

Nonadherence and Unsuppressed Viral Load Across Stages of Adolescent Development in US Youth with Perinatally Acquired HIV in the Pediatric HIV/AIDS Cohort Study: A Longitudinal Analysis

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Background

- Suboptimal adherence and loss of VL suppression more frequent in older youth and in youth vs. adults
- Adolescence a dynamic period of physical, cognitive, social/emotional changes, increasing independence and identity development
- At each stage of adolescent development, individual, behavioral and social factors associated with adherence may vary
- Longitudinal studies needed to identify factors associated with adherence in early and late adolescence and to support prevention/intervention efforts as youth with perinatally-acquired HIV (PHIV) transition to young adulthood

Mellins, 2004; Williams 2006; Nachega, 2009; Usitalo 2013; Agwu, 2013

Study Objectives

- Determine the prevalence of nonadherence to ARVs and unsuppressed viral load, and changes across age among youth with PHIV;
- Identify individual, caregiver and structural factors associated with nonadherence and unsuppressed viral load and compare factors associated with nonadherence across stages of adolescence

Methods

- **Conceptual Framework:** Approach informed by Social Action Theory Model and Biopsychosocial Model of Adolescent Development
- **Study population:** Youth with perinatal HIV infection enrolled in the **Adolescent Master Protocol** of the **Pediatric HIV/AIDS Cohort Study**
 - Prospective study of impact of HIV and ARVs on youth with PHIV
 - Enrolled youth and caregivers at 15 clinical sites in US and Puerto Rico from 3/2007-10/2009 and followed at annual visits
- **Analysis inclusion criteria:** Youth with PHIV with at least 1 youth-reported or caregiver-reported adherence evaluation
- Data as of July 1, 2014:
 - Self-reported nonadherence analysis: N=379 youth, 1190 visits
 - Unsuppressed viral load analysis: N=381 youth, 1257 visits

Outcome Measures

Nonadherence

- Assessed annually via interview w/youth and/or caregiver *
- Defined as at least 1 missed ARV dose in past 7 days
- Classified as nonadherent if either caregiver OR youth reported youth was nonadherent

Unsuppressed viral load

- Included measures taken within +/- 3 months of adherence visit week
- Defined as HIV-RNA >400 copies/mL

*one 1.5 yr. interval between Y 2.5 and Y 4

Covariates

Demographic

- Gender
- Race
- Ethnicity
- Caregiver education
- Annual HH income

Social/Environmental

- Youth exposure to violence
- # Stressful life events
- Stigma [Concern about inadvertent disclosure of HIV status]

Social Interaction Processes

Social Support

- Buddy system to promote adherence
- Youth has boyfriend/girlfriend

Caregiver Functioning

- Health limitations
- Marital status
- Living arrangement

Self and Social Regulation

- Relationship with parents [BASC 2- Personal adjustment composite]
- Youth awareness of HIV status
- Youth alcohol use past 3 mos.

HIV Disease-Related

- Nadir CD4%
- ARV regimen
- Medication burden [Frequency per day taking ARV]
- Distressing physical symptoms
- ARV side effects

Youth mental health functioning

- Emotional Problem : [BASC 2- ESI]
- Behavioral Problem: [BASC 2 – BSI]

Youth-reported violence exposure, past year

Life Events Checklist (see Kang, 2011)

Definition (at least one event)

Direct violence victimization

- Physically attacked
- Raped or sexually assaulted
- Robbed or burglarized

Indirect exposure to violence

- Witnessed fight in which weapon used
- People in neighborhood hit by police
- Someone murdered in neighborhood
- Heard gunshots on their block

Any violence exposure

- Physically attacked
- Raped or sexually assaulted
- Robbed or burglarized
- Witnessed fight in which weapon used
- People in neighborhood hit by police
- Someone murdered in neighborhood
- Heard gunshots on their block

Statistical Analysis

- Calculated proportion with self-reported nonadherence and proportion with unsuppressed viral load at each age and developmental stage;
- Within each age stratum, univariable and multivariable models using generalized linear mixed effects regression to estimate associations of covariates with outcomes;
- Evaluated whether effect of each covariate was modified by age by testing interactions between age and covariates

Sample characteristics of youth with PHIV at first visit

	Total (N=379)
Female	53%
Race	
Black/African American	71%
White, more than one race, other	21%
Unknown	4%
Latina or Latino	21%
Age (yrs)	
8-11	27%
12-14	33%
15-17	35%
18-20	4%
Caregiver graduated high school/GED	74%
Annual household income	
\$10,000 or less	20%
>\$10,000-\$40,000	55%
>\$40,000	24%
Caregiver married	40%
Caregiver living with partner/spouse	51%

HIV clinical and treatment characteristics of youth with PHIV at first visit

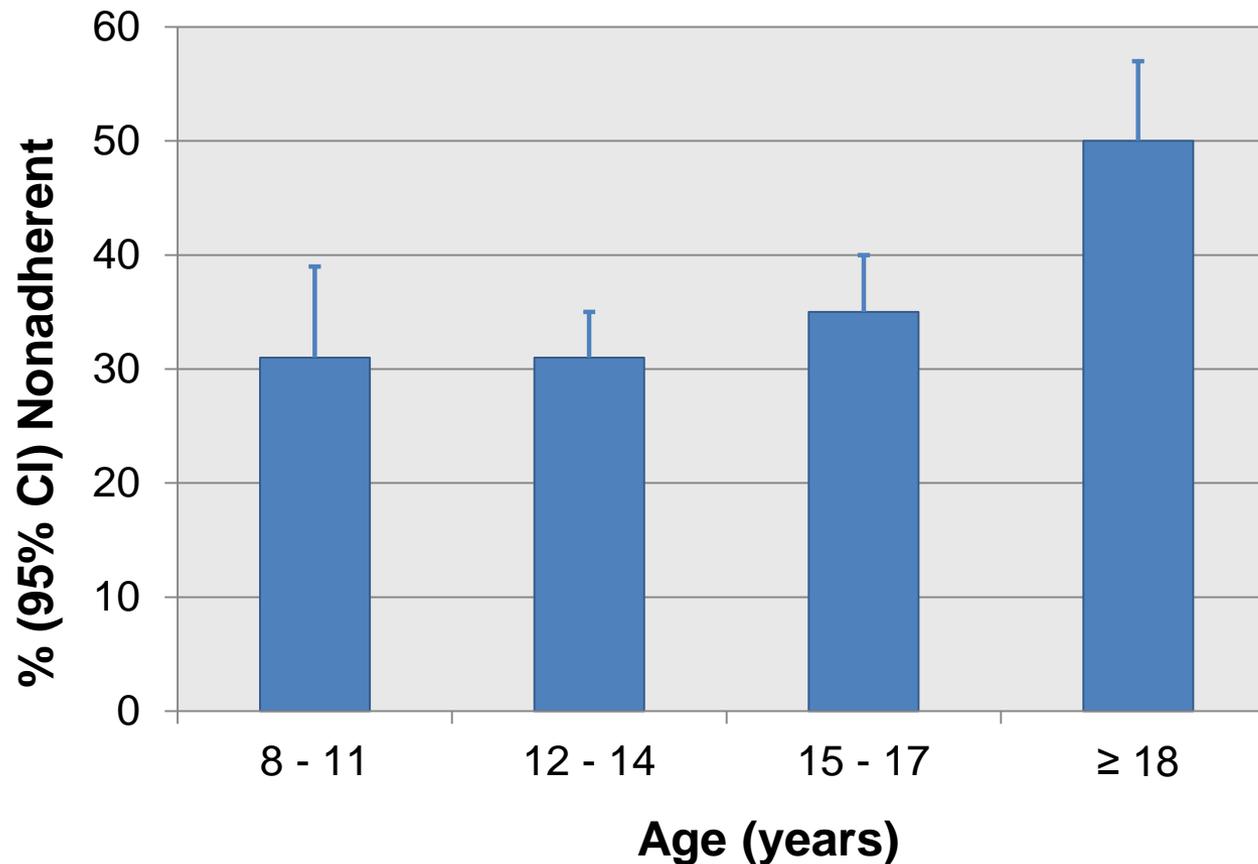
	Total (N=379)
Nadir CD4%	
<15%	36%
15-25%	42%
>25%	22%
Once daily ARV regimen	31%
ARV Regimen	
cART w/PI	57%
cART w/NNRTI or NRTI	10%
Non cART	33%
ARV side effects	9%
Youth aware of their HIV status	79%
Years from first to most recent adherence assessment, mean (SD)	2.6(1.6)

Distribution of visits across age groups (379 youth with PHIV)

	N=1190
	N(%)
Pre-adolescence (8-11 years)	172 (14%)
Early adolescence (12-14 years)	383 (32%)
Late adolescence (15-17 years)	432 (36%)
Emerging adulthood (18-21 years)	203 (17%)

