Factors associated with adherence to antiretroviral therapy among adolescents living in low- and middle- income countries: a systematic review

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Adolescents living in low- and middle-income countries (LMICs) are disproportionately burdened by the global HIV/AIDS pandemic. Maintaining medication adherence is vital to ensuring that adolescents living with HIV/AIDS receive the benefits of antiretroviral therapy (ART), although this group faces unique challenges to adherence. Knowledge of the factors influencing adherence among people during this unique developmental period is needed to develop more targeted and effective adherence-promoting strategies. This systematic review summarizes the literature on quantitative observational studies examining correlates, including risk and resilience-promoting factors, of ART adherence among adolescents living with HIV/AIDS in LMICs. A systematic search of major electronic databases, conference-specific databases, grey literature, and reference lists of relevant reviews and documents was conducted in May 2014. Included studies examined relationships between at least one factor and ART adherence as an outcome and were conducted in primarily an adolescent population (age 10-19) in LMICs. The search identified 7,948 unique citations from which 15 studies fit the inclusion criteria. These 15 studies identified 35 factors significantly associated with ART adherence representing a total of 4,363 participants across nine different LMICs. Relevant studies revealed few consistent relationships between measured factors and adherence while highlighting potentially important themes for ART adherence including the potential impact of (1) adolescent factors such as gender and knowledge of serostatus, (2) family structure, (3) the burdensome ART regimens, route of administration, and attitudes about medication, and (4) healthcare and environmental factors, such as rural versus urban location and missed clinic appointments. Rates of adherence across studies ranged from 16% to 99%. This review identifies unique factors significantly related to ART adherence among adolescents living in LMICs. More research using longitudinal designs and rigorous measures of adherence is required in order to identify the range of factors influencing ART adherence as adolescents living with HIV/AIDS in LMICs grow into adulthood.

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Introduction

As the global HIV/AIDS pandemic matures, the world is witnessing a shift in the burden of HIV infection onto adolescents living in LMICs. Expanded access to ART enables millions of children to grow into young adulthood and manage their HIV infection as a chronic disease (Hazra, Siberry, & Mofenson, 2010; Lowenthal et al., 2014). Approximately 2.1 million adolescents in LMICs were living with HIV/AIDS in 2012, and the 3.3 million children under 15 living with HIV globally (almost 90% living in sub-Saharan Africa) will be growing through adolescence in the coming years (UNAIDS, 2013; WHO, 2013a). Adolescents and young adults represent 41% of new infections globally and are the only age group for which AIDS deaths have risen since 2001 (UNAIDS, 2013; WHO, 2013a). The central role of adolescents in determining the trajectory of the global HIV/AIDS pandemic has prompted amplified efforts to provide treatment and care tailored to the needs of this population (UNICEF., 2011).

Although access to ART has increased in recent years, there remains a disparity between child eligibility and access, with only 34% of children age 0 to 14 living in LMICs receiving ART in 2012 (UNAIDS, 2013). As the number of adolescents on ART continues to rise, sustaining optimal levels of ART adherence (often defined as ≥ 95%, or less than one missed dose per week) has emerged as a major challenge to survival, health, and prevention of sexual transmission for this group (Martin et al., 2008; Jean B. Nachega, Edward J. Mills, & Mauro Schechter, 2010; Paterson et al., 2000; Scanlon & Vreeman, 2013; Van Dyke et al., 2002). While limited adolescent-specific data on adherence is available in LMICs, estimates of ART adherence suggest that adolescents are vulnerable to suboptimal adherence and have difficulty in reducing viral load (van Rossum, Fraaij, & de Groot, 2002). One systematic review of adherence rates among young people age 12 to 24 yielded 50 studies from 53 countries (n=10,725) and produced a global adherence estimate of 62.3% (95% CI 5.71 – 67.6; I²=97.2%), with lower rates of adherence in North and South America compared to Africa and Asia (Kim, Gerver, Fidler, & Ward, 2014). Other systematic reviews of adherence in LMICs among adults and children have produced pooled

adherence estimates of 77% (95% CI 68-85) and 49 to 100%, respectively (Mills, Nachega, Buchan, et al., 2006; Vreeman, Wiehe, Pearce, & Nyandiko, 2008). A study in nine African countries found that half as many adolescents were able to achieve perfect adherence to ART compared with adults (20% versus 40% after six months) (Nachega et al., 2009).

