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Roles of Medication Responsibility, Executive and Adaptive Functioning in Adherence for Children and Adolescents with Perinatally Acquired HIV

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Abstract

Background—Medication adherence is a critical but challenging developmental task for children and adolescents with perinatally acquired HIV (PHIV). Understanding how medication responsibility, executive functions (EF) and adaptive functioning (AF) influence adherence may help prepare adolescents for transition to adulthood.

Methods—Participants included PHIV children and adolescents 7–16 years of age enrolled in the Pediatric HIV/AIDS Cohort Study Adolescent Master Protocol, who were prescribed antiretroviral medications. Measures included: Caregiver report and child self-report measures of adherence,

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medication responsibility, and EF, caregiver report of child AF, examiner-administered tests of EF and processing speed, and demographic and health characteristics.

Results—256 participants with PHIV (mean age 12 years), were 51% female, 80% black, and 79% non-Hispanic. Per 7-day recall, 72% were adherent (no missed doses). Children/adolescents self-reported that 22% had sole and 55% had shared medication responsibility. Adjusted logistic models revealed significantly higher odds of adherence with sole caregiver responsibility for medication (odds ratio (OR)=4.10, confidence interval (CI [1.43,11.8], p=0.009)), child nadir CD4% <15% (OR=2.26, CI [1.15,4.43], p=0.018), better self-reported behavioral regulation (OR=0.65 CI[0.44,0.96], p=0.029), and slower processing speed (OR=0.54, CI[0.38,0.77], p<0.001), adjusting for demographic variables (age, race, caregiver education).

Conclusions—Among children and adolescents with PHIV, continued caregiver medication management, especially during adolescence, is essential. Although global executive and adaptive functioning were not significantly associated with adherence, behavioral regulation was. Given that executive and adaptive functioning develop throughout adolescence, their relationships to adherence should be evaluated longitudinally, especially as youth transition to adulthood and caregiver responsibility diminishes.

Keywords

perinatal HIV; children; adolescents; executive functioning; adherence

INTRODUCTION

Children with perinatally acquired Human Immunodeficiency Virus (PHIV) in the United States (US) are aging into adolescence and assuming greater responsibility for their own HIV medication management, especially as they approach young adulthood. High, sustained antiretroviral (ARV) medication adherence remains necessary for viral suppression.[1–4] Understanding factors that influence medication adherence among children and adolescents with PHIV is critical to promote optimal ARV adherence, health outcomes, and intervention development.

Barriers to ARV adherence for children/adolescents with PHIV include poor medication palatability, pill burden, dietary restrictions, acute and long-term side effects, coordination with daily schedules, forgetting, and treatment fatigue.[5–8] Child, caregiver and family factors associated with PHIV adherence/non-adherence include older child/adolescent age, behavioral functioning, knowledge of HIV status, psychological adjustment, education and problem-solving skills, and caregiver relationship to the child.[9–18] Children/adolescents with PHIV face multiple psychosocial stressors that may negatively affect adherence including poverty, parental HIV disease and death, disclosure, stigmatization, and limited social support.[19]

Among adults with HIV, decreased medication adherence is related to impaired cognition, particularly in the domain of executive functions (EF).[20–24] EFs are involved in goal-directed behavior and include the abilities to initiate behavior, inhibit competing actions, select task goals, plan, organize, shift mental set, problem-solve, and self-monitor.[25–27]

Although research suggests global cognitive functioning does not share the same relationship with adherence in children/adolescents as in adults with HIV,[10] EF has not been examined. EFs are related to treatment adherence in other childhood chronic illnesses (e.g., diabetes),[28–29] and may play an important role as PHIV adolescents assume medication responsibility, potentially providing important intervention targets to improve adherence.

Executive functions are complex and involve multiple cognitive components such as processing speed that may clarify associations of EF with adherence. Thus, evaluating component skills may be important. Processing speed is associated with HIV disease severity in youth[30] and is implicated in ARV adherence in adults with HIV.[21] Similarly, adaptive skills, or the ability to self-manage activities of daily life, may be crucial for successful medication adherence and medication responsibility, especially as caregiver adherence support diminishes.

The effect of cognition on adherence in PHIV children/adolescents may be mitigated by caregiver factors, including medication support.[9] Others have suggested that primary caregiver responsibility for ARVs is essential for sustained adherence throughout adolescence.[17] However, caregiver medication support often wanes in adolescence as youth assume responsibility for their own ARV adherence. With increased child/adolescent shared or sole responsibility for ARVs, it is essential to evaluate the influence of executive and adaptive functioning on the degree of youth assumed medication responsibility.

