

Psychiatric disorder symptoms are associated with longitudinal changes in antiretroviral (ARV) non-adherence in perinatally HIV-infected youth in the US: Results from IMPAACT P1055

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Perinatally HIV-Infected (PHIV+) Youth and ARV Adherence

- ~10,000 PHIV+ youth in the US and Puerto Rico entering adolescence and adulthood
- Most have received antiretroviral therapy throughout their lifetimes, and face challenges to adherence
- Prevalence of psychiatric conditions
 - Exceeds general population prevalence
 - Similar to uninfected youth perinatally HIV-exposed or in HIV-affected families (*Mellins, 2003, 2012; Gadow 2010, 2012*)
- 25-79% with suboptimal ARV adherence (*Simoni, 2007; Koenig, 2011*);
- Depression, anxiety, and conduct problems linked to ARV non-adherence in US PHIV+ youth in some cross-sectional studies (*Malee, 2011; Williams, 2006*)
- Others found no association (*Naar-King, 2013, Rudy 2010*)

Study Objectives

- To evaluate the association between psychiatric conditions and
 - antiretroviral non-adherence over time
 - lack of virologic (VL) suppression over time
- To evaluate the association between psychiatric conditions at baseline and becoming non-adherent to ARVs at follow-up (*“incident non-adherence”*) among PHIV+ youth who were adherent to ARVs at baseline
- To evaluate the association between psychiatric conditions at baseline and loss of VL suppression within two years of follow-up among PHIV+ youth with suppressed VL at baseline

Study Population

- International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) P1055
 - Prospective study of HIV disease and psychiatric conditions
 - 319 PHIV+ and 254 HIV-negative HIV-affected youth, 6-17 yrs
 - 29 clinical sites in US and Puerto Rico
 - Assessed youth and caregivers
 - Enrolled 6/2005-12/2008
 - Baseline, Week 48, Week 96 visits
- **Inclusion criteria for our analysis**
 - **PHIV+, ≥ 1 follow up visit, and ≥ 1 visit on ARVs**

Outcomes

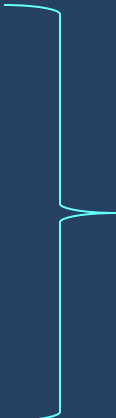
Self-reported ARV non-adherence

3-day recall

- PACTG 3-day recall adherence interview
- Defined as missing >5% of expected doses

Missed a dose within past month

- Defined as last missing a dose within the past month



Reported
by either
youth or
caregiver

Lack of VL suppression

Defined as HIV RNA >400 copies/mL

Exposure: Psychiatric Conditions

Defined as meeting symptom cutoff scores determined by DSM-IV threshold criteria

Psychiatric condition domains (Presence vs. absence):

ADHD: Attention Deficit Hyperactivity Disorder

ODD/CD: Oppositional Defiant and Conduct Disorder

Depression: major depressive disorder and dysthymia

Anxiety: generalized and separation anxiety disorders

Any Targeted Condition: ≥ 1 of above

Rating scales, each visit (*Gadow, 1999, 2005*)

- Caregiver –assessed: *Child and Adolescent Symptom Inventory-4R*
- *Child (Self-report) Inventory*
- *Youth (Self-report) Inventory-4R*

Statistical Analysis

Association of psychiatric conditions and a) non-adherence b) lack of VL suppression over time

- Univariable and multivariable logistic models using Generalized Estimating Equations (GEE). Controlled for demographic, clinical, and family characteristics associated with outcome ($p < 0.1$) in core model.
- Assumed constant effect over time unless psychiatric condition*visit interaction $p < 0.1$

Association of baseline psychiatric conditions and a) incident non-adherence among adherent youth b) loss of VL suppression among youth with VL suppression

Univariable and multivariable logistic regression models. Controlled for demographic, clinical, and family characteristics associated with outcome ($p < 0.1$) in core model.

NOTE: Separate models were fitted for each psychiatric disorder and each outcome.

