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

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HIV/AIDS Prevention Research Synthesis (PRS) Project at CDC

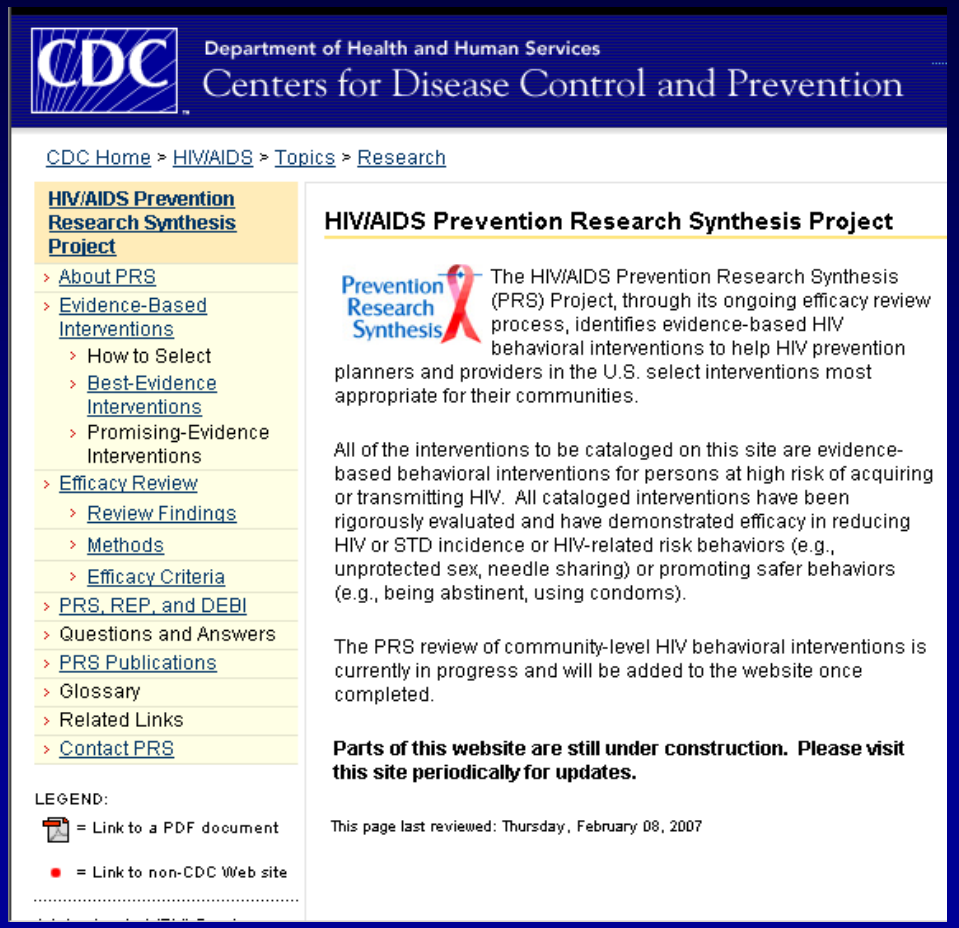
Goal: Review and synthesize cumulative body of evidence from the scientific research literature to help inform policy decisions, programmatic efforts, and future research

- Quantitative (meta-analyses) & qualitative reviews
  - Synthesize evidence across a pool of interventions
- Efficacy Review
  - Identify specific evidence-based behavioral interventions

PRS Project Website

http://www.cdc.gov/hiv/topics/research/prs/index.htm

- 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

Internal and External Consultations

Goal: Solicit input from scientists with expertise in HIV treatment adherence interventions re: methodological, implementation, and analytic issues unique to adherence interventions

DHAP Adherence Interventions Workgroup (AIW)	External Consultants
Mahnaz R. Charania, Ph.D Nicole Crepaz, Ph.D Linda Koenig, Ph.D Cindy Lyles, Ph.D Khiya Marshall, Dr.P.H. David W. Purcell, J.D., Ph.D. Paul Weidle, PharmD, M.P.H.	Christopher Gordon, Ph.D., NIMH Michael Stirratt, Ph.D., NIMH Rivet Amico, Ph.D., Univ of Conn Deborah L. Jones, Ph.D., Univ of Miami Robert H. Remien, Ph.D., Columbia Univ Steve Safren, Ph.D., Mass Gen Hosp Jane Simoni, Ph.D., Univ of Wash 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†