Prevalence of Self-reported Nonadherence by Age

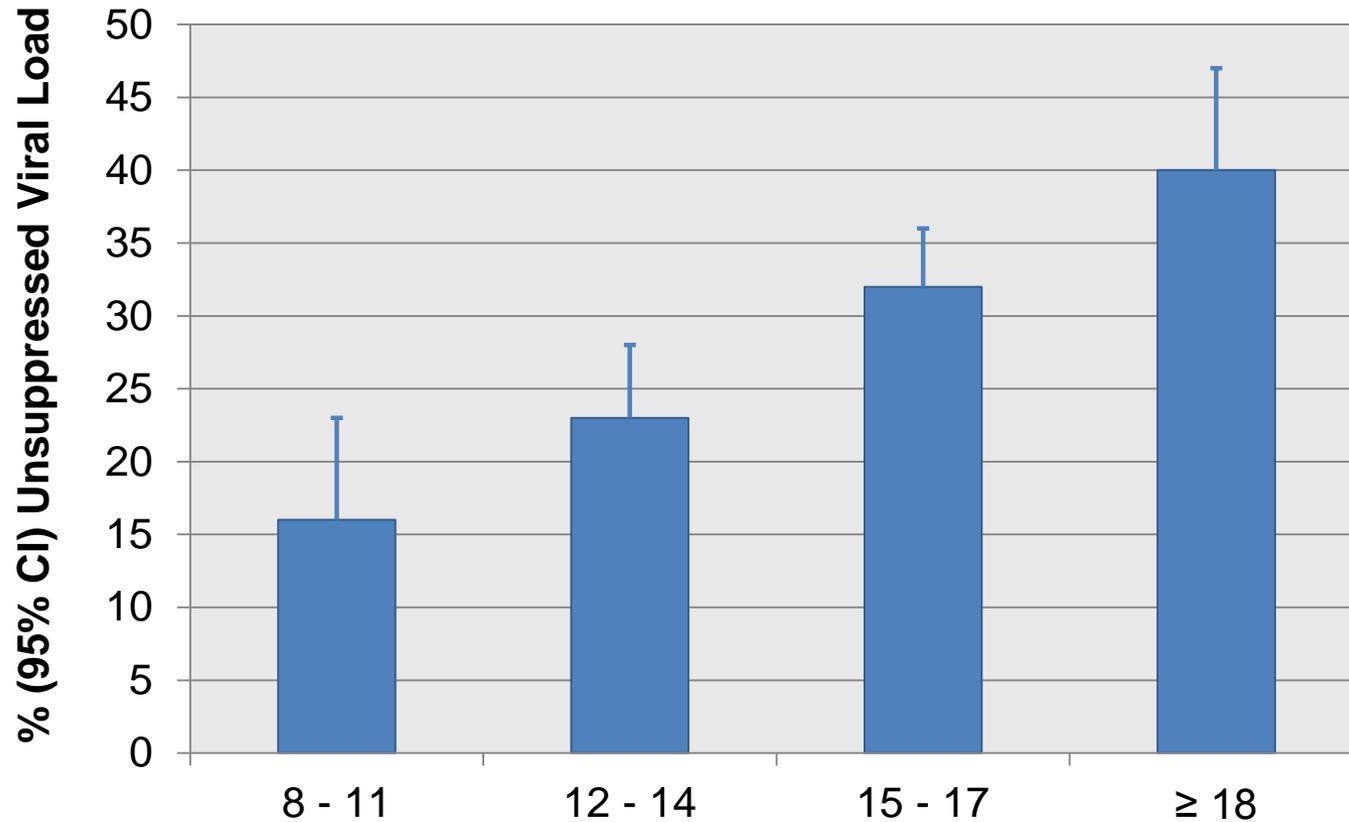
N=1190 visits of 379 Youth with PHIV



	N			
	8 - 11	12 - 14	15 - 17	≥ 18
Total	172	383	432	203
Nonadherent	54	117	153	102

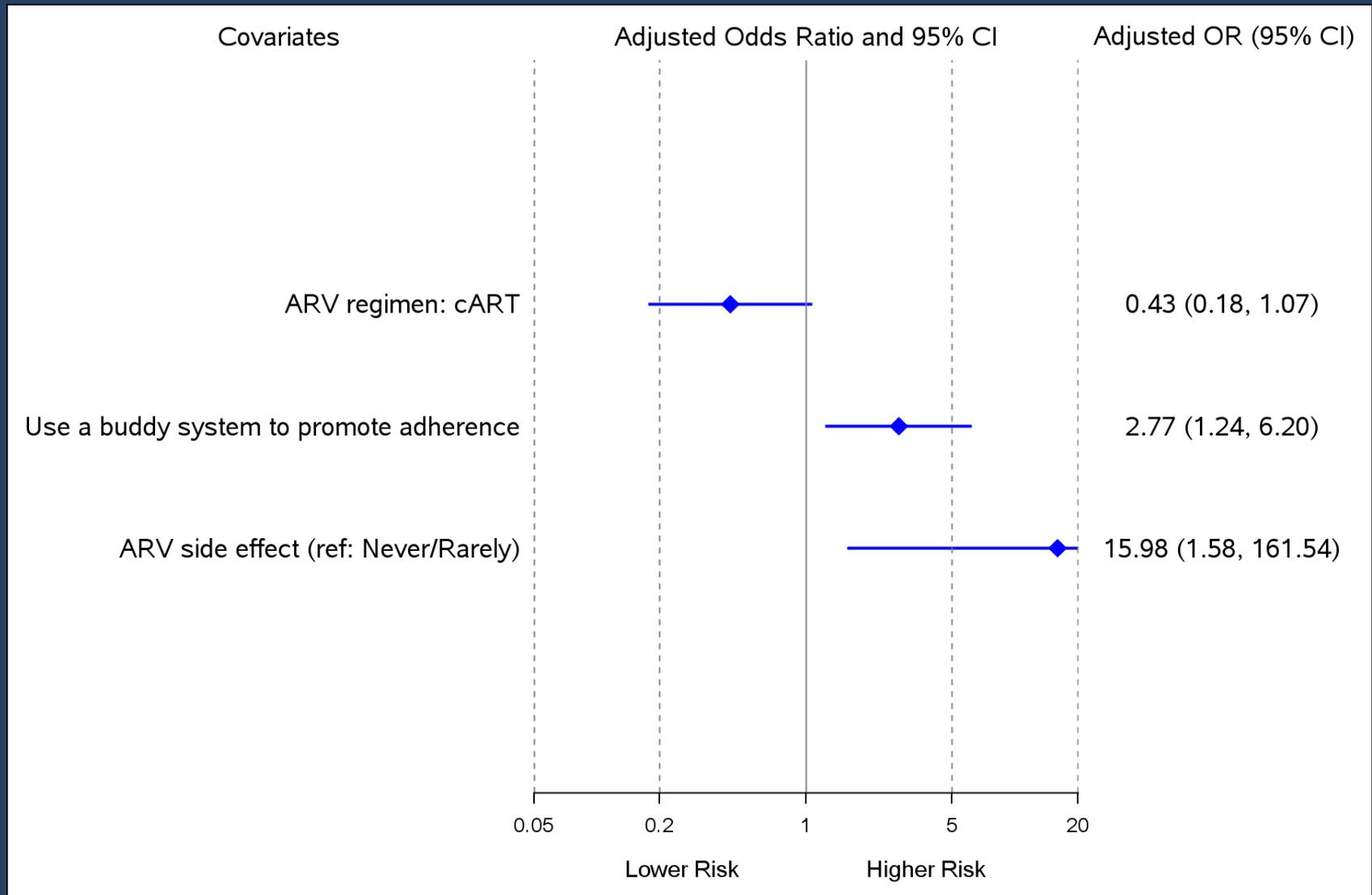
Prevalence of Unsuppressed Viral Load by Age

