CDC Review and Dissemination of Evidence-based HIV Treatment Adherence Interventions

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The findings and conclusions in this presentation are those of the author and do not necessarily represent the views of the Centers for Disease Control and Prevention.
HIV/AIDS Prevention Research Synthesis (PRS) Project at CDC

Goal: Review and synthesize cumulative body of evidence from the scientific research literature to help inform policy decisions, programmatic efforts, and future research

- Quantitative (meta-analyses) & qualitative reviews
  - Synthesize evidence across a pool of interventions
- Efficacy Review
  - Identify specific evidence-based behavioral interventions
• PRS project
• Efficacy review methods
• Best- & Promising-evidence criteria
• **Compendium of evidence-based interventions (EBIs)**
Why Focus on Medication Adherence?

- Intensified focus in HIV prevention and at CDC on:
  - HIV testing
  - PWP (“prevention with positives”) including linkage to and retention in care, prevention services, and improving adherence

- Promoting HIV medication adherence to
  - Maximize benefits of treatment for HIV-positive persons
  - Likely reduce viral load at the population level
Today’s Talk

• Phase 1: Criteria Development Process

• Phase 2: Systematic Review Process

• Phase 3: Evidence-based Interventions
Phase I:
Criteria Development Process

1. Preliminary work by PRS team

2. Internal and External Consultations
Preliminary Work Conducted by the PRS Team

• Comprehensive review of scientific literature

  ➢ Existing PRS efficacy criteria for individual- and small-group level interventions for reducing HIV-related sex and drug behaviors

  ➢ Existing medication adherence intervention literature

  ➢ Medication adherence studies in PRS database as of Dec 08
**Goal:** Solicit input from scientists with expertise in HIV treatment adherence interventions re: methodological, implementation, and analytic issues unique to adherence interventions

<table>
<thead>
<tr>
<th>DHAP Adherence Interventions Workgroup (AIW)</th>
<th>External Consultants</th>
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<tbody>
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<td>Mahnaz R. Charania, Ph.D</td>
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<td>Nicole Crepaz, Ph.D</td>
<td>Michael Stirratt, Ph.D., NIMH</td>
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<td>Deborah L. Jones, Ph.D., Univ of Miami</td>
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<td>Robert H. Remien, Ph.D., Columbia Univ</td>
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<td>David W. Purcell, J.D., Ph.D.</td>
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Ann Williams, Ed.D., RNC, FAAN, Yale Univ
Ira Wilson, M..D., Tufts Univ
• Phase 1: Criteria Development Process

• Phase 2: Efficacy Review Process

• Phase 3: Evidence-based Interventions
Phase 2: Efficacy Review Process

Systematic search of literature†

Efficacy Review Methods

Systematic search of literature†

Screen literature to identify eligible interventions, their evaluation reports, and linked citations

Eligible Interventions

• HIV Medication Adherence focus
  - Educational / behavioral component OR
  - Treatment delivery methods or monitoring devices to facilitate adherence

• U.S. (or U.S. territories) study

• Outcome evaluation report w/ comparison arm

• Published or in press during 1996 to 2009

• Relevant medication adherence behavior or biologic outcome data
  - Behavioral: MEMs caps, pill count, self-report, pharmacy refill
  - Biologic: Viral load

Excluded Interventions

• Interventions comparing treatment regimens
Efficacy Review Methods

Systematic search of literature

Screen literature to identify eligible interventions, their evaluation reports, and any linked citations

Evaluate the evidence for each intervention based on an explicit a-priori set of efficacy criteria

- Independent assessments by 2 CDC scientists
- Reconciliation of all discrepancies
- Group consensus on final assessment
- Contact authors for additional info as needed
The Efficacy Criteria

• Same evaluation domains as HIV risk reduction interventions:
  - Quality of research study design
  - Quality of study implementation
  - Appropriateness of analysis
  - Strength of findings

• Consultant feedback focused on the need to examine each study as a whole

• We propose a set of criteria and overall assessment to reflect current state of science and lead the field forward
The Efficacy Criteria: Identifying interventions at two levels of rigor

• **Best-Evidence** HIV med adherence interventions
  - Rigorously evaluated
  - Significant effects in ↓ HIV RNA viral load (VL) *and*
    - ↑ adherence behaviors
  - Provide *strongest* scientific evidence of efficacy

• **Promising-Evidence** HIV med adherence interventions
  - Rigorously evaluated
  - Significant effects in ↓ VL *or* ↑ adherence behaviors
  - Provide *sufficient* scientific evidence of efficacy
Proposed
Medication Adherence
Efficacy Criteria
Proposed Efficacy Criteria for HIV Medication Adherence Interventions

Quality – Study Design

**Best Evidence**
- Prospective
- Concurrent comparison
- Appropriate comparison
- Random allocation

**Promising Evidence**
- Quasi-prospective
- At least *non*-concurrent
  - +/- 12 mos
  - similar characteristics
- Appropriate comparison
- At least *non-random* w/ minimal-moderate bias
Proposed Efficacy Criteria for HIV Medication Adherence Interventions

Quality – Study Implementation

**Best Evidence**
- Assessment $\geq 3 \text{ mo}$ post-completion (discrete interv)
  $\geq 6 \text{ mo}$ post-initiation (other)
- $>70\%$ retention rate / arm

**Promising Evidence**
- Assessment $\geq 1 \text{ mo}$ post-completion (discrete interv)
  $\geq 3 \text{ mo}$ post-initiation (other)
- $>60\%$ retention rate / arm
Proposed Efficacy Criteria for HIV Medication Adherence Interventions

