of adherence to ART varied across three self-reported measures of adherence: 82% using missed on missed pills, 41% on adherence to medical regimen and 59%

using self-rated adherence on the visual analog scale. The most frequently reported barriers to adherence included: forgetting, being away from home, challenges taking pills at the specified time and sleeping through drug administration times.

In the unadjusted logistic regression models, psychological distress was significantly associated with non-adherence, with magnitudes between 119% - 134% reductions in adherence, across the three self-reported measures. After adjusting for respondents' socio-demographic characteristics and psychosocial resources, psychological distress was associated with 75%, 63% and 79% increase in the odds of non-adherence based on self-reported missed pills, adherence to medical regimen and visual analog scale. In these logistic models, psychosocial resources partially mediated the relationship between psychological distress and non-adherence to ART.

The results of the SEM analyses were consistent with findings of the logistic regression analyses. In the unadjusted SEM model that combined the three self-reported measures of adherence, psychological distress was associated with a 44% increase in the odds of non-adherence, and 31% increase in the odds of non-adherence, after controlling for respondent's socio-demographic characteristics and psychosocial resources. Similar to the logistic regression analyses, psychosocial resources partially mediated the relationship between psychological distress and non-adherence to ART.

Among the socio-demographics factors explored in this study, only household wealth was independently associated with adherence, but this relationship was only marginally significant. Adherence was not significantly associated with age, sex, religion, or level of education. Of the psychosocial resources, only satisfaction with social support were significantly associated with non-adherent across the three self –reported measures. Frequency of praying privately and frequency of attending religious services were significantly associated with increased odds for

non-adherence to the medical regimen schedule and self-rated adherence using the visual analog scale.

These rates of adherence reported in this study across the three self-reported measures of adherence are lower than 95% adherence rates required to achieve therapeutic success. These adherence rates of adherence are lower also than the levels of adherence reported in prior studies conducted among HIV-infected children and adolescents in Uganda. A small study assessing the feasibility of electronic adherence monitoring at the JCRC found that adherence varied with the type of assessment method used- 99% of self-reports, 97% for pill counts, and 88% with electronic medication vials (Wiens et al., 2012). Similarly, a study conducted among 41 HIV-infected children (ages 0 – 18 years) attending the mother-to-child transmission plus program in Kampala, Byakika-Tusiime et al (2009) found that mean adherence was 98.1% and 97.8% based on 3-day self-report and visual analogue scale respectively. Unfortunately, neither the mean nor median age of children in this study was reported, making comparison to the present adolescent sample difficult (Byakika-Tusiime et al., 2009).

The adherence rate documented using the missed pills in the past 3 days (80%) is comparable to findings in another study conducted among children and adolescents in Uganda: in a cross-sectional study conducted among 170 children and adolescents (aged 2 – 18 years) attending the HIV/AIDS clinic at Mulago Hospital in Kampala, Nabukeera_Barungi et al (2007) found that the self-reported rates for adherence among participants was 89.4% based on the 3-day self-report. Additionally, the rates of adherence in this study higher than average rates of adherence among children and adolescents in high-income countries: in a systematic review of adherence among HIV-infected youth aged 13 – 24 years living in the United States, Reisner et

al (2009) found that rates of adherence across the 14 studies reviewed ranged from 28.3% to 69.8% (Reisner et al., 2009).

The variation in adherence rates across the three measures of adherence warrants may reflect the vulnerability of self-reported measures recall and social desirability bias. Of particular concern is the self-reported measure of missed number of pills during the past 3 days. This indicators is frequently used in the JCRC clinic along with pill counts to assess adolescents' adherence to ART. Disclosures of poor adherence are usually followed with berating from clinic staff. As such, adolescents in this study may be sensitive to this measure resulting in under-reporting the actual number of missed pills, resulting in high rates of adherence observed with this measure. For this reason, the following medication regimen and visual analog scale measures may offer more realistic rates of adherence in this population. Despite the variation in adherence rates across the three self-reported measures, there was significant agreement in across the three self-reported measures across the predictors assessed. Nonetheless, the low rates of adherence among adolescents in this study is a cause for concern given that JCRC is one of the most highly resourced ART treatment centers in Uganda.

The relationship between psychological distress and adherence reported in this study is consistent with reports from prior studies conducted in the United States. For example, in a study of 122 HIV-infected youth, Nugent et al (2010) found that distressed youth were more than seven (7) times less likely to adhere to the ART compared to non-distressed youth (Nugent et al., 2010). In a small study of 24 HIV-infected youth (ages 16 – 24), Naar-King et al (2006) found that psychological distress was significantly associated with lower adherence ($\beta = 0.37$, $t = 3.80$, $p < .05$) (Naar-King et al., 2006). Similarly, in a study of 161 HIV-infected youth, Murphy et al (2001) found that higher levels of depression (measured using the CES-DC) were significantly

associated with lower frequency of medication use (OR = 0.3; $p < .03$) (Murphy et al., 2001). These findings are also consistent with the results of studies conducted among HIV-infected adults in Uganda. In a cross-sectional study of 122 HIV-infected persons seeking care from an urban HIV-clinic in Uganda, Nakimuli-Mpungu et al (2009) found that participants with psychologically distress participants were three (3) times were less likely to adhere to ART, compared to participants without psychological distress (Nakimuli-Mpungu, Mutamba, Othengo, & Musisi, 2009).

In general, only a few of the assessed psychosocial resources were associated with adherence- frequency of praying privately, frequency of attending religious services, and satisfaction with social support, and even then, frequency of praying privately and frequency of attending religious services were significantly associated with increased odds for non-adherence to ART. Optimism, spirituality, social support, and coping were not significantly associated with medication adherence. Additionally, the psychosocial resources explored in this study accounted for a small proportion of the differences in the relationship between psychological distress and non-adherence to ART.