N=1257 Measurements from 381 Youth with PHIV

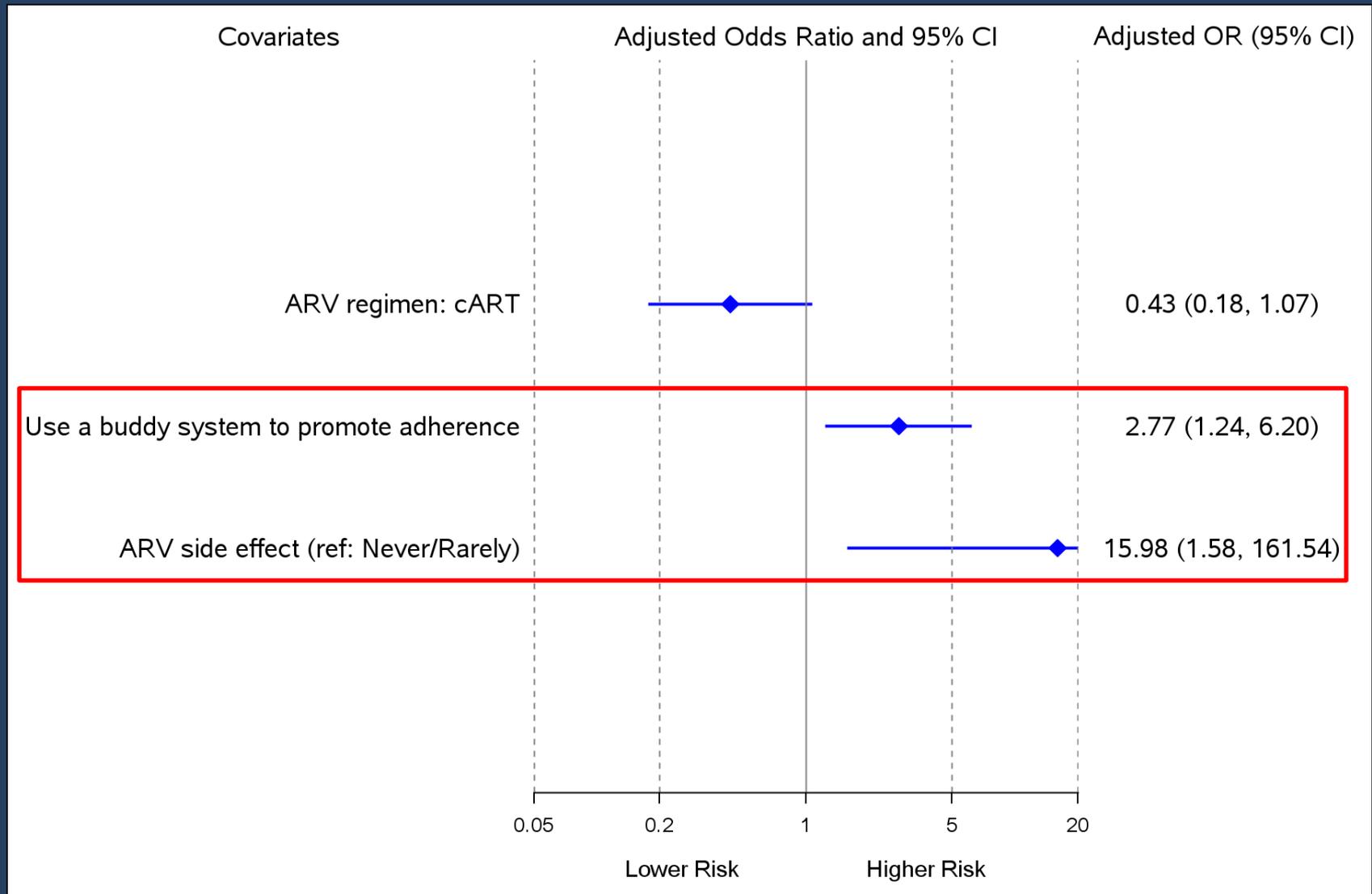


	8 - 11	12 - 14	15 - 17	≥ 18
N				
Total	178	391	462	226
Unsuppressed VL	29	90	147	90

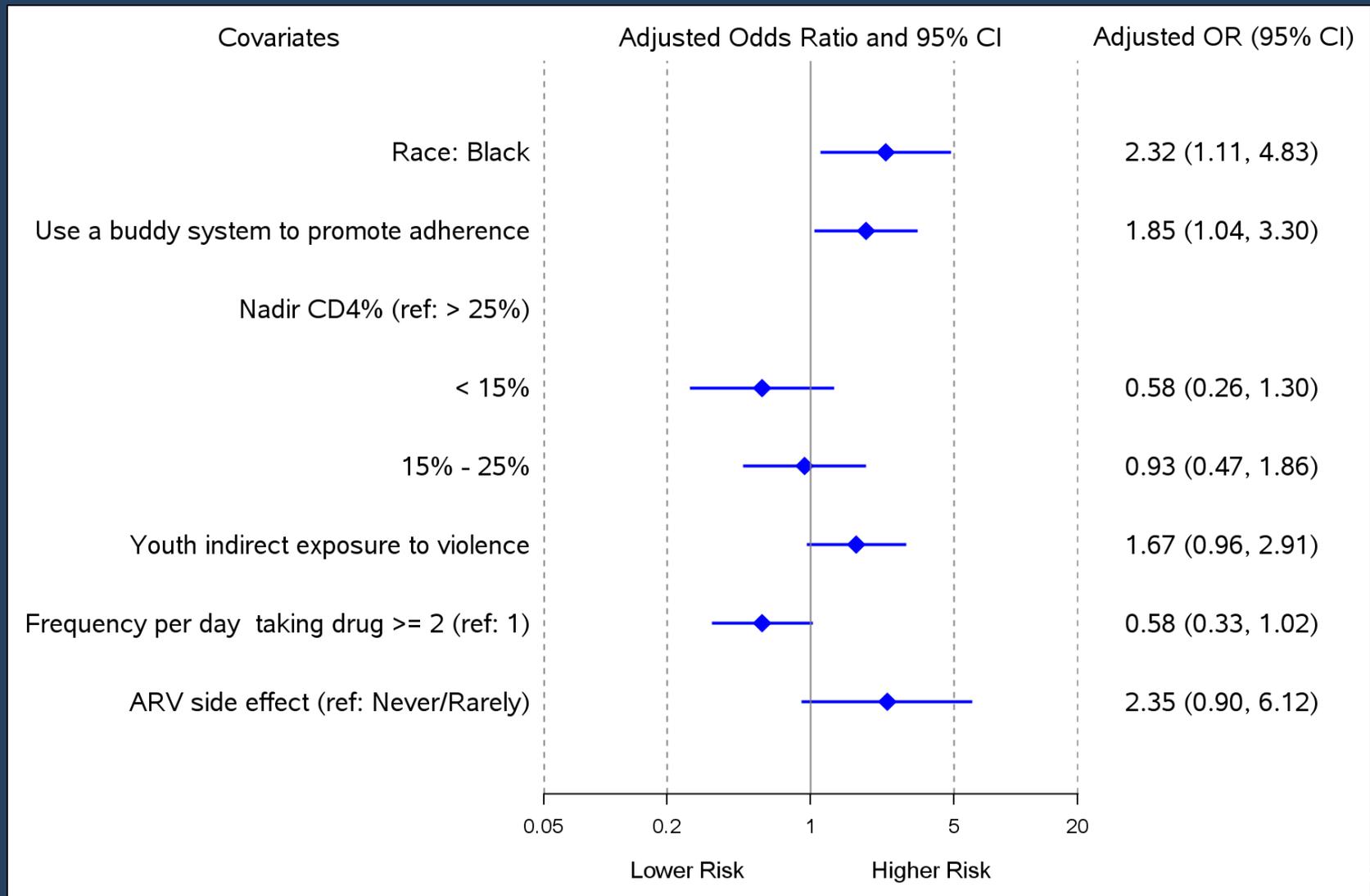
Pre-adolescence (8-11 years): Adjusted associations of covariates with nonadherence



