

# Forty-eight Week Outcomes of a Site-Randomized Trial of Combined Cognitive Behavioral Therapy and Medication Management Algorithm for Treatment of Depression Among Youth with HIV in the U.S.

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**International Maternal Pediatric Adolescent AIDS Clinical Trials  
Network (NIH-funded)**

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# Protocol Team (abbreviated list)

**Medication Algorithm:** Graham Emslie, MD

**CBT Supervision:** Betsy Kennard, PhD

**NIH Medical Officers:** Ellen Townley, MSN, FNP; Adeola Adeyeye, MD, MPA; Sonia Lee, PhD; Susannah Allison, PhD

**Data Manager:** Chelsea Krotje, MPH

**Statisticians:** Miriam Chernoff, PhD; David Shapiro, PhD; Kristin Baltrusaitis, PhD

**Statistical Programmer:** Shirley Traite, MSW

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

# Study Background & Rationale

- ▶ Depression is common among youth with HIV (YWH) and is associated with increased morbidity and mortality.
- ▶ Medication algorithms and cognitive behavioral therapy (CBT) are effective
- ▶ Combination treatment (COMB) is a collaborative, stepped care approach with use of standard measures to guide care
- ▶ Efficacy of COMB for treatment of depression in YWH demonstrated in smaller trial

# Study Objectives

- ▶ **Primary Objectives - To evaluate whether:**
  - Is 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

# Study Objectives

- ▶ **Secondary Objectives - Examine:**
  - Maintenance of depression impact at **48 weeks**
  - Impact on viral suppression rates
  - Safety data - psychological hospitalizations and suicide attempts

# Study Design

**Study Population:** Youth with HIV diagnosed with nonpsychotic depression (structured clinician rating)

**Sample Size:** 13 U.S. sites were randomized to COMB-R or control, to enroll 156 participants

**Enhanced Standard of Care:** Online training in depression treatment. All sites provided access to therapists and antidepressant medication.



# Sample Characteristics at Entry (n= 156)

Age (mean, s.d.)	21.4 (2.8)	QIDS-C severe ( $\geq 16$ )	46%
Male	47%	On antidepressants	22%
Race/ethnicity		RNA, 0-40 copies	58%
Black, non-Hispanic	57%		
Hispanic (any race)	33%		
Route of HIV acquisition			
Perinatal	53%		
Behavioral	47%		

# Health and Wellness CBT Content

Tailored for relevance: stigma, trauma, medical care – 24 weeks

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

# Medication Algorithm

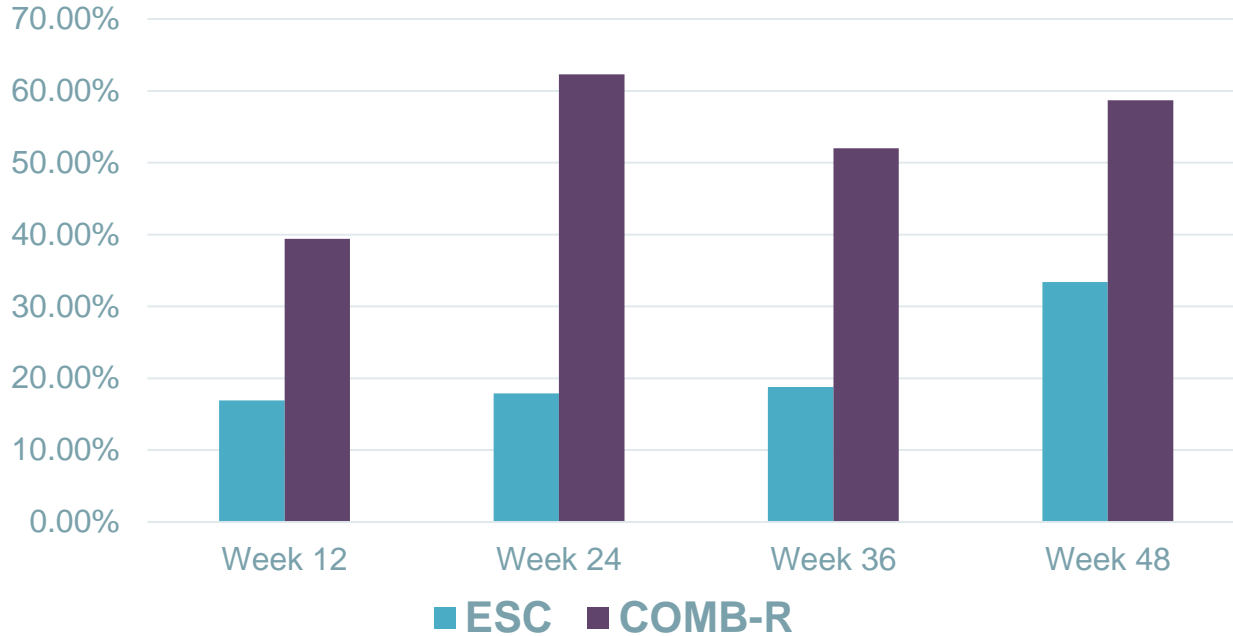
- Framework, not “restrictive,” not a specific medication
- Strategy based on measured care/patient response

