



The Ethiopian Public Health Institute



Predictors and Effective Improvement Strategies of Antiretroviral Therapy (ART) Outcomes: **Rapid Evidence Review**

Foreword

Around 39 million people have died of HIV/AIDS globally over the past few decades. It has been a headache for many families, children, and the economy and health system. The incidence has declined over time; however, it is still significant public health concern.

The world has committed to achieve the 2020 joint UNAIDS program for the last six years. Sub-Saharan Africa carries the highest burden of 71% of the global total. In Ethiopia an estimated 691,362 people were living in 2019. The government of Ethiopia has been working with many collaborators and stakeholders in improving disease detection, viral load testing and adherence on antiretroviral therapy.

The national HIV policies and plans has been updated over the years including; treatment of all children regardless of age, treatment of all adults regardless of CD4 count, implementation of national policy on viral load monitoring .

This report will provide key information on people living with HIV and their status, their ART prevalence, and viral load status. It will generate reliable data for planning and monitoring, evidence based decision, to understand the gaps and challenges faced.

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Acronyms

AIDS	Acquired immunodeficiency syndrome
ART	Antiretroviral therapy
DHS	Demographic and Health Surveys
DHIS	District Health Information Software
EPHI	Ethiopian public health Institute
FHPCO	Federal HIV AIDS Prevention and Control Office
FMoH	Federal ministry of health(Ethiopia)
HIV	Human immune virus
PLHIV	People living with HIV
WHO	World Health Organizations
UNAIDS	United Nations Programme on HIV and AIDS

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What can research evidence tell us about:

Predictors and effective improvement strategies of Antiretroviral therapy(ART) outcomes: **Rapid Evidence Review**

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Key finding

Evidence on effective interventions to improve ART treatment outcomes were mainly targeted on increasing treatment adherence and access to ART service.

Different interventions (Mobile text messaging, behavioral intervention, education, treatment supporters and adherence counseling to increase adherence and task shifting and decentralization to increase access)show improvement in these manner but contextualization to a specific context is vital.

Summary of the review

- Findings from systematic reviews done in Ethiopia indicate sub-optimal adherence to ART, advanced WHO clinical stages, co-infection, CD4 count and HIV-RNA viral load at baseline are some of the determinant factors influence ART treatment outcome.
- Effective strategies or interventions to mitigate the barriers to ART treatment outcome were generally focused on increasing adherence to ART and access to the service.
- Mobile text messaging, behavioral intervention, education, treatment supporters and adherence counseling were some of the intervention associated with improved outcome
- Task shifting (from doctors to not-doctors) and decentralization of service delivery were found to be effective strategies to increase access to ART services.
- Different interventions designed to enhance adherence to ART show improvement but all required contextualizing to the specific setting.

What is Rapid evidence Review?

Rapid evidence review addresses the needs of policymakers and managers for research evidence that has been appraised and contextualized to a specific context in a matter of hours or days. This rapid evidence review goes beyond research evidence and integrates multiple types and levels of evidence

Where did this Rapid Evidence Review come from?

This document was created in response to the request from TB/HIV Reseach Directorate of EPHI to synthesize the the best available evidence related to the predictors of antiretroviral therapy (ART) outcomes and the effective strategies to mitigate the barriers. It was prepared by the Knowledge Translation Directorate and TB/HIV Research Directorate, Ethiopian Public Health Institute.

+ Included:

- **Key findings** from high quality researchs

✗ Not included:

- Recommendations
- Detailed descriptions



Background

Development of highly active antiretroviral therapy (ART) in the mid-1990s revolutionized the care of HIV-infected patients and led to marked reductions in HIV associated morbidity and mortality (WHO, 2016a). Even though ART is not a curative medicine, access to ART has played a vital role in the clinical management of HIV infected individuals through re-establishing the immune function and preventing morbidity and mortality. It has also prolonged the average life expectancy of HIV-infected individuals (UNAIDS, 2019b). The UNAIDS 2019 report indicated, AIDS-related deaths have been declined by more than 56% since the peak in 2004 and by more than 33% since 2010. The global decline in deaths has largely been driven by progress in eastern and southern Africa, which is home to 54% of the world's people living with HIV (UNAIDS, 2019b).

The 2013 WHO ARV guidelines recommended initiating ART for all adults with HIV and a CD4 count at or below 500 cells/mm³, regardless of WHO clinical stage, giving priority to those with severe or advanced HIV disease (WHO clinical stage 3 or 4) or a CD4 cell count at or below 350 cells/mm³ (WHO, 2013, 2016b). As of end of June 2019, 24.5 million people were accessing antiretroviral therapy. According to the report, 62% of all people living with HIV were accessing treatment in 2018 (UNAIDS, 2019a).