This problem of suboptimal adherence can lead to increased risk for viral progression and/or opportunistic infection (Bangsberg et al., 2001; San-Andrés et al., 2003), transmission to sexual partners (Kalichman et al., 2011), and viral resistance in resource-limited settings where second-line treatment is not available in public sector services (Ajose, Mookerjee, Mills, Boulle, & Ford, 2012; Bangsberg et al., 2003). Unfortunately, limited information exists on effective adherence-promoting interventions among adolescents living with HIV/AIDS in LMICs, with one systematic review yielding only three out of sixteen studies conducted in LMICs (Bain-Brickley, Butler, Kennedy, & Rutherford, 2011). The lack of adolescent-specific information, combined with high rates of suboptimal adherence among this group, highlight the need for more knowledge in this area in order to create evidence-based, adherence-promoting interventions.

A growing literature highlights a complex web of correlates that may impact on adherence in different settings; however, the majority of studies are focused on populations over age 18 (See Table 1). Systematic reviews conducted on pediatric populations reveal that most research is conducted in high-income countries and among patients primarily under age 10, and that studies vary in the measures they study and methodological rigor (Simoni et al., 2007; Vreeman et al., 2008). While one systematic review has focused specifically on young adult populations, it was limited to the United States (Reisner et al., 2009).

(TABLE 1: Select Relevant Systematic Reviews of Factors Associated with ART Adherence among Adults, Children, and Youth in High-Income Countries and LMICs)

To our knowledge, no systematic review to date has examined adolescent-specific predictors of adherence in LMICs. Adolescents living with HIV/AIDS in LMICs experience unique challenges to achieving adherence while living in environments where optimal adherence is particularly important. As both access to ART and the number of adolescents living with HIV/AIDS in LMICs increase, understanding the factors that impact on adherence to ART among this population is essential (Havens & Gibb, 2007; Holmes, Bilker, Wang, Chapman, & Gross, 2007; Jean B. Nachega et al., 2010). This review summarizes the literature on quantitative observational studies examining factors associated with adolescent adherence to ART in LMICs.

Methods

Inclusion criteria

Studies included in this review must have met the following criteria:

(1) Was a quantitative observational study (including cohort, case control, and cross-sectional studies) evaluating a statistical relationship between at least one demographic, environmental, behavioral, social, healthcare, or medication-related factor and ART adherence as an outcome (Haberer & Mellins, 2009; Reda & Biadgilign, 2012; Simoni et al., 2007).

(2) Included a sample of primarily adolescents (people age 10 to 19) living with HIV, in accordance with the World Health Organization definition of adolescence (WHO, 2013b). Studies were included if at least 50% of the sample consisted of people age 10 to 19 at some point during the study period. When this information was not available, studies were included if the reported mean or median age of study participants was between 10 and 19.

(3) Was conducted in a LMIC as defined by the 2013 World Bank definition (World Bank 2013).

(4) Explicitly measured ART adherence using any method (e.g. viral load, self-report, pill count, home record, pharmacy refill, healthcare provider assessment, or electronic monitoring).

Studies were excluded that did not analyze factors in relation to ART adherence as an outcome; did not test a statistical relationship between factors and outcome; were qualitative in design; only assessed a

relationship between immunological outcomes and adherence; and/or only examined the effects of an intervention on adherence as an outcome. Studies only examining adherence to pre- or post-exposure prophylaxis or perinatal administration for prevention of mother to child transmission were excluded. Studies without full-text available at the time of conducting this review were excluded. No language restrictions were placed in order to identify as many relevant articles as possible. Non-English language translations were made using an online translator service.

Search strategy

We searched for published and unpublished studies by conducting electronic searches of journal and trial databases, conference databases, ongoing trial registries, and searches of the grey literature in May 2014. Databases searched include MEDLINE (via PUBMED), EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), CINAHL, SIGLE, LILACS, Web of Science, World Health Organization Global Health Library, NLM Gateway, and U.S. Institutes of Health's Clinical Trials Registry. Conference abstracts were identified through AEGIS and the International AIDS Society archives in accordance with Cochrane guidelines (Cochrane HIV/AIDS, 2012). Specific conference archives were also hand-searched or searched via keyword. Search strings and appropriate terms were adapted to each database, and no limits were placed with regard to year of publication. References of included studies and relevant reviews were also checked to identify additional studies (Arrivillaga, Martucci, Hoyos, & Arango, 2013; Bain-Brickley et al., 2011; Haberer & Mellins, 2009; Kim et al., 2014; Lowenthal et al., 2014; Mills, Nachega, Bangsberg, et al., 2006; J. B. Nachega, E. J. Mills, & M. Schechter, 2010; Reda & Biadgilign, 2012; Simoni et al., 2007; Vreeman et al., 2008; Young, Wheeler, McCoy, & Weiser, 2013).

