IMPAACT 2002

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

Larry Brown, MD, Protocol Chair
Rhode Island Hospital; Brown University
23 June 2021

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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

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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 measures to guide care

- COMB-R was underlined 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.

(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

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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

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Study Objectives (Cont.)

▷ **Secondary Objectives - Examine:**
- Maintenance of depression impact at **48 weeks**
- Adherence for HIV and depression treatment
- Safety data - psychological hospitalizations and suicide attempts

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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)

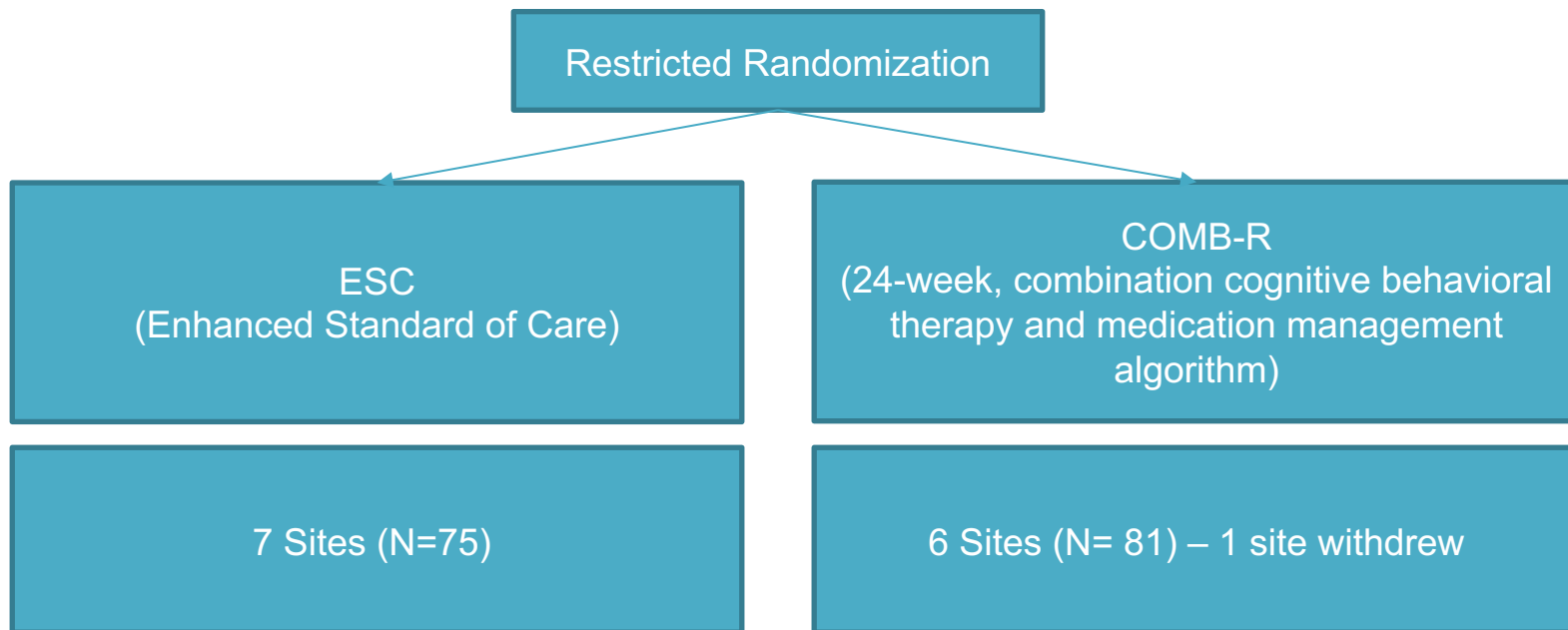**Sample Size:** 13 U.S. sites were randomized, to enroll 156 participants

Study Intervention: <u>Sites</u> 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)

COMB-R
(24-week, combination cognitive behavioral therapy and medication management algorithm)