Analysis Sample

Non-adherence, 3-day recall:

n=270 individuals, 778 records

Non-adherence, missed a dose within past month:

n=272 individuals, 783 records

Lack of VL suppression:

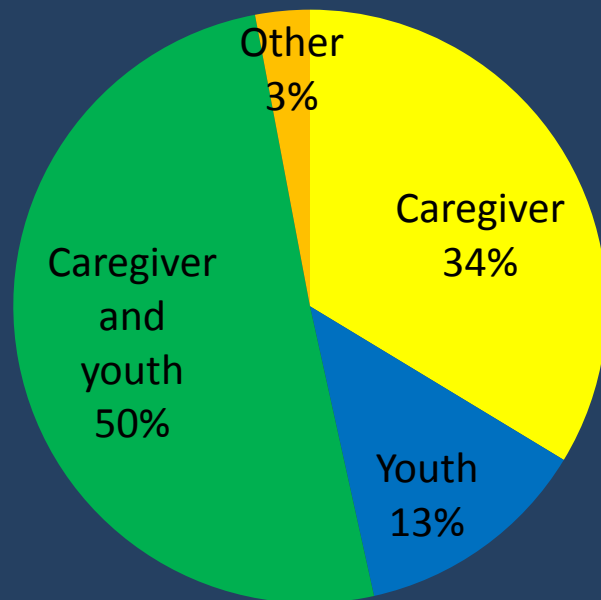
n=294 individuals, 845 records

Demographic Characteristics at Baseline (n=270)

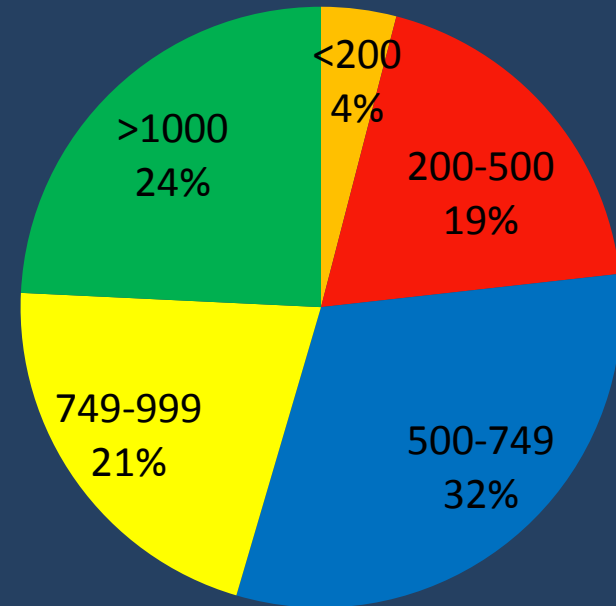
Characteristic	%
Female	49%
Race/Ethnicity	
White, Non-Hispanic, Asian or Other	14%
Black, Non-Hispanic	55%
Hispanic	31%
Age (yrs)	
6-<10	21%
10-<13	29%
13-<16	33%
16-<18	17%
Aware of having HIV infection	70%
Caregiver is biological parent	42%
Caregiver high school graduate	70%
Annual household income >\$20,000	52%
≥1 life stressors	62%

Health and Treatment Characteristics at Baseline (n=270)