Screening Abstracts

Titles, abstracts, and citation information were retrieved, and duplications were removed manually. Titles and abstracts of remaining studies were screened by the lead author using a pre-determined flow chart.

Full text articles were obtained for all articles passing this screening process, and any studies not fitting the inclusion criteria as indicated by the title/abstract, full text, or feedback from authors were excluded.

Data extraction and analysis

For each study meeting eligibility criteria, relevant information was extracted using a pre-determined data extraction form. Microsoft Excel was used for data entry. The first author collected information from each study on the following items: (1) general study information, including citation and setting; (2) participant information; (3) factors related to adherence, including nature of data extractions and method of analysis; and (4) outcomes information, including how adherence was operationalized, rates of adherence in the study, and factors significantly associated with adherence. Questions regarding study eligibility were rectified via discussion between authors. In cases where the title/abstract passed the screening phase but for which no full-text article could be located, attempts were made if possible to contact authors to obtain additional information to determine eligibility.

A critical appraisal tool developed for the appraisal of cohort, case-control, and cross-sectional studies was used to assess methodological quality (Wales, 2004). This tool was utilized because it contains important domains for appraisal in observational studies, which focus on selection methods, measurement of study variables, design-specific sources of bias, confounding, statistical analysis, and relevance of results (Sanderson, Tatt, & Higgins, 2007).

Meta-analysis was not conducted due to the heterogeneity across studies with regard to population, methods, factors analyzed in relation to adherence, and outcome measures (Greenhalgh, 1999). However, this integrative review provides a descriptive account of factors significantly correlated with adherence. The results section distinguishes between outcomes based on different methodological or analytical factors, and the discussion aims to interpret the meaning of different relationships in light of these considerations.

Description of studies

The search of all databases yielded 10,773 citations. After the removal of duplicates, the titles and abstracts of the remaining 7,948 were screened, resulting in an initial exclusion of 7,790 studies (see Figure 1). Full text articles were obtained and/or additional information was sought from authors for the remaining 158 references. 15 studies met the inclusion criteria for this review. Reasons for exclusion of 143 studies passing the title/abstract screening phase were related to the study not being conducted in a LMIC (41%); not fitting age criteria (34%); had no full text article available (15%); had no quantitative study and/or no statistical test of association (6%); had no explicit measurement of ART adherence (2%); had no analysis of factors in relation to adherence (2%); and examined effects of an intervention (1%). Of the 21 articles for which full text could not be obtained, the authors of seven studies were contacted to determine eligibility, while no contact could be made with the authors of 14 studies. See Table 2 for characteristics of the study populations.

(Figure 1: Flowchart of study selection adapted from PRISMA statement]

In total the studies included 4,363 participants. Participants across studies were described as "children", "adolescents", or "youth" and recruited predominantly from pediatric and non-specific hospitals, clinics, and treatment centers. The majority of studies reported a mean or median age between 10 and 19, with three studies specifically studying adolescents ages 10 to 19 (Cardorelle, Toussoungamana-Peka, Miakassissa, & Okoko, 2014; Filho et al., 2008; Machado et al., 2009). Gender distribution ranged across studies (37% - 59% female). Duration of ART was reported as a mean, median, or range in most studies, with duration of use across studies ranging from zero (Cupsa, Gheonea, Bulucea, & Dinescu, 2006) to eight years (Filho et al., 2008). Thirteen studies reported on percentage of study sample who were aware of their HIV status, with rates of disclosure ranging from 15% (Biadgilign, Deribew, Amberbir, & Deribe, 2008) to 100% (Fongkaew et al., 2014). Route of transmission was reported in seven studies, and the majority of participants included vertically infected adolescents (80-100% per study). The number of adolescent participants across studies varied greatly, ranging from 30 to 948 across the thirteen included cross-sectional studies. Two prospective cohort studies were which

followed 190 and 280 participants respectively over 18 months each (Cupsa et al., 2006; Sirikum et al., 2014).