Appropriateness - Study Analysis

Best Evidence
- With appropriate comparison
- Intent to treat analysis
  - As originally allocated
  - Regardless of exposure
  - Imputation of missing data
- Analytic sample $\geq 50$ / arm
- Two-sided test & $\alpha \leq 0.05$
- Adjusting for cluster

Promising Evidence
- With appropriate comparison
- Intent to treat analysis
  - As originally allocated
  - Regardless of exposure
- Analytic sample $\geq 40$ / arm
- Two-sided test & $\alpha \leq 0.05$
Proposed Efficacy Criteria for HIV Medication Adherence Interventions

Quality – Study Analysis (cont’d)

Best Evidence

- Measures Comparability:
  - Identical for repeated measures / change score
  - Of the same construct if BL is a covariate

Promising Evidence

- Measures Comparability:
  - Identical for repeated measures / change score
  - Of the same construct if BL is a covariate
  - For Non-RCT: BL-equivalent on outcome or adjusted
  - For Non-RCT w/ mod bias: BL-equivalent on demographics/ critical variables or adjusted
Proposed Efficacy Criteria for HIV Medication Adherence Interventions

**Strength of Evidence**

**Best Evidence**

- Positive $p \leq 0.05$ effect for $\geq 1$ relevant behav and $\geq 1$ relevant biologic outcome:
  - Behav: MEMs cap, pill count, pharmacy refill, or self-report
  - Bio: viral load lab test
- Effect must meet all criteria
- No negative effect
- No negative replication

**Promising Evidence**

- Positive $p \leq 0.05$ effect for $\geq 1$ relevant behav or $\geq 1$ relevant biologic outcome:
  - Behav: MEMs cap, pill count, pharmacy refill, or self-report
  - Bio: viral load lab test
- Effect must meet all criteria
- No negative effect
- No negative replication
Proposed Efficacy Criteria for HIV Medication Adherence Interventions

Additional Limitations (Best & Promising):

- Intervention and comparison not similar in medication regimens
- Findings based on too many post-hoc analyses
- Inconsistent evidence between effects
- Inconsistent evidence across comparisons arms
- Effects only in biased subgroup analysis
- Substantial (>40%) missing data (attrition + other)
- Differential attrition rates (>10%) or characteristics across arms
- Differences in characteristics between lost & retained participants
- Any other notable bias threatening validity
• Phase 1: Criteria Development Process

• Phase 2: Efficacy Review Process

• Phase 3: Evidence-based Interventions
Results of Efficacy Review

1996-2009 Citations

Eligible citations

Unique studies in review

Promising-Evidence Interventions
DRAFT
Promising Evidence-based HIV Medication Adherence Interventions
### Promising-evidence Interventions \( (n = 8) \)

<table>
<thead>
<tr>
<th>DAART (n=2)</th>
<th>Educational / Behavioral (n=6)</th>
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<tbody>
<tr>
<td><strong>Setting</strong></td>
<td><strong>Setting</strong></td>
</tr>
<tr>
<td>➢ 1 methadone clinic</td>
<td>➢ 4 HIV/AIDS clinics</td>
</tr>
<tr>
<td>➢ 1 mobile van</td>
<td>➢ 1 anywhere</td>
</tr>
<tr>
<td>➢ 1 residential</td>
<td>➢ 1 residential</td>
</tr>
<tr>
<td><strong>Intervention structure</strong></td>
<td><strong>Intervention structure</strong></td>
</tr>
<tr>
<td>➢ 2 repetitive dosing</td>
<td>➢ 1 discrete</td>
</tr>
<tr>
<td></td>
<td>➢ 5 repetitive dosing or combination</td>
</tr>
<tr>
<td><strong>Comparison type</strong></td>
<td><strong>Comparison type</strong></td>
</tr>
<tr>
<td>➢ 2 self-administered therapy</td>
<td>➢ 5 usual care</td>
</tr>
<tr>
<td></td>
<td>➢ 1 attention control</td>
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Promising-evidence Interventions  
\( (n = 8) \)

**DAART (n=2)**

- **% Gender**
  - majority males

- **% Race / Ethnicity**
  - majority minority (AA + Hispanic)

- **Target population**
  - treatment-experienced + naive

**Educational / Behavioral (n=6)**

- **% Gender**
  - 4 majority males
  - 2 50% males / 50% females

- **% Race / Ethnicity**
  - 4 majority minority
  - 2 50% minority / 50% white

- **Target population**
  - 3 treatment-experienced + naïve
  - 2 treatment-experienced
  - 1 treatment-naive
### Promising-evidence Interventions

\( n = 6 \) educational/behavioral interventions

#### Common Elements
- all delivered by nurse or primary care provider
- 6 cognitive-behavioral component (e.g., addressing barriers)
- 4 support partner
- 3 problem solving

#### Relevant Outcomes
6 measured Behavior + Biologic outcomes
- 4 found effects on Beh only
  - 3 MEMs caps
  - 1 self-reported adherence
- 1 found effects on VL only
- 1 found effects on self-reported adherence + VL
Next Steps

• Gather additional input at this conference and from federal partners

• Disseminate the final criteria and list of EBIs on the PRS website

• Work with federal partners and stakeholders to discuss the future translation activities
  ➢ Intervention packages?
  ➢ Adaptation and implementation of the interventions?
  ➢ Dissemination?
  ➢ Technical support?
Thank You….

• Internal Consultants
• External Consultants
• Federal Partners
• Authors who responded to requests for info

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