Developing an implementation science research agenda to improve the treatment and care outcomes among adolescents living with HIV in sub-Saharan Africa

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Developing an Implementation Science Research Agenda to Improve the Treatment and Care Outcomes among Adolescents Living with HIV in Sub-Saharan Africa
Developing an Implementation Science Research Agenda to Improve the Treatment and Care Outcomes among Adolescents Living with HIV in Sub-Saharan Africa

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Project SOAR (Cooperative Agreement AID-OAA-14-00060) is made possible by the generous support of the American people through the President’s Emergency Plan for AIDS Relief and the United States Agency for International Development (USAID). The contents of this guidance document are the sole responsibility of Project SOAR and the Population Council and do not necessarily reflect the views of USAID or the United States Government.

Through operations research, Project SOAR will determine how best to address challenges and gaps that remain in the delivery of HIV and AIDS care and support, treatment, and prevention services. Project SOAR will produce a large, multifaceted body of high-quality evidence to guide the planning and implementation of HIV and AIDS programs and policies. Led by the Population Council, Project SOAR is implemented in collaboration with Avenir Health, Elizabeth Glaser Pediatric AIDS Foundation, Johns Hopkins University, Palladium, and The University of North Carolina.

The Population Council confronts critical health and development issues—from stopping the spread of HIV to improving reproductive health and ensuring that young people lead full and productive lives. Through biomedical, social science and public health research in about 50 countries, the Council works with our partners to deliver solutions that lead to more effective policies, programs, and technologies to improve lives worldwide. Established in 1952 and headquartered in New York, the Council is a nongovernmental, nonprofit organization with an international board of trustees.

Published in July 2016.

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Acknowledgments

The authors gratefully acknowledge the youth who shared their experiences and perspectives living with HIV during the Technical Advisory Network meeting, “Developing an Implementation Science Research Agenda to Improve the Treatment and Care Outcomes among Adolescents Living with HIV in sub-Saharan Africa.” We also acknowledge the expertise and commitment of the other meeting participants who dedicated two days debating and developing implementation science questions to address the needs of young people living with HIV in sub-Saharan Africa. We thank the USAID Project SOAR Management Team, Technical Advisors, and other colleagues who contributed to the conceptualization of the meeting. We also extend our appreciation to the Project SOAR partner representatives who provided input into planning the meeting and writing the literature review that served as the background paper for the meeting. Finally, we thank Ellen Weiss of Population Council for her technical writing and editing skills, Sherry Hutchinson for design and layout skills, and Sherry Hutchinson and Sean Compas of Population Council for organizing the meeting.
## Acronyms and Definitions

### ACRONYMS

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
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<tbody>
<tr>
<td>ALHIV</td>
<td>Adolescents living with HIV</td>
</tr>
<tr>
<td>aOR</td>
<td>Adjusted odds ratio</td>
</tr>
<tr>
<td>aHR</td>
<td>Adjusted hazard ratio</td>
</tr>
<tr>
<td>CDC</td>
<td>The Centers for Disease Control and Prevention</td>
</tr>
<tr>
<td>CHAMP</td>
<td>Collaborative HIV Prevention and Adolescent Mental Health Family Program</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence intervals</td>
</tr>
<tr>
<td>HTC</td>
<td>HIV testing and counseling</td>
</tr>
<tr>
<td>IQR</td>
<td>Interquartile range</td>
</tr>
<tr>
<td>LTFU</td>
<td>Lost to follow-up</td>
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<tr>
<td>OR</td>
<td>Operations research</td>
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<tr>
<td>PEPFAR</td>
<td>United States President’s Emergency Plan for AIDS Relief</td>
</tr>
<tr>
<td>PITC</td>
<td>Provider initiated testing and counseling</td>
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<tr>
<td>PLHIV</td>
<td>People living with HIV</td>
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<tr>
<td>PMTCT</td>
<td>Prevention of mother-to-child transmission</td>
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<tr>
<td>STI</td>
<td>Sexually transmitted infections</td>
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<tr>
<td>SSA</td>
<td>Sub-Saharan Africa</td>
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<tr>
<td>TASO</td>
<td>The AIDS Support Organization</td>
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<tr>
<td>UNICEF</td>
<td>United Nations International Children’s Emergency Fund</td>
</tr>
<tr>
<td>UNAIDS</td>
<td>Joint United Nations Programme on HIV/AIDS</td>
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<tr>
<td>USAID</td>
<td>United States Agency for International Development</td>
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<tr>
<td>VCT</td>
<td>Voluntary counseling and testing</td>
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<tr>
<td>VL</td>
<td>Viral load</td>
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<td>WHO</td>
<td>World Health Organization</td>
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DEFINITIONS

The following definitions are used in this paper:

Adolescence

The World Health Organization (WHO) defines adolescence as the period between childhood and adulthood that encompasses 10 to 19 year olds, which is marked by intense growth and development (WHO 2015a). Adolescents undergo changes in physical, cognitive (e.g., moving from concrete to abstract thinking) and psychological development (e.g., emotional maturity) and take on new and expanded social roles and responsibilities (Sanders 2013). In recognition that adolescence is a developmental process and that a 10 year old may be at a very different point of development compared to a 19 year old, adolescence is often further categorized into early (10–13 years), middle (14–16 years), and late (17–19 years) stages (Sawyer et al. 2012; WHO 2015d). While these age definitions help to focus attention on the second decade of life, the actual beginning and end of adolescence varies across individuals, cultures, and countries with the onset of puberty typically marking the beginning of adolescence and other markers (e.g., age of legal majority, rites of passage, marriage) indicating the end.

HIV care continuum

The HIV care continuum (sometimes also called the HIV treatment cascade) is a model that delineates the sequential steps or stages of medical care that persons living with HIV (PLHIV) go through from initial diagnosis and engagement in care to achieving the goal of viral suppression, showing the proportion of PLHIV who are engaged at each step of care (AIDS.ORG 2015). It is a tool designed to identify where efforts are needed to improve HIV outcomes. The Centers for Disease Control and Prevention (CDC) specifically defines and tracks the following steps of the care continuum: diagnosis, linkage to care, retained in care, prescribed ART and virally suppressed (CDC 2014). This paper uses a slightly modified framework to examine the HIV care outcomes among adolescents living with HIV (ALHIV) with an emphasis on the factors and service delivery approaches related to each step along the continuum:

• Identifying ALHIV through testing and counseling.
• Linking ALHIV to HIV care.
• Retaining ALHIV in care.
• ALHIV adhering to ART and achieving viral load suppression.
• ALHIV transitioning to adult care and self-management.

Implementation science

Under PEPFAR, an implementation science framework consists of three key components: operations research (OR), routine monitoring and evaluation, and focused impact evaluations (Kerrigan et al. 2015; Padian et al. 2011). Within this framework, the purpose of OR, and the focus of the Technical Advisory Network meeting, is to generate evidence that will improve the efficiency, effectiveness, and quality of services delivered, and the availability, accessibility, and acceptability of the service for the users (Fisher et al. 2002). One definition of OR describes this...
focus on service delivery as a continuous process that consists of five main steps: (1) problem identification and diagnosis; (2) strategy selection; (3) strategy testing and evaluation; (4) information dissemination; and (5) information utilization (Fisher et al. 2002).

**Adolescent-friendly services**

The World Health Organization has identified eight global standards for delivering quality healthcare services for adolescents (WHO 2015c). These standards include: (1) adolescents’ health literacy (knowledge about one’s health), (2) community support (including parent/guardian support), (3) appropriate package of services (that fulfills the needs of all adolescents and includes facility services and services provided through referrals and outreach), (4) providers’ competencies (e.g., privacy, non-judgmental, respect), (5) facility characteristics (e.g., convenient operating hours), (6) equity and non-discrimination, (7) data and quality improvement, and (8) adolescents’ participation in the planning, monitoring and evaluation of health services, including their participation in decisions regarding their own care.
Developing an IS research agenda to improve the treatment and care outcomes among ALHIV in SSA
Introduction

Significant advances have occurred in the field of HIV prevention, treatment, and care in recent years. However, progress for the estimated 2.1 million adolescents living with HIV (ALHIV) has been less than optimal (UNAIDS 2014; UNAIDS and WHO 2013). AIDS is currently the leading cause of death among adolescents in sub-Saharan Africa (SSA) and the second leading cause of death globally (Dick and Ferguson 2015). AIDS-related deaths are declining in every age group except 10–19 years old. Additionally, only one in four infected children under the age of 15 has access to antiretroviral therapy (ART) (UNAIDS 2013).

Several new initiatives have recently been formed to respond to this crisis including the “All In” initiative led by UNAIDS, UNICEF, and partners such as PEPFAR. As more attention and resources are focused on ALHIV, it is critical that a strategic implementation science research agenda parallels these efforts. Project SOAR, a USAID-supported global operations research project, implemented by a multi-partner consortium of expert institutions, is in a unique place to bring together leaders in the field to strategize and recommend priority research questions, which if answered, will improve HIV outcomes for adolescents.

On 18–19 February 2016, Project SOAR convened a Technical Advisory Network meeting in Washington DC, “Developing an Implementation Science Research Agenda to Improve the Treatment and Care Outcomes among Adolescents Living with HIV in sub-Saharan Africa.” More than 50 international and domestic thought leaders in adolescent HIV care research and programming participated in the meeting together with a small group of youth from southern Africa who are living with HIV. To prepare the groundwork for the meeting, SOAR produced a background paper synthesizing the literature on HIV continuum of care outcomes among ALHIV in SSA, where most adolescent cases of HIV are concentrated. The care continuum encompasses:

- Identifying ALHIV through testing.
- Linking ALHIV to HIV care.
- Retaining ALHIV in care.
- ALHIV adhering to ART and achieving viral load suppression.
- ALHIV transitioning to adult care and self-management.

This report presents the findings from the literature review and highlights from the Technical Advisory Network meeting. The first section is a summary of the review’s findings, specifically what we know about ALHIV along the care continuum. The complete literature review is found in Appendix 1.

The second section of the report summarizes the outcomes from the meeting, including a set of priority research questions for the larger HIV community, as well as for Project SOAR, to consider addressing as part of new or ongoing studies. See Appendices 2 and 3 for the meeting agenda and the participant list, respectively.
After the meeting, USAID asked Project SOAR to conduct a literature review on prevention of mother-to-child transmission outcomes among ALHIV. The results from this review are found in Appendix 4.

By consolidating existing knowledge about ALHIV along the care continuum and documenting the research priorities identified by global experts, this report can serve as an important resource for catalyzing implementation research that fills important gaps in addressing ALHIV’s unique needs.
Literature Review: A Summary

We conducted a review of the published literature by searching PubMed using terms such as HIV, adolescent, Africa, and adherence. Abstracts were reviewed and articles pulled to assess if they met the eligibility criteria, including having: (1) data on a HIV continuum of care outcome, (2) a study sample from SSA, and (3) data on adolescents with a mean or median age between the ages of 10 and 19 years. Given the existing systematic reviews and meta-analyses on the care continuum (e.g., systematic reviews on adherence among adolescents and children), we searched PubMed for new articles published between 1 January 2014 and 10 March 2016 to capture new manuscripts published after these previous reviews’ inclusion dates. The grey literature was not systematically searched, however, reports and guidance were pulled from sources such as AIDSSTAR and the websites of USAID’s implementing partners. In sum, we found and used the following papers:

- Testing/linkage to care: two systematic reviews, one with 15 age-eligible studies on HIV testing and one with one study on linkages to care, plus three additional studies identified through PubMed and the grey literature.
- Retention: one systematic review with one age-eligible study, plus nine additional studies identified through PubMed and the grey literature.
- Adherence: five systematic reviews identified 20 unique age-eligible studies, plus 16 additional studies identified through PubMed and the grey literature.
- Transitioning to adult care and self-management: one review article found no studies based in SSA, and no studies were identified through PubMed.

Below is a summary of our findings from the literature. As noted above, the entire literature review can be found in Appendix 1.

**EPIDEMIOLOGY OF HIV AMONG ADOLESCENTS IN SUB-SAHARAN AFRICA**

An estimated 85 percent of the 2.1 million adolescents living with HIV reside in SSA with about 1.3 million in East and Southern Africa and 390,000 in West and Central Africa (Idele et al. 2014). Just six countries, five in SSA plus India, account for half of the world’s HIV-infected adolescents (Kasedde 2015).

Among younger adolescents (age 10–14 years), prevalence among males and females is fairly even across countries in SSA, likely reflecting that a majority of these infections were acquired through mother to child transmission of HIV. In mid and late adolescence (age 15–19 years), when sexual transmission of HIV becomes a predominant mode of acquisition among ALHIV, a very significant gap between the sexes emerges, with females up to two to five times more likely to be infected than their male peers (Idele et al. 2014). This age-gender gap reflects the
feminization of the epidemic and the biological, social, and structural factors that increase the risk young females face in acquiring HIV through sexual transmission.

