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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Statisticians: David Shapiro, PhD; Miriam Chernoff, PhD
FHI 360: Kate Lypen, MPH
Participating Sites

- CRS 5114, Bronx-Lebanon Hospital Center
- CRS 5055, Children’s Diagnostic and Treatment Center
- CRS 5030, Emory University School of Medicine
- CRS 5052, The University of Colorado
- CRS 6501, St Jude Children’s Research Hospital
- CRS 5040, Stony Brook University Medical Center
- CRS 5013, Jacobi Medical Center Bronx
- CRS 5048, The University of Southern California LA
- CRS 3801, Texas Children’s Hospital
- CRS 5092, Johns Hopkins University School of Medicine
- CRS 5083, Rush University Medical Center
- CRS 5112, David Geffen School of Medicine at UCLA
- CRS 4601, UCSD
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:** 13 US sites were randomized, to enroll 156 participants

**Study Intervention:** Sites assigned to COMB-R or Enhanced Standard Care (ESC)

**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>

Kennard & Brown, Cogn Behav Practice, 2014
# 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 dose, or augment partial responses (e.g. lithium, bupropion)</td>
</tr>
<tr>
<td>Stage 2</td>
<td>2nd SSRI</td>
<td>Increase dose, or augment partial responses</td>
</tr>
<tr>
<td>Stage 3</td>
<td>Non-SSRI</td>
<td>Increase dose, or 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>
IMPAAACT 2002: Key Milestones

• **August 2016**: Protocol Version 1.0 released to sites

• **November 2016**: Sites randomized to ESC or COMB-R arm

• **December 2016**:  
  ▫ Protocol-specific online training completed  
  ▫ Training material (slides and video) posted to website  
  ▫ Study opened to accrual

• **January-April 2017**: 12 out of 13 sites were activated to initiate study implementation

• **March 2017**: First participant enrolled
Enrollment & Implementation Update

• 45 potential participants contacted and approached for eligibility determination
  ▫ ~ 25% did not consent to formal screening
  ▫ ~ 30% not eligible (generally because symptoms too mild)

• Total accrual of 19 participants as of 21 May 2017
  ▫ COMB-R: n=8
  ▫ ESC: n=11

*Each site is expected to enroll approximately 12 participants*

• Implementation
  ▫ Monthly Monitoring Calls with H&W CBT Therapists & Site Prescribers
  ▫ FAQ list being constructed
Implementation Issues

- Randomization by site unusual IMPAACT and required:
  - Similar COMB-R and ESC consent forms to reduce perceived difference in “burden” by condition
  - Pre-study surveys of patient characteristics & volume
  - Random selection of “blocks” of patients, rather than approaching patients when convenient

- Two stage consent process
  - Screening (one hour mental health evaluation)
  - Enrollment

- At COMB-R sites - Depression self-report score shared with site clinician and Protocol team in timely fashion.

- At COMB-R sites- challenging to have part-time and busy clinicians available for monthly supervision calls.
Questions?