

Test file: Effectiveness of mHealth Interventions for Antiretroviral Therapy Adherence in HIV-Positive Adults: A Systematic Review and Meta-Analysis of Randomized Trials

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Abstract

This systematic review and meta-analysis comprehensively evaluates the effectiveness of mobile health (mHealth) interventions on antiretroviral therapy (ART) adherence among HIV-positive adults. Through rigorous analysis of 38 randomized controlled trials involving 12,847 participants across 25 countries, we demonstrate that mHealth interventions significantly improve medication adherence, viral suppression, and retention in care. The most substantial benefits were observed with two-way text messaging systems that incorporated personalized feedback and medication reminders. Subgroup analyses revealed particularly strong effects among key populations including young adults, pregnant women, and individuals with documented adherence challenges. These findings provide robust evidence to guide the implementation and scale-up of mHealth strategies in diverse HIV care settings.

Keywords: mHealth; HIV; Antiretroviral Therapy; Adherence; Meta-Analysis; Digital Health Interventions; Randomized Controlled Trials

1. Introduction

The global HIV response has made remarkable progress, with antiretroviral therapy enabling millions of people living with HIV to achieve viral suppression and lead healthy lives. However, suboptimal adherence to ART remains a significant challenge, undermining treatment effectiveness and contributing to drug resistance. Current estimates indicate that only 59-83% of people living with HIV achieve adequate adherence levels necessary for sustained viral suppression. The rapid global expansion of mobile technology coverage, particularly in low- and middle-income countries bearing the highest HIV burden, has created unprecedented opportunities for innovative adherence support interventions. Mobile health technologies encompass diverse applications including short message service, interactive voice response, smartphone applications, and wireless medication monitoring devices. While previous reviews have suggested the potential benefits of mHealth for ART adherence, the evidence has been limited by methodological heterogeneity, small sample sizes, and inadequate attention to implementation context. This systematic review and meta-analysis aims to provide a comprehensive and rigorous assessment of mHealth intervention effectiveness, examining differential effects across intervention types, patient populations, and implementation settings to inform evidence-based scale-up in routine HIV care programs.

2. Methods

2.1 Search Strategy and Study Selection

We conducted a systematic literature search following PRISMA guidelines across seven electronic databases including MEDLINE, Embase, Cochrane Central Register of Controlled Trials, PsycINFO, Global Health, Web of Science, and ClinicalTrials.gov from inception through December 2023. The search strategy combined terms related to mHealth, HIV, antiretroviral therapy, and adherence. Additional studies were identified through manual searching of reference lists and conference abstracts. Included studies were randomized controlled trials evaluating mHealth interventions designed to improve ART adherence in HIV-positive adults aged 18 years or older. We excluded studies focusing solely on pre-exposure prophylaxis, those without adherence or clinical outcomes, and trials with less than 3 months follow-up.

2.2 Data Extraction and Quality Assessment

Two reviewers independently screened titles and abstracts, reviewed full-text articles, and extracted data using a standardized form. Extracted information included study characteristics, participant demographics, intervention components, comparison conditions, outcome measures, and results. The Cochrane Risk of Bias tool 2.0 was used to assess study quality across five domains. Disagreements were resolved through consensus or third-party adjudication. We also assessed publication bias using funnel plots and Egger's test, and conducted trim-and-fill analysis where indicated.

2.3 Data Synthesis and Analysis

Random-effects meta-analysis was performed to pool risk ratios for dichotomous outcomes and standardized mean differences for continuous outcomes. Primary outcomes included medication adherence (measured by pharmacy refill, electronic monitoring, or self-report), viral suppression (HIV RNA <50 copies/mL or <1000 copies/mL depending on study definition), and retention in care. Secondary outcomes included CD4 cell count changes, quality of life, and mortality. Pre-specified subgroup analyses examined intervention type, intervention duration, mode of delivery, frequency of contact, level of interactivity, target population characteristics, and geographic region. Meta-regression explored sources of heterogeneity, and sensitivity analyses assessed the robustness of findings to methodological decisions.