The vulnerability of key populations of youth (e.g., men who have sex with men, people who inject drugs) is well established. The 2014 WHO guidelines on HIV among key populations states how adolescents who are members of these groups are at even greater risk than their adult counterparts for poorer health outcomes related to HIV, STIs, and reproductive health. Despite this recognition of their vulnerabilities, little data on the epidemiology of adolescents who may be members of key populations in SSA are available (Bekker, Johnson, Wallace, and Hosek 2015).

ADOLESCENTS AND THE CARE CONTINUUM

The literature review revealed that the published data on care continuum outcomes among ALHIV in SSA are sparse, particularly age-disaggregated data on linking positive youth to care and on transitioning adolescents to self-care and adult HIV clinics. In addition to this general lack of data on ALHIV in SSA, there is even less evidence on program approaches that support ALHIV and their families as they cope with testing for HIV, linking to care, remaining in care, adhering to ART, and transitioning to adulthood and self-management. We also were unable to find any adolescent specific data in the published literature on HIV care continuum outcomes among adolescents in SSA who are members of key populations.

Below we summarize the major findings from the literature on each component of the care continuum.

Identifying ALHIV through HIV Testing and Counseling

HIV testing and counseling (HTC) is a critical entry point to care and treatment, however only an estimated 29 percent of females and 20 percent of males between 15 and 19 years of age in Eastern and Southern Africa have ever taken an HIV test and know their HIV status (UNICEF 2013). Many countries have policies and laws restricting adolescent access to testing in clinic settings, including parental consent requirements, creating barriers to testing for sexually active young people who wish to learn their HIV status (WHO 2013, Annex 15; Sam-Aguda, et al. 2016). Home-based testing has been shown to have the highest uptake among adolescents, but provider-initiated testing and counseling has identified the greatest proportion of ALHIV.

A systematic review of HIV testing among adolescents found 15 eligible studies with data from SSA. These studies examined provider-initiated, outreach, home-based, and family centered HTC. Adolescent uptake was highest with home-based testing (86–99 percent), but detection of positives ranged only from 0.5–3 percent. Uptake varied widely for provider-initiated testing and counseling (40.7–95.5 percent), but it identified the highest proportion of HIV-positive adolescents (6–23 percent) (Govindasamy et al. 2015).

A study comparing mobile HTC with home-based HTC in rural Swaziland found that two percent
of adolescents reached through both approaches tested positive for HIV (Parker et al. 2015). While the overall percentage of positives identified through community-based strategies may be relatively small, community-based approaches may be more successful in diagnosing HIV infection earlier in adolescence, leading to better health outcomes (Govindasamy et al. 2015).

**Three home-based testing studies that required parental/guardian consent for adolescents to test demonstrated high levels of uptake.**

Requiring parental or guardian consent is a potential barrier to accessing testing, care, and treatment in adolescence. Moreover, the process of obtaining consent can be unclear and pose a challenge for health care providers (Govindasamy et al. 2015; Kranzer et al. 2014). Yet three of the home-based testing studies included in the systematic review (Govindasamy et al. 2015) required parental or guardian consent for younger adolescents to participate and still yielded high uptake (85.8–93.6 percent) (Angotti et al. 2009; Dalal et al. 2013; Naik, Tabana, Doherty, Zembe, and Jackson 2012). In addition, the one outreach study that clearly called for parental or guardian consent also had a high proportion accept to undergo testing (90.2 percent). These high levels of parent consent and subsequent adolescent uptake in home-based testing programs may differ greatly from clinic-based testing where parental consent may act as a barrier for sexually active adolescents seeking to learn their HIV status (WHO 2013, Annex 15).

**Linking and Retaining ALHIV in Care**

Very limited data are available on the process of linking adolescents who test positive to HIV care and treatment. A 2015 review found only one eligible article on linkages to care (MacPherson et al. 2015), with most of the available data focusing on ART initiation among adolescents once enrolled in care. Published findings are not yet available on linking ALHIV to care that reflect WHO’s 2015 revised guidelines that eliminated CD4 eligibility requirements for starting ART (Idele et al. 2014; WHO 2015).

**Many adolescents testing positive in Ugandan and South African studies did not enroll in HIV care.**

While the proportion of HIV-positive adolescents enrolling in care increased during the first four years of TASO’s home-based HTC program (from 9 percent to 41 percent), it dropped to 20 percent by 2010 (Livingstone et al. 2014). In South Africa, out of 11,522 adolescents and young adults (15–24 years of age) seen in a stand-alone clinic developed specifically to provide adolescents with HIV management services, 3.6 percent tested positive for HIV (N = 410). Around 25 percent of these youth did not return to enroll in care or have a CD4 cell test conducted (Nkala et al. 2015).

**Older ALHIV appear to have poorer pre- and post-ART retention than younger ALHIV.**

In a Kenyan study of pre-ART retention, an estimated 20 percent of 10–14 year olds and 44 percent of 15–19 year olds (and 49 percent of 15–24 year olds) were lost to follow up (LTFU) 12 months after enrolling in HIV care, indicating poorer retention among older vs. younger adolescents. Clinic data from 160 clinics in Kenya, Mozambique, Tanzania, and Rwanda found that youth ages 15–24 were at greater risk of attrition compared to young adolescents ages 10–14 years (Lamb et al. 2014).
A study of 8,016 young people from 109 clinics in Kenya who had initiated ART found that young adolescents (10–14 years) had lower levels of LTFU at 12 months and 24 months compared to 15–19 year olds (Koech et al. 2014). Data from cohorts in Zimbabwe and South Africa also found that older adolescents experienced greater LTFU compared to younger adolescents, and in Ethiopia adolescents ages 11–19 years were more than twice as likely to be LTFU compared to children (10 years or younger). Some authors discuss how older adolescents may not have the same level of caregiver involvement as younger adolescents and children, contributing to these differences in LTFU by age.

There is a lack of evidence on interventions or program approaches to link or keep adolescents in care.

The 2014 multi-country study by Lamb et al. found no evidence that offering adolescent-specific clinic hours, peer educators, or support groups decreased the risk of attrition among HIV-positive youth, ages 15–24, prior to ART initiation. The authors hypothesize that in the pre-ART phase youth are lost soon after enrollment so they do not have time to engage in or benefit from these types of services (Lamb et al. 2014). Yet 15–24 year olds had significantly lower post-ART attrition if they attended clinics that provided condoms versus their peers who attended clinics that did not provide condoms (Lamb et al. 2014). Also in a Ugandan study, adolescents who refilled their ART at community drug distribution points were consistently at lower risk for attrition compared to their peers refilling at health facilities at 12 months, 24 months, and 36 months (Livingstone et al. 2014). Overall there is a paucity of data testing the effectiveness of interventions to improve linkage to and retention in care.

ALHIV Adhering to ART and Achieving Viral Load Suppression

Five systematic review articles on ART adherence and viral load suppression identified 20 unique studies with data on ART adherence among adolescents in SSA. Only eight of these studies examined outcomes solely among adolescents with HIV, with more than half combining data from adolescents with data from children and/or young adults.

Studies on ART adherence among adolescents vary greatly, based on participants’ age and the way and length of time that adherence is measured.

A systematic review by Hudelson and Cluver (2015), found nine studies in SSA who had at least 50 percent of their study population consisting of adolescents (age range of 6 months to 21 year; only two consisted of adolescents only). These studies generated ART adherence estimates ranging from a low of 16 percent based on monthly self-report among 229 participants in Zimbabwe (Mavhu et al. 2013) to a high of 94 percent using clinic-based pill count among 170 participants in Uganda (Nabukeera-Barungi, Kalyesubula, Kekitiinwa, Byakika-Tusiime, and Musoke 2007). A 2016 literature review that included seven articles from SSA found that the proportion of adolescents achieving viral suppression also varied greatly, ranging from 27 percent to 89 percent at 12 months and 44 percent to 87 percent at 24 months (Ferrand et al. 2016). The few studies that disaggregated adherence data by age found that adolescents were more likely to have incomplete adherence and viral load failure compared to young adults.
The majority of studies assessing factors related to adherence were cross-sectional in design, and several had small sample sizes. These studies yielded mixed findings about the role individual, family, and health factors play in affecting adherence among adolescents.

A few studies have found that females are less likely to be adherent than males while others have found the opposite. Research has revealed contrasting findings about the relationship between a child or adolescent’s knowledge of his/her serostatus and adherence. Several studies found associations between adherence and such family factors as caregiver relations, their involvement in care, and knowledge about ART, while mixed results emerged regarding orphan status in relationship to adherence. There were also mixed findings about the health of adolescents and children and subsequent adherence to ART. It is important to note though, that several of the studies examining adherence among adolescents in SSA were cross-sectional in design and several had relatively small sample sizes (e.g., 82 participants), limiting the potential robustness of the data.

There is some evidence of the positive impact of group interventions on ART adherence by adolescents.

Few published studies provide evidence regarding effective interventions to support ART adherence, specifically among adolescents in SSA. In Zimbabwe, data from 262 adolescents found that participants who attended support groups had greater odds of achieving excellent adherence compared with non-participants (Gross et al. 2015). In South Africa, 10–13 year olds participating in six group sessions with family members had significantly greater improvements in their adherence scores after six months than participants in the comparison arm (Bhana 2014).

ALHIV Transitioning to Adult Care and Self-management

The transition of ALHIV refers to not only the movement from a pediatric or adolescent model to an adult model of HIV care, but also includes the development of self-management skills of adolescents as they grow into adulthood and assume responsibility for their HIV care. Although adolescent and pediatric services exist in SSA, many ALHIV already attend adult HIV care as this is the only service available to them. The search did not find any published data that tested the effectiveness of a transition model or approach among adolescents in SSA.

CONCLUSION

The published literature on the care continuum outcomes among ALHIV in SSA is sparse, particularly age-disaggregated data linking positive youth to care and on transitioning adolescents to self-care and adult HIV clinics. In addition, there is even less evidence on program approaches that support ALHIV and their families as they cope with linking to and retaining in care, adhering to ART, and transitioning into adulthood and self-management.
Technical Advisory Network Meeting

PARTICIPANTS

On 18–19 February 2016, the USAID-funded Project SOAR convened a meeting in Washington, DC, of more than 50 experts to focus on what we know and do not know about ALHIV along the care continuum. The meeting aimed to identify priority research questions that, if answered, would improve HIV policies and programs for this vulnerable population (see Appendix 2 for the meeting agenda).

The participants represented US government agencies (CDC, HRSA, NICHD, NIMH, NIAID, USAID), international agencies (UNICEF, WHO), non-governmental organizations (CHAI, EGPAF, FHI360, Gates Foundation, John Snow, Population Council, Zambart), researchers from US universities (Baylor, Columbia, Indiana University, Johns Hopkins Bloomberg School of Public Health, University of North Carolina, University of Pennsylvania, Yale), international researchers (Mozambique, South Africa, Uganda, Zambia, South Africa, Tanzania) and four youth living with HIV from southern Africa (see Appendix 3 for the participant list).

PROCESS

Youth Panel: Setting the Stage

After brief introductions, the meeting began with a panel of four youth from southern Africa who shared their experiences living with HIV and their perspectives about what helps or hinders adolescents in getting tested, and if positive, receiving continuous care, and adhering to treatment. All four members of the panel were perinatally infected. They highlighted the importance of support from family and peers, having the same provider when they visit the health center, and receiving age-appropriate explanations of their status and medication. Also critical, as they emphasized, is working with adolescents not only to ensure adherence and achieve viral suppression, but more broadly to provide support as they transition into adulthood and deal with challenges around relationships, disclosure, and employment.

They also related their own negative experiences with stigma, depression, and violations of their confidentiality. While some discussed the positive role that teachers played in supporting them, one young woman shared how a teacher she confided in told the whole class she was HIV positive. Throughout the meeting the three young women and one young man kept the discussion focused on issues relevant to ALHIV.
A Review of the Evidence and Expert Panel

Dr. Julie Denison of Johns Hopkins Bloomberg School of Public Health presented a summary of the published quantitative evidence on care continuum outcomes among ALHIV in SSA. This presentation was based on the findings from the comprehensive literature review undertaken by Project SOAR and found in its entirety in Appendix 1. Following this review, an expert panel contextualized the challenges and needs of ALHIV ranging from poor linkages to HIV care after HIV testing to the need for global guidance on better engaging adolescents along the HIV care continuum.

Working Groups and Selection of Priority Research Questions

The remainder of the meeting centered on four working groups:

1. HIV testing and linking ALHIV to care.
2. Retaining ALHIV in HIV care.
3. ALHIV adhering to ART and achieving viral suppression.
4. ALHIV transitioning to adult care and self-management.