[Insert Table 2: Characteristics of included studies (N=15)]

[Note: Italics = Association derived from simple tests of association and did not report on the strength of the relationship controlling for potential cofounders]

The majority of studies analyzed a range of factors in relation to adherence, while three studies evaluated a single measure. These included a study measuring HIV disclosure status (Sirikum et al., 2014), HIV stigma (Fongkaew et al., 2014), and psychosocial function (Lowenthal et al., 2014). Of the two prospective studies included in this review, Cupsa et al (2006) analyzed a range of factors over time in relation to adherence, while Sirkium et al (2014) followed children as they were told their HIV status and examined the relationship between disclosure and adherence. Some studies self-identified as "mixed method" but used quantitative data collected via cross-sectional design in their statistical analysis of correlates of adherence (Fongkaew et al., 2014; Mavhu et al., 2013). Methods of measurement of possible factors related to adherence included interviews, questionnaires, and surveys administered to adolescents (Cardorelle et al., 2014; Filho et al., 2008; Fongkaew et al., 2014; Mavhu et al., 2013; Musiime et al., 2012; Ndiaye et al., 2013), caretakers (Biadgilign et al., 2008; Biressaw, Abegaz, Abebe, Taye, & Belay, 2013; Kikuchi et al., 2012; Lowenthal et al., 2012; Sirikum et al., 2014), or unspecified (Cupsa et al., 2006; Ernesto et al., 2012; Machado et al., 2009; Musiime et al., 2012; Nabukeera-Barungi, Kalyesubula, Kekitiinwa, Byakika-Tusiime, & Musoke, 2007).

Seven of the cross-sectional studies in this review reported response rates, which ranged from 20% (Ndiaye et al., 2013) to 96% (Filho et al., 2008; Nabukeera-Barungi et al., 2007). One prospective cohort study reported information on study attrition (Sirikum et al., 2014).Limited information was available across studies on sampling strategies, though several studies reported data on reasons for excluding particiants (Biressaw et al., 2013; Kikuchi et al., 2012; Mavhu et al., 2013; Ndiaye et al., 2013; Sirikum et al., 2014).

Given that 13 studies were cross-sectional, a major limitation of these findings involves the extent to which causality can be inferred from specific relationships (Carlson & Morrison, 2009). Only one study assessed inter-individual changes in adherence over time while controling for possible confounding variables. In this study, ART adherence was measured pre-and post-disclosure at 6 and 12 months using Wilcoxon matched-pairs signed-rank test, and multivariable analysis was used to evaluate correlation with HIV disclosure (Sirikum et al., 2014). Logistic regression was used in 10 studies to report relationships as odds-ratios adjusted for potential confounders, while one study reported results from both unadjusted and adjusted associations from multivariable logistic regression (Musiime et al., 2012). Four studies used simple tests of statistical comparison to examine factors in relation to adherence (Cardorelle et al., 2014; Cupsa et al., 2006; Fongkaew et al., 2014; Machado et al., 2009). Thus, only 11 studies reported information on the strengths of relationships between variables and adherence, accounting for other variables.

Overall estimates of adherence ranged from as low as 16% among a Zimbabwean population measured by self-report (Mavhu et al., 2013) to 99% among Thai adolescents as measured by pill count (Sirikum et al., 2014). Method of adherence measurement varied greatly across studies (Table 2), consistent with other reviews of adherence among youth (Reisner et al., 2009; Vreeman et al., 2008). Methods used across studies include clinic-based pill count; unannounced home pill count; adolescent or caregiver self-reported number of missed doses; pharmacy refill data. One study explicitly measured adherence via viral load (Lowenthal et al., 2012). Five studies used more than one method for measuring adherence and produced multiple adherence estimates (Biressaw et al., 2013; Ernesto et al., 2012; Filho et al., 2008; Musiime et al., 2012; Nabukeera-Barungi et al., 2007). Several studies found major discrepancies in adherence estimates based on measurement method, with one study demonstrating a sample adherence estimate of 93% when measured by caregiver report compared to an estimate of 35% when measured by unannounced home pill counts (Biressaw et al., 2013).