Responsibility for administering medication

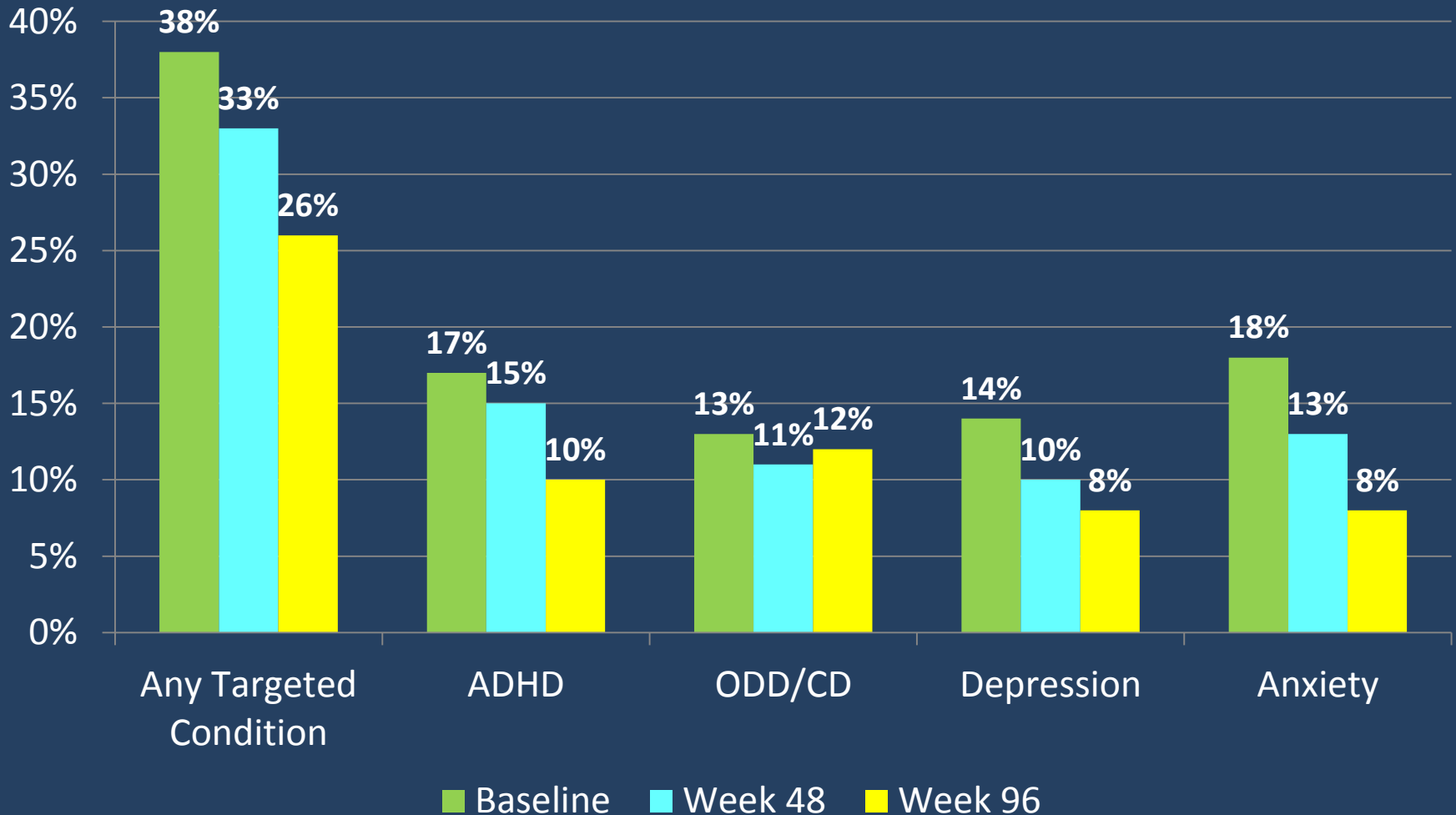


CD4 Count (cells/mm³)