Participants were allowed to choose the working group they joined, with efforts made to make sure each group had members from government, non-government, and university settings. The objectives of the working groups were to: (1) identify research questions for the group’s care continuum topic; (2) select six priority research questions, using criteria provided; and (3) propose potential study designs and platforms, such as research networks and institutions, or ongoing studies, to build upon to answer each of the top six research questions.

The criteria for selecting a priority research question included the ability of the subsequent research to inform the development, evaluation, or scale-up of an intervention along the care continuum; that answering the question was feasible; and that answering the question would be relevant not only locally but also regionally and globally.

After each group reported back to the larger meeting, all participants were asked to select their three priority questions within each topic through silent voting with stickers. Table 1 presents the research questions per topic in the order based on the number of votes each question received from the whole group.
<table>
<thead>
<tr>
<th>HIV testing/linkages to care</th>
<th>Voting results</th>
</tr>
</thead>
<tbody>
<tr>
<td>What are the effects and costs of a stigma reduction intervention on uptake of HIV testing and linkage to care among adolescents?</td>
<td>Tied for 1st</td>
</tr>
<tr>
<td>What is the effectiveness and costs of a peer navigator model in improving linkage to care rates in the context of a community-based or mobile testing program?</td>
<td>2nd</td>
</tr>
<tr>
<td>How do you identify those ALHIV who are at high risk of not linking to care? (Phase 1) What strategies are effective in addressing barriers to linking to care? (Phase 2)</td>
<td>3rd</td>
</tr>
<tr>
<td>Do adolescents who self-test, including members of key populations, get linked to care and if so, how?</td>
<td>4th</td>
</tr>
<tr>
<td>What are effective testing strategies and their costs in identifying ALHIV in low prevalence versus high prevalence contexts?</td>
<td>5th</td>
</tr>
<tr>
<td>How do you create an environment that supports adolescents to test? What are best practices for consenting adolescents for HIV testing?</td>
<td>6th</td>
</tr>
<tr>
<td>What are the right messages/tools/apps to get high-risk adolescents to test, and those testing positive, to link to care?</td>
<td>1st</td>
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<th>Retention in HIV care</th>
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<tr>
<td>Can providers’ enhanced capacity to deliver adolescent services improve retention?</td>
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<tr>
<td>What peer intervention models are effective in improving retention?</td>
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<tr>
<td>What is an appropriate differentiated care model for adolescents?</td>
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<tr>
<td>What are the effects of test and start on retention?</td>
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<tr>
<td>What is the effect of incentives (provider, client, and/or both) on retention?</td>
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<th>Adherence to ART</th>
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<tr>
<td>How can we best identify ALHIV in need of adherence interventions before treatment failure occurs?</td>
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<tr>
<td>What modalities of treatment simplification (regimen and delivery) can improve adherence among adolescents?</td>
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<tr>
<td>What mental health interventions (targeting depression, anxiety, PTSD, ADHD) in the context of adolescent HIV services can improve adherence?</td>
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<tr>
<td>How can mHealth and social network interventions effectively support adherence in adolescents?</td>
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<tr>
<td>Can essential components of treatment literacy training/assessment and autonomy development be effectively standardized using technological solutions?</td>
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<tr>
<td>How do we scale-up existing successful social support and resilience-enhancing models?</td>
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<th>Transitioning to self-management/adult care</th>
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<tbody>
<tr>
<td>What are the key predictors of a successful transition for adolescents who are in HIV care?</td>
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<tr>
<td>What are existing models of delivery of care that facilitate transition for ALHIV?</td>
</tr>
<tr>
<td>Can providers monitor adolescents on modified adult care schedules (e.g., align with their educational/school schedules)?</td>
</tr>
<tr>
<td>Can schools provide a platform to help ALHIV transition to self-care? Are there existing models for strengthening school-based health services to support ALHIV in transitioning?</td>
</tr>
<tr>
<td>What are the comparative effects of the different transition models identified in question 2 on the outcomes below? HIV-related outcomes: viral suppression; adherence; retention in adult care; disclosure of HIV status to the adolescent. Non HIV (well-being outcomes): quality of life; future orientation; life skills; autonomy; mental health; economic stability.</td>
</tr>
<tr>
<td>Can we use m-health technology to achieve a successful transition?</td>
</tr>
</tbody>
</table>
### FINAL PERSPECTIVES

After identifying the priority research questions, the youth panelists shared their final reflections about the meeting. Their inputs reinforced the value of youth participation in developing both research and programs. It also reinforced the need to ensure that youth and researchers/programmers/donors speak the same language. For example, one of the research questions identified as high priority was “to test a peer navigator model to improve linkages to care.” One youth asked what peer navigators were only to realize that he himself was a peer navigator at a youth development program but had never heard the term before. Another youth related that in one of the working groups, she and her peers were asked how they would define transition in the context of transitioning to self-management and adult care. The youth used analogies such as transitioning to a new level in school to talk about the movement from one point in life to another. But they also emphasized that for them and their peers, “transitioning” goes beyond HIV care management to include building life skills and strengthening resiliency necessary for adulthood.

In conclusion, the meeting succeeded in defining a research agenda for improving HIV care continuum outcomes among ALHIV for the larger HIV community as well as Project SOAR to consider addressing as part of new or ongoing studies. To continue the momentum established at the meeting, the research questions and the findings from the literature review will be shared with participants attending the satellite meeting, “Listen Up: What Youth Living with HIV Need to Achieve 90–90–90,” being held as part of the 2016 International AIDS Conference in Durban, South Africa.
Appendix 1
Literature Review

Developing an Implementation Science Research Agenda to Improve the Treatment and Care Outcomes among Adolescents Living with HIV in Sub-Saharan Africa

Prepared for
Project SOAR’s Technical Advisory Network Meeting
18–19 February 2016
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INTRODUCTION

Significant advances have occurred in the field of HIV prevention, treatment, and care in recent years. However, progress for the estimated 2.1 million adolescents living with HIV (ALHIV) has been less than optimal (UNAIDS 2014; UNAIDS and WHO 2013). AIDS is currently the leading cause of death among adolescents in sub-Saharan Africa (SSA) and the second leading cause of death globally (Dick and Ferguson 2015). AIDS-related deaths are declining in every age group except 10–19 years old. Additionally, only one in four children under the age of 15 has access to antiretroviral therapy (ART) (UNAIDS 2013). Several new initiatives have recently been formed to respond to this crisis including the “All In” initiative led by UNAIDS, UNICEF, and partners such as United States Emergency Plan for AIDS Relief (PEPFAR). As both more attention and resources are focused on adolescents globally, particularly ALHIV, it is critical that a strategic implementation science research agenda parallels these efforts. Project SOAR, a United States Agency for International Development (USAID)-supported global operations research project, implemented by a multi-partner consortium of expert institutions, is in a unique place to bring together leaders in the field to strategize and recommend priority implementation research questions, which if answered, will improve HIV outcomes along the care continuum for adolescents.

This literature review serves several purposes. The paper examines and summarizes the existing data on what we know about ALHIV along the care continuum, which encompasses:

- Identifying ALHIV through testing.
- Linking ALHIV to HIV care.
- Retaining ALHIV in care.
- ALHIV adhering to ART and achieving viral load suppression.
- ALHIV transitioning to adult care and self-management.

The paper also presents our knowledge to date regarding the service delivery successes and challenges in engaging and supporting ALHIV to achieve these care continuum outcomes.

Finally, the paper served as a resource for Project SOAR’s Technical Advisory Network meeting held 18–19 February 2016. This meeting aimed to identify the priority implementation science research questions to improve HIV services, program approaches, and outcomes for this vulnerable population.

METHODS

We conducted an initial review of the published literature by searching PubMed using terms such as HIV, adolescent, Africa, and adherence. Abstracts were reviewed and articles pulled to assess if they met the eligibility criteria including having data on a HIV continuum of care outcomes and the study sample was from SSA and had a mean or median age between ages 10 and 19 years. Given the existing systematic reviews and meta-analyses on the care continuum (e.g., there are systematic reviews on adherence among adolescents and children), we searched PubMed for new articles published between 1 January 2014 to 10 March 2016 to capture new manuscripts.
published after these previous review’s inclusion dates. The grey literature was not systematically searched, however, reports and guidance were pulled from sources such as AIDSSTAR and the websites of USAID’s implementing partners.

**FIGURE 1** Disposition of citations during the PubMed search and screening process

- **Records identified through PubMed search (N = 422)**
- **Records published between 2014–2016 and screened (n = 141)**
- **Full-text articles assessed for eligibility (n = 20)**
- **Studies included from the PubMed search (n = 20, 1 report contributes to both adherence/retention)**
  - 2—Testing/linkages
  - 4—Retention
  - 15—Adherence/VL suppression
  - 0—Transitioning care
- **Records excluded (n = 121)**
  - Ineligible ages of study participants (n = 80)
  - Qualitative studies (n = 18)
  - Not about ALHIV (n = 16)
  - Think pieces (n = 5)
  - Not available on line/retracted (n = 2)
- **Additional records identified through other sources (n = 6)**
  - 1—HIV testing and linkages and retention grey literature report
  - 4—HIV testing and linkages
  - 5—Retention
  - 1—Adherence
- **Total material included separate from meta-analyses and review articles**
  - 3—HIV testing and linkages
  - 9—Retention
  - 16—Adherence
  - 0—Transition
RESULTS

Epidemiology of HIV Among Adolescents in Sub-Saharan Africa

An estimated 85 percent of the 2.1 million adolescents living with HIV reside in SSA with about 1.3 million in East and Southern Africa and 390,000 in West and Central Africa (Idele et al. 2014). Just six countries, five in SSA plus India, account for half of the world’s ALHIV (Kasedde 2015). There are two main modes of infection for ALHIV in sub-Saharan Africa. Perinatally acquired infection is when an adolescent acquired HIV as an infant through their mother during pregnancy, labor, delivery, or breastfeeding. The other main mode of infection is sexually acquired HIV (consensual or nonconsensual). The other modes of transmission fall under parenteral transmission, or non-sexual transmission, and include injecting drug use, traditional practices (e.g., female genital mutilation, scarification) and medical procedures (e.g., blood transfusions) (WHO 2013).

Among younger adolescents (age 10–14 years), prevalence among males and females is fairly even across countries in SSA, likely reflecting that a majority of these infections were acquired through mother to child transmission of HIV. In mid and late adolescence (age 15–19 years), when sexual transmission of HIV becomes a predominant mode of acquisition in ALHIV, a very significant gap between the sexes emerges, with females up to two to five times more likely to be infected than their male peers (Idele et al. 2014). This age-gender gap reflects the feminization of the epidemic and the biological, social and structural factors that increase the risk young females face in acquiring HIV through sexual transmission (Dellar, Dlamini, and Abdool Karim 2015). Globally, an estimated 30 percent of new HIV infections in 2014 occurred among 15 to 24 year olds (UNAIDS 2015) with HIV becoming the leading cause of death among adolescents in SSA (Dick and Ferguson 2015). Despite efforts to increase access to ART, the estimated numbers of HIV-related deaths among ALHIV between 2005 to 2012 increased by 50 percent, while the global number of deaths across all ages decreased by 30 percent (WHO 2013).

Adolescents Who are Members of Key Populations

The vulnerability of key populations of youth (e.g., men who have sex with men, people who inject drug) is well established. The 2014 WHO guidelines on HIV among key populations states how adolescents who are members of these groups are at even greater risk than their adult counterparts for poorer health outcomes related to HIV, STIs, and reproductive health. Despite this recognition of their vulnerabilities, little data on the epidemiology of adolescents who may be members of key populations in SSA are available (Bekker, Johnson, Wallace, and Hosek 2015). Moreover, we were unable to find anything in the published literature on HIV care continuum outcomes among such adolescents in SSA. This absence of data highlights the need for innovative research to reach and engage adolescents who are members of key populations in SSA.
HIV Testing and Counseling

HIV testing and counseling (HTC) is a critical entry point to care and treatment; however, only an estimated 29 percent of females and 20 percent of males between 15 and 19 years of age in Eastern and Southern Africa have ever taken an HIV test and know their HIV status (UNICEF 2013). In areas with generalized epidemics, the WHO recommends routine HIV screening of adolescents (10–19 year olds) coupled with initiation of ART for any adolescent who tests positive regardless of his/her CD4 cell count or disease stage (WHO 2015b). WHO and UNICEF also recommend making HTC services adolescent friendly and engaging (UNICEF 2013; WHO 2015b). Box 1 highlights the key findings from the published literature on HTC among ALHIV in SSA, while the text provides a more detailed review of the published evidence found.

