Retention and adherence: evidence-based strategies.

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Adherence in sub-Saharan Africa

3 large reviews of the antiretroviral adherence literature to date:

• Bärnighausen, Lancet 2011
• Thompson, Annals of Internal Medicine 2012
• Chaiyachati, AIDS 2014
Approaches to managing adherence

Systematic literature review; adherence interventions only.

Any ART study with adherence outcome and a comparator group.

Sub-Saharan Africa only.

26 studies (16/26 show benefit)

Intervention categories:
- education and counselling,
- treatment supporters,
- text messages / reminder devices
- DOTs
- food supplements
- health system approaches
Approaches to managing adherence

Clinical Guidelines

Guidelines for Improving Entry Into and Retention in Care and Antiretroviral Adherence for Persons With HIV: Evidence-Based Recommendations From an International Association of Physicians in AIDS Care Panel

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Annals of Internal Medicine, 2012

Intervention categories:
- ART strategies (pill number, dosing)
- education and counselling,
- peer support,
- interactive reminder devices and
- health system / service delivery

Systematic literature review: linkage, retention and adherence.

Any study with adherence as an outcome, including a comparator arm.

325 studies; global
# Quality of the body of evidence

<table>
<thead>
<tr>
<th>Quality of Body of Evidence</th>
<th>Interpretation</th>
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<tbody>
<tr>
<td>Excellent (I)</td>
<td>RCT evidence without important limitations <strong>Overwhelming</strong> evidence from observational studies</td>
</tr>
<tr>
<td>High (II)</td>
<td>RCT evidence with important limitations <strong>Strong evidence</strong> from observational studies</td>
</tr>
<tr>
<td>Medium (III)</td>
<td>RCT evidence with critical limitations <strong>Observational</strong> study evidence without important limitations</td>
</tr>
<tr>
<td>Low (IV)</td>
<td>Observational study evidence with important or critical limitations</td>
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## Strength of Recommendations

<table>
<thead>
<tr>
<th>Strength of Recommendation</th>
<th>Description</th>
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<tbody>
<tr>
<td>Strong (A)</td>
<td><strong>Almost all</strong> patients should receive the recommended course of action.</td>
</tr>
<tr>
<td>Moderate (B)</td>
<td><strong>Most</strong> patients should receive the recommended course of action. However, other choices may be appropriate for some patients.</td>
</tr>
<tr>
<td>Optional (C)</td>
<td>There may be <strong>consideration</strong> for this recommendation on the basis of individual patient circumstances. Not recommended routinely.</td>
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Approaches to managing adherence

Interventions to improve adherence to antiretroviral therapy: a rapid systematic review

Krisda H. Chaiyachati\(^a\), Osondu Ogbuoji\(^b\), Matthew Price\(^b\), Amitabh B. Suthar\(^c\), Eyerusalem K. Negussie\(^c\) and Till Bärnighausen\(^b, d\)

Introduction: Access to antiretroviral treatment (ART) has substantially improved over the past decade. In this new era of HIV as a chronic disease, the continued success of ART will depend critically on sustained high ART adherence. The objective of this review was to systematically review interventions that can improve adherence to ART, including individual-level interventions and changes to the structure of ART delivery, to inform the evidence base for the 2013 WHO consolidated antiretroviral guidelines.

Design: A rapid systematic review.

Methods: We conducted a rapid systematic review of the global evidence on interventions to improve adherence to ART, utilizing pre-existing systematic reviews.

AIDS, 2014

Rapid systematic review (utilises previous reviews), adherence interventions only.

RCT, NRCT: before-after cohort and case-control studies.

124 studies (75/124 show adh. benefit).

Global.

Intervention categories:
- education,
- cognitive-behavioural interventions,
- treatment support,
- active reminder devices and
- DOTs …and combinations
Linkage to care:

Monitor entry and retention.

- **Systematic monitoring of linkage** should be done for all diagnosed (II A)
- **Systematic monitoring of retention** is recommended for all patients (II A) – retention is associated with improved outcome. Use what is available: medical records, administrative databases, pharmacy data etc.

Notice if a visit is missed...
Adherence monitoring:

Monitor adherence and retention.

- **Self-reported adherence** should be obtained routinely in all patients (II A)
- **Pharmacy refill data** are recommended for adherence monitoring when medication refills are not automatically sent to patients (II B)
- The following are not routinely recommended, but can be useful:
  - Use of DAART in routine ART care (IA)
  - Drug concentrations in biological samples (III C)
  - Pill counts performed by staff or patients (III C)
  - Electronic Drug Monitors for clinical use (I C)
Adherence monitoring:

Use the viral load.