The lack of association between social support and adherence in this study is consistent with prior adolescent studies. Contrary to findings from studies conducted among HIV-infected adults (Power et al., 2003; Simoni, Frick, Lockhart, & Liebovitz, 2002; Vyavaharkar et al., 2007), adolescent studies have not found significant associations between social support and adherence to ART (Murphy et al., 2001; Naar-King et al., 2006). The findings on the relationship between religiosity and adherence raise important questions about the relationship religiosity and adolescent wellbeing. In this study, both the frequency of praying privately and frequency of attending religious services associated with increased odds of non-adherence to ART. In the prior

chapter, frequency of praying privately was associated with increased psychological distress. Moreover, religious affiliation, particularly Pentecostalism was also associated with increased psychological distress. Taken together, these findings suggest that religiosity is detrimental to the wellbeing of HIV-infected adolescents. While, the design of this study does not enable assessment of mechanisms that underlie these negative relationships; additional studies are needed to increase underlying of these pathways in order to develop interventions that would eliminate the impact of religiosity on adolescent wellbeing.

While this study is not able to address the important question of what are the important psychosocial correlates associated with adherence among HIV-infected adolescents, the findings in this study raise important questions about the contextually relevant predictors of ART adherence as well factors that could reduce or eliminate the impact of psychological distress on adherence among adolescents in Uganda and other countries in sub-Saharan Africa. Understanding of these factors is critical for developing effective interventions that will improve the adolescents' adherence to ART.

The findings in this study have various public health implications for efforts to curtail the transmission of HIV and expand access to ART in sub-Saharan Africa. Non-adherence has been associated with increased HIV infectiousness and risk of developing resistance to ART. The increased risk of transmission of HIV is especially a concern among adolescents given their propensity for risk-taking behaviors, including unprotected sexual relations. That majority of adolescents in sub-Saharan do not have access to comprehensive sexual and reproductive health information and services that are instrumental to curtailing transmission of HIV further compounds the challenges posed by these low rates of adherence. The wide spread resistance to ART that would emerge secondary to poor adherence threats the viability of HIV treatment

programs in sub-Saharan Africa particularly as transmission of ART resistant strains could compromise these regimens, even for ART naive adolescents. At the population level, increased morbidity due to ART mediated resistance and treatment failure could result in increased strain on already over-burdened health care in sub-Saharan Africa, and also perpetuate increase household poverty due to medical expenditures, while the resulting mortality would deprive sub-Saharan Africa of the much needed labor capital.

The findings have also several implications for both clinical practice and research among HIV-infected adolescents. The documented relationship between psychological distress and non-adherence to ART among HIV-infected adolescents in Uganda underscores the need for interventions to eliminate or reduce psychological distress among HIV-infected adolescents in Uganda and other countries in sub-Saharan Africa. Given that the causes of psychological distress among HIV-infected adolescents are diverse, these findings underscore the need for interventions that could build or foster an equally diverse array of skills to enable these adolescents to effectively cope with whatever challenges they may encounter. The association between satisfaction with social support and lower odds for non-adherence suggests a need for interventions to either improve the quality of social support within adolescents' social support networks in order to improve satisfaction, or to modify adolescents' appraisal of the social support received from significant others.

The positive relationship between religiosity and risk for non-adherence highlights the need for interventions to curtail the deleterious effects of religiosity on adherence. However, prior understanding of the pathways through which religiosity impacts adolescents' wellbeing is needed in order to develop interventions that could effectively address this challenge. In the interim, caution should be exercised in pursuing the involvement of religious persons in care of

HIV-infected adolescents, as religion has been associated with stigmatizing attitudes, which could lead to increased psychological distress (Otolok-Tanga, Atuyambe, Murphey, Ringheim, & Woldehanna, 2007; Pargament et al., 2004; Varas-Díaz, Neilands, Malavé Rivera, & Betancourt, 2010).

This regard to research, the findings also highlight the need for research to establish the most ideal measures for assessing adherence among HIV-infected adolescents with both clinical and research contexts, and research to identify the contextually relevant predictors of adherence, and contextually relevant psychosocial resources that would prevent or reduce the impact of psychological distress on adherence to ART. Unfortunately, there is a scarcity of evidence-based psychosocial interventions for youth in sub-Saharan Africa. For example, a review of ART adherence and intervention studies among HIV-infected youth found only seven unique interventions to enhance adherence but all of these interventions had been conducted in the U.S. (Reisner et al., 2009). The lack of interventions of youth in sub-Saharan Africa is particularly concerning given that more the differences in the HIV epidemic between both adolescents and adults in the global north and sub-Saharan Africa present uncertainty about the relevance of these interventions for adolescents in sub-Saharan Africa. As noted in the prior chapter, the differences in route of transmission, duration of living with HIV/AIDS, prevalence of psychological symptomatology and risky behaviors such as drug and substance abuse create differential risks and barriers that structure the vulnerability of these diverse adolescent sub-populations. Therefore, the success of adolescent HIV treatment programs will depend on how well these programs address the diverse psychosocial needs of this population. As the number of HIV-infected adolescents continues to expand, particularly in countries highly burdened by HIV, there

is a need to develop psychological programs to support this population, including a need to integrate mental health services into HIV care.

The findings in this study should be interpreted within the broader limitations of the study design. First, the cross-sectional nature of this study limits causal inference, particularly in evaluating the temporal relationship between psychosocial resources and medication. Reverse causality must also be considered given that the relationship between psychological distress and health is reciprocal. This studies also utilizes self-reported measures of adherence, which may result in over-estimation (Liu et al., 2001; Wagner, 2002). This study does not include any measures on duration on ART yet this factors has been identified as a predictor of non-adherence to ART. Additionally, this study did not explore other psychosocial factors such as involvement in peer support groups, parent-child relationship characteristics etc., which could potentially mitigate the impact of psychological distress on adherence to ART. The study population is drawn from one urban HIV treatment center, which could limit generalizability of findings to adolescents in other settings; however, this potential selection bias may be minimal, given the considerably large study sample size and the fact that JCRC draws patients from all regions of the country.

Despite these limitations, this study is the first to provide evidence that psychological distress is impacting adherence among HIV-infected adolescents in Uganda, a findings that may have relevance for HIV-infected adolescents in other countries of sub-Saharan Africa. Moving forward, more research is needed to identify the social or structural circumstances, and possible interventions, that can both reduce psychological distress and increase adherence, and better address the psychological needs of this population.