A recent systematic review of published data from SSA assessed the acceptability of HTC and the success of different testing strategies in identifying children and ALHIV (Govindasamy et al. 2015). Out of a total of 21 studies included in the review, 15 studies had participants with a median or mean age between 10 and 19 years, all of which were conducted in East and Southern Africa. These 15 studies examined the uptake of testing and receipt of results among adolescents offered provider initiated testing and counseling (PITC; n = 5, 3 in-patient settings, 2 outpatient settings), outreach testing (mobile clinic or outreach at a central site, n = 5), home-based testing; n = 4) and family-centered testing (testing the families of a person living with HIV; n = 1). Six of the studies provided HIV testing in the context of sero-prevalence surveys.

This review found that the uptake of testing by adolescents varied widely for PITC (40.7–95.5 percent) and outreach (9.9–90.2 percent). For home-based testing the uptake ranged from 85.8–99.4 percent. In the one study examining a family center approach, 99 percent of adolescents offered testing accepted to take the test. Nine of the 15 studies reported adolescent uptake by gender, with only one finding a significant difference with females more likely to accept routine HIV testing in an out-patient setting in South Africa compared to males (Ramirez-Avila et al.)

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**BOX 1**

**Key findings from published literature on HTC among ALHIV in SSA**

- A systematic review of HIV testing among adolescents found 15 eligible studies with data from SSA. These studies examined provider initiated, outreach, home-based, and family centered HIV testing and counseling. Adolescent uptake was highest among home-based testing (86–99 percent). Provider initiated testing and counseling identified the greatest proportion of HIV-positive adolescents (6–23 percent) (Govindasamy et al. 2015).

- Three home-based testing studies that required parental/guardian consent for adolescents to test experienced high levels of uptake (Govindasamy et al. 2015), while data were not found regarding the potential impact of parental consent on adolescent access and uptake of testing in clinic settings.

- A study on HIV self-testing had high uptake (89–100 percent) among 16–19 year olds in Malawi (Choko et al. 2015).

- We did not find any published literature on school-based testing among adolescents in SSA.
The family-centered study, all four home-based testing studies, and three of the outreach studies found no difference by gender in testing uptake (the other studies did not present gender disaggregated data).

The strategy that identified the greatest percent of ALHIV was PITC (ranging from 6.3 percent to 23 percent) supporting the recommendation of routine HIV screening in health facility settings (WHO 2015b). The non-facility based strategies identified a smaller proportion of positive adolescents (home-based HTC ranged from 0.5–3.2 percent, family-centered study had 1.6 percent, and outreach studies ranged from 0.3–2.1 percent). Similar findings were presented in a more recently published study comparing mobile HTC with home-based HTC in rural Swaziland. This study tested 245 adolescents through mobile HTC and 1,924 through home-based HTC, with 2 percent of adolescents reached through both approaches testing positive for HIV (Parker et al. 2015). While the overall percentage of positives identified through community-based strategies may be relatively small, as discussed by Govindasamy et al. community-based approaches may be more successful in diagnosing HIV infection earlier in adolescence, leading to better health outcomes (Govindasamy et al. 2015).

One of the biggest challenges to providing HTC among adolescents discussed in this review article, and in the literature in general, is age of consent. (Govindasamy et al. 2015). Requiring parental or guardian consent is seen as a potential barrier to accessing testing, care, and treatment in adolescence. Moreover, the process of obtaining consent can be unclear and pose a challenge for health care providers (Govindasamy et al. 2015; Kranzer et al. 2014). Three of the home-based HTC studies included in the systematic review required parental or guardian consent for younger adolescents to participate yet still yielded high uptake (85.8–93.6 percent) (Angotti et al. 2009; Dalal et al. 2013; Naik, Tabana, Doherty, Zembe, and Jackson 2012). In addition, the one outreach study that also clearly called for parental or guardian consent also had a high proportion accept to undergo testing (90.2 percent). Further detail on how parental/guardian consent and adolescent assent was obtained within these testing campaigns would help our understanding of how consent challenges may be successfully addressed to create a supportive testing environment for adolescents. In addition, further investigation is needed on how parental consent limits clinic-based HIV testing among adolescents and how providers address these challenges in order to reach sexually active adolescents, particularly young girls (WHO 2013 Annex 15).

In sum, while uptake of HIV testing among adolescents was relatively high in this review article, one of the limitations pointed out by the authors was that none of the studies assessed linkages to HIV care for adolescents who tested positive (Govindasamy et al. 2015). A recent study on self-testing, however, examined both uptake and linkages to care in Malawi (Choko et al. 2015). This study defined HIV self-testing as “an individual performing and interpreting his/her own HIV test” (page 2). This prospective randomized controlled trial enrolled participants age 16 and older. One of the key findings was that adolescents were more likely to undergo self-testing in the first year than adults (uptake was 89.3 percent of adolescent males and 100 percent of adolescent female, a percentage that drops significantly among the older age groups). The percent who tested positive also ranged from 1.1 percent among adolescent males to 3.5 percent among adolescent females. The estimated linkage to care was 56.3 percent, although this data was not
disaggregated by age. The authors did disaggregate though, data on coercion and found that 3 percent of 16–19 year olds reported being coerced into testing and that this percent did not significantly differ from the adults in the study. There were no reported cases of intimate partner violence or suicide related to testing during the first year of follow-up (Choko et al. 2015).

Data on other modes of HTC among adolescents in SSA, such as school-based testing, were not found in the published literature (one article by Bandason et al. that is also included in the Govindasamy review, explores HTC among primary school children; however the median age of study participants was nine years) (Bandason et al. 2013). Cross-sectional data, however, among secondary school students reveal low HIV testing uptake among students in general. Among 400 students in Arusha City, Tanzania, 29.3 percent have undergone HIV voluntary counseling and testing (VCT) and received their results, with students aged 13 to 18 significantly less likely than 19–24 year olds to test (aOR 0.37; 95 % CI 0.19–0.71), and males less likely to test than females (aOR 0.29; 95 % CI 0.17–0.50)(Sanga, Kapanda, Msuya, and Mwangi 2015). Another cross-sectional study in Ethiopia found only 8.8 percent of 339 students 18–24 years of age had undergone VCT (Sisay, Erku, Medhin, and Woldeyohannes 2014). Findings from Zambia echo these trends; in a community-based survey of 550 adolescents between 16 and 19 years of age, out-of-school youth were significantly more likely to have taken an HIV test compared to those attending school (aOR 2.95; 95 % CI = 1.32–6.59). This study also found that participants who had discussed with a family member whether or not to take an HIV test were more than three times as likely to have tested than their peers who had never had such discussions (aOR 3.51; 95 % CI = 1.08–11.47) (Denison, McCauley, Lungu, and Sweat 2014). A recent study in South Africa found that out of 2970 students between the ages of 14 and 27, 71.8 percent reported being willing to have an HIV test at the school (Madiba and Mokgatle 2015). While these studies indicate potential for school-based HIV testing, experts during the Project SOAR Technical Advisory Network meeting debated the merits of testing in schools, particularly among younger adolescents, compared to more targeted testing approaches as a way to reach adolescents who are living with HIV.

Linkages to Care

At the end of 2012, an estimated half of adolescents in low- and middle-income countries who were eligible for ART at that time (based on WHO 2010 guidelines) had been started on therapy (Idele et al. 2014). Since then the WHO guidelines have changed, first raising the CD4 threshold for ART initiation to 500 cells/µL in 2013 and then completely removing the CD4 eligibility requirements in 2015. Both these actions increased the numbers of adolescents eligible for ART who had not yet been initiated (Idele et al. 2014; WHO 2015b), highlighting the need for effective mechanisms linking adolescents who test positive to immediate care and treatment. Box 2 highlights the key findings from the published literature on linking ALHIV in SSA, while the text provides a more in-depth look at the evidence we found.

Very limited data are available on the process of linking adolescents who test positive to HIV care and treatment. The available data tend to focus on ART initiation among adolescents once enrolled in care. For example, The AIDS Support Organization (TASO) in Uganda implemented a home-based HIV testing and counseling program from 2005–2011 and tested 22,089 adolescents, aged 10–19 years, of whom 461 were positive and 140 were enrolled in HIV care
at TASO (30.4 percent). Out of these 140 enrolled adolescents, 26 percent (n = 37) were eligible for care, and 89 percent of these started ART (n = 33). Overall, the proportion of HIV-positive adolescents enrolling in TASO care increased during the first four years of the home-based HIV testing and counseling program (from 9 percent to 41 percent), but then dropped to 20 percent by 2010 (Livingstone et al. 2014). Cohort data from Kenya, Tanzania, Mozambique, and Rwanda found that youth (15–24 years) in HIV care were more likely to be female (85 percent vs. 65 percent) and referred to care from prevention of mother and child transmission (PMTCT) programs than their adult counterparts age 25 and older (20 percent vs. 9 percent), highlighting the role of PMTCT efforts to link female ALHIV to HIV care (Lamb et al. 2014).

In South Africa, out of 11,522 adolescents and young adults (15–24 years of age) seen in a stand-alone clinic developed specifically to provide adolescents with HIV management services in Soweto, 3.6 percent tested positive for HIV (N = 410) of whom only 109 had their CD4 cell count assessed and only 12 were eligible for treatment (Nkala et al. 2015). Moreover, around 25 percent of the youth who tested positive did not return to enroll in care or have a CD4 cell test conducted (Nkala et al. 2015). These studies did not systematically assess the reasons adolescents chose to link or not link with HIV care. Overall data on linking ALHIV to care in SSA are sparse.

**Retention**

The following section examines retention to care among adolescents once enrolled in HIV care but prior to initiating ART, known as pre-ART retention, followed by an examination of the literature on retention once on ART.
**Pre-ART retention**

**BOX 3**

**Key findings from published literature on pre-ART retention for ALHIV in SSA**

- Two studies examined pre-ART initiation retention (Koech et al. 2014; Lamb et al. 2014). An estimated 19 percent of 10–14 year olds and an estimated 44 percent of 15–19 year olds (and 49 percent of 15–24 year olds) were lost to follow up (LTFU) 12 months after enrolling in HIV care, indicating a higher LTFU among older vs. younger adolescents.

- 15–24 year olds entering care through PITC, PMTCT and HIV/TB services experienced greater pre-ART attrition than peers enrolled following VCT.

- Only one study examined program factors related to pre-ART retention and found no evidence that offering adolescent-specific clinic hours, peer educators, or support groups decreased the risk of attrition.

**Levels of pre-ART retention**

A 2015 systematic review (MacPherson et al. 2015) found only one article on ART retention among adolescents in SSA (Lamb et al. 2014). This study analyzed routine clinic data from 312,335 patients enrolled in care between 2005–2010 in 160 clinics in Kenya, Mozambique, Tanzania, and Rwanda (Lamb et al. 2014). This study categorized age into four groups: 10–14 years (young adolescents), 15–24 years (youth), 25–54 years, and 55 and over. One year after joining care, but before initiating ART, 49 percent of the youth and 20 percent of the young adolescents experienced attrition defined as lost to follow-up or known death, with LTFU accounting for 98 percent and 87 percent of attrition respectively. The adjusted hazard ratio (aHR) for attrition, compared to the reference population of 25–54 year olds was 1.50 (95% CI 1.45–1.54) for youth; and 0.71 (95% CI 0.64–0.79) for the young adolescents. When compared directly, youth were at greater risk of attrition compared to the young adolescents (sHR = 2.11, 95% CI 1.88–2.37).

Another study identified through the PubMed search assessed data from 22,832 patients, aged 10–24 years, enrolled in care between 2006 and 2011 in 109 clinics in Kenya (Koech et al. 2014). This study found that at 12 months 19 percent (95% CI 17.5–20.5) of the 10–14 year olds were lost to follow-up (LTFU); not including death or transfer) compared to 44 percent (95% CI 42.6–46.0) of the 15–19 year olds and 44 percent (95% CI 43.4–45.1) of the 20–24 year olds. Similar results were found at 24 months with an estimated 22 percent of the 10–14 year olds compared to 50 percent of the 15–19 and 20–24 year olds being LTFU. Mortality did not differ by age at either 12 or 24 months.

**Factors related to pre-ART retention**

The Lamb et al. study also examined the factors related to pre-ART attrition at 12 months specifically for youth (15–24 year olds) (Lamb et al. 2014). In an adjusted analysis, youth across four countries who entered HIV care from PMTCT, PITC, TB/HIV clinics, and unknown sources were more likely to experience attrition than youth who enrolled following voluntary counseling and testing (VCT). Non-pregnant females were also less likely to experience attrition than males.
Developing an IS research agenda to improve the treatment and care outcomes among ALHIV in SSA  ■  A-11

(0.90, 95% CI 0.86–0.94) while no difference in attrition was found between males and pregnant females. Youth with CD4 counts between 100 and 200 cells/µL were also significantly less likely to experience attrition compared to youth with who had missing CD4 counts or CD4 results that were less than 100 cells/µL or greater than 200 cells/µL. Finally, youth from Kenya, Mozambique and Tanzania had greater risk of attrition compared to their counterparts in Rwanda.