† *DeLuca, J. B., Mullins, M. M., Lyles, C. M., Crepaz, N., Kay, K., Thadiparthi, S. (2008). Developing a comprehensive search strategy for evidence based systematic reviews. Evidence Based Library and Information Practice, 3, 3-32.*

Efficacy Review Methods

Systematic search of literature†

↓

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

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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 ≥3 mo post-completion (discrete interv) ≥6 mo post-initiation (other)*
- *≥70% retention rate / arm*

Promising Evidence

- *Assessment ≥1 mo post-completion (discrete interv) ≥3 mo post-initiation (other)*
- *≥60% retention rate / arm*

Proposed Efficacy Criteria for HIV Medication Adherence Interventions

Appropriateness - Study Analysis

Best Evidence

- *W/ appropriate comparison*
- *Intent to treat analysis*
  - As originally allocated
  - Regardless of exposure
  - Imputation of missing data
- *Analytic sample ≥50 / arm*
- *2-sided test & α ≤ .05*
- *Adjusting for cluster*

Promising Evidence

- *W/ appropriate comparison*
- *Intent to treat analysis*
  - As originally allocated
  - Regardless of exposure
- *Analytic sample ≥40 / arm*
- *2-sided test & α ≤ .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 ≤ .05 effect for ≥1 relevant behav **and** ≥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 ≤ .05 effect for ≥1 relevant behav **or** ≥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**

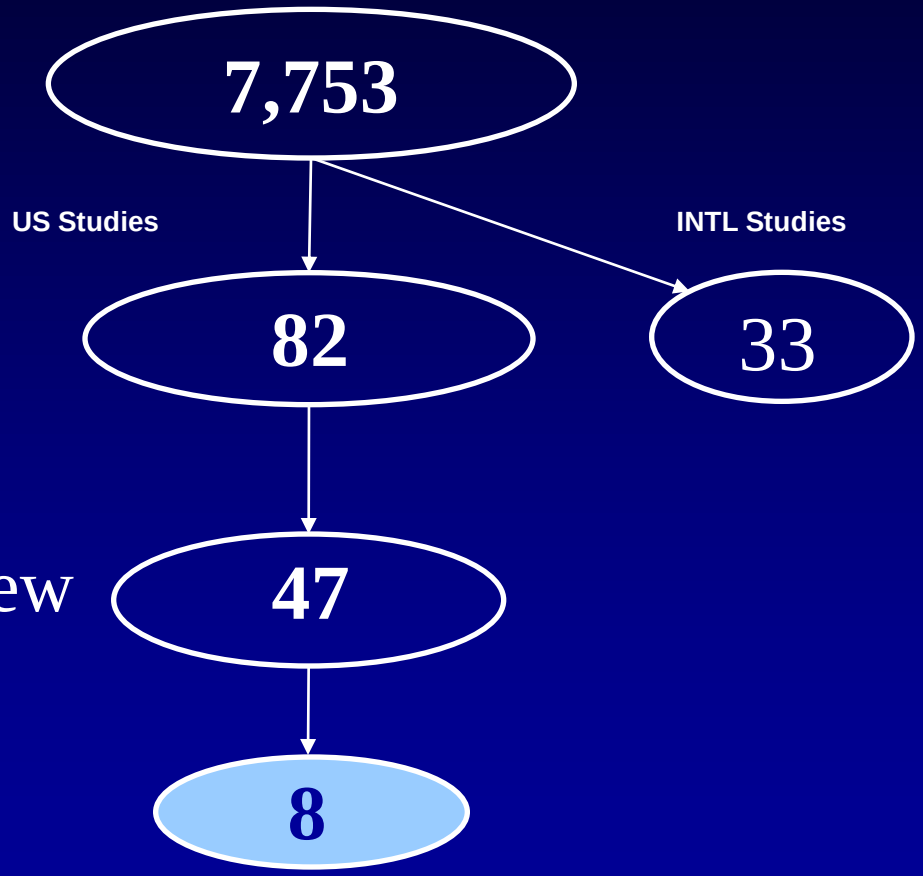
Results of Efficacy Review

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)*

DAART (n=2)

Setting
- 1 methadone clinic
- 1 mobile van

Intervention structure
- 2 repetitive dosing

Comparison type
- 2 self-administered therapy

Educational / Behavioral (n=6)

Setting
- 4 HIV/AIDS clinics
- 1 anywhere
- 1 residential

Intervention structure
- 1 discrete
- 5 repetitive dosing or combination

Comparison type
- 5 usual care
- 1 attention control

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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