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Figure 4.2. Barriers to adherence among HIV-infected adolescents at the Joint clinical Research Center, Kampala (N = 462).

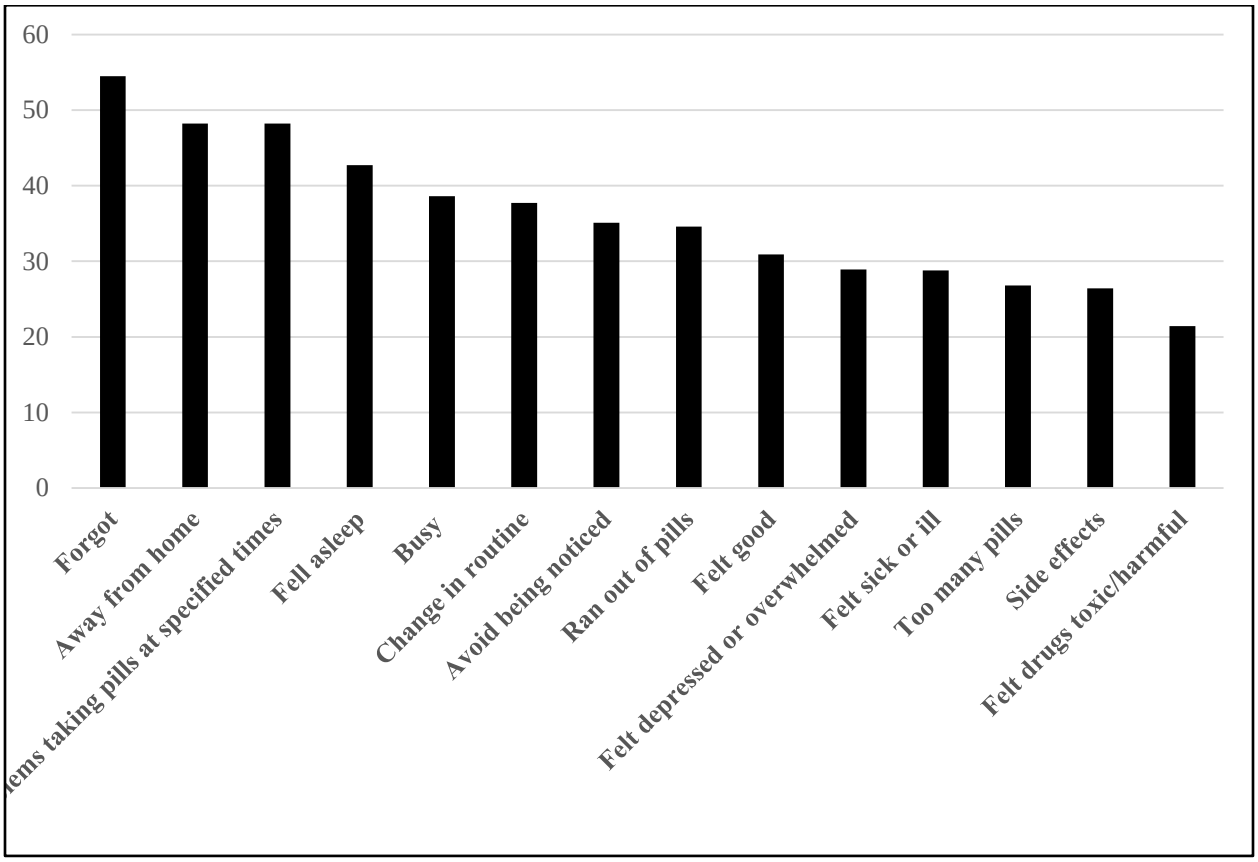


Table 4:1: Socio-demographic characteristics of the HIV-infected adolescents at the Joint Clinical Research Center in Kampala, Uganda (N = 462)

Variable	Percent (frequency) / Mean (SD)	Variable	Percent (frequency)
Age	M = 15.58 (SD = 2.44)	Education level	
12 & 13	26.8 (125)	None	5.4 (25)
14 & 15	24.3 (113)	Primary	37.8 (176)
16 & 17	14.6 (68)	Secondary	49.6 (231)
18 & 19	34.3 (160)	Tertiary	7.3 (34)
Sex		Orphan-hood	
Males	46.6 (217)	Both parents alive	32.6 (152)
Females	53.4 (249)	Mother alive	26.4 (123)
Household wealth index score	M = 2.78 (SD = 0.94)	Only father alive	19.5 (91)
		Both parents deceased	21.5 (100)
Religion			
Protestant	25.9 (121)	Relation to caregiver	
Catholic	37.3 (174)	Biological parents	57.7 (269)
Muslim	16.7 (78)	Aunt or uncle	18.2 (85)
Pentecostal	7.1 (33)	Grandparents	11.6 (54)
Other e.g. SDA	12.9 (60)	Other e.g. foster parents	12.5 (58)

Table 4:2: Descriptive summary of psychosocial resources, including the internal reliability of each scale (N = 462)

Variable	Mean (SD)	Median	Range	Internal reliability (alpha)
Spirituality	1.63 (0.28)	1.7	1 - 2.9	0.44
Frequency of praying privately	5.51 (1.7)	6.0	1 - 8	n/a
Optimism	1.33 (0.38)	1.43	0 – 1.7	0.75
Social support	2.64 (0.71)	2.73	0 - 4	0.87
Coping	1.69 (0.26)	1.7	1 - 2.7	0.70
	Percentage (N)			
Frequency of attending religious services				
More than once a week	4.5% (21)			n/a
Every week or more often	12.9% (60)			
Once or twice a month	56.1% (259)			
Every month or so	15.6% (72)			
Once or twice a year	10.8% (50)			

Table 4:3: Results of Logistic regressions on predictor of adherence to ART, using self-reported measures of adherence-missed number of pills, following medical regimen and self-rated adherence