To our knowledge, no prior studies have investigated the relationship of executive functions, processing speed and adaptive functioning to ARV adherence in children/adolescents with PHIV, even though adherence involves complex behaviors that rely on problem-solving and adaptive skills. Additionally, the relationship of child/adolescent executive and adaptive functioning to medication responsibility has not been studied among PHIV children/adolescents. The aims of this study were to determine whether executive functions, adaptive skills and processing speed influence medication adherence and degree of medication responsibility among PHIV children/adolescents.

MATERIALS AND METHODS

Participants

The Pediatric HIV/AIDS Cohort Study (PHACS) Adolescent Master Protocol (AMP), a prospective cohort study of the long-term effects of PHIV and treatment on pre-adolescents and adolescents biomedical and neurobehavioral outcomes (https://phacsstudy.org/), enrolled participants between March 2007 and October 2009 at 15 AMP sites throughout the US and Puerto Rico. Eligibility criteria included perinatal HIV infection or exposure, age 7 to <16 years at enrollment, and accessible treatment history. To assess adherence outcomes, analyses presented herein included AMP PHIV participants who were prescribed ARVs and had available valid data through January 1, 2012 for: 1) caregiver-report and/or child/adolescent self-report of medication adherence and responsibility; 2) caregiver-report and child/adolescent self-report (participants ≥11) of executive function; 3) caregiver report of child/adolescent adaptive functioning; and, 4) examiner administered pencil-and-paper tests of child/adolescent executive functions and processing speed as described below.

Procedure

Institutional Review Boards at the Harvard T.H. Chan School of Public Health and each participating PHACS site approved the study. Written informed consent and age-appropriate assent were obtained for all participants according to institutional guidelines.

Measures

Primary Outcomes

Adherence: ARV adherence assessment was based on the work of the Adult and Pediatric AIDS Clinical Trials Groups, modified by the AMP team.[12,31–33] Caregivers and children/adolescents (whose caregivers provided consent) were interviewed separately and asked to report ARVs prescribed, primary person responsible for administering ARVs, and number of doses missed in the past 7 days. Consistent with prior studies,[15] non-adherence was defined as either child *or* caregiver report of ≥1 missed dose of any ARV in the prior seven days. Significant associations of caregiver and child/adolescent 7-day adherence recall with concurrent HIV RNA viral load (VL) has been established in AMP,[32] thus validation was not repeated herein.

Medication Responsibility: During the adherence interview, children/adolescents and/or caregivers independently reported whether the: 1) Caregiver was solely responsible for the child's/adolescent's ARV adherence; 2) child/adolescent and caregiver shared responsibility; or, 3) child/adolescent was solely responsible.

Potential Predictors of Adherence and Medication Responsibility

Adaptive Functioning (AF): The Adaptive Behavior Assessment System-Second Edition (ABAS-II) Parent Report[34] is a comprehensive, norm-referenced proxy inventory that assesses an individual's adaptive skills for ages 5–21 years. The General Adaptive Composite (GAC) was evaluated as a global predictor of adherence; Conceptual, Social, and Practical Composites also were explored. Composites have a standard score mean (M)=100 and standard deviation (SD)=15.

Executive Function (EF): The *Behavior Rating Inventory of Executive Function, Parent-Report Form* (*BRIEF-PR*)[26] and the *BRIEF-Self-Report (BRIEF-SR)*[27] are standardized age-normed inventories for rating EF in the performance of everyday tasks across multiple domains. The Behavioral Regulation Index (BRI), Metacognition Index (MI), and Global Executive Composite (GEC) were examined in relation to adherence. T-scores (M=50, SD=10) are computed. Caregivers completed the BRIEF-PR regardless of participant age. Per standard administration guidelines, children/adolescents ≥11 years of age completed the BRIEF-SR. Because the BRIEF was not available in Spanish during data collection, it was not administered to children or caregivers without English proficiency.

The *Children's Color Trails Test (CCTT)*[35] is a standardized paper-and-pencil assessment of alternating and sustained visual attention, sequencing, psychomotor speed, cognitive flexibility, planning and inhibition-disinhibition. Age-norm-referenced scores include T-scores (M=50; SD=10) for each trial (CCTT-1 and CCTT-2) completion time (i.e.,

processing speed), and percentile ranges for the Interference Index, which assesses inhibition and cognitive flexibility.

