HIV Treatment Adherence Interventions: A Cycle of Evolution and Change

Moderator: Jane M. Simoni, Ph.D., University of Washington
Virtual Conference, November 2-3, 2020
Historical Perspective
15 years ago at the first conference
*NIMH/IAPAC International Conference on HIV Treatment Adherence*
*March 8-10, 2006, Jersey City, New Jersey*
ART Adherence Interventions

Simoni et al., 2003; 2005:

- Field is in a “nascent stage of development”
- Most of the 21 studies published through 1/2003 were pilot or feasibility studies
- Only four randomized controlled trials were conducted with adequate methodological rigor
- Conclusion: Lack of empirical data necessary to make strong recommendations regarding the most efficacious way to improve antiretroviral therapy adherence
A Systematic Review and Meta-Analysis of RCTs to Enhance HAART Adherence
Overall Descriptives \( (k = 19) \)

- All studies reported since 1998
  - Published since 2003 74%

- Studies conducted in the
  - U.S. 74%
  - Spain 11%
  - France 11%
  - Switzerland 5%

- Study sites
  - Outpatient HIV primary care clinics 84%
### Overall Descriptives \((k = 19)\)

<table>
<thead>
<tr>
<th>Category</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage of male subjects</td>
<td>75%</td>
<td>0 - 91%</td>
</tr>
<tr>
<td>MSM</td>
<td>53%</td>
<td>0 - 77%</td>
</tr>
<tr>
<td>Ethnic/racial minorities in U.S. Studies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- African-Americans</td>
<td>54%</td>
<td>21 - 88%</td>
</tr>
<tr>
<td>- Latino/a-Americans</td>
<td>19%</td>
<td>1 - 46%</td>
</tr>
<tr>
<td>26% of studies restricted inclusion based on marker of risk for nonadherence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Poor baseline adherence</td>
<td>16% ((n = 3))</td>
<td></td>
</tr>
<tr>
<td>- Detectable VL</td>
<td>16% ((n = 3))</td>
<td></td>
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</tbody>
</table>
## Intervention Characteristics

<table>
<thead>
<tr>
<th></th>
<th>$n$</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention provided by:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health care provider</td>
<td>8</td>
<td>(47%)</td>
</tr>
<tr>
<td>Pharmacist</td>
<td>2</td>
<td>(12%)</td>
</tr>
<tr>
<td>Counselor</td>
<td>5</td>
<td>(29%)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of intervention sessions</td>
<td>4</td>
<td>1 – 54</td>
</tr>
<tr>
<td>Duration of each session</td>
<td>1 hr</td>
<td>45 min– 2.5 hrs</td>
</tr>
<tr>
<td>Intervention duration (days)</td>
<td>70</td>
<td>1 day–1 yr</td>
</tr>
<tr>
<td>Post Intervention follow-up (k=16)</td>
<td>56 days</td>
<td>14 days– 1 yr</td>
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</tbody>
</table>
Intervention Components

**HAART information** 79%
Didactic provision of generic information about HIV, HAART in general, and the patient’s prescribed regimen

**Cognitive strategies** 79%
Interactive discussion involving patient-specific information addressing cognitions, motivations and expectations about taking HAART

**Behavioral strategies** 84%
Such as external rewards or cue-dosing

**External reminders** 32%
Such as pagers, diaries, or calendars
Meta-Analysis Results:  
95% Adherence \((k = 18)\)

<table>
<thead>
<tr>
<th>Overall OR</th>
<th>95% CI</th>
<th>Z</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.50</td>
<td>1.16, 1.94</td>
<td>3.10</td>
<td>.002</td>
</tr>
</tbody>
</table>

Homogeneity Analysis

<table>
<thead>
<tr>
<th>Q</th>
<th>df</th>
<th>p</th>
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<tbody>
<tr>
<td>20.27</td>
<td>17</td>
<td>.26</td>
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</table>

Sensitivity Analyses (no “outliers”)

*Note. Used outcomes for first follow up. If not available, used immediate post intervention data.*