Variable	*Missed pills in past 3 days*			*Following medical regimen schedule*			*Self-rated adherence using visual analog scale*		
	1 OR [95% CI]	2 OR [95% CI]	3 OR [95% CI]	1 OR [95% CI]	2 OR [95% CI]	3 OR [95% CI]	1 OR [95% CI]	2 OR [95% CI]	3 OR [95% CI]
Global distress score	2.08*** [1.37 - 3.16]	2.29*** [1.47 – 3.57]	1.75** [1.04 – 2.95]	2.34*** [1.66 – 3.29]	2.29*** [1.59 – 3.29]	1.63** [1.08 – 2.46]	2.19*** [1.56 – 3.08]	2.13*** [1.49 – 3.05]	1.79*** [1.19 – 2.69]
Frequency of praying privately			1.02 [0.86 – 1.19]			1.22*** [1.07 – 1.39]			1.15** [1.19 – 2.69]
Frequency of attending religious services			0.89 [0.67 – 1.18]			1.38*** [1.09 – 1.74]			1.21 [0.97 – 1.51]
Spirituality			0.97 [0.86 – 1.09]			0.98 0.89 – 1.07]			1.01 [0.92 – 1.09]
Optimism			0.99 [0.90 – 1.09]			0.96 [0.89 – 1.03]			0.97 [0.89 – 1.04]
General social support			1.01 [0.98 – 1.04]			1.01 [0.99 – 1.04]			1.01 [0.98 – 1.03]
Satisfaction with social support			0.42*** [0.22 – 0.79]			0.42*** [0.26 – 0.67]			0.69** [0.44 – 1.11]
Receive support for adherence			1.14 [0.63 – 2.07]			1.01 [0.64 – 1.59]			0.88 [0.57 – 1.36]
Coping strategies			0.98 [0.94 – 1.03]			0.99 [0.96 – 1.03]			0.99 [0.96 – 1.03]

***p < 0.001; **p < .05; *p < .10

Model 2 and 3 adjust for socio-demographic variables: age, sex, household wealth, level of education, orphan-hood and type of caregiver

Figure 4.3. Unadjusted SEM Model on Relationship between psychological distress and non-adherence to ART

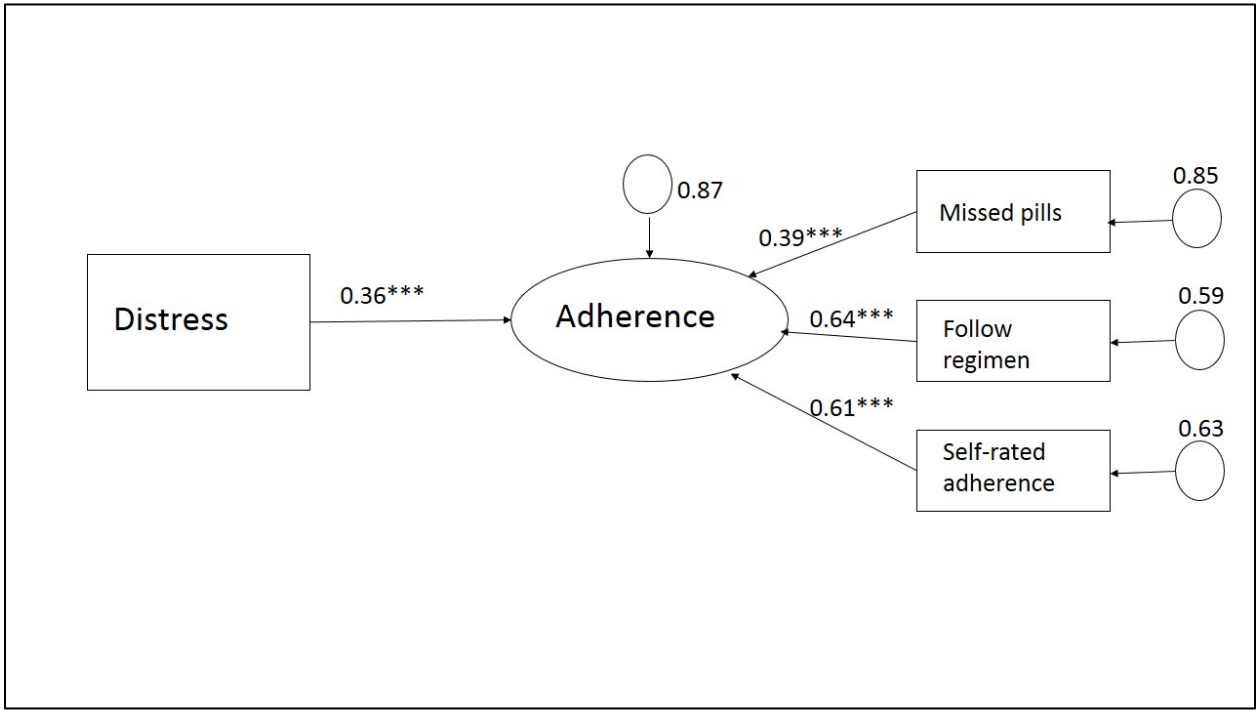
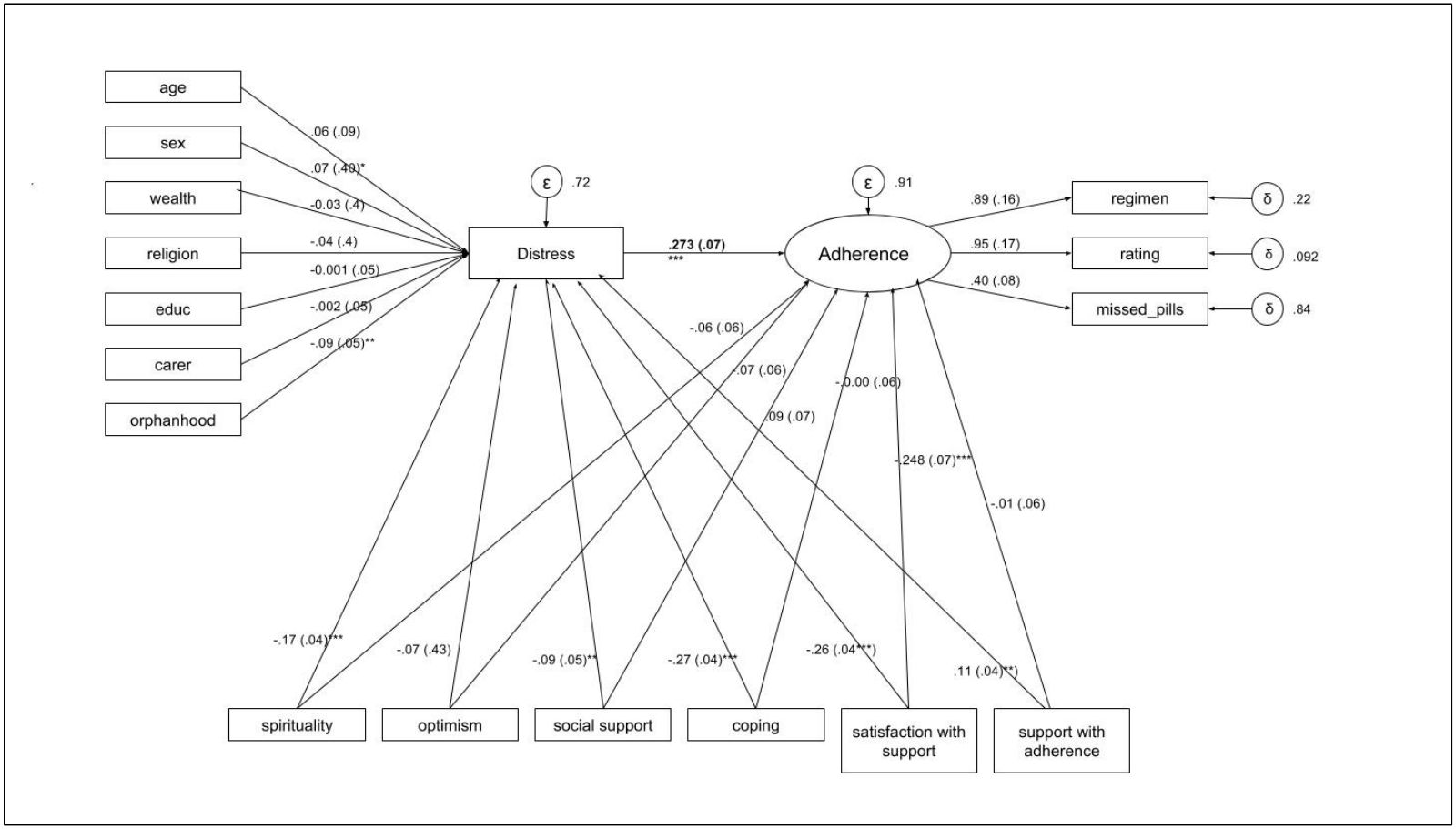