Processing Speed: The Processing Speed Index (PSI) of the Wechsler Intelligence Scale for Children, 4th Edition (WISC-IV)[36] was included, and is normed with M=100, SD=15.

Potential Confounding Variables

Demographic, Caregiver and Health Information: Demographic information collected via structured interview with the primary caregiver included child age, sex, race/ethnicity, and primary language, household income, child HIV disclosure status, and caregiver relationship to child, HIV status, and education. Medical chart abstraction provided current (at study entry) and peak HIV-1 RNA VL; current and nadir CD4+ T-lymphocyte count (CD4) and percent (CD4%); Centers for Disease Control (CDC) HIV disease classification and age at classification; diagnosis of encephalopathy and age at diagnosis; and current ARV regimen.

Other Measures of Child and Caregiver Functioning: The following measures of child academic and child and caregiver cognitive functioning administered within AMP were included as potential confounders: Child/adolescent WISC-IV Full Scale IQ (FSIQ),[36] Wechsler Individual Achievement Test, 2nd Edition, Abbreviated (WIAT-II-A)[37] Word Reading subtest score, and caregiver FSIQ (Wechsler Abbreviated Scale of Intelligence (WASI)[38]).

Data Collection—Administration of baseline measures was staggered in AMP to minimize participant burden. Semi-annual visits included physical exam, chart review of health and medication status, and demographic interviews. At study entry, child/adolescent participants were administered the WISC-IV, caregivers completed the ABAS-II, and child medical and developmental histories were assessed. At the 6-month visit, caregivers were administered the WASI. At the 1-year visit, children/adolescents completed the CCTT, WIAT-II-A, and BRIEF-SR; caregivers completed the BRIEF-PR. At the 1.5-year visit, adherence self- and caregiver-reports were obtained. All cognitive, behavioral, and health status variable data of interest preceded the adherence assessments.

Statistical Analyses

Descriptive statistics were used to summarize demographic variables. The odds of 7-day adherence and the child/adolescent having sole responsibility for ARVs were modeled. Logistic regression was used to estimate odds ratios (OR) while adjusting for potential confounders selected *a priori* based on associations within the literature and previous AMP analyses. Covariates included the participant's age, sex, race, ethnicity, WISC-IV FSIQ, WIAT-II-A reading level, peak HIV RNA VL, nadir CD4%, degree of medication responsibility, and history of encephalopathy. Caregiver characteristics included: Education, FSIQ, and biological relationship to the participant. Regression analyses were used to reduce the number of potential confounders. Core model adjustment variables were selected as follows: Variables with a p-value <0.20 in univariate models were included in a core multivariable adjustment model, and retained if p-value was <0.15. Analyses with p-values

<0.05 were considered statistically significant; confidence intervals (CI) are reported as 95%. SAS 9.2 and 9.4 (Cary, NC) were used for the analyses.

RESULTS

Participant Demographics (Tables 1 and 2)

Child/adolescent PHIV participants included in the analyses (n=256) were of average age 12 years (SD=2.51; range, 7–16 years), primarily black race (80%), and non-Hispanic (79%), with both genders equally represented (female, 51%).

Adherence

Available adherence reports included in the analysis were as follows: Caregiver only, n=51, child/adolescent self-report only, n=20, both caregiver and child/adolescent reports, n=185. Seventy-two percent of participants were identified as adherent by child self- and/or caregiver report (no missed doses) with moderate agreement between child/adolescent and caregiver reports of adherence (Kappa=0.53, CI[0.38,0.68], p<0.0001).

Predictors of Adherence (Table 3)

Executive Function

BRIEF: Based on child/adolescent self-report (n=156), lower odds of adherence were associated with higher behavioral regulation T-scores (greater impairment; OR=0.65 CI[0.44,0.96], p=0.029). There were no significant relationships of adherence with caregiver (n=200) or self-reported metacognition or GEC, or with caregiver-reported behavioral regulation.

CCTT: The relationship of the CCTT Interference Index, a measure of EF, with adherence was non-significant.

Adaptive Functioning

ABAS-II: In adjusted models there were no significant relationships of adherence with caregiver-reported Global Adaptive functioning or Conceptual, Social or Practical subdomains with adherence.