Interventions to improve pre-ART retention
Overall there is limited evidence regarding interventions to improve pre-ART retention among ALHIV in SSA. The Lamb article was the only published article that examined the relationship between interventions and pre-ART retention among adolescents in sub-Saharan Africa. This study found no evidence that offering adolescent-specific clinic hours, peer educators or support groups decreased the risk of attrition among youth. The authors hypothesize that in the pre-ART phase youth are lost soon after enrollment so they do not have time to engage in or benefit from these types of services (Lamb et al. 2014).

Post-ART retention

Eleven studies (10 published and 1 report) present data specifically on retention to care after ART initiation among ALHIV in SSA. These cohort studies analyzed routine clinic data collected either prospectively or retrospectively and give insight into retention among adolescents after they initiate ART (Bakanda et al. 2011; Berheto, Haile, and Mohammed 2014; Bygrave et al. 2012;
Loss to follow up
In a study of 10–24 year olds from 109 clinics in Kenya (described above), 8,016 youth had initiated ART (Koech et al. 2014). The young adolescents (10–14 years) had lower levels of LTFU: 10 percent (95% CI: 8.7–11.5) at 12 months and 18.5 percent (95% CI 16.6–20.6) at 24 months compared to 15–19 year olds with 19.8 percent (95% CI 17.7–22.2) LTFU at 12 months and 30.3 percent (95% CI 27.7–33.2) at 24 months (Koech et al. 2014). Similarly in the Lamb study, among the 140,798 patients who started ART and had 1 year of potential follow-up, 27.2 percent of the 15–24 year olds were LTFU (defined as documented death or LTFU) compared to 9 percent of the 10–14 year olds (HR 2.45, 95% CI 2.15–2.80). Loss to follow-up, rather than death, accounted for the majority (>95 percent) of this post-ART initiation attrition for both youth and young adolescents (Lamb et al. 2014).

Data from a cohort of 898 patients who initiated ART between 2005 and 2008 in rural Zimbabwe also found that older adolescents experienced greater LTFU compared to younger adolescents, with a rate per 100 person years of 4.2 (95% CI 2.5–7.0) among 10–14 year olds and 10.9 (95% CI 6.2–19.1) among 15–19 year olds (aHR 2.54, 95% CI 1.17–5.49) (Bygrave et al. 2012). Similar data emerged from a retrospective analysis of data from seven clinics across urban Gauteng and rural Mpumalanga in South Africa, with LTFU rates per 100 person years lowest among young adolescents 10–14 years at 6.1 and highest among older adolescents 15 to 19 years at 23.3. Compared to adults over 25 years old, older adolescents were almost twice as likely to be LTFU (HR 1.78, 95% CI 1.34–2.36), while young adolescents had less risk (HR 0.43 95% CI 0.26–0.69) (Evans et al. 2013). A retrospective chart review among 2,133 Ethiopian patients revealed that the 74 adolescents (aged 11–19 years) were more than twice as likely to be LTFU when compared to the 128 children who were less than 10 years of age (HR 2.1, 95% CI 1.3–3.4) (Berheto et al. 2014). Both Evans (2013) and Berheto (2014) discuss how older adolescents may not have the same level of caregiver involvement as younger adolescents and children, potentially leading to these differences in LTFU by age.

Data from Uganda shows much higher retention proportions for adolescents. Among a cohort of 156 adolescents who had started ART in 2012 and were sampled from 10 districts in Uganda, 90 percent were still in care one year later (Nabukeera-Barungi et al. 2015). A cohort study conducted among 617 HIV-positive adolescents (10–19 years) enrolled between January 2006 and December 2011 in TASO’s ART clinics in Uganda also generated high retention proportions for adolescents: 96 percent at 12 months, 83 percent at 24 months, 76 percent at 36 months and 71 percent at 48 months (Livingstone et al. 2014). The authors state these proportions were similar when compared to adult patients who were age 20 years and older. This study also explored differences among various cohorts of adolescents based on when they started ART, with virtually no change existing in the first 6 months in the ART program with retention ranging from 93 percent in the 2010 cohort to 100 percent in the 2006 cohort. However, there were greater variations as more time passed with earlier cohorts from 2006 to 2009 having over 90 percent retention at 12 months compared to the 2010 cohort that had 79 percent retention at 12 months. This study also found that older adolescents, 15–19 years, were significantly more likely
to experience non-retention during the first two years after ART initiation than younger 10–14 year olds: aHR 1.88 (95% CI 1.01–3.48) at 12 months and aHR 1.30 (95% 1.02–1.66) at 24 months, a trend that becomes non-significant by 36 months.

Some studies, however, did not find significant differences in LTFU by age, including an earlier study of 23,267 TASO patients who initiated ART between 2004 and 2009 (Bakanda et al. 2011) and a study in Kenya with 924 patients comparing LTFU among those under 20 to those 20 years and older (Ojwang et al. 2015). Similarly, data from among 883 patients enrolled in a prospective cohort study in a public sector community-based ART program in Cape Town South Africa also found no significant difference in LTFU or mortality between age groups comparing 9–19 year olds to 20–28 year olds. This study did find, however, an increased risk in virological failure (aHR 2.06, 95% CI 1.11–3.81) in adolescents compared to adults (Nglazi et al. 2012).

Post-ART initiation LTFU due to mortality among ALHIV
While LTFU was clearly higher among older adolescents compared to younger adolescents, data from four studies showed no significant differences in mortality by age (Bakanda et al. 2011; Evans et al. 2013; Koech et al. 2014; Nglazi et al. 2012). Data from a cohort of 898 patients who initiated ART between 2005 and 2008 in rural Zimbabwe did find that young adolescents (10–14) had the lowest rate of death per 100 person years compared to adolescents (15–19 years) and young adults (19.1–24 years): 3.6 (95% CI 2.0–6.3); 5.4 (95% CI 2.4–12.1); and 6.6 (95% CI 3.7–11.9) respectively (Bygrave et al. 2012).

Factors related to post-ART retention
Among 10–19 year olds attending TASO clinics in Uganda, factors related to non-retention at 12 months included having a WHO stage 3 or 4 at ART initiation (aHR 2.21, 95% CI 1.19–4.09), a variable that was no longer significant at 24 or 36 months. On the other hand, having a pre-ART CD4 cell count of >100 cells/µL was not significantly related with attrition at baseline, but was at 24 and 36 months. This analysis also found no differences between the sexes in terms of LTFU at 12 months, but with time females had significantly less risk of being LTFU compared to males: aHR 0.68, 95% CI 0.52–0.88 at 24 months and aHR 0.79, 95% CI 0.64–0.98 at 36 months. In the multi-country study by Lamb et al. (2014) an analysis specifically on 15–24-year-old youth found that male youth had greater attrition than female youth and, similar to pre-ART loss to follow up, patients entering care through PITC or unknown points of entry had greater attrition rates than youth entering through VCT. This analysis also found less attrition among youth with a CD4 count of 100–200 cells/µL when compared to either counts that were higher than 200 cells/µL or lower than 100 cells/µL at ART initiation, and that youth attending clinics in Kenya, Mozambique and Tanzania had higher rates of post-ART attrition compared to youth attending clinics in Rwanda.

Interventions to improve post ART initiation retention
Only one study provides information solely on adolescents that examines retention by specific program strategies. In Uganda, adolescents who refilled their ART at health facilities were consistently at greater risk for attrition compared to their peers refilling at community drug distribution points: aHR 2.58 (95% CI 1.26–5.29) at 12 months; aHR 1.59 (95% CI 1.23–2.05) at 24 months and aHR 1.3 (95% CI 1.05–1.61) at 36 months (Livingstone et al. 2014).
Two other studies examined how different program strategies may relate to adherence among young adults. For example, 15–24 year olds in Lamb’s multi-country study had significantly lower post-ART attrition if they attended clinics that provide condoms versus their peers who attended clinics that did not provide condoms (RR = 0.47, 95% CI 0.32–0.70) (Lamb et al. 2014). This study found no evidence of differences in attrition when other youth friendly services were offered in addition to regular services, including adolescent specific clinic hours, screening for STI’s and the provision of hormonal contraceptives. In a study in Kenya of 10–24 year olds (median age 21 years, IQR 19–23) the authors found no difference in attrition at a six month follow up among youth attending clinics with youth friendly services compared to peers attending clinics without youth friendly services (Teasdale et al. 2015).

**Adherence to ART and Achieving Viral Load Suppression**

**BOX 5**

**Key findings from published literature on adherence to ART and achieving viral load suppression among ALHIV in SSA**

- Estimates of ART adherence among adolescents in SSA vary greatly from 16 percent to 94 percent based on the age of the study participants, the way adherence was measured, and the time frame covered.

- Five systematic reviews identified data from 20 unique published studies containing data on adolescents living with HIV in SSA. Out of these 20 articles, only 8 reported exclusively on adolescents, with the rest combining data from adolescents with data from children and/or young adults.

- Studies examining factors related to adherence among adolescents in SSA tend to have cross sectional study designs and often smaller sample sizes.

- Three studies that disaggregated adherence data by age found that adolescents were more likely to have incomplete adherence and viral load failure compared to young adults and adults.

- The factors related to adherence among adolescents (gender, disclosure, family factors, and medical/health factors) varies depending on whether the sample is combined with children or focused on adolescents only, and if the measure of adherence is a caregiver report versus other measures of adherence (e.g., self-report, pill counts).

- Few published articles examine the impact of interventions on adherence among adolescents and those that do provide preliminary data on the positive impact of group sessions on adolescents’ adherence behaviors.

**Levels of adherence**

Several systematic reviews and a meta-analyses have assessed ART adherence among adolescents and children, both globally and specifically in middle and low income countries, producing adherence estimates ranging from 16–94 percent (Hudelson and Cluver 2015; Kim et al. 2014; Vreeman et al. 2008). However critical questions remain regarding how well the existing literature provides insight and evidence regarding the adherence behaviors of ALHIV in SSA.
In the first review by Vreeman et al. published in 2008, only six out of the 17 studies that met the eligibility criteria were from SSA, and out of those only two had participants with a median age that fell within 10 to 19 years. In one of these studies, conducted among 170 HIV-infected children between the ages of 2 and 18 years in Uganda, caregivers estimated that 89.4 percent of participants achieved >95 percent adherence based on a three-day self-report, a percentage that increased to 94.1 percent with clinic based pill counts and dropped to 72 percent during a home-based unannounced pill count a few weeks later (Nabukeera-Barungi, et al.,2007). In the other study, in–depth interviews were conducted with 42 Uganda children and their caregivers jointly, with 29 percent of these pairs reporting excellent adherence (never missed any dose, with the time frame not specified (Bikaako-Kajura et al. 2006). Adherence in both articles was not disaggregated further by age.

Kim et al. published the next review in 2014 with data from 50 eligible studies that assessed ART adherence among adolescents and young adults living with HIV globally. Eight of these studies were conducted in sub-Saharan Africa and produced a pooled adherence estimate of 83.8 percent [95% CI 78.9–88], a percentage that is much higher when compared to the overall global estimate of 62.3 percent [57.1–67.6]. Unlike the measures used in the articles in the Vreeman systematic review, six of the SSA articles in the Kim meta-analysis used viral load test results to assess adherence, and one article had data from pill counts (Nabukeera-Barungi et al. 2007), one used pharmacy refill data (Nachega et al. 2009), and one used self-reports (Wiens et al. 2012). Four of the studies contributing to the largest samples sizes for the SSA meta-analysis adherence estimate, however, included young adults up to age 24 (Evans et al. 2013; Mutevedzi et al. 2011; van Cutsem et al. 2010) and age 28 (Nglazi et al. 2012). In two of these articles the authors disaggregated the data by age. In one study they found that young adolescents (10–14) had higher virologic failure rates (6.3 per 100 person years) compared to older adolescents (3.8 per 100 person years) and that younger adolescents (10–14) (HR 2.94 95% CI 1.63–5.31), older adolescents (15–19) (HR 2.90 95% CI 1.74–4.86) and young adults (20–24) (HR 1.53 95% CI 1.13–2.08) all had greater risk of viral failure when compared to adults 25 years and older (Evans 2013). Another study found that adolescents (ages 9–19) had a greater risk of viral failure compared to young adults (ages 20–28) (aHR 2.06, 95% CI 1.11–3.81) (Nglazi et al. 2012). Nachega et al. also found that when compared to adults, 154 adolescents in South Africa were less likely to achieve 100 percent adherence measured through pharmacy refill data (20.7 percent vs. 40.5 percent at 6 months; 6.6 percent versus 20.6 percent at 24 months).