Figure 4.4. Adjusted SEM Model on Relationship between Psychological Distress and Adherence to ART



Chapter 5

CONCLUSION

Summary of introduction and purpose

Anti-retroviral therapy (ART) has been instrumental in reducing HIV/AIDS mortality and morbidity worldwide (Baker et al., 2008; Fielden et al., 2008; Lima et al., 2009; UNAIDS, 2013; World Health Organization, 2003), but rates of ART adherence among HIV-infected children and adolescents living both low-income and high-income countries, remain low (Vreeman et al., 2010). Although prior studies have found high rates of psychological distress among HIV-infected adolescents in both the United States and Uganda (Murphy, Moscicki, Vermund, & Muenz, 2000; Musisi & Kinyanda, 2009; Naar-King et al., 2006), the relationship between psychological distress and adherence has not been explored in sub-Saharan Africa, where approximately 69% of HIV-infected youth reside. Moreover, psychological distress has been associated with non-adherence to ART (Brown, Danovsky, Lourie, DiClemente, & Ponton, 1997; Brown, Lourie, & Pao, 2000; Murphy et al., 2001; Pao et al., 2000; Shrier, Harris, Sternberg, & Beardslee, 2001; Stevens, Murphy, & McKnight, 2003; Tapert, Aarons, Sedlar, & Brown, 2001), which in turn increases adolescents risk of mortality and morbidity (Bangsberg et al., 2000; García et al., 2002; Mannheimer, Friedland, Matts, Child, & Chesney, 2002).

The purpose of this study was to develop and test a new measure of psychological distress among HIV-infected adolescents (age 12-19 years) in Uganda, generating new knowledge on predictors of psychological distress in this cohort, and to assess the impact of

psychological distress on adherence to HIV care, net of mitigating factors such as adolescents' psychosocial resources.

Summary of results

Chapter 2 describes the steps and procedures used to develop a local measure of psychological distress- in-depth interviews, focus group discussions, expert panel review, cognitive testing, and pilot-testing. Following these procedures resulted in a 46-item scale, which was subsequently reduced in a large-scale survey, to 25 items with 6 six subscales corresponding to anhedonia, depressive-anxiety, isolation, suicidal ideation, sleep problems, and somatic symptoms. Exploratory factor analysis of the sub-scales, revealed a one-dimensional factor, thus supporting the use of a composite global psychological distress score. The scale reliability was high: reliability of the entire scale was 0.89, and between 0.615 and 0.732 for the individual sub-scales. The scale had adequate convergent validity, as demonstrated by the statistically significant positive correlation with the Functional Assessment of Human Immunodeficiency Virus Infection FAHI scale ($r = 0.5483$; $p < .001$), a measure of quality of life among HIV-infected persons, and negative correlation overall happiness ($r = -0.3054$; $p < .001$), and self-rated health ($r = -0.2478$; $p < .001$). The results of confirmatory factor analysis indicated that the factor structure of the scale had excellent fit to the data: chi-square (260) = 470.772 ($p < 0.000$), RMSEA) = 0.042 (CI: 0.036 – 0.048), CFI = 0.922, and TLI = 0.910.