Ethiopia is one of the low-income countries experiencing high communicable disease burden, including HIV/AIDS (Roser, 2018). Access to highly active antiretroviral therapy (HAART) in Ethiopia started in 2005, and reached 448,500 people from 690,000 people living with HIV/AIDS by 2018 ART (UNAIDS, 2019b). Even though many HIV-positive clients have accessed to ART, first or second-line treatment failure, which could be due

How this Rapid Evidence Review was prepared?

The methods used to prepare in this rapid evidence review were adapted from the SURE Rapid Response Service.

In this review, we have searched for relevant evidence related to - predictors of anti-retrovirus therapy (ART) outcomes and effective strategies to mitigate the barriers.

The evidence in this summary comes from systematic reviews and guidelines.

It was prepared based on structured searches of the literature and selected evidence-based healthcare databases (SUPPORT Summaries, PDQ-Evidence, Epistemonikos, Health systems evidence, Medline, Cochrane Library, and JBI database for systematic reviews).

to clinical, immunologic or virology failure, continues to grow in resource limited countries like Ethiopia calling for solution strategies (MoH, 2013; Oosterhout et al., 2009; Pujades-Rodríguez M et al., 2010).

This rapid evidence review, therefore, focused on summarizing the best available evidence regarding:

1. The determinant factors that affect antiretroviral treatment outcomes (clinical, immunological, or virological) in Ethiopia using local evidence, and
2. Effective strategies or interventions to mitigate the barriers that hinder treatment success from global evidence with the similar settings.

Review findings

We searched for relevant support summaries and systematic reviews from national and global evidence with similar settings to summarize the findings in our review. For similar systematic reviews (with the same PICO), the methodological quality of the systematic reviews were assessed using AMSTAR and we included only one systematic review with highest AMSTAR score. Based on our search, we found highly relevant systematic reviews that provide evidence on the above-mentioned two concerns. The summary of the findings from these systematic reviews are presented below based on the search results on the two specific concerns mentioned.

1. Determinant factors that affect antiretroviral treatment outcomes in Ethiopia

We found two systematic reviews dealing with first-line and second-line treatment failures (Assemie et al., 2019; Edessa et al., 2019). According to Assemie *et al*, treatment failure, among first-line ART users in Ethiopia was significant. Adherence, co-infection, advanced WHO clinical stage, regimen change, and disclosure were the determinant factors for treatment failure (Assemie et al., 2019).

More over, the systematic review by Edessa and his colleagues showed that common failure rates occurred at a 12–18 month period of follow-up after second-line therapy start in Sub-Saharan Africa including Ethiopia. According to this systematic review, suboptimal adherence to second-line ART, higher HIV-RNA viral load at baseline, lower peak values for CD4 cells, and advanced WHO clinical stages were the key factors that have accelerated second-line HIV treatment failure in the setting. In addition, prolonged delays in switching prior therapy, tuberculosis co-treatment, and other patient factors including younger age, depressive symptoms, underweight, and traditional medicine use were linked with the occurrence of second-line treatment failure (Edessa et al., 2019).

2. Effective strategies or interventions to mitigate the barriers that hinder treatment success

We found support summaries and relevant systematic reviews that summarise effectiveness of different strategies or interventions to improve ART treatment outcome. The findings were further thematically classified according to their focus area of interventions. The summary of the findings from the most relevant documents are presented below in table 1.

Table 1: Key findings from best available evidence related effective interventions or strategies to enhance antiretroviral treatment outcomes

Type of document	Focus Area/Area of intervention, and setting	Key findings	Authors Conclusion
Interventions that improve adherence to ART			
SUPPORT Summary (Gagnon, 2017)	Effectiveness of text message on ART adherence Setting (Kenya and Cameroon)	<ul style="list-style-type: none"> ▪ Mobile phone text messages compared to standard care improves adherence to ART for up to 12 months. ▪ Weekly text messages probably improve adherence compared to daily text messages and interactive text messages probably improve adherence compared to non-interactive text messages. ▪ Motivational content and the length of the text messages may lead to little or no difference in adherence. 	<ul style="list-style-type: none"> ▪ The authors conclude that text messaging can support antiretroviral therapy adherence
SUPPORT Summary (Reda, 2017)	Behavioural interventions (information, interactive discussion, behavioral therapy, and reminders) Setting (Any setting)	<ul style="list-style-type: none"> ▪ Behavioral interventions probably lead to slightly better adherence to ART. 	<ul style="list-style-type: none"> ▪ Behavioral interventions probably lead to slightly better adherence to ART
A rapid systematic review (KH et al., 2014)	Evaluate ART adherence-enhancing interventions (cognitive-behavioural interventions)	<ul style="list-style-type: none"> ▪ Cognitive-behavioural interventions that includes education, treatment supporters, DOT, and active adherence reminder devices interventions can significantly increase ART adherence in some settings, but each 	<ul style="list-style-type: none"> ▪ The authors suggest consideration of effective adherence-enhancing interventions found here, to be implemented in routine programme and care settings

