IMPAACT 2002

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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Rhode Island Hospital; Brown University
23 June 2021
Protocol Team (abbreviated list)

Medication Algorithm: Graham Emslie, MD

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Statistical Programmer: Shirley Traite, MSW

Clinical Trials Specialists: Kate Lypen, MPH; Sarah Buisson, MSW, MPH

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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
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 measures 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.


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 Enhanced Standard Care (ESC)

- COMB-R is associated with improved biological measures of health over 24 weeks (CD4 and HIV RNA) compared to ESC
Secondary Objectives - Examine:
- Maintenance of depression impact at 48 weeks
- Adherence for HIV and depression treatment
- Safety data - psychological hospitalizations and suicide attempts
Study Schema

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

Study Population: Youth living with HIV, 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 was 24 months. Participants completed assessments to 48 weeks.

Enhanced Standard of Care: Online training in depression assessment/monitoring, supportive psychotherapy, and use of antidepressants.

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Study Design

Restricted Randomization

ESC (Enhanced Standard of Care)
7 Sites (N=75)

COMB-R (24-week, combination cognitive behavioral therapy and medication management algorithm)
6 Sites (N=81) – 1 site withdrew
Accrual by Site and Treatment Arm

<table>
<thead>
<tr>
<th>Treatment Arm</th>
<th>Site</th>
<th>Enrollment</th>
</tr>
</thead>
<tbody>
<tr>
<td>COMB-R</td>
<td>Univ. of Colorado Denver NICHD CRS</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>South Florida CDTC Ft Lauderdale NICHD CRS</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>Rush Univ. Cook County Hosp. Chicago NICHD CRS</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>Johns Hopkins Univ. Baltimore NICHD CRS</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>David Geffen School of Medicine at UCLA NICHD CRS</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>St. Jude Children’s Hospital CRS</td>
<td>11</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>81</td>
</tr>
<tr>
<td>ESC</td>
<td>Texas Children’s Hosp. CRS</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>University of California San Diego CRS</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>Jacobi Med. Ctr. Bronx NICHD CRS</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>Emory University School of Medicine NICHD CRS</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>SUNY Stony Brook NICHD CRS</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>USC LA NICHD CRS</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Bronx-Lebanon Hospital Center NICHD CRS</td>
<td>16</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>75</td>
</tr>
<tr>
<td>All</td>
<td>Overall Total</td>
<td>156</td>
</tr>
</tbody>
</table>
## Sample Characteristics at Entry (n=156)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (mean, s.d.)</strong></td>
<td>21.4 (2.8)</td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td>47%</td>
</tr>
<tr>
<td><strong>Race/ethnicity</strong></td>
<td></td>
</tr>
<tr>
<td>Black, non-Hispanic</td>
<td>57%</td>
</tr>
<tr>
<td>Hispanic (any race)</td>
<td>33%</td>
</tr>
<tr>
<td><strong>Route of HIV acquisition</strong></td>
<td></td>
</tr>
<tr>
<td>Perinatal</td>
<td>53%</td>
</tr>
<tr>
<td>Behavioral</td>
<td>47%</td>
</tr>
<tr>
<td><strong>QIDS-C severe (≥16)</strong></td>
<td>46%</td>
</tr>
<tr>
<td><strong>QIDS-SR severe (≥16)</strong></td>
<td>44%</td>
</tr>
<tr>
<td><strong>On antidepressants</strong></td>
<td>22%</td>
</tr>
<tr>
<td><strong>RNA, 0-40 copies</strong></td>
<td>58%</td>
</tr>
<tr>
<td><strong>CD4, ≥ 500 cells</strong></td>
<td>68%</td>
</tr>
<tr>
<td><strong>CDC class, stage 0/1</strong></td>
<td>56%</td>
</tr>
<tr>
<td><strong>Integrase Inhibitor-based ARV</strong></td>
<td>74%</td>
</tr>
</tbody>
</table>
Health and Wellness CBT Content
Tailored for relevance: stigma, trauma, medical care – 24 weeks