- WHO recommends **VL monitoring** with other adherence measures.
- Raised viral load indicates a risk of failure, so **DO** something.
- 56-68% can re-suppress with an adherence intervention.
Adherence interventions are successful

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>n</th>
<th>Intervention</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>Berki-Benhaddad</td>
<td>2006</td>
<td>15</td>
<td>Personal adh support</td>
<td>Ave decrease VL by 2.3 log</td>
</tr>
<tr>
<td>Calmy</td>
<td>2007</td>
<td>23</td>
<td>Counseling, pill boxes, support group, treatment partner</td>
<td>77% achieved VL&lt;400</td>
</tr>
<tr>
<td>DeFino</td>
<td>2004</td>
<td>45</td>
<td>Counseling, pill boxes, alarm reminders, repeat education...</td>
<td>Ave decrease VL by 0.6 log</td>
</tr>
<tr>
<td>Khan</td>
<td>2013</td>
<td>40</td>
<td>Structured adh counseling, including families</td>
<td>78% achieved resuppression</td>
</tr>
<tr>
<td>Orrell</td>
<td>2007</td>
<td>43</td>
<td>Pill box, dosing diaries, counseling, home visit</td>
<td>68% achieved resuppression</td>
</tr>
<tr>
<td>Parker</td>
<td>2013</td>
<td>20</td>
<td>Intensive adh counseling</td>
<td>48% achieved resuppression</td>
</tr>
<tr>
<td>Pirkle</td>
<td>2009</td>
<td>56</td>
<td>1 month mDAART, weekly f/u visits</td>
<td>36% decreased VL by &gt;1 log</td>
</tr>
<tr>
<td>Wilson</td>
<td>2009</td>
<td>40</td>
<td>Counseling and education</td>
<td>90% resuppression</td>
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Bonner, JAIDs 2013
Interventions to improve adherence:

**ART strategies:**

- Among regimens of similar efficacy and tolerability, **once-daily regimens** are recommended for treatment-naive patients beginning ART (II B).
- **Simplify** where possible...
- Among regimens of equal efficacy and safety, **fixed-dose combinations** are recommended to decrease pill burden (III B).

Thompson et al.
Adherence interventions:

Counselling and education:
• Individual ART education is recommended (IIA); can be done in a group (IIIC).
• Providing one-on-one adherence support to patients through adherence counselling approaches is also recommended.
• Multidisciplinary education and counselling intervention can be useful too – use the skills of the team: nurse, Dr, CCW, psychologist (IIIB)
• Positive outcome: 79-88% adherence; 21-63% biological.

Thompson, Bärnighausen and Chayachati.
Adherence interventions:

Peer support:

• Offering peer / treatment support may be considered (IIIC).
• Some discrepant findings... 62% had a positive adherence outcome, 19% positive biological outcome.
• Treatment supporter role is not clear.

Thompson, Bärnighausen and Chayachati.
Adherence interventions:

*Cognitive behavioural therapy:*
Chaiyachati reports 60 studies; 67% had a positive adherence outcome and 20% a positive biological outcome. Includes motivational interviewing, self-efficacy and skills building, stress management, patient empowerment.
Adherence interventions:

*Interactive reminder devices:*

- **Reminder devices (e.g. pillboxes)** and use of communication technologies with an interactive component are recommended. (IB)

Thompson, Bärnighausen and Chayachati.
Adherence interventions:

*Interactive reminder devices:*

8 recent RCT using SMS messaging...

**Only 5 noted improved adherence;** only 2 showed biological improvement.

Successes to date include:

- Weekly messaging
- Interactive component
- Targeting those with poor adherence
Adherence interventions:

**Health system approaches:**

• Using nurse- or counsellor-based care is recommended where resources are limited: task-shifting. (IIB)

• **Monthly food supplementation** packages improve early adherence to first-line antiretroviral therapy and are recommended. (IIB)

43% of seven studies showed biological improvement.

Thompson, Bärnighausen and Chayachati.
Adherence interventions:

**Health system approaches:**

- DOTS vs no DOTS: discrepant findings

Thompson: DAART not recommended in routine clinical settings (IA)

Chaiyachati: of 20 studies, 85% showed adherence benefit; 30% biological.

Bärnighausen: assess within context!
Vulnerable populations:

- Mentally ill (including anxiety and depression)
- Pregnant women
- Children and adolescents
- Substance use
Summary 1

• Simplify the treatment to be taken...
• Education and counseling is beneficial.
• Monitor adherence on treatment: PR, SR.
• Notice if people miss visits.
• Use the viral load! Target interventions to those not doing well.
• Consider the use of food supplementation / reminders...
• Watch for high-risk groups; consider use of DOTs.
Summary 2

Still room for more learning:

• For each intervention with a significant outcome there is one without.
• Many studies use only subjective adherence measures and have only shown short-term benefit;
• Lack of cost-effectiveness information;
• Little data on vulnerable populations;
• Value of single vs. combination adherence interventions (prevention);
• Improving long-term adherence / retention.
What works to improve adherence?

Develop your adherence toolkit:
• Medication factors,
• Service / provider factors,
• Patient factors

We can do a lot with what we have already!
Acknowledgements

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• Melanie Thompson and IAPAC guideline team