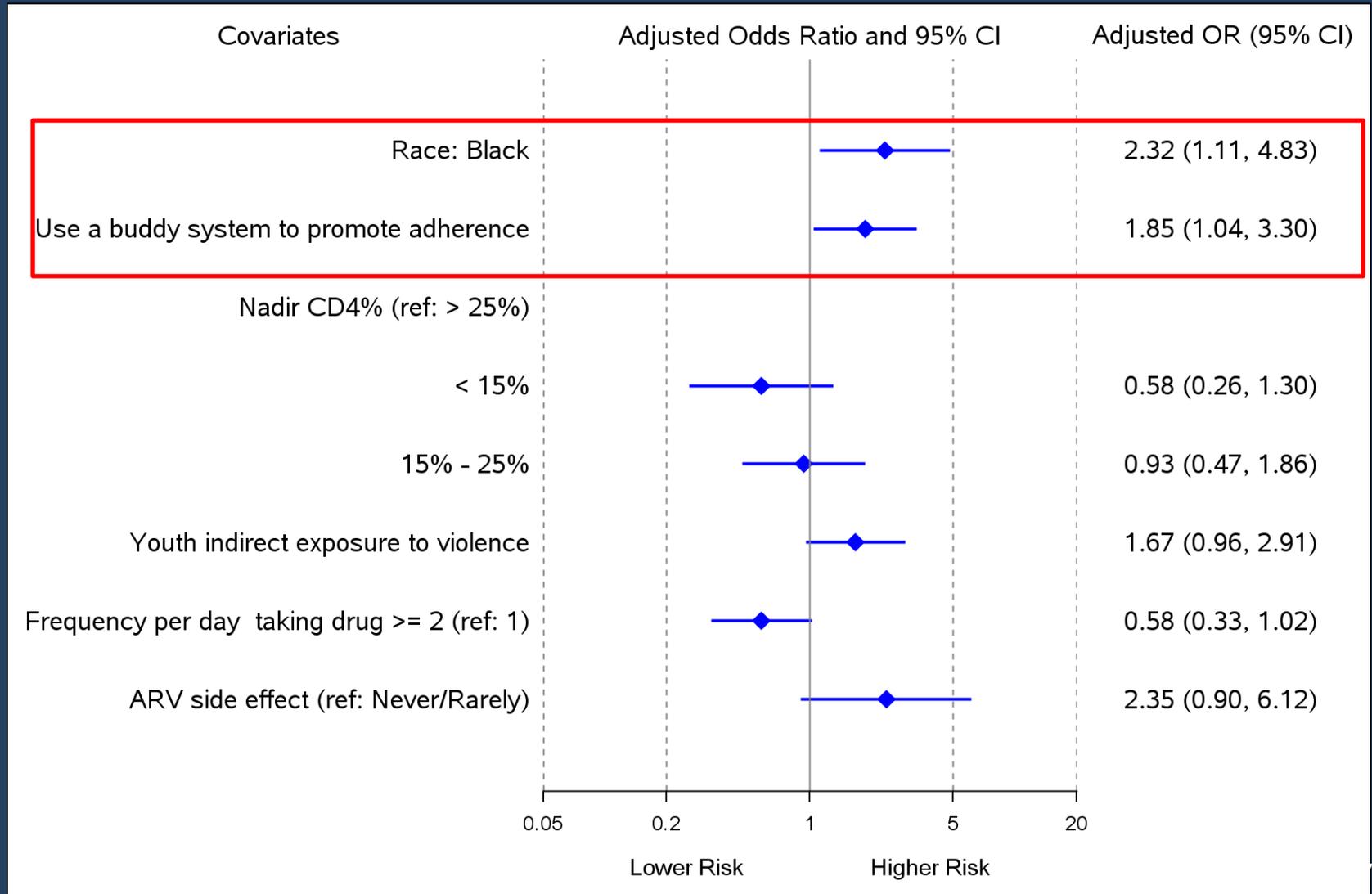
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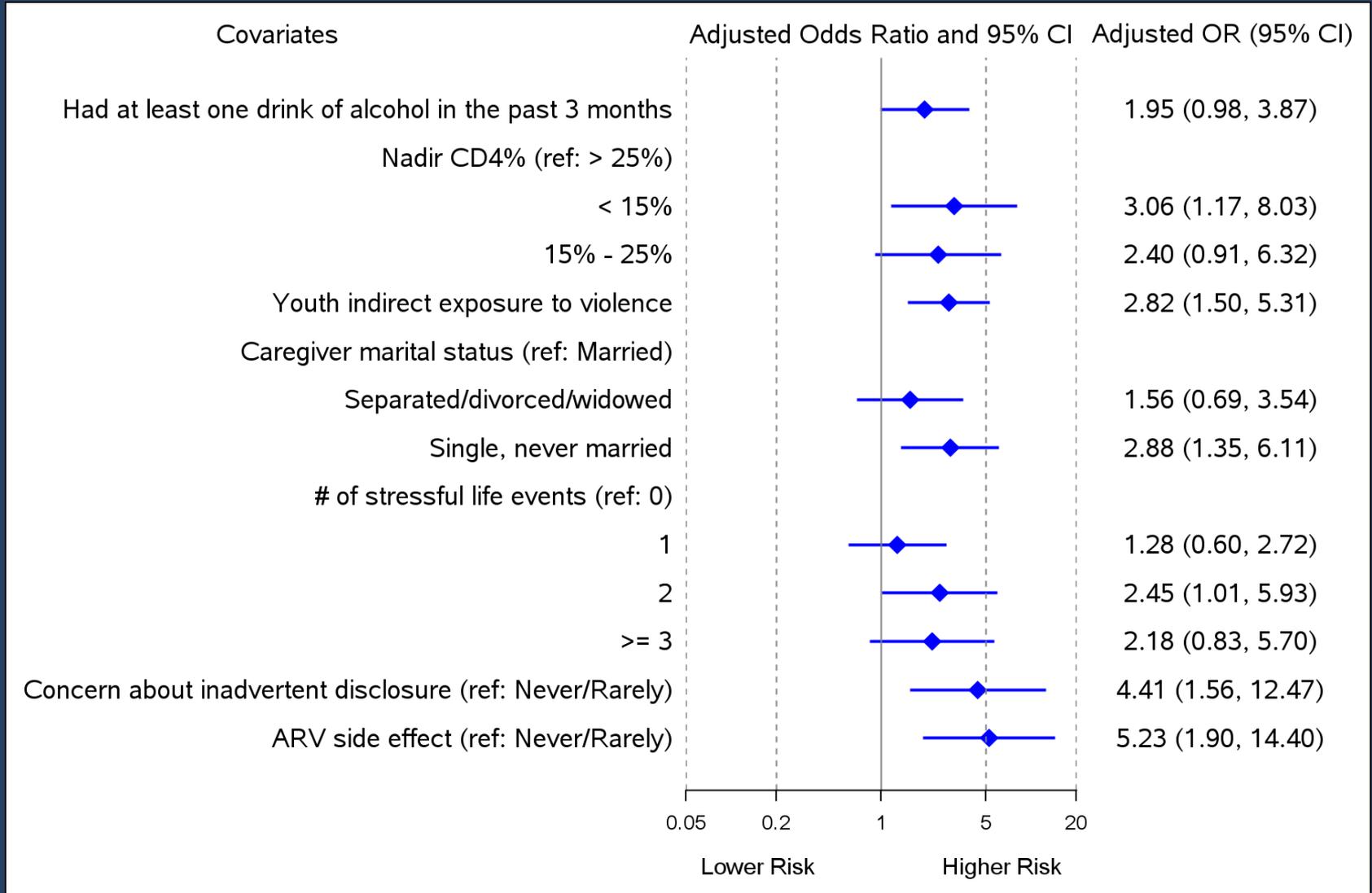
Early adolescence (12-14 years): Adjusted associations of covariates with nonadherence



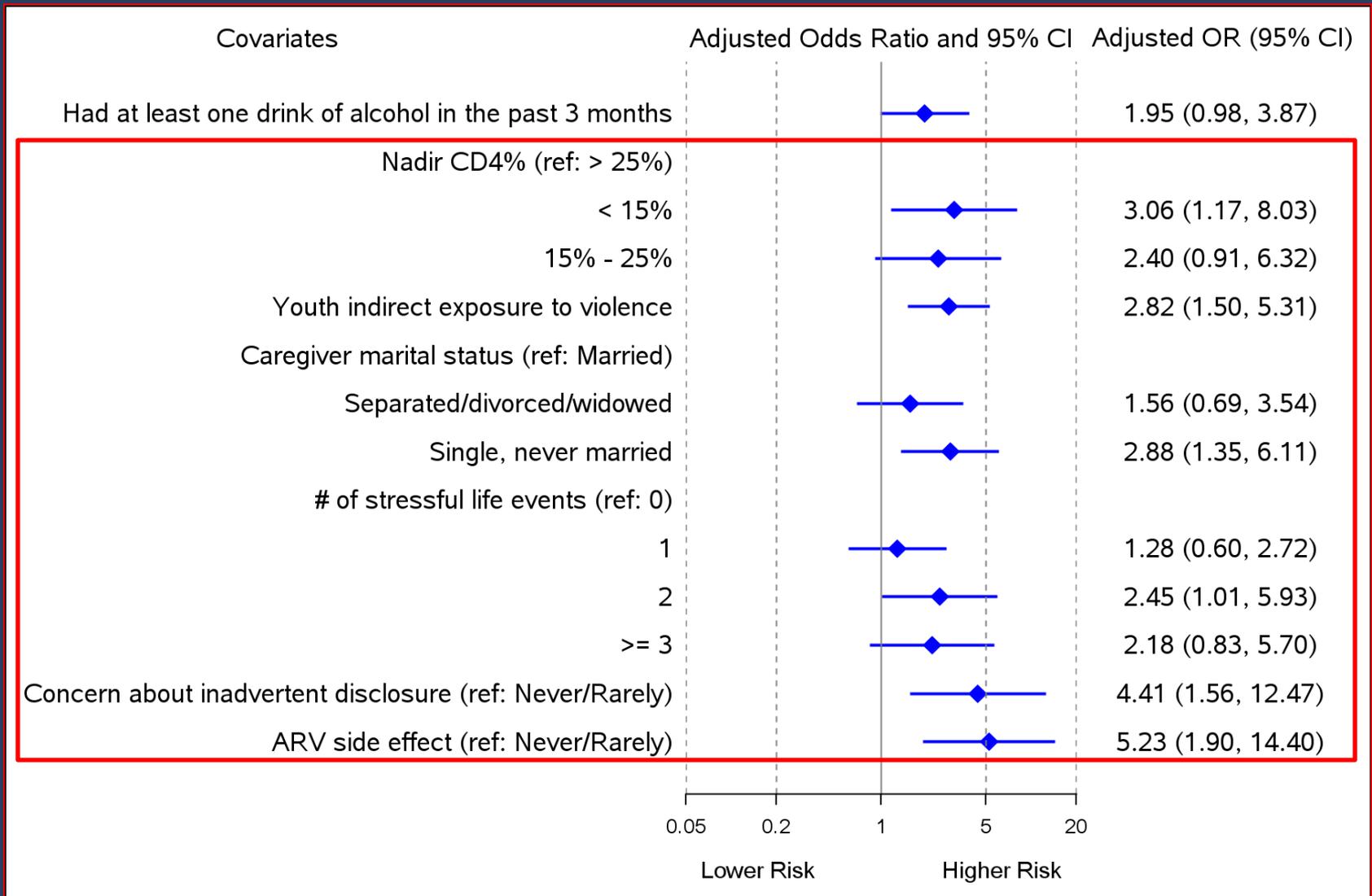
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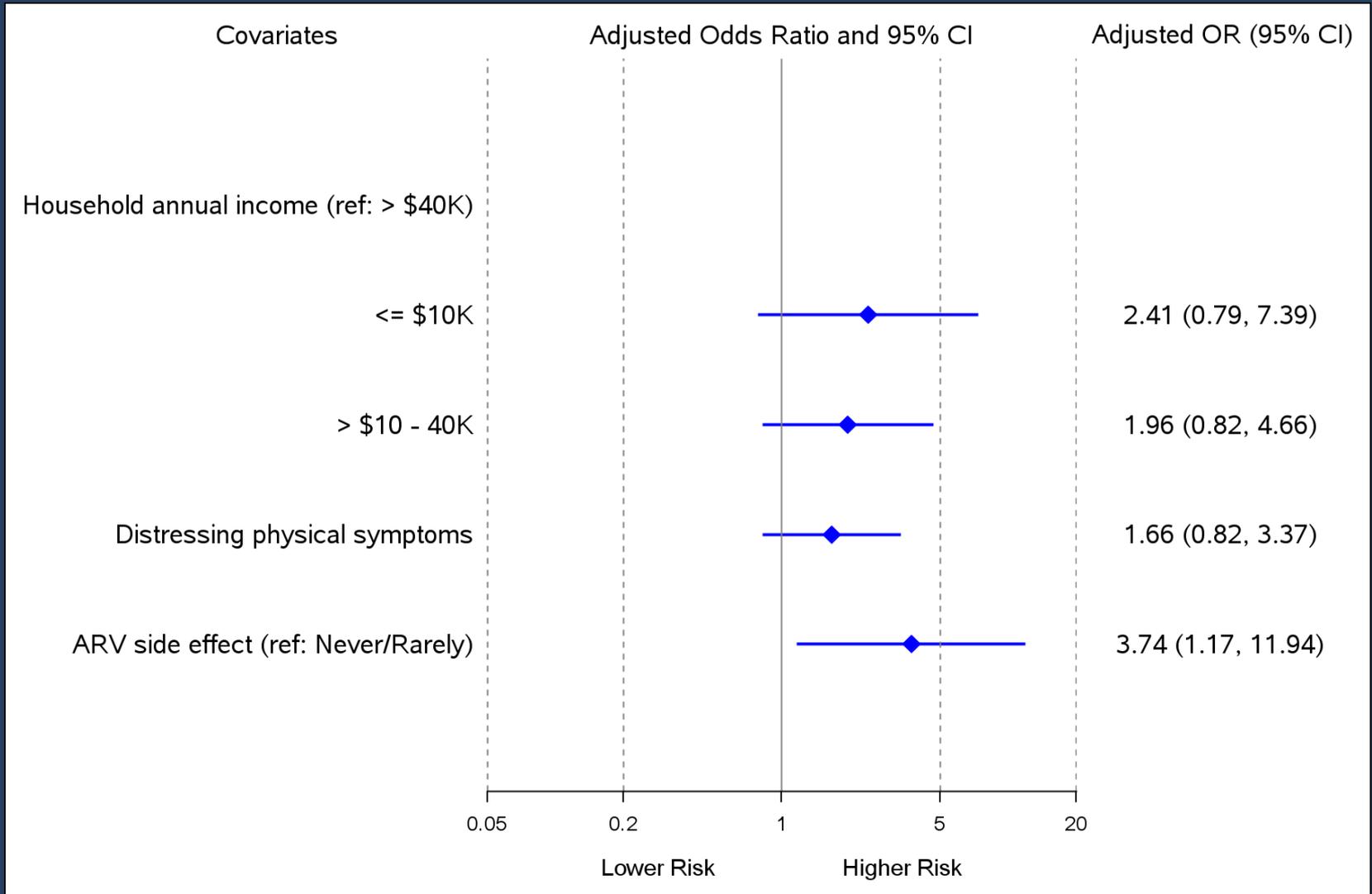
Late adolescence (15-17 years): Adjusted associations of covariates with nonadherence