Of the 15 studies identified by this review, 12 studies reported a total of 34 significant associations between factors measured in the study and ART adherence. These studies included 10 correlates associated with good adherence and 24 associations with suboptimal adherence. Across studies, 25 associations were derived from multivariate analysis and reported as adjusted odds ratios (Table 3). Overall, the results reveal a range of diverse factors associated with adherence that can be loosely categorized as related to the adolescent; caregiver; medication; or social, physical, or healthcare environment. While many of the same factors were analyzed across studies, these results demonstrate few consistent relationships.[Insert Table 3: Factors associated with good and suboptimal adherence across studies, n=15]

[Caption: Italics = Association derived from simple tests of association and did not report on strength of relationship controlling for potential confounding variables]

Adolescent-related factors

Studies in this review analyzed a range of adolescent sociodemographic factors (i.e. age, gender, race/ethnicity, education), health-related factors (i.e. mental health, previous hospitalization, stunted growth), orphan status, knowledge of serostatus, substance use, and level of sexual activity in relation to adherence. Significant but inconsistent relationships were reported for gender across studies; being male was associated with good adherence in a study of 946 children and adolescents in Uganda (crude OR=1.9 [1.2-3.1], p=0.005) (Musiime et al., 2012), while it was associated with suboptimal adherence in Botswana (adj. OR=3.29 [1.13-9.54], p=0.03, age range 13-18) (Ndiaye et al., 2013). Gender was not significantly correlated with adherence in 10 other studies in which it was analyzed. Lack of awareness of serostatus was significantly associated with good adherence in one Ethiopian (median age 11) (Biressaw et al., 2013). Other factors significantly associated with good adherence across studies included having previous hospitalizations (Nabukeera-Barungi et al., 2007) younger age of adolescence (Cardorelle et al., 2014), and lack of awareness of caregiver's health problems (Biadgilign et al., 2008). Double orphan status (Kikuchi et al., 2012), stunted growth (Kikuchi et al., 2012), low mental health score (Lowenthal et

al., 2012), and sexual activity (Cardorelle et al., 2014) were correlated with worse adherence across studies. No significant relationships were reported for race/ethnicity, social support, quality of life, or substance use across studies.

Caregiver-related factors

Several factors were significantly associated with adherence across studies that emphasize the potential importance of family structure, caregiver support, and caregiver involvement in adolescent adherence. Biressaw et al (2013) found that Ethiopian adolescents with married (OR=7.85, [2.11-29.13], p<0.05) or widowed/divorced caregivers (OR=7.14, [2.00-25.46], p<0.05) had significantly better ART adherence than those with single caregivers. Conversely, low caregiver involvement (Kikuchi et al., 2012), widowed caregiver (Musiime et al., 2012), "disorganized" family (Cupsa et al., 2006) were associated with suboptimal adherence across studies. Low caregiver education level (Cupsa et al., 2006) and caregiver being the only one knowing child's serostatus (Nabukeera-Barungi et al., 2007) were also correlated with worse adherence.

Medication-related factors

Analysis of medication-related factors highlight the challenges associated with burdensome regimens, ease of administration, and the potential impact of caregiver versus adolescent administration. Administration of medication by adolescents was associated with suboptimal adherence in one study (Ernesto et al., 2012), while caregiver administration of drug was correlated with good adherence in another study using a simple test of association (Cardorelle et al., 2014). Difficulty of administration by caregiver was associated with suboptimal adherence in one study (Ernesto et al., 2012), while adolescents who were taught how to take ART by a healthcare worker were more likely to have good adherence (Filho et al., 2008). Relationships between burdensome regimens and suboptimal adherence were reported; taking three or more pills per day (Kikuchi et al., 2012) and having a high number of ART schemes (Machado et al., 2009) were correlated with suboptimal adherence. One study examining

adolescent attitudes toward medication found that adolescent "lack of concern" about ART and never carrying ART while out were associated with suboptimal adherence (Filho et al., 2008).

Social, environmental, and healthcare-related factors

Few factors related to social environment and healthcare were measured and correlated with adherence across studies. Urban versus rural residence was inconsistently but significantly associated with adherence; one Ugandan study found that adolescents living in urban areas were less likely to be adherent (OR=0.6, [0.4-1.0], p=0.038) (Musiime et al., 2012), while another study found that living in rural areas was correlated with suboptimal adherence (Biadgilign et al., 2008). Several studies assessed the relationship between adherence and measures of socioeconomic status such as monthly income and/or caregiver employment, but no study found a significant relationship. One study analyzed the relationship between HIV stigma and adherence to ART but found no significant relationship (Fongkaew et al., 2014). Receipt of clinic nutritional support (Biadgilign et al., 2008) and missed clinic appointments (Ernesto et al., 2012) were also healthcare-related factors associated with suboptimal adherence.