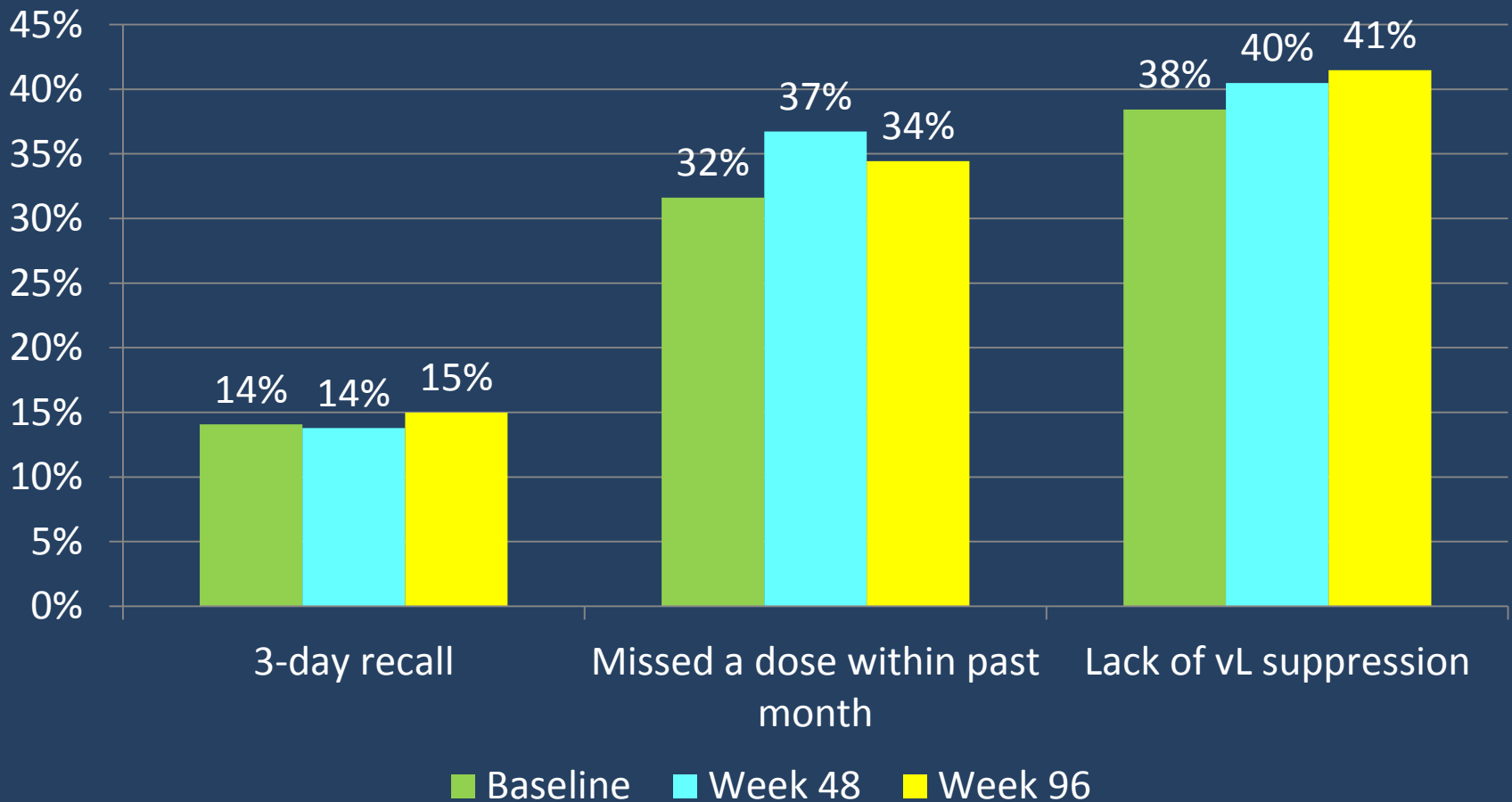


- 73% on a PI-based HAART regimen
- 14% currently using psychotropic medication

Prevalence of psychiatric conditions by visit among PHIV+ youth in IMPAACT P1055



Prevalence of non-adherence and lack of VL suppression by visit



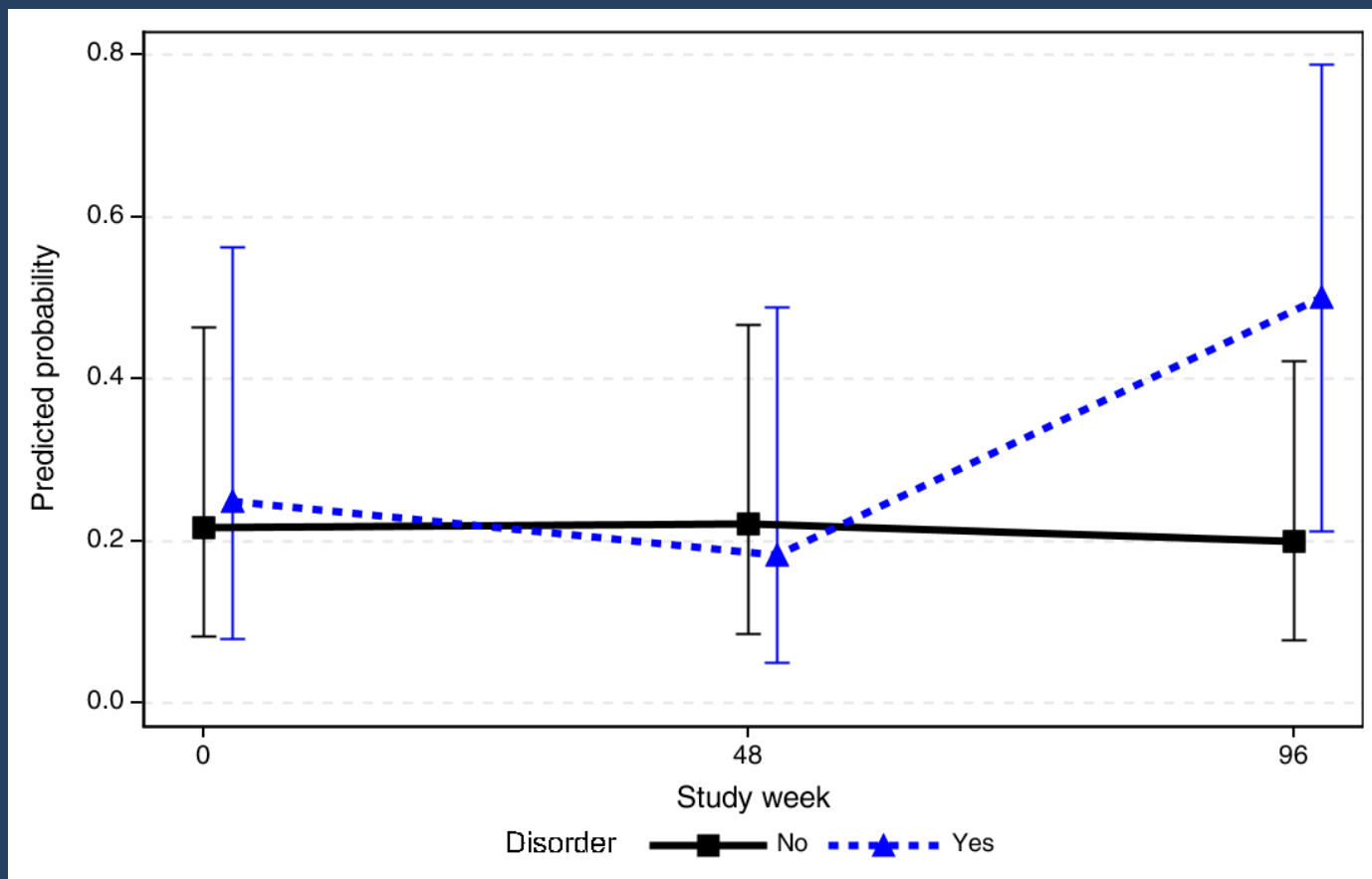
Summary of multivariable GEE results

Odds of non-adherence and odds of lack of VL suppression for youth with vs. without psychiatric conditions

	3-day recall	Missed dose in past month	Lack of VL suppression
ADHD	--	--	Greater odds , but at later visits
ODD/CD	Greater odds, but at week 96	--	--
Depression	Greater odds, but at week 96	Greater odds, but at week 96	--
Anxiety	--	--	Reduced odds
Any Targeted Condition	--	--	--

Predicted probability of non-adherence (3-day recall) for youth with vs. without ODD/CD over time