The results of these analyses affirmed the multi-dimensionality of psychological distress, which is consistent with findings from prior conceptualizations of psychological distress (Cimprich, 1999; Derogatis & Fitzpatrick, 2004; Goldberg & Hillier, 1979; Massé, 2000). The study findings also highlighted suicidal ideation as an important domain of psychological distress among HIV-infected adolescents in this study. The 25-item psychological distress measure

developed in this study provides a tool for providers and researchers to assess psychological distress symptomatology among HIV-infected adolescents in Uganda. This would facilitate early recognition, treatment and referral (as needed) for adolescents experiencing distress, and prevent an escalation towards clinical morbidities such as psychiatric disorders. This measure also provider clinicians and researchers with a tool to accrue data on the psychological wellbeing of HIV-infected adolescents in Ugandan and other countries in sub-Saharan Africa, and to tailor their clinical care and counseling to the adolescent's needs. Additionally, the information accrued in using this measure could inform the development of locally relevant psychosocial interventions for this population.

Chapter 3 assessed the relationships between specific stressors and measurable psychosocial resources with psychological distress among HIV-infected adolescents in Uganda, and explored the potential mediating effects of these psychosocial resources on the stressors. Results indicated that HIV-infected adolescents encounter a diverse array of challenges including negative events such as bereavement, stigma, worries and HIV-related concerns, and these stressors were consistently associated with increasing levels of psychological distress. Among the stressors, psychological distress was positively associated with worries ($\beta = .118$, $t(462) = 2.52$; $p < 0.05$), negative life events ($\beta = .209$, $t(462) = 5.50$; $p < 0.001$), HIV concerns ($\beta = .229$, $t(462) = 7.08$; $p < 0.001$), and stigma ($\beta = .089$, $t(462) = 2.36$; $p < 0.05$). Psychological distress was negatively associated with the psychosocial resources: frequency of praying privately ($\beta = .079$, $t(462) = 2.26$; $p < .05$), spirituality ($\beta = -.083$, $t(462) = -2.40$; $p < .05$), satisfaction with social support ($\beta = -0.169$, $t(462) = -4.28$; $p < .001$), and coping ($\beta = -0.160$, $t(462) = -4.15$; $p < .001$). However, psychological distress was not significantly associated with optimism and social support. The psychosocial resources partially mediated the effects of worries and stigma

on psychological distress. The findings of these analyses are consistent with Lazarus and Cohen's Transactional Model of Stress and Coping (Lazarus & Folkman, 1991), and with findings from prior studies that have explored the relationship between psychosocial resources (e.g. coping) and psychological distress among HIV-infected youth (Brown & Lourie, 2000; Murphy et al., 2000; Thorsteinsson, Sveinbjornsdottir, Dintsi, & Rooke, 2013). The findings highlight the potential salutogenic effects of spirituality on adolescents' psychological wellbeing, thereby contributing to the scanty literature on the relationship on the role of spirituality in coping with HIV-related challenges among HIV-infected adolescents in Uganda.

Chapter 4 examined the relationship between psychological distress and adherence to ART, and explored the potential mediating effects of psychosocial resources on adherence. Study findings indicated a negative association between psychological distress and adherence to ART. In the logistic regression analyses, the odds for non-adherence associated with psychological distress ranged from 63% to 79% across the three self-reported measures of adherence, net of socio-demographic factors and psychosocial resources. In the SEM analyses using a latent adherence variable, psychological distress was associated with a 30% increase in the odds for non-adherence to ART. Results from the logistic regression and SEM analyses indicated that psychosocial resources partially mediate the effect of psychological distress on adherence. Of the socio-demographics factors explored in this study, only household wealth was significantly associated with non-adherence, but this relationship was only marginally significant. Age, sex, religion, level of education, orphan-hood and type of caregiver were significantly associated with non-adherence to ART. Among psychosocial resources, only satisfaction with social support and frequency of praying privately were significantly associated with non-adherence across the three self-reported measures of adherence. Moreover, frequency of praying privately was associated

with increased odds of non-adherence to ART. Optimism, spirituality, social support, coping, and adherence specific support were not significantly associated with medication adherence. The findings in this study highlighted the need to prevent or reduce psychological distress in order to promote adherence to ART among HIV-infected adolescents in Uganda.

Implications

The findings in this study have several public health implications for the prevention and treatment of HIV/AIDS in Uganda and other countries in sub-Saharan Africa. Among HIV-infected adults, psychological distress has been associated with changes in the endocrine and immune systems, which may reduce the efficacy of ART, resulting in accelerated disease progression and increased risk of mortality (Cohen, Janicki-Deverts, & Miller, 2007; Leserman, 2003, 2008). Moreover, psychological distress has also been associated with risky behaviors e.g. drug and substance abuse and sexual risk-taking, which in turn, compromise an adolescent's ability to engage in self-caring behaviors such as adherence to ART.

The low rates of ART adherence documented in this study present a substantial threat to the success of HIV prevention and treatment programs in sub-Saharan Africa, yet less than 60% of the ART eligible population in Uganda has access to these lifesaving medications (Uganda AIDS Commission, 2012; UNAIDS, 2013). As noted in Chapter 1, non-adherence to ART has dire consequences for the HIV-infected adolescent, as it contributes to poor clinical outcomes such as poor immunologic (CD4 counts) and virologic responses (HIV RNA), leading to accelerated progression to AIDS and death (Bangsberg et al., 2000; García et al., 2002; Mannheimer et al., 2002). Non-adherence has been associated with development of ART resistance, leading to treatment failure. ART resistance compromises the viability of drugs within a particular class(s) once a person develops resistance to a drug within that class, thus

necessitating changes to ART treatment regimen. However, there is a limited range of treatment options within ART programs in sub-Saharan Africa, and wide spread resistance could compromise the efficacy of these medications across sub-Saharan Africa. Additionally, these second line medications are often more expensive. For this reason, wide spread resistance to the cheaper first-line regimens also threatens the sustainability of ART programs in sub-Saharan Africa because majority of these programs are largely funded by international donors and aid organizations. Several countries in sub-Saharan Africa cannot afford to sustain large numbers of HIV-infected persons on expensive medications, and rampant poverty, particularly within AIDS-affected households would limit the number of persons who can access these medications.