A more recent systematic review on adherence was published in 2015 by Hudelson and Cluver. The purpose of this review of adolescents living with HIV in low- and middle-income countries was to identify the factors related to adherence. Out of 15 eligible studies, 9 were conducted in SSA and only one overlapped with the articles in the earlier reviews (Nabukeera-Barungi et al. 2007). While all studies had at least 50 percent of participants who were between 10 and 19 years, the age ranges across articles encompassed 6 months to 21 years. In addition, all the studies used cross sectional designs, and all but one used a 95 percent cutoff for good adherence based on caregiver and self-reports and pill count (Kikuchi et al. 2012, used a cutoff of 85 percent). Only one study assessed adherence by viral load (Lowenthal et al. 2012). Adherence estimates across these studies ranged from a low of 16 percent based on monthly self-report among 229 participants in Zimbabwe (Mavhu et al. 2013) to a high of 94 percent using clinic-based pill count among 170 participants in Uganda (Nabukeera-Barungi et al. 2007).
A separate meta-analysis article, published in 2016, examined viral suppression among adolescents on ART (Ferrand et al. 2016). This review identified seven articles from SSA, five of which have appeared in earlier adherence reviews. The proportion of adolescents achieving viral suppression varied greatly, ranging from 27 percent to 89 percent at 12 months, 44 percent to 87 percent at 24 months and two studies reported an overall proportion with virological suppression at 61–62 percent. Sample sizes for these studies ranged from 65 to 652 participants. Another study examining routine viral load monitoring in Swaziland found 48 percent of 277 adolescents were never linked to their viral load (VL) test result or underwent VL testing. Out of the adolescents who underwent VL testing, 30 had a detectable viral load of whom 14 had confirmed virologic failure (Jobanputra et al. 2014). In another analysis of the Swaziland data, the authors found adolescents (n = 588) were significantly more likely to have a detectable viral load than adults (aOR 3.2, 95 % CI 2.2–4.8) and significantly less likely to re-suppress after adherence counseling compared to adults (aOR 0.3, 95% CI 0.2–0.8) (Jobanputra et al. 2015). In Khayelitsha, South Africa, among 118 study participants from two primary care clinics (median age 10, IQR 5–14), 33 percent were failing their ART and had not achieved viral suppression (Bernheimer et al. 2015). A study among 161 adolescents and children in Tanzania compared VL test results from 2008–2009 to a second set of results from 2012–13. Sixty percent (44/65) of the participants who were 12 or older during the study remained on first line regimens and virally suppressed compared to 95 percent of those who were younger than 12 years during the assessments. Overall the authors found a significant and large (3.3 fold) increase in the odds of virologic failure among adolescents, and an even greater odds of virologic failure (8.8, CI not reported, p < 0.01) for participants who remained in adolescence during the study (Dow et al. 2014).

Factors related to adherence and viral suppression

Out of the literature found, 20 studies (9 identified by Hudelson and Cluver 2015, 10 identified through PubMed, and 1 found in the grey literature) examined factors associated with adherence to ART among ALHIV. Adolescents comprised at least 50 percent of the study populations in these articles, with 5 articles exclusively enrolling adolescents between the ages of 10 and 19 years old. Around half of these articles assessed the factors associated with adherence while half assessed non-adherence as their primary outcome. These studies in general were cross-sectional with relatively small sample sizes (ranging from 82 up to 1,000 participants) producing mixed results. The key findings from these articles are grouped by theme/factors below.

Gender

Four studies had adherence data disaggregated by sex. Two studies found that males were more adherent than females. In Uganda, data from 948 children and young adolescents between 3 and 15 years of age found that males were more likely than females to have 95 percent or more adherence using a three day self-report measure that was completed by the child or caregiver [crude OR 1.9, 95% CI 1.2–3.1] (Musiime et al. 2012). In Tanzania, a study among 183 HIV-infected children and adolescents between the ages of 2 and 17 years found that males were more than twice as likely to have good adherence across three measures: pill count, 2 day measure and a 30 day measure [OR 2.55, 95% CI 1.05–4.87] (Nsheha et al. 2014).
The opposite, however, was found in a study in Botswana conducted among only 13–18 year olds (n = 82). This study found that males were significantly more likely to have suboptimal adherence compared to females when assessing pill count data over the past month [OR 3.29, CI 1.13–9.54] (Ndiiaye et al. 2013). Data from 285 adolescents aged 15 to 19 in Zambia also found that males had greater odds of missing two consecutive days of ART in the past 3 months than females [aOR 1.92, 95% CI 1.05–3.54], while there was no difference between males and females in terms of having less than 90 percent of their 6 month pharmacy refill pills (Denison 2015 unpublished).

Disclosure
Six published quantitative studies have examined the relationship between adherence and the adolescent’s knowledge of his/her HIV serpositive status. Three studies from Ethiopia, all conducted among young adolescents combined with children, found that participants who were unaware of their HIV status were significantly more likely to adhere to ART. Two of the studies assessed adherence using unannounced home-based pill counts one week after the clinic visit [n = 210, aOR = 2.35, 95 CI 1.09–5.06] (Biressaw et al. 2013) and the other used caregiver 7-day adherence reports [n = 390 OR 2.53, 95% CI 1.24–5.19] (Biadgilign et al. 2008). Another study conducted in Ethiopia also used caregiver reports and found disclosure to a child significantly related to a reduced odds of adherence [n = 342, aOR = 0.27, 95% CI:0.24–0.32] (Dachew, Tesfahunegn, and Birhanu 2014).

These data are in stark contrast to findings from another study in Ethiopia (n = 464) which found that participants who knew their status were more likely to have achieved adherence based on caregiver reports of >95 percent adherence in the past month [aOR = 3.47 95% CI 2.10–6.81] (Araga, Tessema, and Kassa 2014). Just one study, conducted in South Africa, enrolled only adolescents and found that when participants knew their HIV-positive status they were more than twice as likely to self-report higher adherence in the past week [OR 2.18, 95% CI 1.47–3.24] (Cluver et al. 2015). Among those adolescents who were perinatally infected and learned their HIV status prior to turning 12 years old, adherence was also significantly higher [OR 2.18, 95% CI 1.47–3.24] compared to adolescents who learned their HIV status after turning 12 years old (Cluver et al. 2015). A study in Uganda found no difference in adherence based on the participant’s knowledge of his/her serostatus [n = 170, CI 091, 95% CI 0.39–2.07] (Nabukeera-Barungi et al. 2007).

Family and household factors
Several studies found family level factors related to ART adherence among adolescents. In Botswana, Lowenthal et al. (2015) found that the odds of virologic failure at the 3-month clinic visit was much greater among adolescents who did not have their parents or guardian attending the clinic with them compared to those who did [n = 300, OR 4.5, 95% CI 1.5–4.1]. A similar finding emerged from data from 262 adolescents in Zimbabwe with adolescents whose parents were always in the room during clinic visits having greater self-reported adherence than those without their parent or guardians present [OR 2.1, 95% CI 1.3–3.5] (Gross et al. 2015). Another study conducted in Uganda found that when the only person who knew the child’s serostatus was the primary caregiver, versus others also knowing the child’s serostatus, the odds of non-adherence was three times greater [OR 3.34, 95% CI 1.14–9.82] (Nabukeera-Barungi et al.
Young adolescents and children in Ethiopia who were not aware of their caregiver’s health problem were also more adherent than their peers who were aware [OR = 2.45, 95% CI 1.25–4.81] (Bladgilign et al. 2008).

Another study found that caregivers’ knowledge about ART [aOR 2.72, 95% CI 1.82–5.39] and caregivers not currently using substances (i.e. alcohol, chat and/or cigarettes) [aOR 2.21, 95% CI 1.34–7.13] were related to caregivers’ reports of adherence in the past month among 440 young adolescents and children in Ethiopia. This same study found that adolescents whose caregivers had at least a secondary education compared to those who could not read or write were less likely to be adherent [aOR 0.59, 95% CI 0.21–0.83] (Arage et al. 2014). Another study from Ethiopia also found that caregivers’ knowledge about ART was significantly related to adherence [aOR 4.7, 95% CI 3.7–5.6] (Dachew et al. 2014).

In Ethiopia, children and young adolescents were more likely to adhere if their caregiver was married [aOR = 7.85 (95% CI: 2.11,29.13)] and widowed/divorced [aOR = 7.14 (95% CI: 2.00,25.46)] compared to single caregivers (Biressaw et al. 2013), while participants with widowed caregivers in Uganda experienced worse adherence that those with married caregivers (Musime et al. 2012). In Rwanda, multivariate analysis revealed less adherence among adolescents who were double orphaned compared to maternal, paternal or non-orphans (n = 717) (Kikuchi et al. 2012). A study in South Africa did not find any evidence of a relationship between adolescent adherence and if their caregiver was a biological parent or not (Cluver et al. 2015).

In two studies, the authors did not find evidence of a significant relationship between adherence and several family level measures including family support, caregiver relations, and discussions of adherence (n = 82) (Ndiaye et al. 2013) or orphan status, having an HIV-infected sibling, and social support (Nabukeera-Barungi et al. 2007). In a study in Tanzania, children and adolescents were more adherent if the caregivers could afford to bring the child to the clinic (OR = 3.4, CI 1.60–7.36), provide additional food (OR = 2.93, CI 1.23–6.90), and had a monthly household income above 1000,000 Tanzanian shillings [OR = 0.44, CI 0.21–0.96] (Nsheha et al. 2014). In Brazzaville, Congo, among 10–19 year olds, being younger and parents’ administration of ART were both significantly associated with adherence (Mbika et al. 2014).

**Medical- and health-related factors**

There are mixed findings about the health of adolescents and children and subsequent adherence. Hospitalization (OR 0.44 for non-adherence, 95% CI 0.20–0.92) (Nabukeera-Barungi et al. 2007), and having a baseline WHO clinical stage III/IV [OR = 3.18, 95% CI: 1.21–8.40] (Biressaw et al. 2013) were related to adherence in two studies. In other studies, worse adherence and virologic failure were associated with side effects and symptoms (Nsheha et al. 2014) and mental health measures (Dow et al. 2016; Lowenthal et al. 2012; Lowenthal et al. 2015; Mavhu et al. 2013). One study also found that children on d4T/3TC/EFV combination ART were less likely to be adherent [OR = 0.10, 95% CI: 0.02–0.53] (Biressaw et al. 2013), and another study among 1–18 year olds in Botswana found that adherence less than 95 percent, VL failure (VL >400 copies/mL), and CD4 percentage less than 15 percent were all associated with short stature (Joel et al. 2014).
Another factor related to adherence included rural and urban residency. In one Ugandan study, adolescents had greater odds of poorer adherence among 183 rural participants compared to 1573 urban participants (aOR 2.64, 95% CI 1.28–5.43) (Nabukeera-Barungi et al. 2015). Another study from Uganda, however, found no difference by rural/urban status in terms of self-reported adherence of greater than 95 percent (91.3 percent among rural participants vs. 88.2 percent urban participants, p = 0.131) but did find that rural adolescents were significantly more likely to have pill counts of 95 percent or greater than urban adolescents (88.8 percent vs. 78.8 percent, OR 0.5, 95% CI 0.3–0.7). Adherence was also related to proximity to health care in Ethiopia (Arage et al. 2014), and in Tanzania (Nsheha et al. 2014) with non-adherence related to not attending the clinic regularly and having missed drug doses in the past six months. One author also found that in Uganda parents not paying for treatment and having received nutritional support were related to non-adherence, while taking co-trimoxazole medication/syrup increased the odds of adherence [OR = 3.65 (95% CI 1.24, 10.74)](Biadgilign et al. 2008).

**Interventions to improve adherence**

Few published studies provide evidence regarding effective interventions to support ART adherence specifically among adolescents in SSA. MacPherson’s 2015 review of the literature from 2001–2014 on this topic resulted in only one published article (MacPherson et al. 2015). This study piloted the “VUKA” program among 10–13 year olds living with HIV in South Africa (Bhana et al. 2014). VUKA is the adapted version of the Collaborative HIV Prevention and Adolescent Mental Health Family Program (CHAMP) that is a multi-session and family-based intervention (Bhana et al. 2010; McKay et al. 2007). The intervention consisted of six group sessions delivered over three months to 10–13 year olds living with HIV and their families. Based on self-reported missed ART over the past six months, the VUKA intervention arm participants had significantly greater improvements in their adherence scores than participants in the comparison arm (VUKA = 1.10; Control = –0.43 at baseline and follow up, p < 0.05; n = 65).