	Setting (Any setting)	<p>intervention has also been found not to produce significant effects in several studies.</p> <ul style="list-style-type: none"> Combination interventions tended to have effects that were similar to those of single interventions. 	by contextualizing specific intervention to a particular setting.
(Ridgeway et al., 2018)	<p>Strategies to improve adherence among adolescents living with HIV</p> <p>Setting (LMIC)</p>	<ul style="list-style-type: none"> Task shifting, community-based adherence support, mHealth platforms, and group adherence counseling emerged as strategies used in adult populations that show promise for adaptation and testing among adolescents 	<ul style="list-style-type: none"> Unlike adults, limited studies were high quality and no single intervention strategy warrant adaptation for adolescents.
Systematic review of RCT (Mbuagbaw et al., 2015)	<p>Effectiveness of interventions designed to improve adherence to antiretroviral therapy (ART)</p>	<ul style="list-style-type: none"> Adherence counselling (two studies); a once-daily regimen (compared to twice daily); text messaging; web-based cognitive behavioral intervention; face-to-face multi-session intensive behavioral interventions (two studies); contingency management; modified directly observed therapy; and nurse-delivered home visits combined with telephone calls improved adherence to ART. 	<ul style="list-style-type: none"> The authors support testing more interventions to address adherence challenges and the need to develop a gold standard (or uniform adherence measures) for adherence outcome ascertainment
Systematic review of a network meta analysis (EJ et al., 2014)	<p>Comparative effectiveness of different interventions for improving ART adherence with standard of care(SOC)</p> <p>Setting (Africa)</p>	<ul style="list-style-type: none"> There were important improvement in self-reported adherence comparing SOC with enhanced SOC, weekly SMS messages, counselling and SMS combined, and treatment supporters. Treatment supporters with enhanced SOC and weekly SMS messages were significantly better than basic SOC 	<ul style="list-style-type: none"> In conclusion, the study provides strong inferences that a standard of care that includes patient counseling on adherence, SMS messaging, and treatment supporters can improve adherence for patients residing in Africa but sustainable efforts to promote adherence will be required.

Systematic review (Rueda et al., 2006)	Effectiveness of patient support and education for promoting adherence to HAART Setting (any setting)	<ul style="list-style-type: none"> Interventions targeting practical medication management skills, those administered to individuals vs groups, and those interventions delivered over 12 weeks or more were associated with improved adherence outcomes. The study also found that interventions targeting marginalized populations were not successful at improving adherence. 	<ul style="list-style-type: none"> The authors found evidence that support the effectiveness of patient support and education interventions intended to improve adherence to ART.
Systematic review and meta-analysis of randomised trials (Ford et al., 2009)	Service delivery approach to enhance adherence (Directly observed versus self-administered ART) Setting (Any setting)	<ul style="list-style-type: none"> A pooled effect has shown no difference between the two approaches namely directly observed versus self-administered treatment for treatment adherence 	<ul style="list-style-type: none"> Directly observed antiretroviral therapy seems to offer no benefit over self-administered treatment, which calls into question the use of such an approach to support adherence in the general patient population.
Strategies to increase access to ART services			
Systematic review (ND & Chindove, 2014)	Effectiveness and cost implications of the home-based ART and mobile clinic ART models Setting (Uganda & Kenya)	<ul style="list-style-type: none"> Home-based ART is as effective as health facility-based ART The finding also indicate that health facility-based ART is the most cost-effective, followed by mobile-clinic ART, and then home-based ART. 	<ul style="list-style-type: none"> Eventhough the limited available studies suggest home-based ART can potentially be as effective as health facility-based ART, there is a need for more research before robust conclusions can be made.
Systematic review	Effectiveness of taskshifting on ART	<ul style="list-style-type: none"> Task-shifting from doctors to nurses, or from health care professionals to mid-level workers or 	<ul style="list-style-type: none"> The findings suggest that task-shifting can be