At the population level, ART mediated virologic suppression and reduced infectiousness has been associated with reduced transmission of HIV within communities (Das et al., 2010; Montaner et al., 2010; Tanser, Bärnighausen, Grapsa, Zaidi, & Newell, 2013). For this reason, ART is a critical component of HIV prevention strategies worldwide. Among adolescents, the potential over HIV-transmission raises serious concerns given the high propensity for drug experimentation and sexual risk-taking among adolescents. This challenge is compounded by the low levels of comprehensive sexual and reproductive health (SRH) information, including knowledge about HIV/AIDS and the limited access to comprehensive SRH services, which increases adolescents' vulnerability to HIV acquisition (or re-infection) and transmission. The potential to transmit of ART resistance strains raises additional concerns, as this would compromise the efficacy of ART treatment regimens even among ART naïve adolescents.

From a public health perspective, the relationship between viral suppression and reduced risk of HIV underscores the importance of ensuring that HIV-infected adolescents have access to ART and adhere to these medications. The relationship between psychological distress and

adherence suggests that preventing psychological distress among HIV-infected adolescents is critical to promoting ART adherence in this population. While this study cannot provide data on the prevalence of psychological distress among HIV-infected adolescents in Uganda, this findings support earlier calls for the integration of HIV and mental health services, to promote a holistic approach to the health needs of HIV-infected persons. Within the clinical context, these study findings specifically highlight the need: (1) increase awareness of about psychological distress and its causes among health care providers and caregivers, as this will facilitate early recognition, treatment and referral of adolescents experiencing psychological distress; (2) expand clinical assessments on adolescent well-being beyond physical well-being to include the social, psychological, and spiritual domains in order to identify potential risk factors that could impact adolescents' well-being and health behavior; (3) identify the psychosocial resources which prevent or attenuate the risk of psychological distress among HIV-infected adolescents.

The psychological distress measure developed in this study provides a tool for health care providers to identify and monitor psychological wellbeing among HIV-infected adolescents. Within the context of routine HIV-care, this measure could provide a starting point for dialogue for psychological wellbeing, thereby creating an opportunity to break the silence and address the stigma surrounding mental wellbeing. The findings on predictors of psychological distress may be used to tailor health counseling within routine HIV care, and also inform development of interventions at either individual or group level.

These study findings highlight the need for interventions to prevent psychological distress among HIV-infected adolescents. At the individual level, the study findings suggest that HIV-infected adolescents should be equipped with the skills and psychosocial resources to deal with the diverse array of stressors they will most likely encounter encounter, and prevent or

reduce psychological distress. Of particular relevance would be skills that could modify appraisal process that underlie an adolescent's evaluations of stressful stimuli. Resilience, life skills trainings, and interventions using cognitive based therapy techniques to influence adolescents' feelings or thoughts regarding stressful stimuli may also be helpful. Indeed, resilience and life skills training interventions have been effective in reducing psychological distress among HIV-infected youth in the United States (Bhana et al., 2013; Naar-King, Parsons, Murphy, Kolmodin, & Harris, 2010) and also among HIV un-infected children and adolescents (Kerrigan et al., 2011; Parker et al., 2011). Additionally, interventions that promote psychosocial resources such as coping strategies, spirituality, building and maintaining social networks as well as evaluation social support may also be useful in reducing psychological distress among HIV-infected adolescents. However, few such interventions have been tested and/or validated among adolescents in Uganda and other countries in sub-Saharan Africa. Therefore, the efficacy of these interventions within these contexts remains unknown.

At the inter-personal level, these study findings highlight the need to address stigma against HIV-infected persons. HIV-related stigma remains rampant within households and schools, the ecological spaces of most significance to adolescent wellbeing. For example, unpublished study conducted among 28 adolescents (aged 10 – 19 years) at the JCRC found low levels of household disclosure of the adolescent's HIV status. Several respondents reported stigma and discrimination within at home and school. Majority of these adolescents had not disclosed their HIV status to peers or school authorities at school due to fear of stigmatization. The low rates of disclosure within households and schools reinforced these adolescents' feelings of isolation, and limited their ability to seek social support and adherence to ART. These findings also highlighted the need for interventions to reduce stigma within the households and

schools of HIV-infected adolescents in Uganda (Mutumba et al; unpublished). Further, the deleterious effect of poverty-related worries and hardships documented in this study call for concerted efforts to eliminate or reduce household poverty within HIV-affected households in Uganda and other countries in sub-Saharan Africa.

In this study psychosocial resources partially mediated the effect of stressors on psychological distress and also partially mediated the relationship between psychological distress and non-adherence to ART. The finding suggests that this study has only identified a minority of the contextually important psychosocial resources that could prevent or eliminate psychological distress among HIV-infected adolescents. Therefore, there is a need for additional research to identify other important psychological resources that could inform clinical counseling and interventions within this population. This study explored a minority of psychosocial resources, largely at the intra-personal level. Future research could explore the potential role of family, peers and health facility attributes.

Contribution to the literature

Data on the mental well-being among HIV-affected adolescents in Uganda and other countries in sub-Saharan Africa are scarce, yet these data are critically important to support the counseling dimensions of AIDS-related care in HIV-endemic regions of Africa, and in facilitate development of contextually relevant policies and interventions. The notable barriers to expanding the knowledge base on mental health in sub-Saharan Africa include: stigma, lack of understanding of local expression of mental health, lack of locally validated measures of mental health, and lack of mental health providers. This study specifically addresses the lack of local measures to facilitate mental health assessment and the paucity of data on the contextually relevant determinants of health and wellbeing among HIV-infected adolescents in sub-Saharan

Africa. To the best of my knowledge, this is the first study to develop a local measure of psychological distress among HIV-Infected adolescents in sub-Saharan Africa, and the first to explore the relationship between psychological distress and adherence to ART among adolescents in Uganda. The measure developed in this study addresses some of these barriers to addressing the mental wellbeing of HIV-infected adolescents in Uganda and other countries in sub-Saharan Africa. First, it addresses the lack of locally developed measures of psychological distress for HIV-infected adolescents, and provides a reference for future research on studies assessing mental health and developing tools for adolescents in Uganda and other countries in sub-Saharan Africa. This measures provides clinicians and researchers with a contextually meaningful and reliable tool to assess psychological distress among adolescents. However, additional work to establish reference criterion and test-retest reliability is needed to ensure that this measure is locally applicable to populations beyond the present sample. With validation, this measure could be utilized in a variety of setting and populations across sub-Saharan Africa.