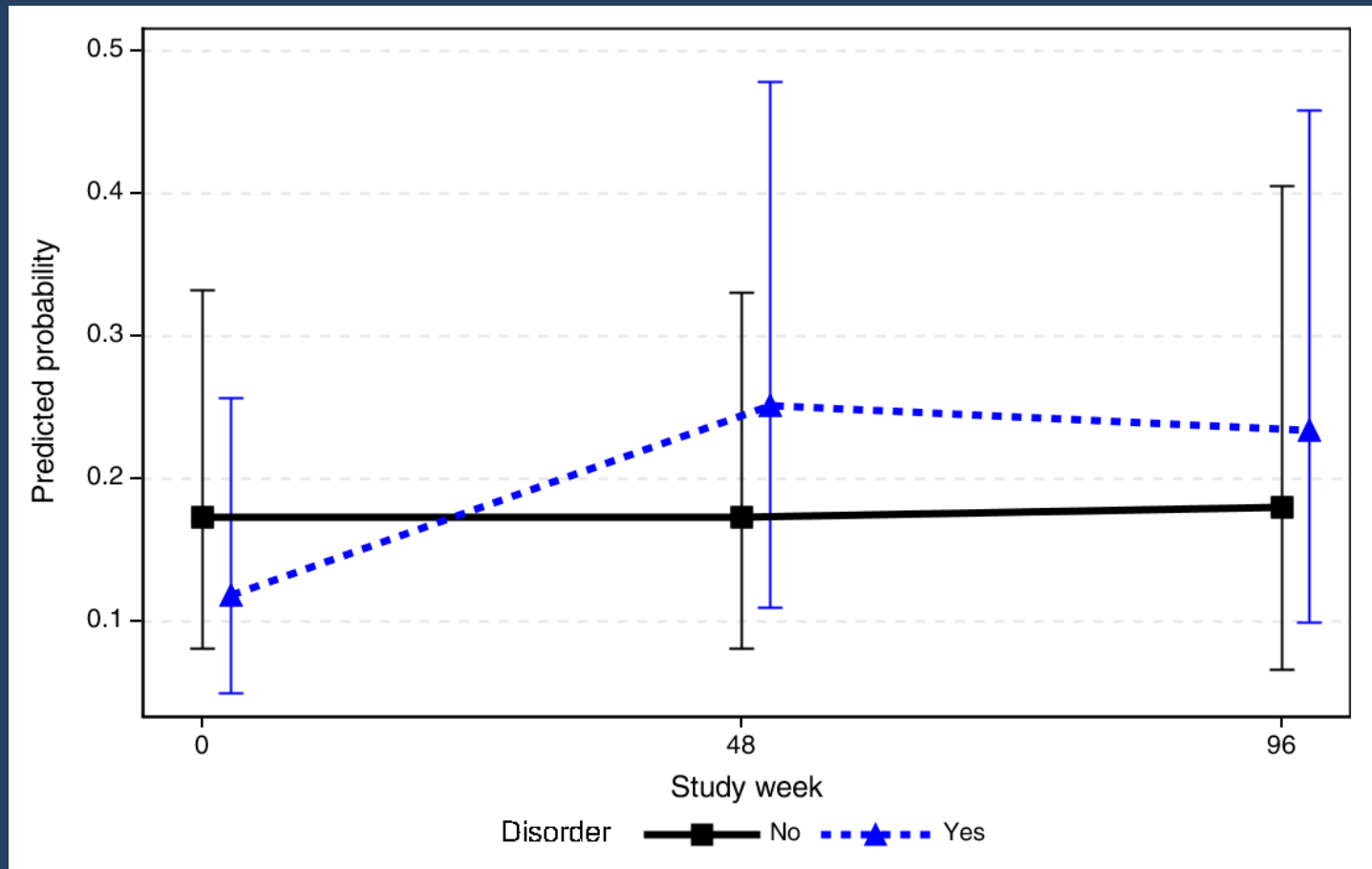
ODD/CD* week
interaction
overall p=0.05



Those with ODD/CD (aOR=3.36; 95%CI:1.02-11.10) vs. without had greater odds of non-adherence at week 96, but not at earlier visits. Models adjusted for age and CD4 count at baseline.

Predicted probability of lack of VL suppression for youth with vs. without ADHD over time

ADHD*week
interaction
overall p=0.01



Those with ADHD vs. without had greater odds of lack of VL suppression at week 48 (aOR=2.51; 95% CI:1.28-4.9) and 96 (aOR=2.17; 95% CI:1.0-4.69) vs. baseline. Models adjusted for age, race/ethnicity, income at baseline.

Association between anxiety and lack of virologic suppression

	Adjusted OR (95% CI)	P-value
Anxiety vs. none	0.61 (0.40, 0.93)	0.03
Age		
10-<13 vs. 6-10	1.43 (0.75, 2.73)	0.02
13-16 vs. 6-10	1.47 (0.75, 2.86)	
>16-18 vs. 6-10	3.32 (1.56, 7.08)	
Race/ethnicity		
Black vs. White	2.79 (1.37, 5.69)	0.02
Hispanic vs. White	2.19 (1.02, 4.72)	
Income >\$20,000/yr vs. <\$20,000/yr	0.57 (0.36, 0.90)	0.02
Week 48 vs. Baseline	1.11 (0.88, 1.41)	0.66
96 vs. Baseline	1.10 (0.84, 1.43)	

Incident non-adherence and loss of VL suppression

3-day recall:

Among 232 adherent youth at baseline, 17% reported non-adherence during follow-up.

Missed a dose within past month:

Among 186 adherent youth at baseline, 33% reported non-adherence during follow-up.

Loss of VL suppression:

Among 181 youth with VL suppression at baseline, 25% had loss of VL suppression during follow-up.

Association between psychiatric disorders at baseline and incident non-adherence (3-day recall)

	Crude OR (95% CI)	Adjusted OR (95% CI)*
Any targeted disorder	1.51 (0.75, 3.02)	1.50 (0.73, 3.08)
ADHD	1.94 (0.85, 4.40)	1.89 (0.82, 4.36)
ODD/CD	3.14 (1.33, 7.43)	3.01 (1.24, 7.31)
Depression	0.44 (0.13, 1.50)	0.43 (0.12, 1.55)
Anxiety	0.72 (0.28, 1.83)	0.68 (0.25, 1.86)

**Each model adjusted for age at baseline*

Summary and Conclusions I

- High prevalence of psychiatric disorder symptoms in PHIV+ youth
- Prevalence of non-adherence remained similar over time and was greatest for last missed dose in past month measure
- No single psychiatric condition associated with all measures of non-adherence but direction of association and pattern over time similar for some
 - Youth with anxiety disorder symptoms had greater odds of VL *suppression* throughout the study period.
 - Associations between a)depression and each adherence measure, b)ODD/CD and 3-day recall non-adherence, and c) ADHD and lack of VL suppression were seen at later visits but not at enrollment – why?

Summary and Conclusions (cont.)

- Among youth adherent at baseline those with ODD/CD had greater odds of developing non-adherence at followup.
 - No effects seen for other disorders, incident non-adherence (last missed dose past month) or loss of VL suppression.
- Older age independently associated with both non-adherence measures and lack of VL suppression
- Black and Hispanic race/ethnicity and higher income independently associated with lack of VL suppression in GEE analyses

Limitations

- Self-report data on non-adherence may lead to overestimates
- Last missed dose measure includes psychotropic medication
- Clinic-based convenience sample may not be generalizable to PHIV+ youth

Implications

- Ongoing screening for presence of psychiatric condition symptoms and increased supports for PHIV+ in adolescence and young adulthood are needed;
- Adherence interventions for adolescents and young adults should address existing and potentially emerging psychiatric comorbidities;
- Future research should examine impact of psychiatric conditions on non-adherence and evaluate interventions as PHIV+ enter young adulthood.