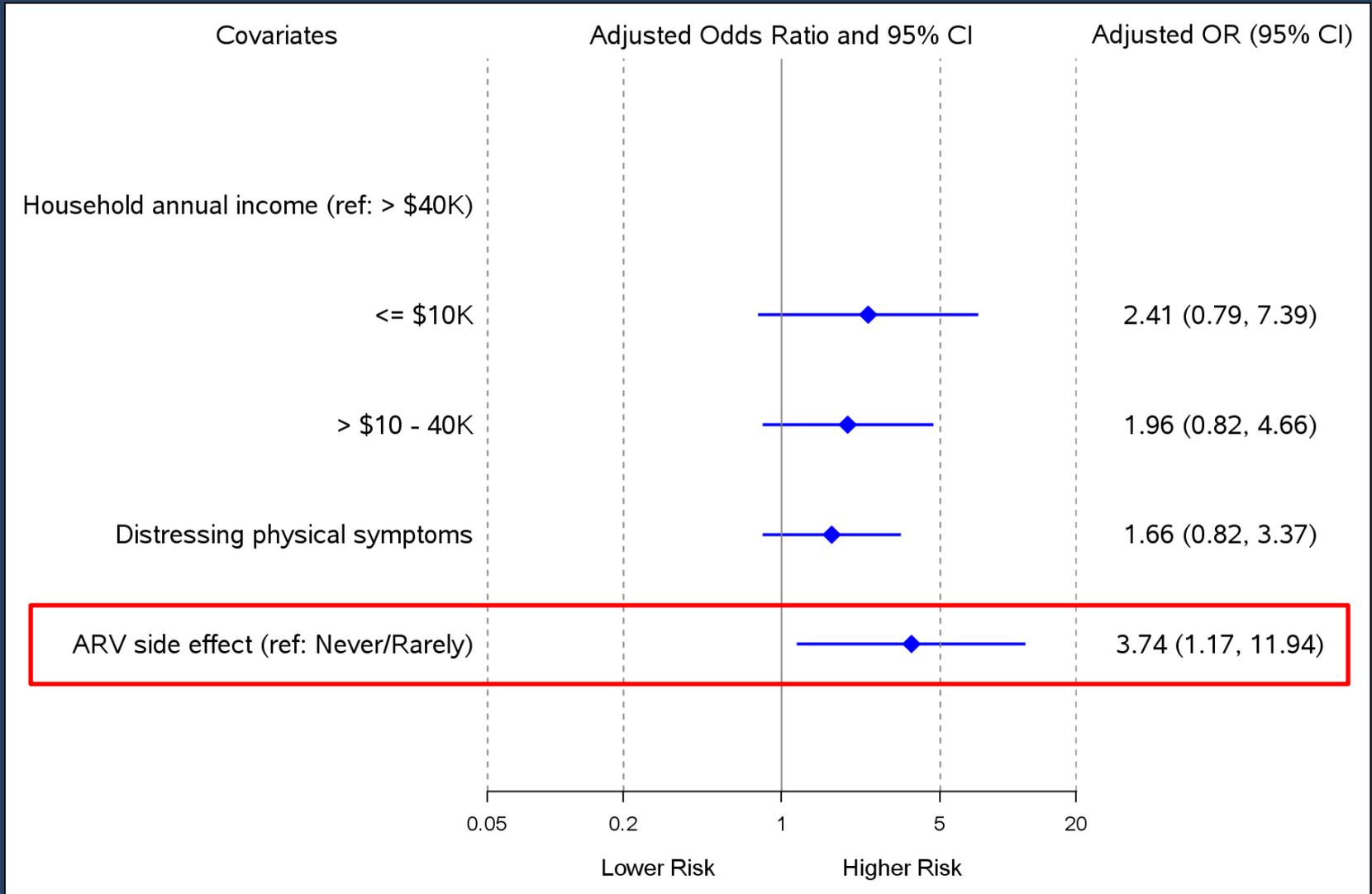
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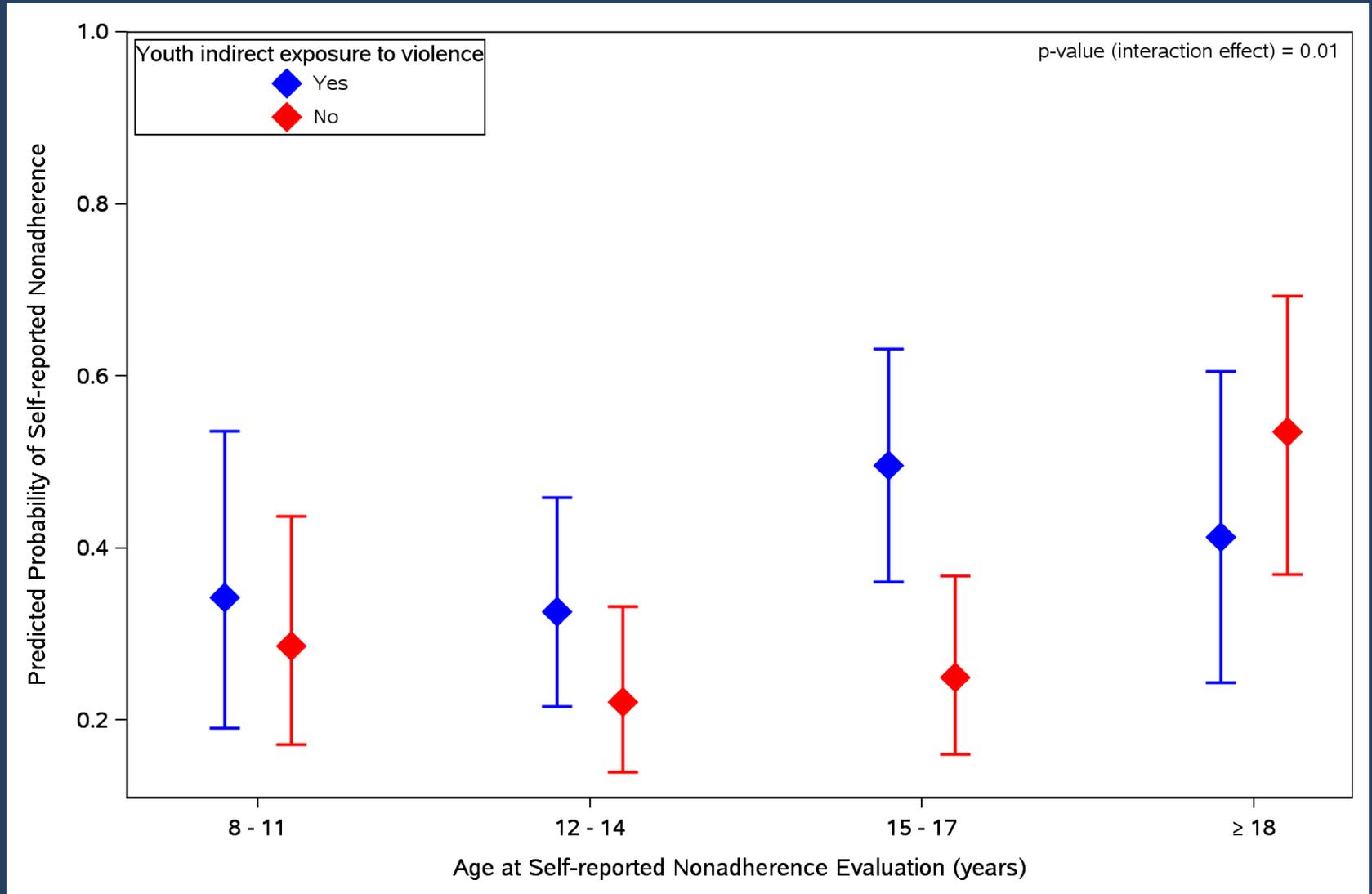
Emerging adulthood (≥ 18 years): Adjusted associations of covariates with nonadherence