Secondly, this measure has been developed for use within clinical and research settings, and allows for screening by laypersons, with some basic training on mental health. In this regard, the measures open up opportunities to expand access to mental health services by facilitating screening and referral for adolescents in need of future care. Lastly, the experienced amassed in this study provides some insights on how to address the effect of imposed by stigma on discussing adolescents' psychological wellbeing. The pilot phase of this study also explored language used to describe mental health. One of the issues that arose in the course of this study was that the term "mental health" raised alarm and fear among adolescents and caregivers alike, highlighting the burden of stigma against mental illness in Uganda. However, we found a more acceptable term "ebiloowo" translating into "thoughts", and this was more acceptable compared

to “obulwadde bwo’mu mutwe”- the direct translation of mental health. Therefore, future researchers are advised to adapt a more locally acceptable terminology to facilitate discussions about mental health thus avoiding potential barriers through use of terms that arouse stigma.

The findings on predictors of psychological distress in this study extend our understanding of predictors of wellbeing among HIV-Infected adolescents, and highlight contextually relevant stressors such as major negative life events and financial worries that are particularly relevant for adolescents in sub-Saharan Africa, where AIDS-related mortality and household poverty, especially among AIDS-affected households remain high, and social services are scarce and unprepared to address the varied needs of these youth. Lastly, the findings in this study extend the current literature on the importance of psychological wellbeing in predicting adherence to ART in both low- and high-income countries, and highlight the role of psychosocial resources in mitigating the impact of psychological distress on adherence, thereby highlighting potential intervention points that could be leveraged to improve adherence to ART.

Study Limitations

This study has several notable limitations that should be taken into consideration when interpreting the study findings. First, the cross-sectional nature of this study limits causal inference, particularly in evaluating the temporal relationship between psychosocial resources and medication. Reverse causality must also be considered given that the relationship between psychological distress and health is reciprocal. This studies also utilizes self-reported measures of adherence, which may result in over-estimation of adherence (Liu et al., 2001; Wagner, 2002). The study did not include any measures on duration of ART, yet this could influence adherence to ART. Additionally, this study did not explore other psychosocial factors such as involvement in peer support groups, parent-child relationship characteristics etc., which could potentially

mitigate the impact of psychological distress on adherence to ART. The study population is drawn from one urban HIV treatment center, which could limit generalizability of these to adolescents in other settings; however, this potential selection bias may be minimal, given the considerably large study sample size and the fact that JCRC draws patients from all regions of the country.

Future research

The measure developed in this study warrants further refinement prior to its use among HIV-infected adolescents in other parts of Uganda, and countries in sub-Saharan Africa. Additional research is required to establish the cut-off points for this measure- total score, and sub-scale score, a score two standard deviations above the mean in the study population could serve as a preliminary cut-off point for differentiating between adolescents with or without psychological distress. Future research is also needed to establish reference criterion and test-retest reliabilities for the scale and its subscales, and also investigate the validity of the derived factor structure across diverse populations. Additional explorations on tobacco, alcohol and substance abuse in relation to psychological distress are also needed, given the prominence of themes related alcohol and substance abuse within adolescent's narratives about psychological distress symptomatology.

There is a need for longitudinal study to explore causal relationships between predictors, and also explore how risk factors for both psychological distress and adherence may change over the life course. The findings on spirituality and religiosity documented in this study call for additional research to explore the role of spirituality and religiosity in coping with adversity among HIV-infected youth. In this study, measures of religiosity (frequency of attending religious services and religious affiliation as Pentecostal) were associated with increased distress.

Some measures of spirituality (frequency of praying privately) were associated with lower adherence while others (spirituality measured using brief RCOPE Spirituality subscale) were associated with increased adherence. These findings suggest differential effects of spiritualty and religiosity across different health domains and highlight the importance of investigating potential pathways through which spirituality and religiosity affect adolescents' well-being.

Additionally, more research is needed to identify the social or structural circumstances, and possible interventions, that can both reduce psychological distress and increase adherence, and better address the psychological needs of this population. Unfortunately, there is a scarcity of evidence-based psychosocial interventions for youth in sub-Saharan Africa- infected youth, as all current interventions have been conducted in high-income countries (Reisner et al., 2009). Concerted efforts to address the needs of adolescents in sub-Saharan Africa are warranted.

Lastly, there is a need for future research on how tobacco, alcohol and substance abuse could be incorporated into measures of psychological distress, given the prominence of themes related alcohol and substance abuse within adolescent's narratives about distress, and the documented association between alcohol and substance abuse and psychological distress among adolescents, both HIV-infected and uninfected (Fleischmann, Bertolote, Belfer, & Beautrais, 2005; LaFromboise & Howard-Pitney, 1995; Mc Manama, Kimberly, & Berzin, 2012; Page & West, 2011; World Health Organization, 2014).

With regard to adherence, future research is needed to establish the most reliable measure of adherence among adolescents, and establish adherence cut-off to enable comparision of findings across studies. There is also a need to elaborate on the relationship psychological distress, adherence to ART and biological markers of treatment outcomes among HIV-infected persons, that is CD4 counts and viral RNA. Future studies should also explore the impact of

psychological distress on immune-mediated pathways; biochemical markers such as cortisol and other stress markers as this would increase understanding of the mechanims through which psychological distress impacts the health and wellbeing of HIV-infected adolescents.

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