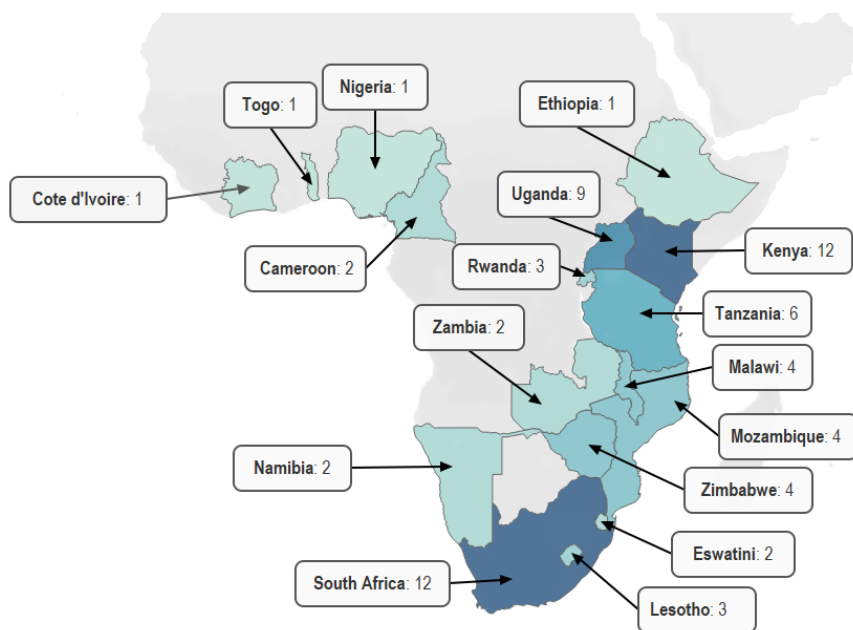


Overview: Literature review of linkage, adherence, and retention interventions for seropositive children and young people in Africa

In the era of the UNAIDS 95-95-95 goals, HIV testing, engagement in HIV care, and viral suppression, achieved through proper adherence to antiretroviral treatment (ART), are crucial steps toward controlling the HIV epidemic. Considerable work has already been conducted on HIV testing and related interventions to identify HIV-positive infants (<1 year); children (1–9 years); adolescents (10–19 years); and youth (20–24 years). However, these children and young people living with HIV are less likely to be linked to care and adherent to ART, compared to adults.¹ Furthermore, there has been less focus, to date, on adolescents in the development, implementation, and evaluation of interventions to facilitate ART delivery, retention in care, and adherence to treatment.

Nevertheless, various strategies have been implemented in countries around the world to reduce barriers to engagement in care and adherence to ART among these vulnerable communities, and to support young people living with HIV to achieve viral suppression. Strategies to engage people living with HIV in care and to improve ART adherence can be categorized as: 1) individual-level interventions, such as information and communication technology-enhanced solutions or education and counselling; 2) group-level interventions, such as community support groups; and 3) policy or systems interventions, such as changes to healthcare delivery models.

Despite these diverse programmatic strategies, a comprehensive understanding of what works best for children and adolescents in sub-Saharan Africa is lacking. To address this gap, Project SOAR conducted a systematic review of the peer-reviewed literature to: 1) document interventions that support engagement in care and ART adherence for infants, children, adolescents, and youth living with HIV in sub-Saharan Africa (SSA), including orphans and other vulnerable children; and 2) inform future policy decisions.



Number of interventions by country, sub-Saharan Africa

METHODS

We conducted a comprehensive literature search of online databases to identify relevant articles published from 2010 through 2018. The search included keywords focusing on terms used to describe orphaned and vulnerable populations living with HIV in sub-Saharan African nations.

We developed eligibility criteria with respect to the population, outcomes of interest, and publication type. Studies were eligible for inclusion if they presented an intervention to improve linkage to care, retention, adherence to ART or viral suppression among individuals who were under the age of 18 and living with HIV in sub-Saharan Africa. Using these criteria, the research team independently screened titles and abstracts for inclusion.


RESULTS

We identified a total of 5,012 unique articles through database searching. Of those, we excluded 4,943 articles during the screening phases, leaving 69


articles that met all eligibility criteria for inclusion. Of those, 25 studies reported ART initiation as an outcome, 36 reported on retention in HIV care and/or ART adherence as an outcome, and 12 reported on viral suppression as an outcome. In cases where study populations included those under as well as over age 18, we included findings pertaining to these older participants (i.e., youth up to age 24).