Discussion

This systematic review identified fifteen studies assessing correlates and predictors of ART adherence representing 4,363 participants across ten LMICs. Factors associated with adherence are categorized into four broad themes related to the (1) adolescent, (2) caregiver, (3) medication, and (4) physical, social, and/or healthcare environment. Although the results of this review reveal few consistent relationships, the diverse range of factors identified across a relatively small number of studies sheds light on potential avenues for intervention among certain sub-groups while highlighting the need for further investigation. Certain themes emerged as potentially important across studies, including the possible impact of (1) gender and knowledge of serostatus (2) the influence of family structure, (3) the impact of burdensome ART regimens, route of administration, and attitudes about medication, and (4) healthcare and environmental factors, such as rural versus urban location and having missed clinic appointments.

While this is the first systematic review to focus specifically on correlates of adherence among adolescents in LMICs, the results highlight a diverse range of correlates consistent with the findings of previous reviews among pediatric, adult, and youth populations in high- and low-income countries (Mills, Nachega, Bangsberg, et al., 2006; Reisner et al., 2009; Vreeman et al., 2008). Financial constraints, complicated regimens, and side effects have been reported as significant barriers to adherence among adults in LMICs (Mills, Nachega, Bangsberg, et al., 2006), and caregiver relationship, adherence strategies, and child beliefs about medication were similarly identified as factors impacting on adherence among children (Vreeman et al., 2008). These commonalities shed light on various concurrent influences, such as the transfer in responsibility of medication administration combined with a burdensome ART regimen, which could interact during the adolescent period to increase risk for suboptimal adherence.

Comparison of these results with previous literature also highlights gaps that could be important for future study. Certain factors such as substance use, sexual risk factors, housing instability, and quality of life were significantly associated with adherence among youth living with HIV/AIDS in the U.S., while few studies in this review examined those variables (Reisner et al., 2009). Most variables studied in this review were focused on the individual-level factors, and there was a lack of focus on broader environmental, social, healthcare, and structural forces, including adolescents' changing legal status, social capacity, and access to "adolescent-friendly" services (Binagwaho et al., 2012; Sawyer et al., 2012; Tanner et al., 2014). Additionally, the results of this review demonstrate a troubling lack of published research on factors impacting on adherence in adolescent populations in many LMICs with emerging adolescent HIV epidemics, such as in South Asia, the Middle East, and the Caribbean (UNICEF., 2011).

The majority of studies identified by this review were cross-sectional, thus limiting our ability to infer causal relationships between adherence and potential risk- and resilience-promoting factors. These results emphasize the need for more methodologically rigorous prospective cohort studies that measure inter-individual change in factors over time while controlling for confounders, which would better capture the changing influences of adherence over time as children living with HIV/AIDS transition to adulthood.

Furthermore, these results also highlight to the importance of method of measurement of adherence. There exists debate on the best method for measuring adherence among young people who may rely on caregivers, and each method has its own strength and limitations (Berg & Arnsten, 2006; Haberer & Mellins, 2009). Few studies used multiple measures of adherence and/or incorporated objective immunological measurements into their definition of adherence, and only one study defined and measured adherence as viral load (Lowenthal et al., 2012).

This review has several limitations. We did not exclude any studies due to methodological rigor, given the limited number of studies conducted on adolescents in LMICs. The cross-sectional nature, use of simple tests of association without controlling for confounders, and general heterogeneity among studies limits the extent to which inferences can be made about causal mechanisms. Furthermore, this review does not include qualitative data. However, these results contribute to a larger body of knowledge related to the determinants of HIV-related outcomes among adolescents in LMICs. Targeting intervention design around potentially important risk- and resilience-promoting factors, such as caregiver support and level of ART administration, could be important in achieving optimal effectiveness. These results also clearly identify the need for more rigorous research to better captures the diverse range of factors impacting on the lived experience and adherence-related behaviors of adolescents living with HIV/AIDS in LMICs.

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