7 Sites (N=75)

6 Sites (N= 81) – 1 site withdrew

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Accrual by Site and Treatment Arm

Treatment Arm	Site	Enrollment
COMB-R	Total	81
	Univ. of Colorado Denver NICHD CRS	16
	South Florida CDTC Ft Lauderdale NICHD CRS	13
	Rush Univ. Cook County Hosp. Chicago NICHD CRS	13
	Johns Hopkins Univ. Baltimore NICHD CRS	15
	David Geffen School of Medicine at UCLA NICHD CRS	13
	St. Jude Children's Hospital CRS	11
ESC	Total	75
	Texas Children's Hosp. CRS	8
	University of California San Diego CRS	16
	Jacobi Med. Ctr. Bronx NICHD CRS	16
	Emory University School of Medicine NICHD CRS	12
	SUNY Stony Brook NICHD CRS	5
	USC LA NICHD CRS	2
	Bronx-Lebanon Hospital Center NICHD CRS	16
All	Overall Total	156

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Sample Characteristics at Entry (n= 156)

Age (mean, s.d.)	21.4 (2.8)		QIDS-C severe (≥16)	46%
Male	47%		QIDS-SR severe(≥16)	44%
Race/ethnicity			On antidepressants	22%
Black, non-Hispanic	57%		RNA, 0-40 copies	58%
Hispanic (any race)	33%		CD4, ≥ 500 cells	68%
Route of HIV acquisition			CDC class, stage 0/1	56%
Perinatal	53%		Integrase Inhibitor-based ARV	74%
Behavioral	47%			

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Health and Wellness CBT Content
Tailored for relevance: stigma, trauma, medical care – 24 weeks

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

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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

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Results:
Depression over 48 weeks

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QIDS-SR Over 48 Weeks
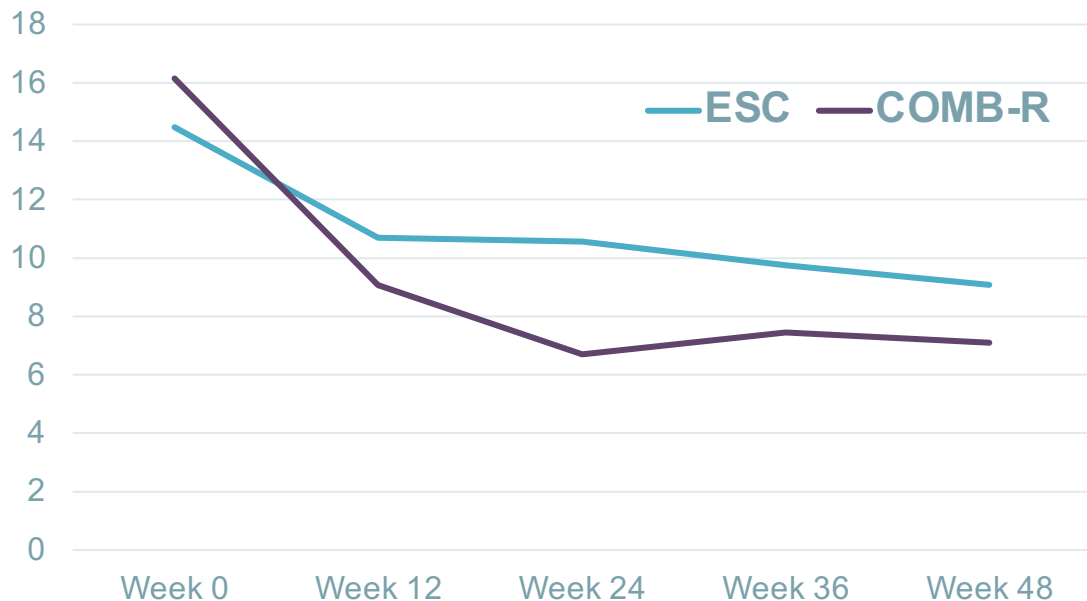
Difference between ESC and COMB-R sites in QIDS-SR:

Week 24, [-3.9, (CI =-6.8, -0.9), *p* = 0.01]

Week 36, *p* = 0.05

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QIDS-SR Response over 48 Weeks
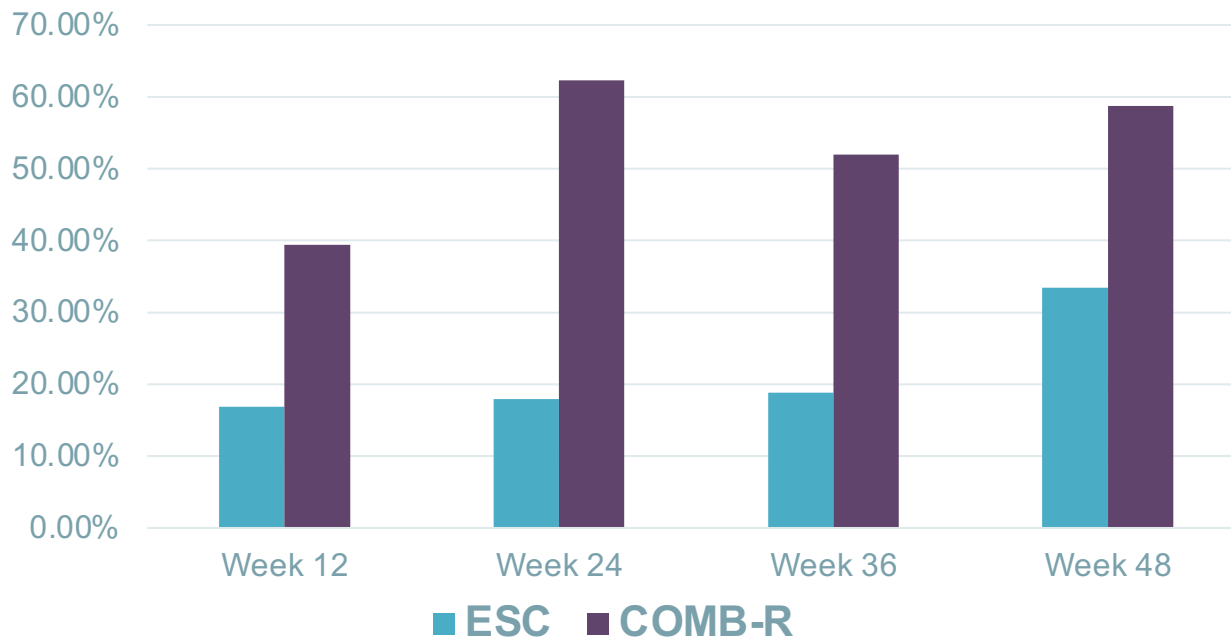
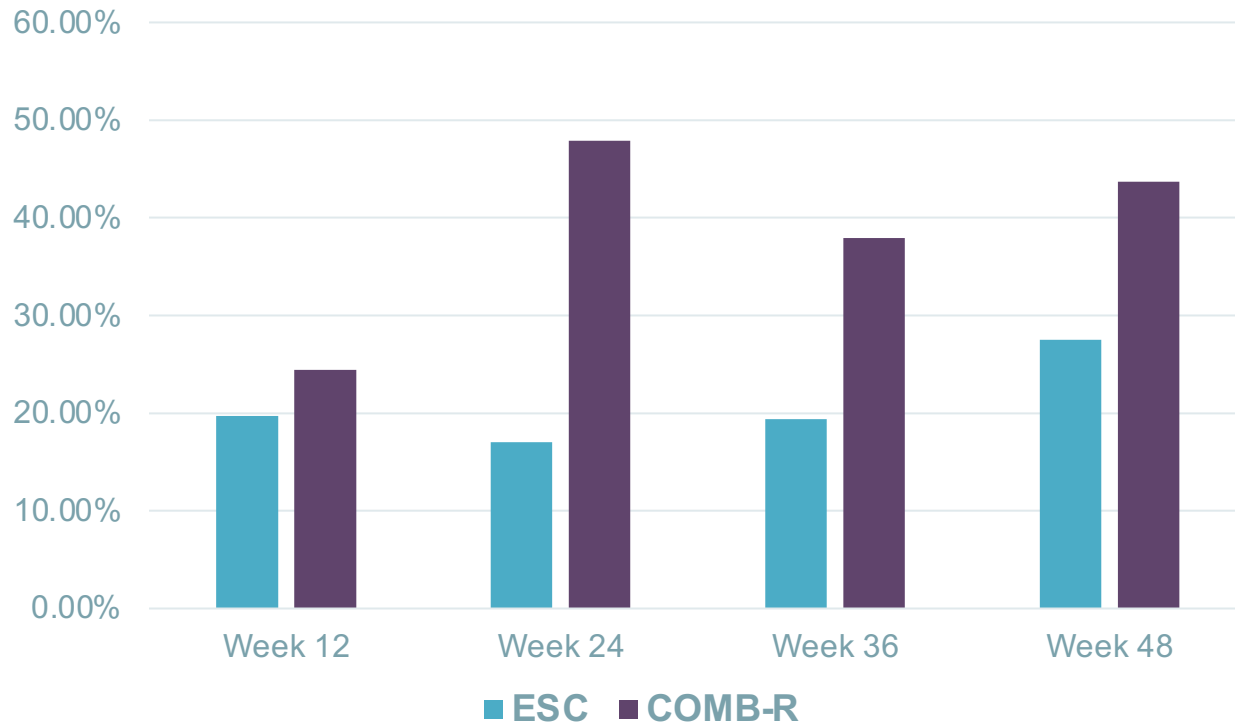Difference between ESC and COMB-R sites in response (>50% reduction in QIDS-SR):

