IMPAACT 2002

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

Chair: Larry Brown, MD
Vice-Chairs: Betsy Kennard, PsyD; Patricia Emmanuel, MD
Statisticians: David Shapiro, PhD; Miriam Chernoff, PhD
fhi360: Kate Lypen, Lisa Levy, JL Ariansen

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CC Meeting

- Site 5114, Bronx-Lebanon Hospital Center
- Site 5055, Children's Diagnostic and Treatment Center
- Site 5030, Emory University School of Medicine
- Site 5052, The Regents of the University of Colorado
- Site 6501, St Jude Children's Research Hospital
- Site 5040, Stony Brook University Medical Center
- Site 5013, Jacobi Medical Center
- Site 5048, The University of Southern California- MCA Center
- Site 3801, Texas Children's/Baylor
- Site 4001, Chicago Children's
- Site 5092, Johns Hopkins University School of Medicine
- Site 5083, Rush University Medical Center
- Site 5112, David Geffen School of Medicine at UCLA
- Site 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.

(APA) APA. Practice Guideline for the Treatment of Patients with Major Depressive Disorder, Third Edition. 2010.

Kennard, B., Brown, L., Hawkins, L., Risi, A., Radcliffe, J., Emslie, G., ... the Adolescent Trials Network for HIV/AIDS Interventions, S. (2014). Development and Implementation of Health and Wellness CBT for Individuals with Depression and HIV. *Cognitive and Behavioral Practice*, *21*(2), 237–246. http://doi.org/10.1016/j.cbpra.2013.07.003

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)

	Treatment Stage	Frequency	Month
I.	Motivation to engage; psychoeducation	Weekly	1
II.	Reduce symptoms with core skills; identify strengths	Weekly	2
III.	Wellness skills—relapse prevention	Every other week	3, 4
IV.	Consolidate gains	Monthly	5, 6

Kennard & Brown, *Cogn Behav Practice*, 2014

Medication Algorithm

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

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

Developed from Children's Medication Algorithms Project; STAR*D Trial; Bialer, 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

Hayes RJ, Moulton LH. Cluster Randomised Trials: Taylor & Francis; 2009.

IMPAACT 2002: Key Milestones

- **August 2015:** Site Selection and Accrual Plan approved by IMPAACT 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 IMPAACT 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