Emerging adulthood (≥ 18 years): Adjusted associations of covariates with nonadherence



Adjusted Predicted Probabilities (with 95% Confidence Intervals) of Nonadherence among Youth with vs. without indirect exposure to violence



Model adjusted for sex, race, caregiver living arrangement, and household annual income.

Conclusions

- The prevalence of nonadherence and unsuppressed viral load increased with age among youth with PHIV
- Associated factors varied by developmental stage and by outcome
 - At multiple developmental stages, ARV side effects associated with both nonadherence and unsuppressed viral load
 - In pre- and early adolescence, unexpected association of buddy system with nonadherence--Why?
 - In late adolescence, fear of inadvertent disclosure was associated with nonadherence, and in early adolescence, youth awareness of HIV status was associated with reduced odds of unsuppressed viral load, highlighting salience of stigma
 - In late adolescence, indirect exposure to violence, and stressful life events were associated with nonadherence and lower income was associated with unsuppressed viral load

Limitations and Strengths

- Small sample size in some age strata limited statistical power to evaluate associations
- Clinic-based sample may not be generalizable to all youth with PHIV
- Includes large sample of youth with PHIV who were followed longitudinally over a longer duration than previous studies

Implications

- Recognition of age- and stage-specific factors is essential when considering prevention and intervention strategies for youth with HIV.
- Addressing social environmental factors including violence and disclosure concerns early as part of adherence support interventions may be particularly important for youth approaching late adolescence and the transition to adult care.
- Attention to and support for caregivers and families of youth may still be critical even at older ages.
- Future research should evaluate whether the findings from this study generalize to settings outside of the US.

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PHACS US Clinical Sites

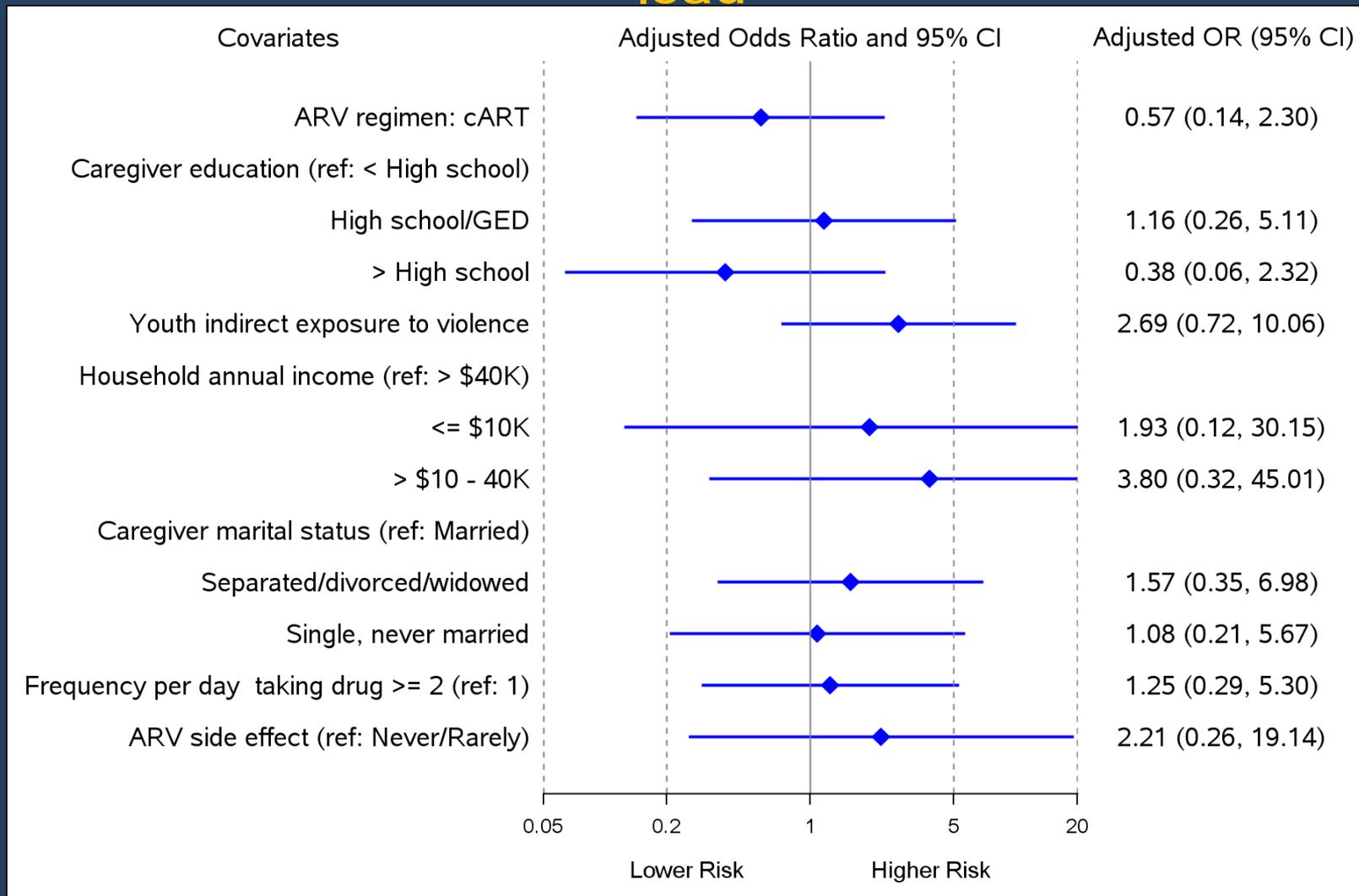
- Ann & Robert Lurie Children's Hospital of Chicago
- Baylor College of Medicine
- Bronx Lebanon Hospital Center
- Children's Diagnostic & Treatment Center
- Children's Hospital, Boston
- Children's Hospital of Philadelphia
- Jacobi Medical Center
- New York University School of Medicine
- St. Christopher's Hospital for Children
- St. Jude Children's Research Hospital
- San Juan Hospital/Department of Pediatrics
- SUNY Stony Brook
- SUNY Downstate Medical Center
- Tulane University Health Sciences Center
- University of Alabama, Birmingham
- University of California, San Diego
- University of Colorado Health Sciences Center
- University of Florida/Jacksonville
- University of Illinois, Chicago
- University of Maryland, Baltimore
- Rutgers- New Jersey Medical School
- University of Miami
- University of Southern California
- University of Puerto Rico Medical Center

For more information...