Table 1 (on page 4) provides a summary of experimental studies included in the systematic review. An Excel spreadsheet summarizing all studies included in the systematic review can be found on the Project SOAR website at: https://projsoar.org/wp-content/uploads/2021/01/ChldrnYngPpl_LinkageRetention_LitReviewMatrix.xlsx

ART initiation as an outcome

 **Total number of included studies:** 25

 **Populations targeted:** infants (12); children (15); adolescents (14); and youth (6)

 **Study designs:** non-experimental and no comparison group (20); non-experimental with a comparison group (3); and experimental (2)


 **Effectiveness:**

- Diagnostic testing interventions for infants, such as point-of-care PCR testing and electronic patient monitoring systems, were effective at shortening the time until diagnosis, and increasing the number of patients who both received results and, when appropriate, initiated ART.²⁻⁶
- Task-shifting from clinical officers to nurses as a standalone intervention was not effective at improving ART initiation rates.⁷
- Comprehensive service delivery models that reduced client visits, improved family-centered care, offered multi-disease services, and home-based follow-up were effective at increasing ART initiation among children.⁸⁻¹¹

Retention/adherence as an outcome

 **Total number of included studies:** 36

 **Populations targeted:** infants (11); children (23); adolescents (28); and youth (11)

 **Study designs:** non-experimental and no comparison group (21); non-experimental with a comparison group (9); and experimental (6)

 **Effectiveness:**

- There was mixed evidence for the impact of education and counseling intervention models on retention in care and adherence among children and adolescents.¹²⁻¹⁴
- Case management models showed efficacy for care retention among adolescents in one quasi-experimental evaluation,¹⁵ and weaker evidence of efficacy in a study with a more rigorous randomized controlled trial (RCT).¹⁶
- There was good support for the effectiveness of phone-based outreach interventions to promote care retention among children and adolescents.^{17,18}
- Electronic infant tracking system in Kenya¹⁹ and point-of-care PCR HIV testing for newborns were also effective at improving retention when evaluated in an RCT.³
- Decentralization or down-referral models improved retention outcomes among children and adolescents in multiple countries.²⁰⁻²²
- There was mixed evidence from clinic-level interventions for improving retention and adherence outcomes. The majority of these interventions involved differentiated care models, with a focus on either family- or youth-friendly services, and most interventions indicated differentiated care was effective for either retention in care or adherence.^{1,9,23-29}

Viral suppression as an outcome



Total number of included studies: 12



Populations targeted: infants (2); children (9); adolescents (12); and youth (3)



Study designs: non-experimental and no comparison group (5); non-experimental with a comparison group (5); and experimental (2)



Effectiveness:

- Three studies documented significant reductions^{16,30,31} and one study found no difference in viral load³² through case management approaches using a mix of experimental and non-experimental designs among children, adolescents, and youth.
- The use of an illustrated book led to improved disclosure and viral suppression³³ while a medication diary led to no change in viral suppression among a small sample of infants, children, and adolescents.³⁴
- An economic empowerment intervention was evaluated with a cluster RCT that led to 10 times greater viral suppression among adolescents in the intervention group compared to the control group.³⁵
- In an adolescent-friendly clinic, researchers observed improved viral load suppression among adolescents and youth after more than five years of follow-up.¹
- In a transition to universal test and treat, children were less likely to be virally suppressed after six months of follow-up.³⁶

CONCLUSIONS

This review identified a variety of effective strategies for improving engagement in HIV and ART adherence among children, adolescents, and youth living with HIV in sub-Saharan Africa. Approaches included phone-based reminder and tracing programs, group education and peer support, and expedited care delivery. Given this broad menu of options, the most appropriate strategy for any given context will likely need to be tailored to ensure it fits the specific objectives and target audience. Furthermore, to foster progress in generating evidence for future interventions, more rigorous study designs should be employed.