Processing Speed

CCTT: In adjusted analyses, significantly higher odds of adherence was associated with slower CCTT Trial 1 psychomotor speed (OR=0.54, CI[0.38,0.77], p<0.001), consistent with observed lower WISC-IV Processing Speed Index scores (OR=0.63, CI[0.44,0.89], p=0.009). The relationship of adherence with CCTT Trial 2 was nonsignificant.

Demographic Covariates of Adherence

In unadjusted analyses of caregiver characteristics (not shown), participants with HIV+ caregivers were less likely to be adherent (p=0.045). Adherent participants had lower nadir CD4% (p=0.02) and were more likely to have controlled VL at study entry (p<0.001). In adjusted models, after selection of potential confounders, the core model adjustment

variables for multivariable analyses included age, race, caregiver education, caregiver relationship, medication responsibility, and nadir CD4%. In a multivariable model (see Table, Supplemental Digital Content 1), black race was associated with lower odds of adherence (OR=0.39, CI[0.18,0.86], p=0.02). Higher odds of adherence were associated with younger child age (OR=3.94, CI[1.15,10.320], p=0.005), caregivers being high school graduates (OR=2.80, CI[1.41,5.56], p=0.003), caregiver solely responsible for medications (OR=4.10, CI[1.43,11.81], p=0.009), and participant nadir CD4% <15% vs. >15% (OR=2.26, CI[1.15,4.43] p=0.018). Child history of encephalopathy (p=0.837) and knowledge of HIV status (p=0.856) were not associated with adherence.

Medication Responsibility

Overall, there was 73% child-caregiver congruence for medication responsibility (Kappa=0.56, CI[0.46,0.66], p<0.0001). Per participant self-report, 22% reported sole medication responsibility, 21% sole caregiver responsibility, and 55% shared responsibility. By caregiver report, 15% reported sole child/adolescent responsibility, 34% sole caregiver responsibility, and 47% shared responsibility. A significantly higher proportion of adherent (39% and 26%) than non-adherent (20% and 9%) children/adolescents had caregivers with sole responsibility for medication management per both caregiver (p=0.017) and child reports (p=0.012), respectively.

Predictors of Medication Responsibility

Core model adjustment variables for child/adolescent medication responsibility included child/adolescent's age and FSIQ (see table, Supplemental Digital Content 2). Adolescents ≥12 years of age had ten-fold higher odds of being solely responsible for medication administration. Although nonsignificant, FSIQ was marginally higher (OR=1.40, CI[0.96,2.06], p=0.083) for children/adolescents with sole responsibility for their medications. Given the moderate agreement between child/adolescent and caregiver reports of medication responsibility, and the greater availability of caregiver reports, modeling for this analysis was based on caregiver report. In adjusted models, there were no statistically significant associations of executive or adaptive functioning or encephalopathy with caregiver report of medication responsibility (Table 4). Additionally, there was no other significant demographic, HIV health status, or cognitive predictor of medication responsibility.

DISCUSSION

Sustaining optimal adherence to ARV treatment in children/adolescents with PHIV is crucial. The roles of executive functions, adaptive functioning, processing speed, and cognitive and behavioral constructs not previously examined were assessed as potential predictors of PHIV ARV adherence. Similar to other studies of children with HIV in the US,[39] 72% of children/adolescents in our sample were identified as adherent. While these results demonstrate that optimal adherence is attainable by many PHIV children/adolescents, a still sizable number experience adherence difficulties and are at risk for suboptimal viral suppression. Nearly one-third of participants had detectable VL at study entry, which is of great clinical concern.

A critical finding in this study is the role of medication responsibility in relation to ARV adherence. The odds of adherence were significantly higher when caregivers maintained sole responsibility for their child's/adolescent's medication management. Per both caregiver and participant reports, significantly greater numbers of adherent than non-adherent children/adolescents had caregivers with sole responsibility for their ARVs. Relationships between child age and adherence also were observed; older children/adolescents were less likely to be adherent. Additionally, those >12 years of age were 10 times more likely to be solely responsible for their medications. Findings are consistent with prior reports demonstrating that PHIV adherence is better with parent involvement,[40–43] even in adolescence, highlighting the need for sustained participation of caregivers in medication management, careful evaluation of readiness for transition of responsibility from caregiver to youth, and ongoing caregiver support and monitoring even after youth assume sole responsibility. No relationships of child/adolescent executive or adaptive functioning were observed in relation to degree of medication responsibility further supporting the notion that responsibility for ARVs likely is shifted based on child/adolescent age rather than readiness.