<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>

Developed from Children’s Medication Algorithms Project; STAR*D Trial; Bialer, 2006; Caballero, 2005
Results:
Depression over 48 weeks
QIDS-SR Over 48 Weeks

Difference between ESC and COMB-R sites in QIDS-SR:

Week 24, [-3.9, (CI = -6.8, -0.9), p = 0.01]
Week 36, p = 0.05
QIDS-SR Response over 48 Weeks

Difference between ESC and COMB-R sites in response (>50% reduction in QIDS-SR):

- Week 12, \( p = 0.06 \)
- Week 24, \( p < 0.001 \) [44 (CI =23.1, 65.5), \( p < 0.001 \)]
- Week 36, \( p = 0.02 \)
- Week 48 \( p = 0.05 \)
QIDS-SR Remission over 48 Weeks

Difference between ESC and COMB-R sites in remission (QIDS-SR ≤ 5):

Week 24, [31 (CI = 8.9, 52.9), p = 0.01]
Week 36, p = 0.05
Results:
Viral Load / CD4 Over 48 Weeks
Viral Suppression and CD4 <200 over 48 weeks (COMB-R vs. ESC)

The site mean viral load, % viral suppression, CD4 level, and % CD4 < 200 were not significantly different between arms at any week.
The proportions of participants with a psychiatric hospitalization or suicide attempt were not significantly different between arms at any point (7% vs. 4% by week 48).

Note: non-parametric sensitivity analyses largely confirmed all findings being presented.
Results:
Medication use over 48 weeks
Antidepressant and SSRI use over 48 Weeks

Difference between sites in antidepressant use:
Week 24, $p = 0.06$

Difference between sites in SSRI use:
Week 24, $p = 0.02$
Adherence to care over 48 weeks

- Youth at the COMB-R sites, compared to ESC sites:
  - Attended more medication and therapy visits, but not significantly different
  - Self-report of adherence to HIV or antidepressants not different between groups
Conclusions

- Combination of medication algorithm and tailored CBT using measured care for 24 weeks resulted in:
  - Improved depression at 24 weeks with effects to 36 and 48 weeks
  - Greater use of SSRIs, but therapy visits not significantly increased
  - No impact on viral load or self-report of adherence – contrary to hypotheses
    - ESC received excellent, supportive care – adherence good in both groups
    - Depression is just one of many factors influencing adherence to ART
Future Analysis Plans

- Secondary analyses and publications
  - Effect modification – gender, age, level of depression on entry
  - Outcomes for those not on medication (~45%)
  - Behavioral risk outcomes
  - Implementation fidelity
  - Acceptability

THANKS

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Acknowledgments

The protocol team would like to thank the adolescents who participated in the trial in addition to the site investigators and research teams: Bronx-Lebanon Hospital Center, Children’s Diagnostic & Treatment Center, Ft. Lauderdale Florida, David Geffen School of Medicine at UCLA, Emory University School of Medicine, Jacobi Medical Center, Johns Hopkins University School of Medicine, Rush University Medical Center, St. Jude Children’s Research Hospital, State University of New York (SUNY) Stony Brook, Texas Children’s Hospital, The University of California San Diego, The University of Colorado Denver, The University of Southern California.

Overall support for the International Maternal Pediatric Adolescent AIDS Clinical Trials Network (IMPAACT) was provided by the National Institute of Allergy and Infectious Diseases (NIAID) with co-funding from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) and the National Institute of Mental Health (NIMH), all components of the National Institutes of Health (NIH), under Award Numbers UM1AI068632-15 (IMPAACT LOC), UM1AI068616-15 (IMPAACT SDMC) and UM1AI106716-09 (IMPAACT LC), and by NICHD contract number HHSN275201800001I. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.
THANKS!
To IMPAACT, Staff, Participants

Any questions?
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