IMPAACT 2002

COMBINED COGNITIVE BEHAVIORAL THERAPY AND A MEDICATION MANAGEMENT ALGORITHM FOR TREATMENT OF DEPRESSION AMONG YOUTH LIVING WITH HIV IN THE UNITED STATES

Protocol Version 1.0, with LoA #1 and CMs #1-2

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PROTOCOL CHAIR

JUNE 12, 2019

IMPAACT

International Maternal Pediatric Adolescent AIDS Clinical Trials Network

IMPAACT 2002 PROTOCOL TEAM
(ABBREVIATED LIST)

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PARTICIPATING SITES

- **CRS 5114,** Bronx-Lebanon Hospital Center
- **CRS 5055**, Children's Diagnostic and Treatment Center
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- **CRS 6501**, St Jude Children's Research Hospital
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- **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
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STUDY BACKGROUND & RATIONALE

- **Medication algorithms and cognitive behavioral therapy (CBT) are effective** for the treatment of depression, as demonstrated in smaller trial in ATN 080
- Combination treatment (COMB) is a collaborative, stepped care approach with use of standard measure to guide care
  - COMB-R was adapted for easy dissemination.
  - 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)

Sample Size: 13 U.S. 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)

	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 dose, or augment partial responses (e.g. lithium, bupropion)
Stage 2	2nd SSRI	Increase dose, or augment partial responses
Stage 3	Non-SSRI	Increase dose, or 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

KEY STUDY MILESTONES

- **August 2016:** Protocol Version 1.0 released to sites
- **December 2016:** Study opened to accrual
- **March 2017**: First participant enrolled
- **March 2019:** Study closed to accrual (i.e. last participant enrolled)
- **September 2019**: Anticipated primary completion date
- **March 2020**: Study anticipated to close to follow-up (i.e. final study visit completed)

ENROLLMENT / ASSESSMENT UPDATE

- Target accrual of 156 participants (to achieve at least 140 evaluable for primary study outcomes) was achieved on 5, March 2019 (in 24 months!)
  - A total of 81 participants were enrolled in the COMB-R arm
  - A total of 75 participants were enrolled in the ESC arm
  - 93 participants have completed the study, and 63 currently remain in study follow-up
  - Visit completion at 24 weeks is currently 89%

SAMPLE CHARACTERISTICS AT ENTRY (N= 156)

Male	74 (47%)	QIDS-C severe (≥16)	72 (47%)
Age (mean, s.d.)	21.4 (2.8)	QIDS-SR severe(≥16)	68 (44%)
Race/ethnicity		On antidepressants	71 (46%)
Black, non-Hispanic	88 (56%)	RNA, 0-40 copies	90 (58%)
Hispanic (any race)	52 (33%)	CD4, ≥ 500 cells	106 (68%)
Route of HIV acquisition		CDC class, stage 0/1	85 (54%)
Perinatal	83 (53%)	Integrase Inhibitor-based ARV	
Behavioral	73 (47%)		102 (65%)

IMPLEMENTATION ISSUES

- Monthly CBT and Med Management supervision for COMB-R site staff has been smooth.
  - Many participants start the protocol not wanting medication.
  - Sites have enjoyed opportunity to collaborate and strategize on participant case management challenges.
- Site randomization has required frequent monitoring of the demographic and diagnostic characteristics of the two conditions (COMB-R and ESC).

IMPLEMENTATION ISSUES

- Sites found the enrollment procedure (random ordering of blocks of potential participants) cumbersome and many patients were no longer depressed because of lengthy delays before screening.
- The LoA #1 removed the requirement that sites approach participants in a randomly assigned order, which increased the pace of enrollment. Accrual was completed in the expected timeframe.

FUTURE ANALYSIS PLANS

- **Fall 2019 -** Primary outcome analyses (depression and VL at 24 weeks)
- **Spring 2020** – Secondary analyses
  - Maintenance of impact on depression and VL at 48 weeks
  - Secondary outcomes – adherence, risk behavior
  - Moderators of impact – demographics, behavioral and biological factors

QUESTIONS?