In another review by Adejumo et al. identified through the PubMed search, the authors identified six studies that described effective intervention programs to improve ART adherence (Adejumo et al. 2015). Out of these six, only three focused on adolescents, including the VUKA study described above, as well as a conference abstract presenting data on adolescent peer support groups in Uganda (Musiime et al. 2007) and a psycho-social support group intervention in Zimbabwe (Mavhu et al. 2013). The program in Uganda consisted of monthly meetings on Saturday that included health education talks, indoor and outdoor games, art, crafts and music. This program was led by counselors, nurses and doctors and involved adolescents and their caregivers. Out of the 27 percent of the participants who were identified as having poorer adherence at baseline (adherence measure not defined) all 16 achieved 95 percent or greater adherence within 3 months. The other study by Mavhu et al. (2013) found that the majority of the 229 interviewed participants attended monthly psycho-social support groups for HIV-infected adolescents in Zimbabwe and that 95 percent found the groups to be helpful. Based on the results of their formative research, the authors propose an adolescent and family-based intervention consisting of community adolescent treatment support, cognitive-behavioral therapy, and caregiver training to enhance adolescent support (Mavhu et al. 2013).
Since these review articles, two other studies have been published providing data on program effects on adolescent adherence. In Zimbabwe, data from 262 adolescents found that participants who attended professionally run support groups had greater odds of achieving excellent adherence compared with non-participants [OR 1.8, 95% CI 1.1–3.0] (Gross et al. 2015). A medical file review of 200 patients in Swaziland, however, found that enhanced adherence counseling was not significantly associated with increased odds of viral suppression (Jobanputra et al. 2015).

Transition to Self-management and Adult Care

As ALHIV transition into adulthood it is critical that they gain the skills to successfully manage their HIV and their health. This process is unique for adolescents given the stages of development they undergo and the many challenges they, their families, and health care providers face such as cognitive and developmental delays, disorganized social environments (parental illness and loss, school absences), health risk behaviors, and co-morbidities (Sawyer et al. 2007). To address these issues and to maximize resilience among adolescents, the PEPFAR/USAID guidance on the transition of care for ALHIV emphasizes several key issues: (1) for some adolescents this process includes a physical transition from a pediatric or adolescent model of care to an adult facility; (2) that many ALHIV in SSA already receive care in adult HIV clinics and while these adolescents are not changing care providers or facilities, they still need support to develop the skills to self-manage their HIV; and (3) this period of transition and concept of HIV self-management is a complex and “multifaceted, active process that attends to the medical, psychosocial, and educational or vocational needs of adolescents” (Duffy and Sharer 2014). In the PEPFAR/USAID technical brief on transitioning ALHIV they further break down the factors that self-management encompass and the support that ALHIV need into two specific categories: (1) individual growth and environmental support, and (2) clinical support (Sharer and Fullem 2012). Examples of these follow the key findings in Box 6.

**BOX 6**

**Key findings from published literature on transitioning to self-management and adult care among ALHIV in SSA**

- The transition of ALHIV refers to not only the movement from a pediatric or adolescent model to an adult model of HIV care, but also includes the development of self-management skills as ALHIV grow into adulthood and assume responsibility for their HIV care, regardless of where they receive treatment.

- While adolescent and pediatric services exist in SSA, many ALHIV already attend adult HIV care as this is the only service available to them.

- The search did not find any published data on the effectiveness of a transition model or approach among adolescents in SSA.
Individual growth and environmental support

This aspect of self-management as presented in the technical brief consists of psychosocial support (mental health, grief and bereavement), sexual and reproductive health, substance use, and future planning. In a review article of adolescents living with chronic conditions, the authors found emerging evidence that ALHIV are at least as likely, if not more likely, to engage in risk behaviors such as drinking, drug use, and having sex, as their healthy peers (Sawyer et al. 2007). Furthermore, 20 percent of women globally have had a child by age 18, a proportion that is much higher in many SSA countries (UNICEF 2013). Overall there is a growing body of literature on the sexual and reproductive health needs of ALHIV (Birungi 2011; Birungi et al. 2009a; Birungi et al. 2009b; Birungi et al. 2011; Obare and Birungi 2010; Obare, Birungi, and Kavuma 2011; Obare, van der Kwaak, and Birungi 2012) and the importance of viewing adolescent health care from a human rights perspective (Mburu et al. 2013).

Clinical support

This aspect of self-management consists of supporting adolescent self-care and their clinical management of HIV and mental health issues (Sharer and Fullem 2012). Clinical needs may vary between perinatally infected adolescents and their horizontally infected peers, with adolescents infected since birth more likely to experience greater complications, side effects, and developmental delays (Sharer and Fullem 2012). These differences may mean more perinatally infected youth are receiving second line treatment and are at greater risk for drug failure and resistance (Sharer and Fullem 2012). Co-morbidities (e.g., psychiatric illness) and emerging health challenges (e.g., cardiovascular disease risk and bone health) also need to be considered as adolescents transition into adult care (Lee and Hazra 2015). Evidence is mounting that adolescent females have worse PMTCT outcomes when compared to adults (Fatti et al. 2015; Horwood et al. 2013) and use maternal health care less frequently when pregnant (Birungi et al. 2011). A study conducted in South Africa also found that the most common reason for changing an ART regimen among older adolescents was pregnancy, something the authors point out as evidence indicating the need for contraceptive counseling and access to birth control among ALHIV (Evans et al. 2013).

Overall, an integrated approach to transitioning ALHIV to self-manage their HIV is supported by the literature specifically on ALHIV (Lee and Hazra 2015) as well as the literature on pediatric chronic illness management more broadly (Modi et al. 2012). These models and guidance also emphasize the important role that families have in supporting adolescents living with chronic conditions, including HIV (Amzel et al. 2013; Rosen et al. 2003; Sawyer et al. 2007), especially as the majority of the self-management behaviors ALHIV need to perform such as adherence, HIV status disclosure, and safe sexual behaviors, occur in their homes and communities, not in the clinic. This role of family is reflected in a definition of pediatric self-management as the “interaction of health behaviors and related processes that patients and families engage in to care for a chronic condition” (Modi et al. 2012). This role varies greatly with some caregivers actively engaging in the care and treatment of ALHIV and others shifting treatment responsibility to the ALHIV as they reach mid adolescence (Denison et al. 2015). Fears of stigma and disclosure also often isolate adults and ALHIV from sources of family and community support and the connection between adult caregivers of ALHIV and the clinic where ALHIV receive care is often weak (Denison et al. 2015). Furthermore, there is evidence that managing a chronic illness
can have a negative impact on caregivers and families, particularly in low-income and highly stigmatized environments (Thurman, Jarabi, and Rice 2012). These issues reinforce the need to “consider healthcare transition as a continuum and not separate, discrete moves from pediatric to adolescent to adult clinic settings” (Lee and Hazra 2015).

While there is an international call to support HIV self-management among adolescents (Chakraborty et al. 2013; Gilliam et al. 2011; WHO 2013), including adhering to ART, practicing safer-sex behaviors, and transitioning to adult care (Pequegnat et al. 2001; Pequegnat and Bell 2011; Pequegnat and Szapocznik 2000; Perrino et al. 2000; Thurman et al. 2012), the reality is that ALHIV in SSA often do not have access to adolescent-specific services or opportunities to build life skills (WHO 2013).

Often the only program provided in response to the needs of adolescents in SSA are elements of youth friendly services (e.g., special clinic hours) and the provision of clinic-based support groups for ALHIV. However, such group programs are often vulnerable to changes in staff and funding and are often not systematically incorporated into service provision. In the next section the data available on transitioning adolescents to adult HIV care in SSA will be examined.

**Transitioning to adult care**

Several guidelines exist on transitioning adolescents from a pediatric or adolescent model of care to an adult HIV care service (IAPAC 2015; Rosen et al. 2003; Sharer and Fullem 2012). Such guidelines often emphasize a comprehensive approach to adolescent health care that engages young people and transfers youth based on cognitive and emotional readiness rather than on age alone. Despite this guidance, there is a paucity of data on the use of these guidelines and their impact on the care continuum outcomes of transitioning ALHIV. A 2014 review article on transitioning from pediatric to adult HIV care did not find a single article based in sub-Saharan Article (Hussen et. al 2014). In the WHO testing guidelines for adolescents, data from a survey conducted among 477 youth living with HIV (10–24 years of age) from 57 countries is presented. While the majority of participants were enrolled in HIV care, only 282 were attending pediatric or adolescent HIV care facilities. This reflects the reality that many adolescents often already attend adult HIV clinics for their care. Out of those 282 in pediatric or adolescent settings, the following percentages of youth have had discussions with their provider about transitioning to adult care: 38 percent had at least one discussion, 40 percent 2–3 discussions and 22 percent more than three discussions (WHO 2013). No other data on models or outcomes related to transitioning adolescents to adult HIV care in SSA were found.

**CONCLUSION**

This paper provides a summary of key findings related to the care continuum outcomes among ALHIV in SSA. We have prepared the table below to highlight our main conclusions and implications that emerged from the literature we reviewed according to the key care continuum domains. The table also includes the number of studies found related to each of the domains.

As illustrated in Table 2, the published literature on the care continuum outcomes among ALHIV in SSA is sparse, particularly age disaggregated data on linking positive youth to care and on
### TABLE 2  Summary of published literature on the care continuum outcomes among ALHIV in SSA

<table>
<thead>
<tr>
<th>Domain</th>
<th># of studies</th>
<th>Main findings</th>
<th>Potential Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>HTC and linkages to care</td>
<td></td>
<td>• 2 systematic reviews with 16 studies on adolescents.*</td>
<td>• Evaluate different models of HTC to reach adolescents and identify ALHIV earlier in their infection.</td>
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<tr>
<td></td>
<td></td>
<td>• 3 studies (one a program report, two published) with linkage to care data.</td>
<td>• Examine ways to obtain parental or adult permission to test.</td>
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<tr>
<td></td>
<td></td>
<td>• Home-based testing had high uptake among adolescents even when adult permission was required.</td>
<td>• Identify linkage mechanisms for different HTC strategies given WHO new guidelines on ART initiation.</td>
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<td></td>
<td></td>
<td>• PITC yielded the largest proportion of ALHIV.</td>
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<td></td>
<td></td>
<td>• None of the HTC studies assessed linkages to care for adolescents who tested positive.</td>
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<td></td>
<td></td>
<td>• Significant percentage of adolescents who tested positive do not enroll in HIV care.</td>
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<tr>
<td>Retention</td>
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<td>• 1 systematic review.</td>
<td>• Disaggregate data by age to assess retention among ALHIV in country programs.</td>
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<tr>
<td></td>
<td></td>
<td>• 9 additional studies identified through PubMed and a literature review.</td>
<td>• Rigorously test different models of care in improving retention among ALHIV.</td>
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<tr>
<td></td>
<td></td>
<td>• Older ALHIV (15–19) appear to have poorer retention rates compared to younger ALHIV (10–14) both before and after ART initiation.</td>
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<td></td>
<td></td>
<td>• One study found less attrition with ART refills at community drug distribution points vs. health facilities.</td>
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<td></td>
<td></td>
<td>• Other studies that combined ALHIV with young adults produced mixed findings on the relationship between youth-friendly services and retention in care.</td>
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<tr>
<td>Adherence</td>
<td></td>
<td>• 5 systematic reviews, data from 20 unique studies.</td>
<td>• Conduct intervention studies to assess program impact on adherence among ALHIV.</td>
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<tr>
<td></td>
<td></td>
<td>• 16 additional studies identified through PubMed and the grey literature.</td>
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<td></td>
<td></td>
<td>• Adherence estimates range from 16–94 percent</td>
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<td>• Adherence studies often combine ALHIV with children and/or young adults.</td>
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<td>• ALHIV adhere less than young adults in the few studies that disaggregated the data.</td>
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<td>• Few studies examined factors related to adherence, with preliminary data showing a positive relationship with group sessions.</td>
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<td>Transition to self-management and adult care</td>
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<td>• 1 systematic review</td>
<td>• Identify and test different models of care to support HIV self-management among older adolescents</td>
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<td>• 0 additional studies identified through PubMed and the grey literature</td>
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<td>• Many ALHIV already attend adult HIV care</td>
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<td>• HIV self-management includes retention and adherence as well as other issues such as sexual behavior and self-disclosure</td>
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transitioning adolescents to self-care and adult HIV clinics. This paucity of data on ALHIV in SSA is often attributed in part to donor driven reporting requirements that in the past often defined children as 0–14 years of age and adults as 15 years of age and older (Mburu et al. 2013). In addition to this general lack of data on ALHIV in SSA, there is even less evidence on the program approaches that support ALHIV and their families as they cope with retention to care, adhering to ART, and transitioning into adulthood and self-management.

Some limitations to this review must be noted. The focus of the literature search was on quantitative data and qualitative studies were not systematically assessed. We also did not grade the quality of the studies included in this paper, nor did we systematically review the grey literature.