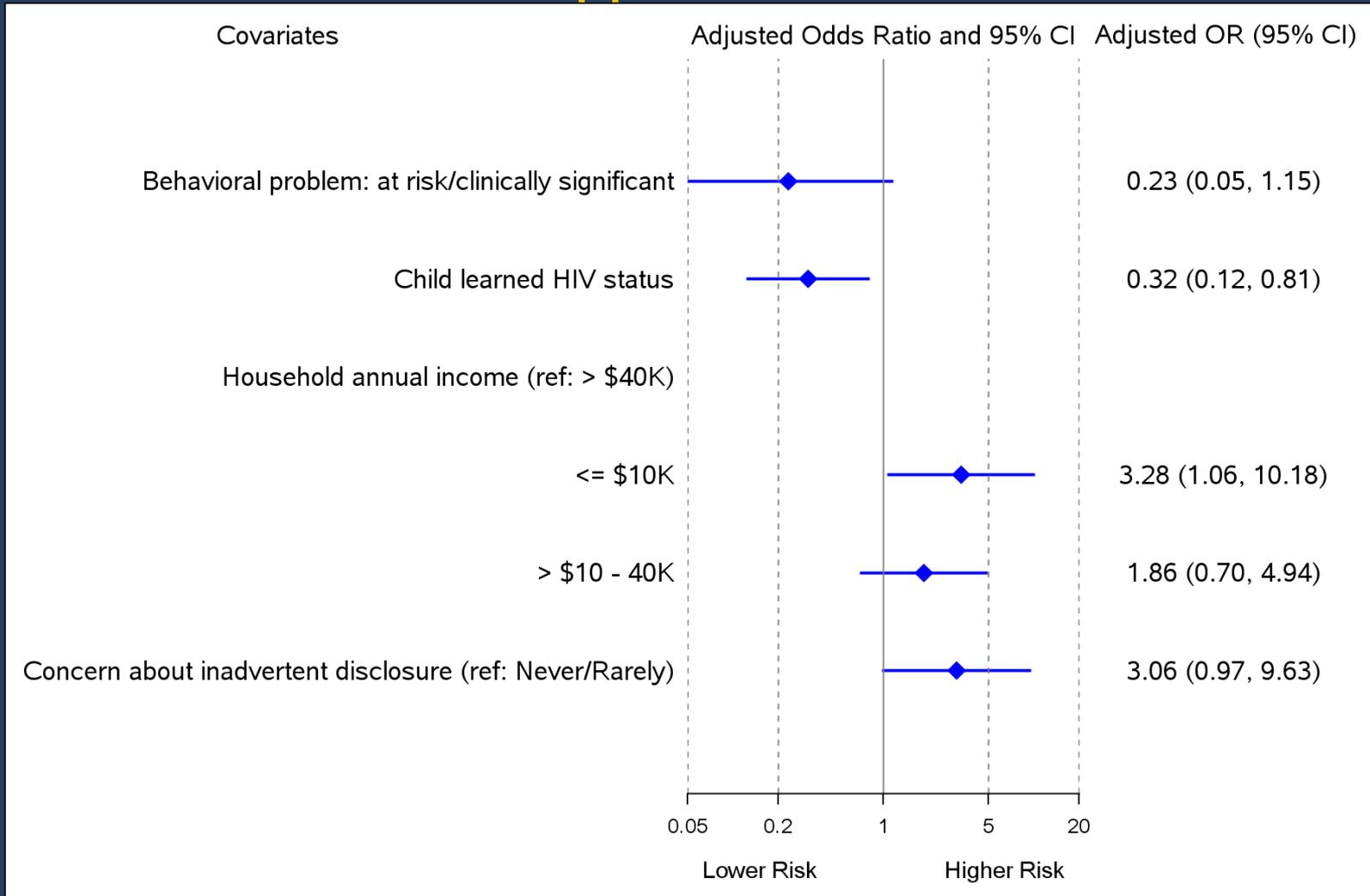
- www.phacsstudy.org
- dkacane@sdac.harvard.edu

Extra slides

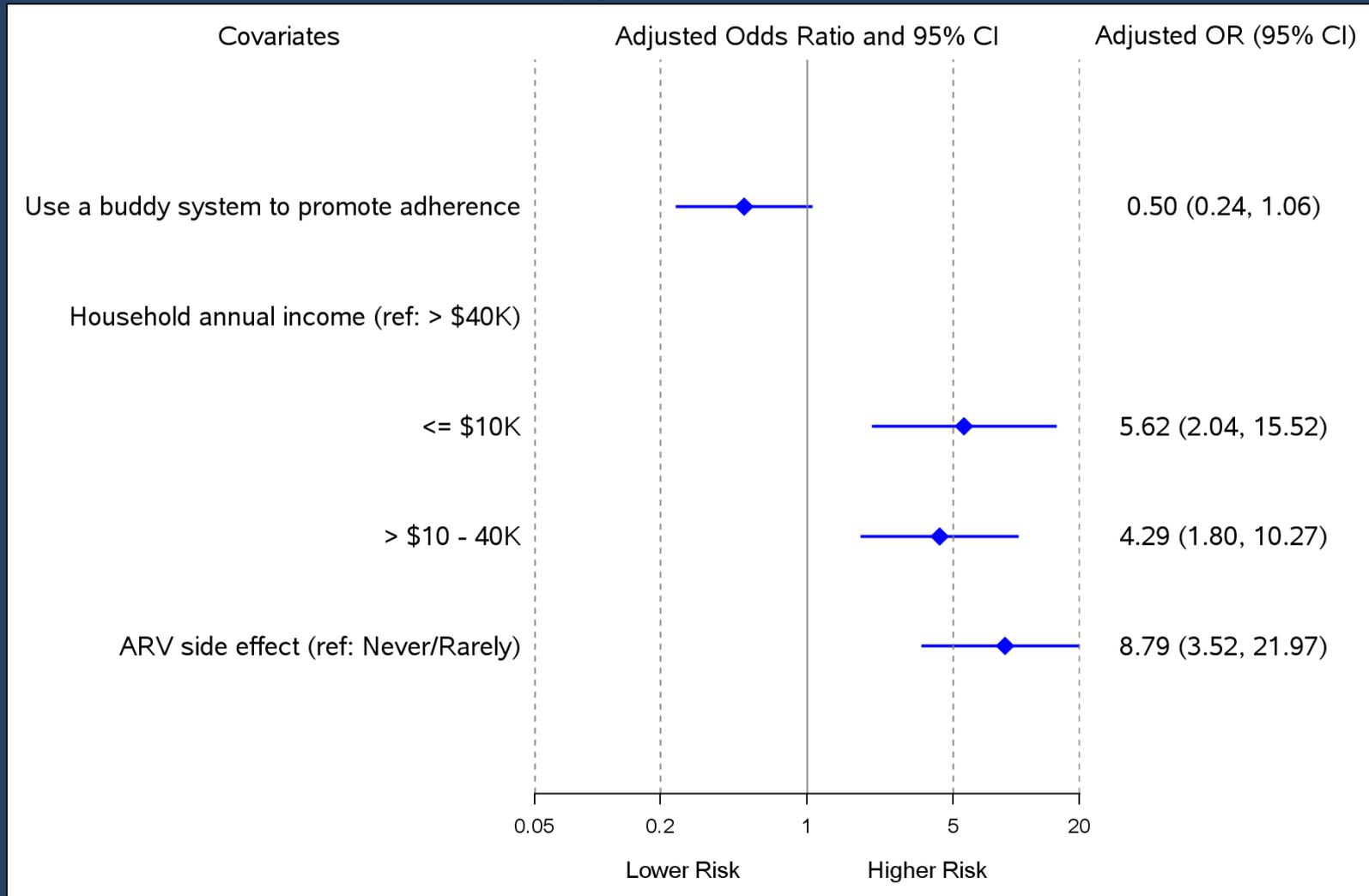
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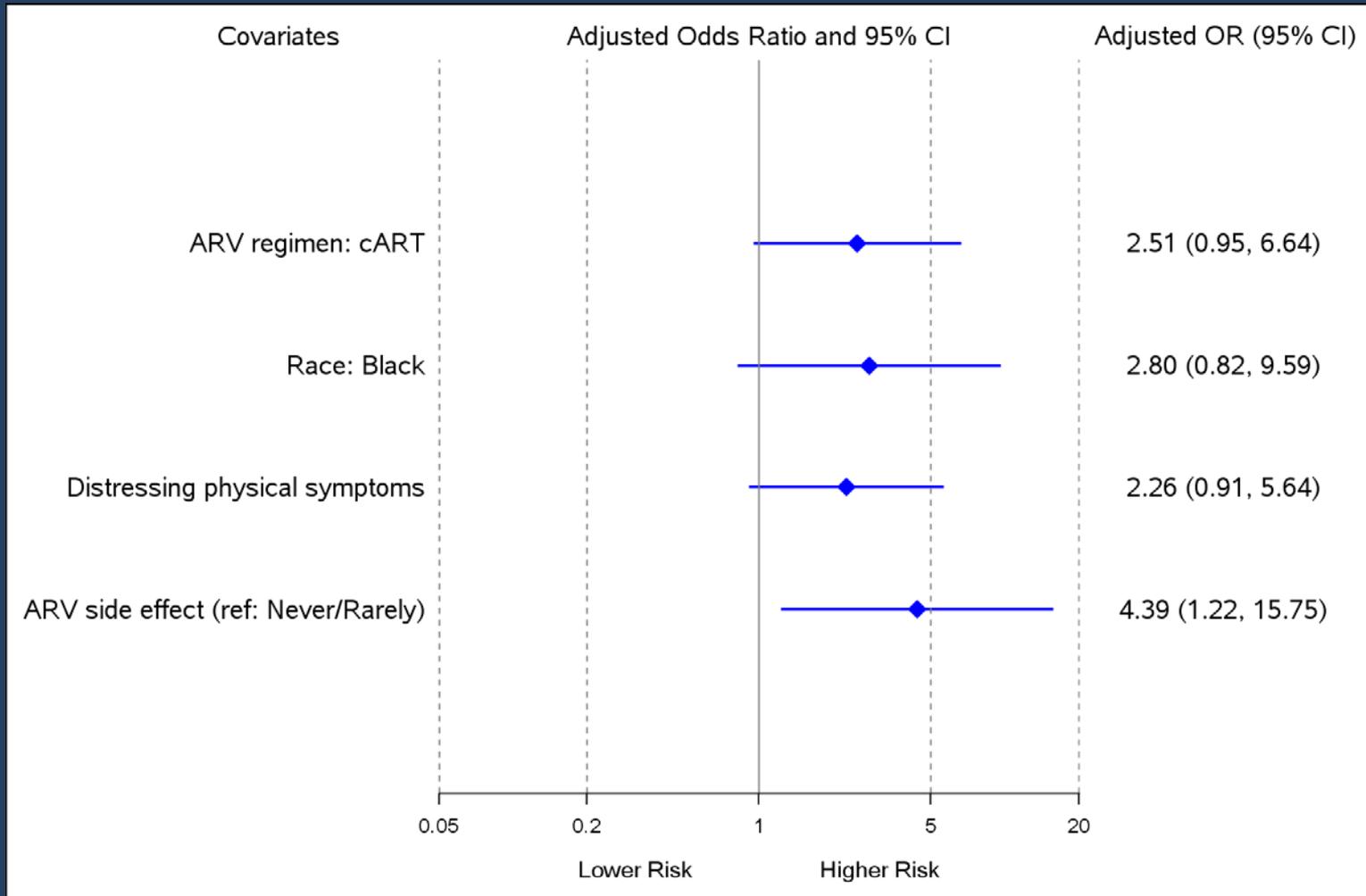
Early adolescence (12-14 years): Adjusted associations of covariates with unsuppressed viral load