3. Results

3.1 Study Characteristics and Quality Assessment

Our search identified 4,832 records, of which 38 randomized controlled trials involving 12,847 participants met inclusion criteria. Studies were conducted across 25 countries, with substantial representation from sub-Saharan Africa, Asia, and North America. Intervention types included one-way text messaging, two-way interactive messaging, smartphone applications, interactive voice response, and electronic dose monitoring with feedback. Follow-up duration ranged from 3 to 24 months, with a median of 12 months. Risk of bias assessment indicated low risk for 22 studies, some concerns for 12 studies, and high risk for 4 studies, primarily due to missing outcome data and measurement of the outcome.

3.2 Primary Outcomes: Adherence and Viral Suppression

mHealth interventions significantly improved medication adherence across all measurement methods. The pooled risk ratio for achieving $\geq 95\%$ adherence was 1.32. For viral suppression, mHealth interventions increased the likelihood of achieving HIV RNA <50 copies/mL, with a pooled risk ratio of 1.28. Retention in care was also significantly improved. Subgroup analysis revealed that interventions incorporating two-way communication demonstrated larger effects

than one-way messaging systems. Personalized messages tailored to individual adherence patterns and preferences showed superior effectiveness compared to standardized content.

3.3 Secondary Outcomes and Subgroup Analyses

Modest but significant improvements were observed in CD4 cell counts and self-reported quality of life measures. Mortality outcomes showed no significant difference between intervention and control groups, though event rates were low. Subgroup analyses identified several important modifiers of intervention effectiveness. Young adults demonstrated particularly strong benefits, with effect sizes approximately 40% larger than older age groups. Pregnant and postpartum women showed significant improvements in adherence and viral suppression. Individuals with documented prior adherence challenges responded well to more intensive intervention approaches. Geographic context also influenced effectiveness, with larger effects observed in resource-limited settings compared to high-income countries.

4. Discussion

4.1 Interpretation of Key Findings

This comprehensive meta-analysis provides robust evidence that mHealth interventions effectively improve ART adherence and clinical outcomes across diverse settings and populations. The findings are particularly significant given the global challenge of sustaining lifelong ART adherence and the urgent need for scalable, cost-effective support strategies. The superior performance of interactive and personalized interventions suggests that engagement and tailoring are critical success factors. The substantial benefits observed among traditionally challenging populations highlight the potential of mHealth to address health inequities in HIV care.

4.2 Implementation Considerations and Scalability

Successful implementation requires attention to several key factors. Integration with existing healthcare systems emerges as crucial for sustainability, while maintaining data privacy and security remains paramount. The digital divide presents implementation challenges, particularly for smartphone-based interventions in low-resource settings. Cost-effectiveness considerations favor text messaging approaches in most contexts, though more sophisticated platforms may be justified for high-risk populations. Long-term sustainability requires planning for technology updates, staff training, and ongoing content refinement.

4.3 Limitations and Research Gaps

Several limitations warrant consideration. The heterogeneity in outcome measures and intervention characteristics complicates direct comparisons. Most studies had relatively short follow-up periods, limiting understanding of long-term effectiveness. Few studies examined implementation outcomes or cost-effectiveness, creating evidence gaps for policy decisions. Future research should focus on optimal intervention intensity, long-term sustainability, implementation in routine care settings, and integration with other health services.

5. Conclusion

mHealth interventions represent an effective and scalable approach to support ART adherence across diverse global settings. The evidence supports widespread implementation, particularly of interactive text messaging systems, as part of comprehensive HIV care programs. Policy makers and program managers should prioritize integration of evidence-based mHealth strategies while addressing implementation barriers related to digital infrastructure, workforce capacity, and

sustainable financing. Future innovation should focus on personalized approaches, multi-language platforms, and integration with emerging technologies to further enhance intervention effectiveness and reach.

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