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	2 <sup>nd</sup> SSRI	Increase dose or augment partial resp.
Stage 3	Non-SSRI	Increase dose or augment partial resp.
Stage 4	Combination Treatment	Two antidepressants or antidepressant plus lithium

# **Results:**

## **Depression over 48 weeks**

# QIDS-SR Response over 48 Weeks



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

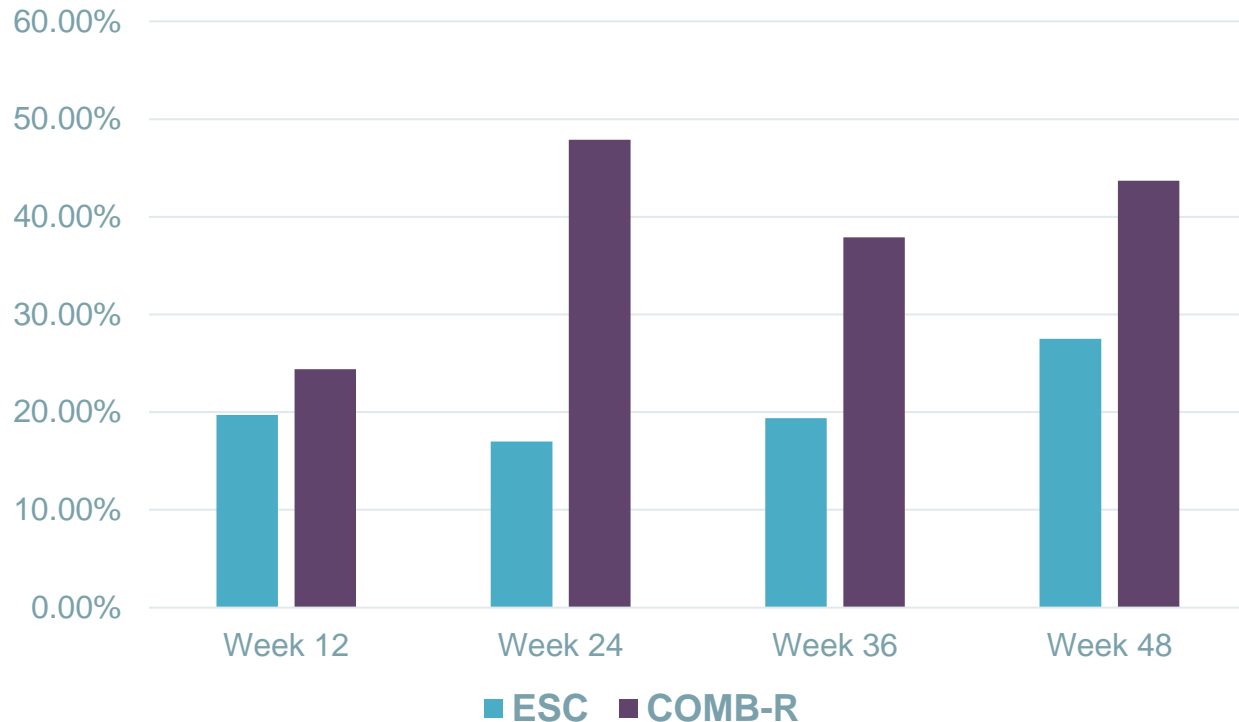
Week 12,  $p = 0.06$

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  $\leq 5$ ):