Despite these limitations the data are clear that disaggregating data by age and gender can provide powerful and useful insight in the status of and issues confronting adolescents as they transition through different developmental stages to become adults. Such disaggregation also highlights the disparities adolescents experience in comparison to adults in remaining in HIV care and adhering to ART. This information provides a critical foundation for developing a research agenda that will strengthen our response to and engagement of ALHIV in SSA to improve their HIV continuum of care outcomes.
Appendix 2
Meeting Agenda

Project SOAR Technical Advisory Network (TAN) Meeting:
Developing an Implementation Science Research Agenda to
Improve the Treatment and Care Outcomes among
Adolescents Living with HIV in sub-Saharan Africa

18–19 February 2016
Carlyle Hotel, 1731 New Hampshire Ave, NW, Washington, DC 20009

Objectives
• Take stock of the current state of knowledge of the HIV care continuum among adolescents living
  with HIV in sub-Saharan Africa.
• Identify priority implementation science research questions that if answered, will contribute to
  improving HIV care continuum outcomes among adolescents living with HIV.
• Identify potential study designs and platforms to build upon in answering the priority research
  questions.

Day 1

8:00–8:30  Registration and Breakfast (Taylor Room)

8:30–8:45  Welcome and introductions (Taylor Room)
           Julie Pulerwitz, Population Council/Project SOAR
           Anouk Amzel, United States Agency for International Development

8:45–9:30  Setting the stage: Youth panel (Taylor Room)
           Rebecca Marcus, Desmond Tutu HIV Centre, South Africa (facilitator)

9:30–10:15 A review of the evidence: what do we know about the continuum of care among
           ALHIV in sub-Saharan Africa? (Taylor Room)
           Julie Denison, Johns Hopkins University, Bloomberg School of Public Health/SOAR

10:15–10:30 Break (Taylor Room)
10:30–11:45  **Expert panel on key challenges and needs of ALHIV** (Taylor Room)
Lynne Mofenson, Elizabeth Glaser Pediatric AIDS Foundation/SOAR, USA (facilitator)
Audrey Pettifor, University of North Carolina at Chapel Hill, USA
Rebecca Marcus, Desmond Tutu HIV Centre, South Africa
Stephen Okoboi, The AIDS Support Organization (TASO), Uganda
Harriet Birungi, Population Council, Kenya
Susan Kasedde, UNICEF, USA

11:45–12:15  **Initial brainstorming of research gaps and ongoing research** (Taylor Room)
Julie Denison

12:15–1:15  **Lunch** (Taylor Room)

1:15–3:00  **Working groups: Identify research questions**
Identifying adolescents living with HIV (HIV testing) and linkages to care: Audrey Pettifor (Taylor Room)
Retention in HIV care: Stephen Okoboi (Taylor Room)
ART adherence, viral suppression, treatment as prevention: Rebecca Marcus (Ellington Room)
Transition to self-management of HIV (including transitioning from pediatric to adult care, acquiring self-disclosure skills, and addressing reproductive and maternal health needs): Harriet Birungi (Horn Room)

3:00–3:15  **Break** (Taylor Room)

3:15–4:30  **Working groups: Select six priority research questions and potential study designs and platforms** (Assigned rooms)

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**Day 2**

8:00–8:30  **Breakfast** (Taylor Room)

8:30–10:00  **Working groups: Discuss study designs and platforms and finalize presentations** (Assigned rooms)

10:00–10:15  **Break** (Taylor Room)

10:15–12:15  **Full group: Working groups present priority research questions to all meeting participants** (Taylor Room)
15 mins of presentation and 10 mins of discussion per group

12:15–1:15  **Lunch** (Taylor Room)

1:15–1:45  **Full group exercise: Select priority research questions** (Taylor Room)
Sara Bowsky, Palladium/SOAR
1:45–2:15  **Feedback on process: Youth perspectives on top priorities** (Taylor Room)

2:15–2:45  **Wrap up/reactions** (Taylor Room)
Scott Geibel, Population Council/SOAR
Elizabeth Berard, United States Agency for International Development

2:45  **Adjourn**
Appendix 3
Participant List

Project SOAR Technical Advisory Network Meeting:
Developing an Implementation Science Research Agenda to
Improve the Treatment and Care Outcomes among
Adolescents Living with HIV in Sub-Saharan Africa

18–19 February 2016
Carlyle Hotel, 1731 New Hampshire Ave NW, Washington, DC 20009

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Appendix 4
Prevention of Mother-to-child Transmission of HIV among ALHIV

USAID requested an additional review be added to this document to examine the published evidence regarding the prevention of mother-to-child transmission (PMTCT) of HIV among adolescents living with HIV. This topic is touched upon in the transition to adult care section in the complete literature review in Appendix 1, but in this section we present a more comprehensive review of PMTCT among adolescents in sub-Saharan Africa.

METHODS

We conducted a review of the published literature by searching PubMed using terms such as HIV, adolescent, Africa and prevention of mother-to-child transmission. Abstracts were reviewed and articles pulled to assess if they met the eligibility criteria including having data on PMTCT outcome and the study sample was from SSA and had a mean or median age between ages 10 and 19 years. The grey literature was not systematically searched. The results of this process are shown in the flow chart on the next page (Figure 1).

RESULTS

As noted above in the transitioning to adult care section, evidence is mounting that adolescent females have worse PMTCT outcomes when compared to adults (Fatti et al. 2015; Horwood et al. 2013) and use maternal health care less frequently when pregnant (Birungi et al. 2011). A 2013 systematic review of the barriers and facilitators of PMTCT in sub-Saharan Africa identified 20 quantitative and 8 mixed-methods studies (Gourlay et al. 2013). Out of these studies, only two provided data on adolescents 10–19 specifically. A study among women attending ANC services in Moshi Tanzania found no difference in an adjusted odds ratio between age groups (14–19 year olds, 20–24 year olds and 25 years and older) in terms of having a male partner attend the ANC service for HIV testing (Msuya et al. 2008).

The other study was a multi-country study that examined the cord blood of 27,893 women who had given birth for HIV antibodies, and for those found positive, the presence of nevirapine (Stringer et al. 2010). Study samples were from Cameroon, Cote d’Ivoire, South Africa and Zambia. While the median age of participants was 27 years (IQR 23–21) the authors assessed differences in nevirapine coverage comparing mothers younger than 20 vs. adult women older than 30 years of age (age range not provided). This analysis found that the teen mothers (aOR 1.44; 95% CI, 1.18–1.76) and mothers 20–24 years of age (aOR 1.28; 95% CI 1.07–1.54) were
both significantly more likely to experience failed coverage (not provided nevirapine), while there was no difference in nevirapine coverage between the 26–30 year olds and those older than 30. When provided with nevirapine, there was no difference between mothers younger than 20 compared to those older than 30 in terms of non-adherence to the medication (aOR 1.24; 95% CI 0.83–1.84).

The remaining published studies were found through the PubMed search and by reviewing the references of eligible articles. A cohort study among HIV-positive pregnant women in South Africa followed 312 young women (up to age 24 years) of whom 65 were adolescents aged 19 years or less (Fatti et al. 2015). This multivariable analysis found that adolescents, compared to adult women age 25 and older, were at greater risk of being unaware of their status, not receiving lifelong ART by time of delivery and to experience maternal mortality, although the results from this model should be considered with caution as several variables had perfect 95% confidence intervals (Fatti et al. 2015). Another study among 9,803 mothers, including adolescent mothers under 20 years of age, found that the adolescent mothers were more likely to be unaware of their status (aOR 2.2, 95% CI 1.5–3.3), and to have dropped out at CD4 count testing or not receive result (aOR 1.7, 95% CI 1.1–2.7) than mothers over 20 years of age (Woldesenbet et. al 2015).

In another study, 1,059 HIV-positive adolescents in Kenya participated in a quantitative interview, of whom 393 had ever been pregnant for a total of 506 pregnancies (Birungi et al. 2011).
Adolescents accessed prenatal care during 84 percent of the 506 pregnancies, but only accessed PMTCT services during 67 percent of the pregnancies. Overall, less than half of these 393 female adolescents attended four or more prenatal care visits (45 percent). Those who attended 4 or more prenatal care visits, however, compared to their peers who had not, were 6.5 times more likely to access PMTCT services (95% CI 2.8–15.3), 4.7 times more likely to have a skilled attendant at birth or during an induced or spontaneous abortion (95% CI 2.4–9.0), and 5.1 times more likely to receive post abortion/postnatal care (95% CI 2.8–15.3). Overall, adolescents whose husbands were responsible for the pregnancy were also more likely to access PMTCT services compared to adolescents impregnated by someone other than a husband (OR 4.9, 95% CI 1.8–13.1).

In South Africa, 18,363 mothers attending well-child clinics with children six years of age or younger participated in a cross-sectional survey (Horwood et al. 2013). Out of these mothers, 6,467 self-reported living with HIV - 687 adolescents 12–19 years of age and 5,780 adults age 20–39. Among these HIV-positive mothers, more adults compared to adolescent mothers have had a CD4 cell count test during pregnancy (81 percent vs.66.5 percent, p < 0.0001), received their results (84.4 percent vs. 75.4 percent, p < 0.0001) and had CD4 cell counts <200 (24.5 percent vs. 10.6 percent, p < 0.0001). Both adult and adolescent mothers received ART prophylaxis (96.2 percent vs. 94.9 percent), however, adolescent mothers were less likely to receive ART for their own health compared to adult mothers (3.6 percent vs. 14.7 percent, p < 0.0001), and were less likely to receive the full recommended PMTCT regimen (76.7 percent vs. 81.2 percent, p = 0.007). After birth the adolescent mothers were more likely than their adult counterparts to exclusively breastfeed (58.9 percent vs 50 percent p < 0.0001) and to have a higher proportion of infected infants (10.8 percent vs. 6.6 percent, OR 1.7, 95% CI 1.2–2.4). This greater odds in having an HIV infected infant, however, disappeared after controlling for whether or not a mother received a recommended ART regimen compared to an ineffective regimen. The authors comment that this finding highlights poor access to service, rather than biological factors, as an underlying cause in HIV transmission among adolescent mothers and their infants, echoing findings found in Stringer et al. 2003 presented above.

The last study found that presented data specifically on adolescents living with HIV was a community cohort study conducted in Kisesa, Tanzania (Gourlay et al. 2015). This study assessed if women of reproductive age and living with HIV accessed PMTCT or HIV care either before or during their pregnancy, and if they accessed ART during pregnancy. Out of 9,692 women of childbearing age in Kisesa who had an HIV test as part of the study survey, 420 were HIV positive and pregnant resulting in 756 pregnancies. Of these pregnancies, 4.8 percent occurred among 15–19 year old females (n = 36 pregnancies). None of these adolescent mothers, however had enrolled in HIV care or accessed ART (Gourlay et al. 2015).

The remaining study provides PMTCT related information on adolescents in general. A cross-sectional study among 225 pregnant women attending ANC in a primary health care center for the first time examined PMTCT behaviors in Nigeria by asking “have you ever presented in any PMTCT center before” and defining utilization as “attendance in any PMTCT service provider center including voluntary counseling and testing (VCT) prior to presentation for ANC at the PHC center” (page 3, Amoran, Salami, and Oluwole 2012). This study found that adolescents in general (not segregated by HIV status) were less likely to have utilized PMTCT services compared
to older pregnant women (unadjusted OR 0.34, 95% CI 0.1–1.00). This study did not define the specific ages encompassed by the terms adolescent and older pregnant women.

CONCLUSIONS

The data on PMTCT utilization and outcomes among ALHIV is sparse. As the number of adolescents living with HIV continues to grow, it is critical to examine reproductive health access and behaviors in order to fully support ALHIV’s transition into adulthood. The data available, however, shows a clear gap in reaching adolescent pregnant mothers with PMTCT services. A few studies even indicate that when an adolescent mother has access to recommended PMTCT ART regimens, their outcomes do not differ significantly from older women (Horwood et al. 2013; Stringer et al. 2010). These findings highlight the importance of making PMTCT services accessible for female adolescents and their partners. In addition, none of the studies presented above provided evidence regarding intervention strategies for engaging ALHIV in PMTCT. Currently a systematic review/meta-analysis is underway to examine interventions to improved PMTCT uptake and retention of HIV-infected pregnant and breastfeeding women and their infants (Ritchie et al. 2015). Such reviews, if they are able to find data on adolescents and to examine the findings disaggregated by age, may be coupled with our experiences to date with reproductive health programs among adolescents in general, to inform a research and program agenda to improve PMTCT access and outcomes among ALHIV.
References


Developing an IS research agenda to improve the treatment and care outcomes among ALHIV in SSA ■ A-35


Developing an IS research agenda to improve the treatment and care outcomes among ALHIV in SSA


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