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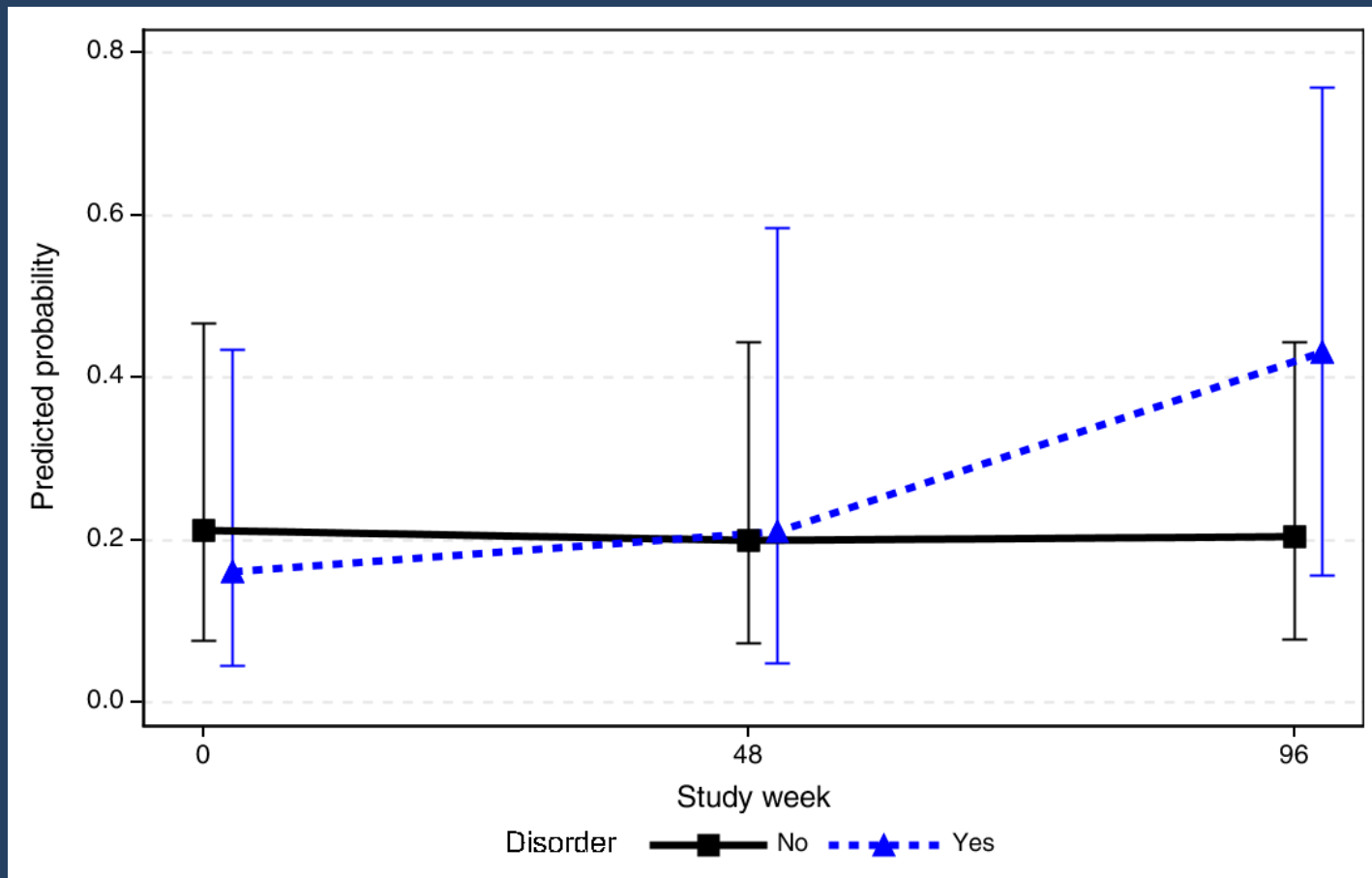
National Institute
of Mental Health



EXTRA SLIDES

Predicted probability of non-adherence (3-day recall) for youth with vs. without major depression or dysthymia over time