*\(p < .05\)
Meta-Analysis Results:
Undetectable VL ($k = 14$)

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<th>Overall OR</th>
<th>95% CI</th>
<th>Z</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>1.25</td>
<td>.99, 1.59</td>
<td>1.84</td>
<td>.067</td>
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</tbody>
</table>

Homogeneity Analysis

<table>
<thead>
<tr>
<th>Q</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.19</td>
<td>13</td>
<td>.83</td>
</tr>
</tbody>
</table>

Sensitivity Analyses (no “outliers”)

*Note.* Used outcomes for first follow up. If not available, used immediate post intervention data.
Limitations of the Individual RCTs

- Few theory-driven
- Small samples
- No or limited follow-up
- Measure of adherence usually limited to either self-report or MEMS only
- Many lacked virologic or immunologic outcomes
Correlates of Patient Adherence

- Patient Characteristics
- Aspects of the provider and the patient-provider relationship
- Variables related to the treatment regimen or illness
- Contextual / Environmental Factors
• These 4 correlates of adherence represent 4 possible junctures for intervention...
• Most intervention studies have targeted only patient characteristics
• …and have done so in one of the four following types of interventions:
  – Cognitive Behavioral
  – Behavioral
  – Directly Observed Therapy
  – Affective interventions
Suggestions for Future Research (1)

• More RCTs, perhaps comparing intervention strategies
• Clear hypotheses and operationalization of key outcomes to decrease Type I error
• More consistent measures so study results can be compared
• Reporting of null findings
• Targeting of specific at-risk groups, e.g., IDUs, homeless, pregnant women
Suggestions for Future Research (2)

- Tailored interventions to better meet patient needs
  - Better to offer patients a range and ask them to choose?
- Examination of effectiveness (vs. efficacy)
- Translation and dissemination studies
- Cost-effectiveness of interventions
- Better communication and collaboration among investigators may enhance the development of knowledge and reduce duplication of efforts (e.g., frequent reviews, adherence research listserv)
Lingering concern…

• Potentially low exportability to resource poor settings for interventions requiring high level of training, complexity, and expense

• Lack of implementation science research

Implementation research on HIV adherence interventions: no time to wait

Two decades since the development of antiretroviral therapy (ART) for HIV, adherence remains the primary obstacle to achieving the best outcomes for patients receiving treatment. Indeed, despite the increased availability and affordability of potent once-daily regimens worldwide, the UNAIDS goal of 90% viral suppression has not been reached, partly because of poor adherence.13 Dedicated funding has generated a wave of rigorous research on developing and assessing interventions to promote ART adherence in both high-income and low-resource settings.10 Notably, a research synthesis project by the US Centers for Disease Control21 has identified 13 interventions that are supported by good evidence.29 In the Lancet Infectious Diseases, Marinj de Bruijn and colleagues21 present the results of their multicentre randomised trial of an intervention to improve adherence to treatment for HIV—an outstanding addition to the scientific literature on adherence. In their 15-month study, they assessed the effectiveness of a nurse-based counselling intervention (the Adherence Improving self-Management Strategy [AIMS]) involving promotion of self-management guided by review of electronically collected medication adherence data. The comparator enhances the likelihood that intervention effects are generalisable and can be sustained through scale-up. AIMS requires no additional or greatly lengthened clinic visits, extensive provider training, ongoing supervision, or patient incentives. Notably, effectiveness did not vary by ethnicity, treatment experience, or by nurse, suggesting that the results might be generalisable beyond the study population. Despite some minor methodological limitations (eg, the shortage of analysable data for ART adherence), AIMS merits the Dutch national rollout in progress. Indeed, Dutch clinics that do not have the substantial adherence support available at the treatment-as-usual sites might have results surpassing those in the trial.

Further dissemination and implementation research will be essential to ensure widespread adoption of the AIMS intervention, especially in resource-constrained settings. Feasibility and cost must be determined across a range of health systems. Provider training, however brief, might be burdensome in settings with high staff turnover, and a task-sharing approach using a cadre of adherence specialists with less training24 might prove more feasible. Additionally,
Thank you