Table 1 Experimental study summary (n=7)

Study	Intervention	Effect size	Conclusion/recommendations
Bermudez et al., 2018	Suubi+Adherence: A savings-led economic empowerment intervention on viral suppression for adolescents (10–16 years)	Proportion of virally suppressed participants in the intervention cohort increased tenfold ($\Delta T_2 - T_0 = +10.0$, $p=0.001$) relative to the control group ($\Delta T_2 - T_0 = +1.1$, $p=0.733$).	Interventions addressing economic insecurity have the potential to bolster health outcomes, such as HIV viral suppression, by improving ART adherence among vulnerable adolescents living in low resource environments.
Bigna et al., 2013, 2014	Mobile phone appt. reminders for infants, children and adolescents (0–15 years)	Appointment attendance (retention in care): OR 7.5 (95% CI 2.9–19.0; $p<0.0001$) for call+SMS; OR 5.5 (2.3–13.1; $p=0.0002$) for call; OR 2.9 for SMS (1.3–6.3; $p=0.012$)	The most effective method of appointment reminder was a text message followed by a phone call, but a text message alone was the most cost-effective method though the use of text messaging alone significantly improved attendance at the appointment compared with control.
Ferrand et al., 2017	ZENITH: Decentralized primary healthcare clinic-based HIV care plus structured support home visits for caregivers by trained community health workers targeting children and adolescents (6–15 years)	Retention in care: aOR 0.92 (95% CI 0.49–1.74; $p=0.79$) Self-reported nonadherence: aOR 0.75 (95% CI 0.24–2.35; $p=0.62$) Viral suppression: aOR 0.46 (95% CI 0.23–0.89; $p=0.02$)	The case management intervention improved viral suppression in children and adolescents, however, a substantial proportion in the intervention group still had poor outcomes leading the authors to conclude that it is unlikely that one intervention will suffice to achieve optimum outcomes. To scale up community-based interventions, careful attention needs to be paid to training and mentoring community workers, addressing contextual issues, and monitoring for quality assurance.
Finocchiaro-Kessler et al., 2018	HIV Infant Tracking System (HITSsystem): a web-based intervention linking providers, laboratory technicians, and mothers and infants for quality improvement of early infant diagnosis (EID)	ART initiation: 100% of 21 HIV-positive infants at intervention sites initiated ART (73% of 11 HIV-positive infants at control sites) Retention in care: aOR 3.7 (95% CI 2.5–5.5; $p<0.0001$)	Implementation of the HITSsystem was associated with more than a two-fold increase in both EID retention and initiation of ART among infants living with HIV compared to historical controls. The HITSsystem's integration of customized alerts (Internet and SMS-based) with dedicated prospective tracking proved to be feasible and effective in both settings (urban, peri-urban) and in both types of hospitals (large maternity and district).
Graves et al., 2018	Family Clinic Day (FCD) differentiated care model including: patient scheduling, health education, patient flow prioritizing children, and their families for care over other patients (19 months to 19 years)	Retention in care (at least 1 appt in the last 3 months of study): aOR 1.11; (90% CI 0.63–1.97; $p=0.75$) Adherence to last appointment with sufficient ARV: aOR 1.64 (90% CI 1.27–2.11; $p<0.001$)	The FCD did not improve retention but was associated with improved adherence to last appointment scheduled. Patient health outcomes may benefit following an increase in knowledge as a result of health education, and peer support. Broad challenges facing ART clinics, such as under-staffing and poor filing systems, should be addressed in order to improve patient care.
Jani et al., 2018	Point-of-care (POC) early infant HIV testing	ART initiation: aRR 7.34, (95% CI 4.7–11.5; $p<0.001$) Retention in care: aRR 1.40 ($p<0.027$)	POC infant HIV testing enabled clinics to more rapidly diagnose and provide treatment to HIV-infected infants. This reduced opportunities for pretreatment loss to follow-up and enabled a larger proportion of infants to receive test results and initiate antiretroviral therapy. The benefits of faster HIV diagnosis and antiretroviral treatment may also improve early retention in care.
Linnemayr et al., 2017	SMS reminder messages on antiretroviral and cotrimoxazole prophylaxis adherence targeting adolescents and youth (15–22 years)	Adherence 67% in control group, 64% in SMS only, 61% in message + response option; $p=0.35$.	SMS reminder messages did not have an effect on multiple measures adherence to ART. Simple reminder messages may not be enough to capture the attention of recipients, and considering other functions of SMS messages such as communicating adherence feedback, sending small incentives, or integration into a more involved mHealth approach may lead to more fruitful future interventions.

aOR adjusted odds ratio; aRR adjusted risk ratio; CI confidence intervals; OR odds ratio

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