HIV Treatment Adherence Interventions: A Cycle of Evolution and Change

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- I am or have been funded by the US National Institutes of Health, Bill and Melinda Gates Foundation, and USAID
- I serve as a consultant to Merck
• Scoping review of recent ART adherence interventions in Africa
• Comparison with prior interventions
• Thoughts on future work
A Cascade of Interventions to Promote Adherence to Antiretroviral Therapy in African Countries

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Background

• We wanted to summarize adherence interventions in the Treat All era with the UNAIDS 90-90-90 goal in mind.

• Adherence needs differ during uptake of ART, execution of adherence, and persistence over time that should be considered with adherence interventions.

• We conducted a scoping review of recent ART adherence interventions to understand how best to support adherence at different stages in the HIV care cascade.
Methods

• Literature reviewed from January 2014 to December 2019
• Studies excluded if not conducted in the Treat All era
• Databases: PubMed, EMBASE, Cochrane, Web of Science
• Five steps in the adherence cascade
  • PLWH who know their status and have not yet initiated ART
  • All PLWH prescribed ART
  • ART users with known sub-optimal adherence
  • ART users with stable adherence
  • PLWH initiated on treatment who later disengaged
Overview of findings

• 51 articles were identified, of which 27 were randomized controlled trials

• Most studies focused on ART initiation

• Most studies were conducted in East and Southern Africa

• Many studies involved specific patient populations
PLWH with known status but not yet on ART

General adult population
• Promising approaches
  • Home- or community-based services to identify PLWH and initiate ART
  • Point-of-care services (POC): CD4 plus counseling to facilitate care
  • Escorted transportation or reimbursement
  • Improved care within facilities (e.g., provider education, POC CD4)
  • Combination intervention strategies: modified counseling, SMS reminders, POC CD4, accelerated ART initiation, non-cash incentives, collocated services
PLWH with known status but not yet on ART

**General adult population**
- Home visits to encourage ART initiation had more modest effects
- No benefit seen with conditional economic incentives, weekly SMS, or trauma coping intervention

**Adolescents and young adults**
Peer-delivered interventions are promising
- Interlinked community- and facility components (youth-oriented)
- May be mobile phone-based
- Involving targeted counseling and health education
PLWH with known status but not yet on ART

Pregnant women and infants
• Integration of PMTCT with primary care services is promising
• Expert mothers were associated with mixed results

Female sex workers
• Mixed results were seen with community-based HIV testing, immediate ART or ART counseling
• Unclear benefit from combination prevention-treatment centers
• Peer delivery of self-HIV testing did not improve ART initiation

TB/HIV co-infection
Signal of improved entry into care with identifying PLWH in care for TB
All PLHIV prescribed ART

General adult population
• SMS reminders alone and scheduled SMS reminders (not “as needed”) in combination with real-time adherence monitoring were beneficial
• Mixed findings with unconditional cash transfers; effect may be dependent on addressing food insecurity
• Peer support groups were modestly beneficial
• No benefit from culturally appropriate images to prime adherence

Pregnant women
Effective to engage male partners in PMTCT
ART users with sub-optimal adherence

General adult population
• Promising approaches
  • Self-regulation counseling over the phone
  • Economic strengthening activity
  • Active visualization intervention

• Mixed results with enhanced adherence counseling. Improvements seen with:
  • Attention to depression, substance use and extended session duration
  • Options of reinforcement strategies (pill organizers, SMS or calls, home visits, self-help groups, limiting non-ART medications)
ART users with stable adherence

General adult population and post-partum women

• ART adherence clubs work as well as standard of care with less patient burden

• Retention higher for clinic-based clubs (versus community-based) in one study of general adults
PLWH initiated on ART, later disengaged from care

**General adult population**
- Training and supervision of expert patients and staff in best practices and telephone follow-up was marginally beneficial, especially for younger patients.
- Face-to-face tracing by a peer worker helped for select patients, but was considered inefficient.

**High risk groups**
- Small cash transfers conditional on appointment attendance were promising for PMTCT (up to 6 weeks post-partum), especially among poorest women.
- Food baskets for food insecure patients was also beneficial.
Summary

- Beneficial interventions were identified across stages of adherence
  - Community outreach and linkage to facilities
  - POC services
  - Integration of services
  - SMS reminders
  - Peer support with adolescents
  - Adherence clubs
  - Cash or food incentives with demonstrated need
  - Ongoing intensive counseling for those with viremia
  - Face-to-face tracing
Summary caveats

- Most effects were dependent on context and/or methodology
- Evidence quality ranged widely with ~half of studies using RCT designs
- Gaps in research quality
  - Lack of specificity (e.g., “counseling”)
  - No use of theory
  - No objective adherence measures
- Details of each intervention are reviewed in the paper
Ongoing and future work

Published protocols indicate much ongoing work

- Research is largely oriented in the community (e.g., with community workers, peers) and focused on high risk of virologic failure (e.g., men, youth, fisher folk)
- Other studies are targeting comorbid mental health disorders (e.g., depression)
- Community-based differentiated care delivery and expansion of adherence clubs to high-risk groups
Reflection on prior interventions

Review - Antiretroviral Adherence Interventions  Volume 11  Issue 6  November/December 2003

Review

Antiretroviral Adherence Interventions: A Review of Current Literature and Ongoing Studies

Jane M. Simoni, PhD, Pamela A. Frick, PharmD, MPH, David W. Pantalone, AB, Barbara J. Turner, MD, MSeD
Review of 2003 findings

- 21 published studies involving
  - Cognitive-behavioral therapy
  - Behavioral therapy
  - Directly observed therapy
  - Affective interventions

- Limited number of RCTs showed promise for
  - Pharmacist-led individualized intervention
  - Cognitive-behavioral educational intervention based on self-efficacy theory
  - Cue-dose training when combined with monetary reinforcement
Summary of 2003 findings

- Ongoing work at the time offered “superior methodologic sophistication” and innovation:
  - Handheld devices
  - 2-way pagers
  - Alarmed medication vials
  - Enhanced social and emotional support
Progress since 2003

- Lots of research has been done and is ongoing
- We have a more sophisticated approach to understanding the stages of adherence (i.e., what is needed when) and the differences among populations (e.g., adolescents, pregnant women)
- More recognition of the structural barriers to adherence
Lack of progress since 2003

• Still struggle with rigor in study design, including use of theory and objective measurement of adherence

• Studies are often limited in scope for a problem that requires more comprehensive solutions
Thoughts on future work

• The field is moving in the right direction in terms of recognizing the complexity and nuance of effective adherence support

• We face a challenge of relevancy in some settings where adherence is felt to be a solved problem and many settings are reaching the 90-90-90 targets

• However, even at 90-90-90, 27% of people are not suppressed and durability of suppression is a concern
Thoughts on future work

Intervention research should continue to address key areas of concern

- Populations at high risk for non-adherence
- Health systems
- New formulations (e.g., injectables) which appear promising but may come with different challenges
- Continued attention to the key role of mental health
Thank you!

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