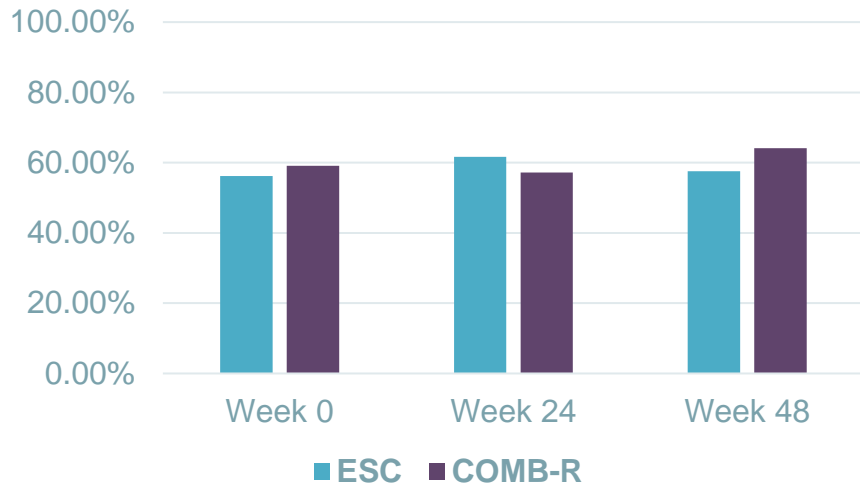
Week 24, [31 (CI = 8.9, 52.9),  $p = 0.01$ ]

Week 36,  $p = 0.05$

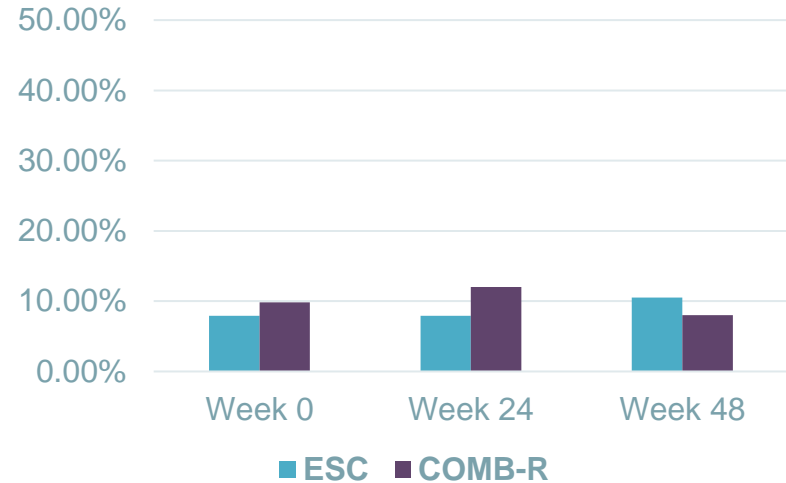
# **Results: Viral Load / CD4 Over 48 Weeks**

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

## 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



# Safety Results Over 48 Weeks

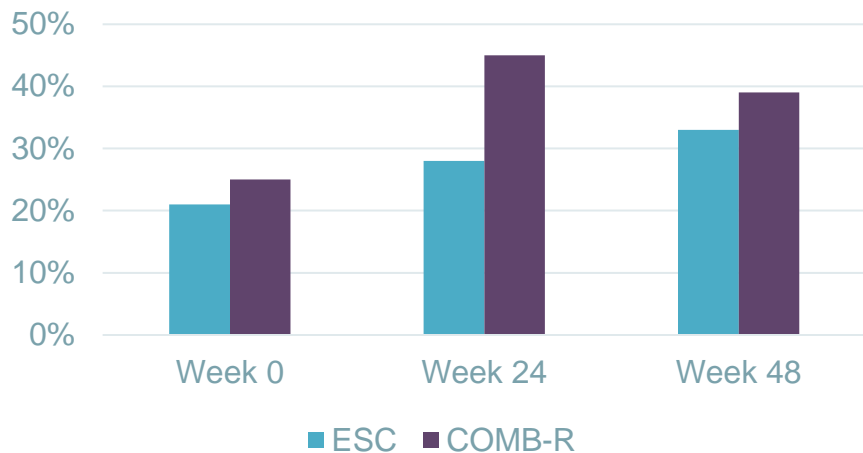
- ▶ The proportions of participants with a psychiatric hospitalization or suicide attempt were not significantly different between arms at any point (7% vs. 4% by week 48).
- ▶ Note: non-parametric sensitivity analyses largely confirmed all findings being presented.