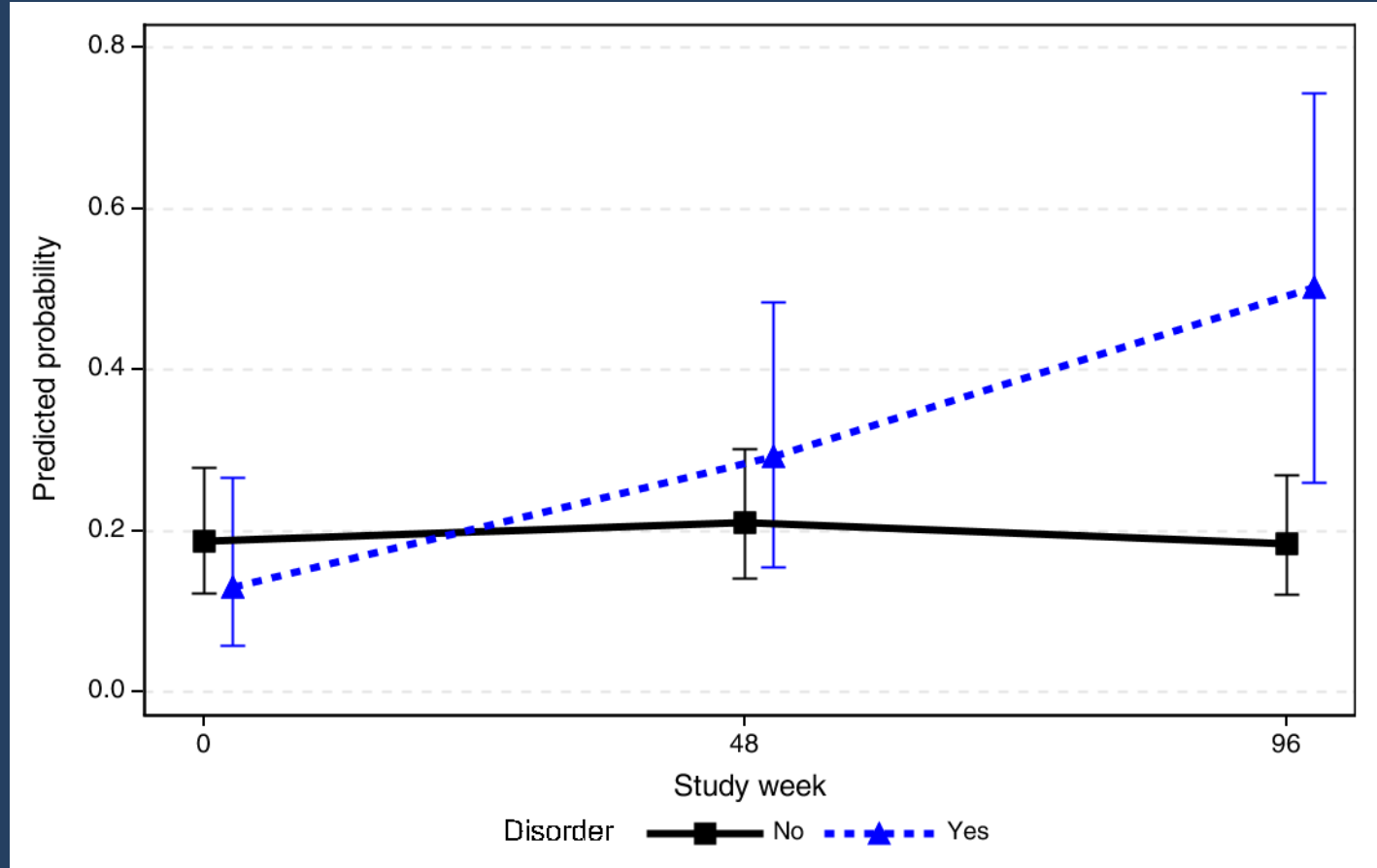
Depression*week
interaction overall
 $p=0.1$



Those with depression ((aOR)=4.14; 95% CI: 1.11-15.42) versus without had greater odds of non-adherence at week 96, but not at earlier visits. Models adjusted for age and CD4 count at baseline.

Predicted probability of non-adherence (last missed ARV dose last month) for youth with vs. without major depression or dysthymia over time

Depression*
week
interaction
overall
 $p=0.03$



Odds of non-adherence (last missed dose last month) for those with depression versus without were greater at week 96 (aOR=6.96; 95% CI:1.6-30.3) versus entry. Models adjusted for age at entry.

Other covariates

Demographic

- Age at enrollment
- Sex
- Race/ethnicity
- Life stressors
- Knowledge of HIV status

Clinical and Treatment

- CD4 count
- CD4%
- ARV regimen
- Current psychotropic medication use

Family

- Caregiver educational attainment
- Annual household income
- ≥ 1 psychiatric symptoms
- Caregiver relationship to youth