Combined Cognitive Behavioral Therapy and a Medication Management Algorithm for Treatment of Depression among Youth Living with HIV in the United States

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Background and Rationale

- Medication algorithms and cognitive behavioral therapy (CBT) are effective for the treatment of depression.

- IMPAACT 2002 builds on a combined CBT and medication algorithm (COMB) found efficacious in ATN 080:
  - Test the “core components” of COMB with all essential elements of collaborative, stepped care but is adapted for easy dissemination (COMB-R).
  - Examine the impact of COMB-R on biological and medical adherence outcomes with a larger sample with greater power to detect impacts.
  - Examine moderators of COMB-R impact, such as gender and initial level of depression.


Study Objectives

Primary Objectives – To evaluate whether:

• Cognitive Behavioral Therapy and Medication Management Algorithm (COMB-R) is associated with improved depression outcomes at 24 weeks, compared to Standard Care.

• COMB-R is associated with improved biological measures of health over 24 weeks (CD4 cell numbers and copies of HIV RNA in plasma) compared to Standard Care.

Secondary Objectives - Examine:

• Adherence for HIV and depression treatment.
• Maintenance of depression impact at 48 weeks.
• Moderators of impact: demographic, behavioral, and biological factors
• Behavioral risk outcomes (alcohol/drug use; sex-risk behaviors)
• Use of therapy and medication at all sites.
• Adverse Events - psychological hospitalizations and suicide attempts
Study Schema

**Design:** Multi-site, two-arm, cluster-randomized study

**Study Population:** HIV-infected youth, ages 12 to 24 years, diagnosed with nonpsychotic depression (structured clinician rating).
- Prior or current treatment is not an exclusion criteria.

**Sample Size:** 14 US sites will be randomized, enroll 156 participants

**Study Intervention:** Sites assigned to COMB-R or Standard Care

**Study Duration:** Accrual will be approximately 24 months. Participants will complete assessments to 48 weeks.

**Enhanced Standard of Care:** Online training in depression assessment/monitoring, supportive psychotherapy, and use of antidepressants.
## Health and Wellness CBT Content
(tailored for relevant issues: stigma, trauma, medical care)

<table>
<thead>
<tr>
<th>Treatment Stage</th>
<th>Frequency</th>
<th>Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Motivation to engage; psychoeducation</td>
<td>Weekly</td>
<td>1</td>
</tr>
<tr>
<td>II. Reduce symptoms with core skills; identify strengths</td>
<td>Weekly</td>
<td>2</td>
</tr>
<tr>
<td>III. Wellness skills—relapse prevention</td>
<td>Every other week</td>
<td>3, 4</td>
</tr>
<tr>
<td>IV. Consolidate gains</td>
<td>Monthly</td>
<td>5, 6</td>
</tr>
</tbody>
</table>
Medication Algorithm

- Framework, not “restrictive,” not a specific medication
- Strategy based on measured care/patient response

<table>
<thead>
<tr>
<th>Stage</th>
<th>Treatment</th>
<th>Medication Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>No medication</td>
<td>N/A</td>
</tr>
<tr>
<td>Stage 1</td>
<td>SSRI Mono Therapy</td>
<td>Increase or augment partial responses (lithium or bupropion)</td>
</tr>
<tr>
<td>Stage 2</td>
<td>2nd SSRI</td>
<td>Increase or augment partial responses</td>
</tr>
<tr>
<td>Stage 3</td>
<td>Non-SSRI</td>
<td>Venlafaxine, bupropion, mirtazapine augment partial responses</td>
</tr>
<tr>
<td>Stage 4</td>
<td>Combination Treatment</td>
<td>Two antidepressants or antidepressant plus lithium</td>
</tr>
</tbody>
</table>

Developed from Children’s Medication Algorithms Project; STAR*D Trial; Blier 2006; Caballero, 2005
Statistical Considerations

• Randomization:
  ▫ Sites will be randomized (instead of individuals) to prevent spillover effects
  ▫ Restricted randomization procedure designed to balance key characteristics of the site populations
    • Pre-study survey: number behaviorally HIV-infected, gender and age
    • Before randomization sites will identify potentially eligible participants and their characteristics
    • Computer program will generate all possible site allocations that meet balance criteria and select one randomly

• Primary Analyses:
  ▫ Cluster-level analyses, where the unit of analysis is the site
**IMPAAACT 2002: Key Milestones**

- **August 2015:** Site Selection and Accrual Plan approved by IMPAAACT Management Oversight Group (MOG)
- **September 2015:** Teleconference held with Protocol Chairs and Site Representatives
- **December 2015:** Received final protocol team sign-off and submitted to the IMPAAACT Multidisciplinary Protocol Review Group (MPRG)
- **January 2016:** MPRG review
- **February 2016:** Study budget approved by the MOG
- **February-March 2016:** Protocol team addressed comments/concerns received from MRPG.
- **May 2016:** DAIDS Clinical Sciences Review Committee Review (CSRC) - voted to move forward
Upcoming Reviews/Projected Timelines

- **June/July 2016**: DAIDS Regulatory Review & Medical Officer Review
- **August 2016**: Regulatory Affairs Branch final sign-off
- **August 2016**: Version 1.0 released to participating sites
- **September/October 2016**: Site training to occur (via webinar)
- **October/November 2016**: Sites expected to be activated for participation