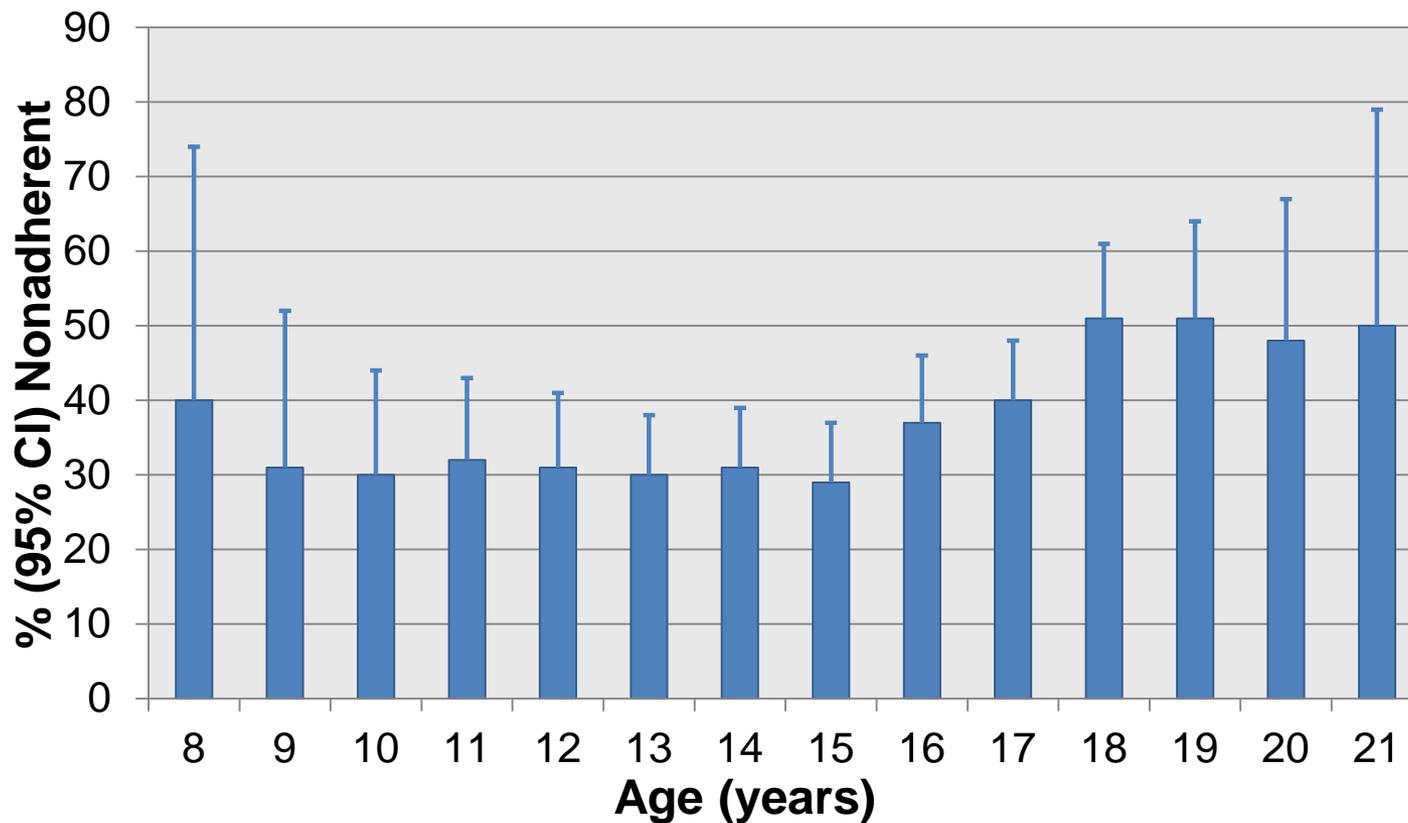
Late adolescence (15-17 years): Adjusted associations of covariates with unsuppressed viral load



Emerging adulthood (≥ 18 years): Adjusted associations of covariates with unsuppressed viral load



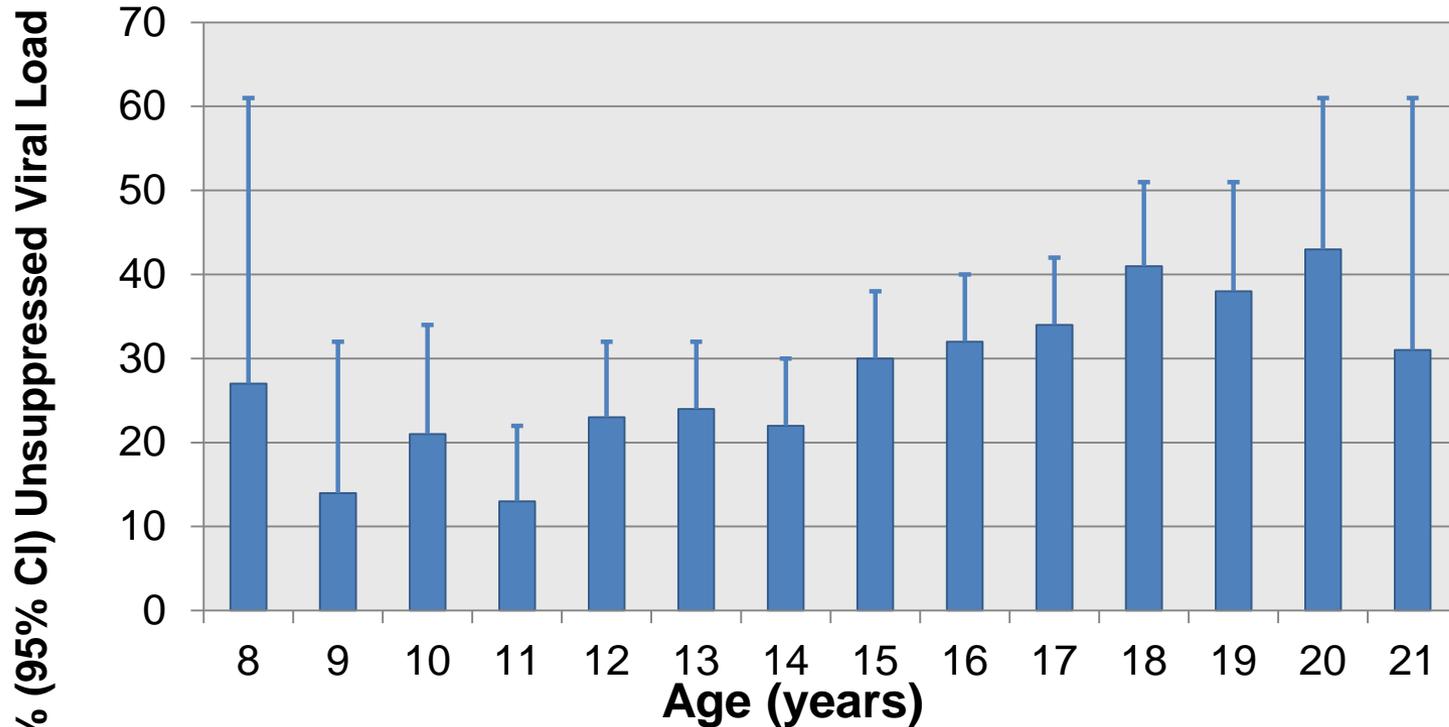
Prevalence of Self-reported Nonadherence by Age N=1190 visits of 379 Youth with PHIV



	8	9	10	11	12	13	14	15	16	17	18	19	20	21
N														
Total	10	26	54	82	115	137	131	139	150	143	91	68	31	12
Nonadherent	4	8	16	26	36	41	40	40	56	57	46	35	15	6

Prevalence of Unsuppressed Viral Load by Age

N=1257 Measurements from 381 Youth with PHIV



	8	9	10	11	12	13	14	15	16	17	18	19	20	21
N														
Total	11	29	53	85	116	133	142	148	160	154	107	68	37	13
Unsuppressed VL	3	4	11	11	27	32	31	44	51	52	44	26	16	4