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

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QIDS-SR Remission over 48 Weeks

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

Week 24, [31 (CI = 8.9, 52.9), p = 0.01]

Week 36, p = 0.05

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Results:
Viral Load / CD4 Over 48 Weeks

Viral Suppression and CD4 <200 over 48 weeks (COMB-R vs. ESC)

Viral Suppression
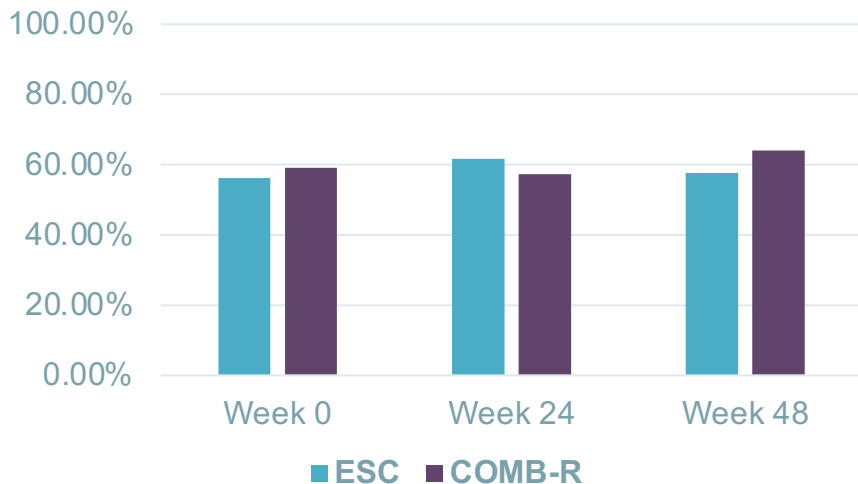
CD4 < 200
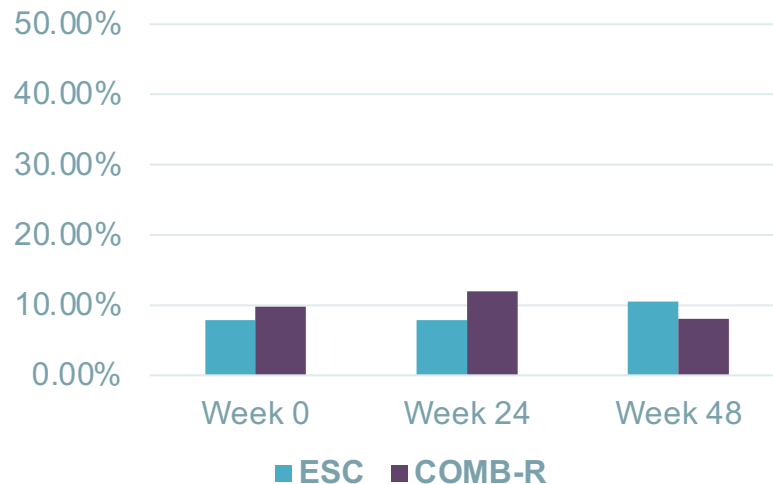
The site mean viral load, % viral suppression, CD4 level, and % CD4 < 200 were not significantly different between arms at any week