# **Results:**

## **Medication use over 48 weeks**

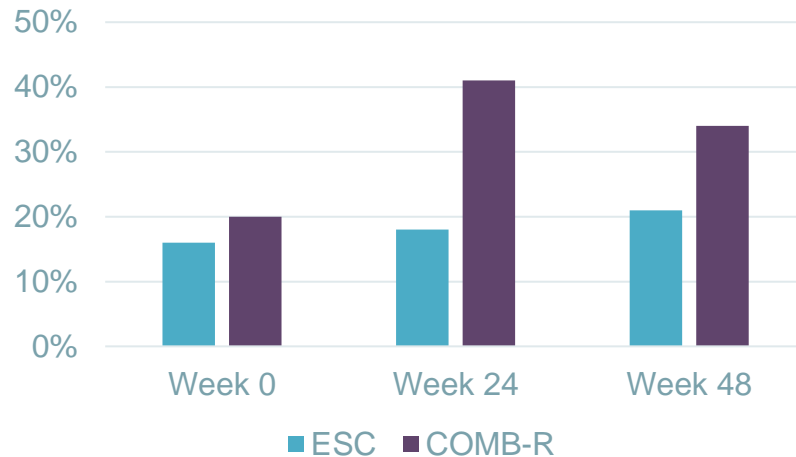
# Antidepressant and SSRI use over 48 Weeks

## Antidepressant use



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

## SSRI use



Difference between sites in SSRI use:  
Week 24,  $p = 0.02$

# 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 & 48
  - Greater use of SSRIs, but therapy visits not increased
  - No impact on viral load – contrary to hypotheses
    - ESC received excellent, supportive care
    - Depression is just one of many factors influencing adherence
    - Adherence skills mainly in early COMB-R sessions

# THANKS!

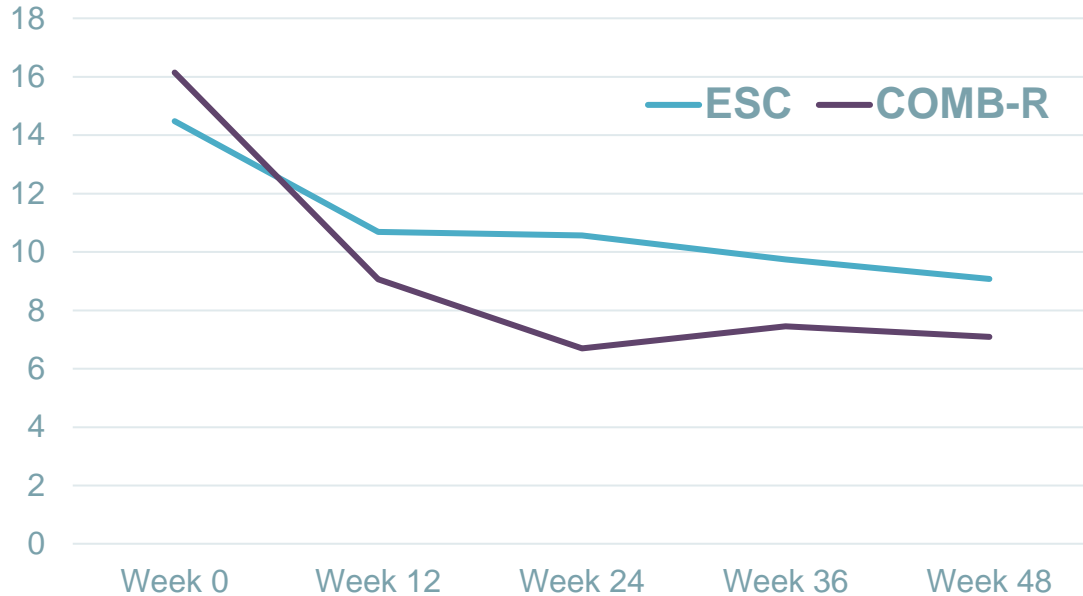
## To IMPAACT, Staff, Participants

**Any questions?**

You can find me at

- [Larry\\_Brown@brown.edu](mailto:Larry_Brown@brown.edu)

# 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,  $p = 0.05$

# Study Background & Rationale

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- ▶ COMB-R was adapted for easy dissemination – training and supervision reduced, and all online, videotaped
- ▶ A larger sample for greater power to detect differences:
  - Viral suppression
  - Demographic characteristics: gender, route of infection

(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>