(ND et al., 2013)	provision and cost implication Setting (sub-Saharan Africa)	lay health workers showed non-inferior patient outcomes. <ul style="list-style-type: none"> Task-shifting resulted in substantial cost and physician time savings. 	potentially effective and cost-effective approach to address the human resource limitations to ART rollout.
Systematic review (JV et al., 2014)	Service delivery models (decentralization and task shifting) Setting (sub-Saharan Africa)	<ul style="list-style-type: none"> There was a strong evidence found related to the feasibility of decentralisation and task-shifting 	<ul style="list-style-type: none"> The authors concluded that decentralisation and task-shifting appear to be effective strategies to increase access to ART services.
Systematic review (Kredo et al., 2014)	Comparing service delivery models(task shifting from doctors to non doctors) Setting (Africa)	<ul style="list-style-type: none"> There were no clear difference seen across the studies, whether a doctor deliver care in the hospital or specially trained field workers (nurse or clinical officer) provide home-based maintenance care and antiretroviral therapy 	<ul style="list-style-type: none"> Substitution of nurses or community workers for doctors to initiate and maintain ART in adults in lower- and middle-income countries is feasible and probably does not compromise the quality of care provided
Systematic review (Decroo et al., 2013)	Assess models of community-based ART program Setting (sub-Saharan Africa)	<ul style="list-style-type: none"> Community ART programs made treatment more accessible and affordable. But community programs need to be driven, owned by and embedded in the communities and, An enabling and supportive environment is needed to ensure that task shifting to lay staff and PLWHA is effective and quality services are provided. 	<ul style="list-style-type: none"> Authors highlight the need for exploration of the cost, effectiveness, and sustainability of the models in different contexts. Long term vision and commitment also required from governments and international donors.
(Bain-Brickley et al., 2011)	Evaluations of interventions for	<ul style="list-style-type: none"> Homebased nursing programme showed a positive effect of the intervention on medication refills. 	<ul style="list-style-type: none"> The authors stated that home-based nursing, have the potential to improve ART

	<p>improving paediatric ART adherence.</p> <p>Setting (any setting)</p>	<ul style="list-style-type: none"> ▪ A peer support group therapy for adolescents demonstrated no change in self-reported adherence ▪ A trial found that children adherence was no different between children on a lopinavir-ritonavir (LPV/r) regimen compared to children on a non-nucleosidereverse transcriptase regimen 	<p>adherence, but more evidence is needed.</p> <ul style="list-style-type: none"> ▪ Medication diaries, peer support for adolescents and LPV/r-containing regimens do not appear to have an effect on adherence.
<p>Systematic review and meta-analysis (AB et al., 2013)</p>	<p>Effect of integrating ART into antenatal care (ANC) and maternal and child health (MCH) clinics</p> <p>Setting (LMIC)</p>	<ul style="list-style-type: none"> ▪ Increased enrolment and coverage of pregnant women in ART was observed in ANC clinics that had integrated ART. ▪ Rate of retention in ART was similar in ANC clinics with and without ART integration. 	<ul style="list-style-type: none"> ▪ Although few data were available, ART integration appears to lead to higher rates of ART enrolment and coverage. Retention in ART remain similar to those observed in referral-based models.
<p>Scoping review (Hagey et al., 2018)</p>	<p>Assessed the health, acceptability, and cost-effectiveness of differentiated HIV care models</p>	<ul style="list-style-type: none"> ▪ These approaches(HIV care modeles) had similar outcomes in viral load suppression and retention in care and were acceptable alternatives to standard HIV care. ▪ There were no clear results that can be inferred for task shifting and those reporting cost-effectiveness outcomes 	<ul style="list-style-type: none"> ▪ The authors suggest further evaluation, quality improvement and research studies to be performed as different care models are rolled out.
<p>Systematic review (Handford et al., 2017)</p>	<p>Organization of care interventions on medical, immunological, virological, psychosocial and economic outcomes</p>	<ul style="list-style-type: none"> ▪ Of the interventions examined in the review, sustained in-person case management and outreach interventions were most consistently associated with improved medical and economic outcomes, in particular antiretroviral prescribing, immunological outcomes and healthcare utilization. 	<ul style="list-style-type: none"> ▪ The authors conclude that case management interventions were most consistently associated with improvements in immunological outcomes.

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Conflicts of interest

No conflicting of interest.

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