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Safety Results Over 48 Weeks

▹ 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).

▹ <u>Note:</u> non-parametric sensitivity analyses largely confirmed all findings being presented.

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Results:
Medication use over 48 weeks

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Antidepressant and SSRI use over 48 Weeks
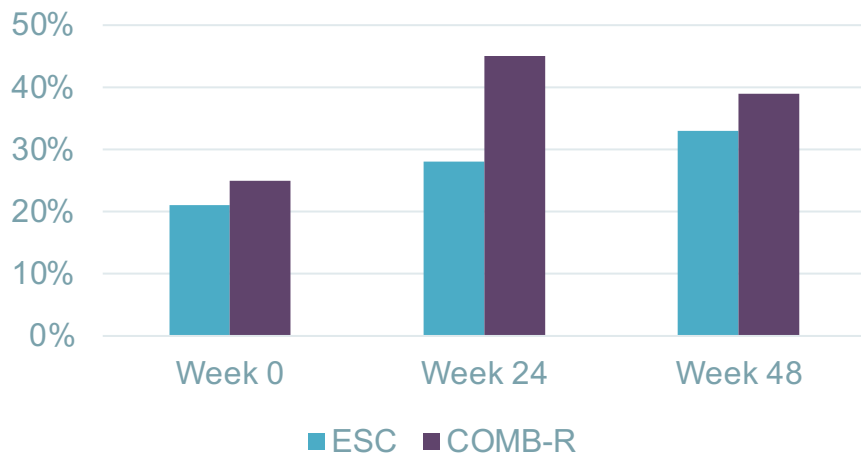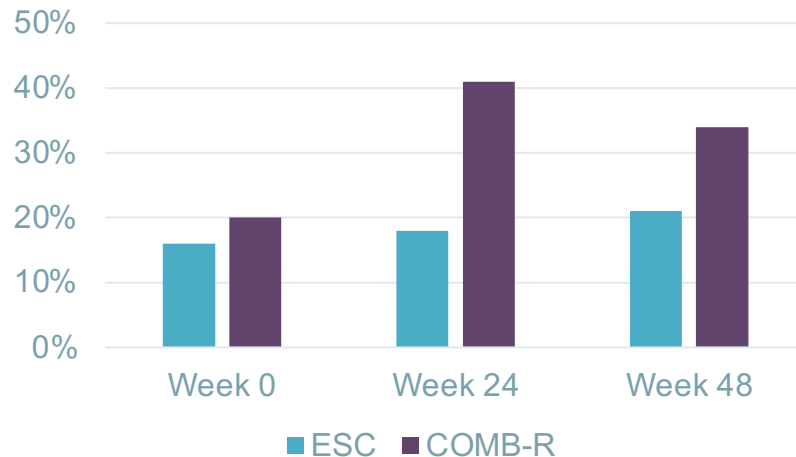
Adherence to care over 48 weeks

▹ 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

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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

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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

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THANKS!
To IMPAACT, Staff, Participants

Any questions?

You can find me at

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