Caregivers who were high school graduates were significantly more likely to have youth who were adherent, suggesting that at minimum high school completion may contribute to overall health literacy and consistent access to care. On the other hand, black race was significantly associated with non-adherence, raising questions regarding contributing roles of minority status, health disparities, and stigmatization; limited access to adequate educational and community-based social resources also may be implicated.

The importance of examining components of EF was supported by the increased likelihood of nonadherence among children/adolescents with self-reported behavioral dysregulation. Adherence may be challenging among children/adolescents who experience difficulties with aspects of behavioral regulation, such as inhibition, cognitive shift, and emotional control, as suggested in prior studies of caregiver-reported behavioral difficulties and adherence.[10] Routine assessment of behavioral regulation may provide information to guide behavioral interventions for youth with adherence difficulties.

A significant relationship between adherence and processing speed was observed, albeit in the opposite direction of that seen in adults. One possible explanation is that for "slower processors," caregivers may be aware of their child's limitations, and may intentionally maintain adherence support, despite their child's advancing age or expectations for increased autonomy. However, this requires further investigation to better understand the observed counter-intuitive relationship.

Contrary to expectations, no significant effects of global executive or global adaptive functioning on adherence were observed. Global indices may obscure the effects of selective skills that influence performance on a specific task and may not be adequately sensitive to detect subtle executive or adaptive differences. It is also important to consider that health and developmental consequences of intermittent or persistently poor adherence may have an impact on the developmental trajectory of executive functions, adaptive skills, and processing speed in children/adolescents with PHIV. Clarifying this relationship warrants future longitudinal investigation.

Regardless of executive or adaptive functioning and observed adherence behaviors, caregivers of children/adolescents with PHIV may assume their child is ready for autonomous medication management by virtue of their age and expect pre-adolescents/adolescents to assume sole or minimally supervised joint management of ARVs. Children/adolescents with "age-typical" organizational skills and working memory who have moderate supervision around medication management still may experience fluctuations in adherence behaviors related to emerging executive skills and/or other challenges, including emotional/behavioral concerns, burgeoning peer relationships and associated pressures to fit in,[44] or acute or chronic psychosocial stressors that limit independence. Thus, it is important to counsel caregivers that age is not a sufficient indicator of readiness for sole medication responsibility, and to transfer medication responsibility based on youth age alone may be unwise. Ideally, caregivers should be encouraged to calibrate supervision over time, congruent with youth's emerging autonomy, demonstrated cognitive and behavioral capabilities, and emotional health necessary for sustained success as they approach young adulthood.

This study is not without limitations, including those inherent with self-report measures, such as recall bias and social desirability. This sample may not reflect the population of children/adolescents with PHIV who do not participate in research studies like AMP that involve extensive monitoring. Those who kept study visits may be more likely to adhere to ARV medications than those who did not enroll, missed appointments, or were lost-to-follow-up. While executive and adaptive skills develop throughout adolescence and into adulthood, the mean age of our sample is one at which executive and adaptive skills are still emerging and may be better developed in later adolescence, thus limiting findings. Further, given the spacing of initial assessments, we cannot account for potential changes over the 1.5 year timeframe.

Conclusions

Among children/adolescents with PHIV, continued caregiver involvement in medication management during adolescence is essential, despite emerging expectations of autonomy. Global ratings of executive function and adaptive skills were not significantly associated with medication adherence, but self-reported behavioral regulation was. Therefore, components of executive functions should be monitored as youth age into young adulthood. In contrast to observations of adults with HIV, slower processing speed was associated with better adherence, which may reflect ongoing caregiver support resulting from perceptions of youth impairment, which warrants further examination. Given that adaptive behaviors and executive functions develop throughout adolescence and young adulthood, relationships with adherence should be evaluated longitudinally to guide development and implementation of effective adherence-promoting interventions.

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Table 1

Child and Caregiver Characteristics

Characteristic		Total (N=256) n (%)
Child Age at Study Entry	Mean (SD)	11.99 (2.51)
Child Gender	Female	130 (50.8%)
Child Race	Black	194 (80.2%)
	White	47 (19.4%)
	Other	1 (0.4%)
	Missing[1] (n)	14
Child Ethnicity	Hispanic	53 (20.7%)
Child Primary Language	English	220 (88.0%)
	Spanish	12 (4.8%)
	French	2 (0.8%)
	Bilingual, English/Spanish	14 (5.6%)
	Other, specify	2 (0.8%)
	Missing[1] (n)	6
English Primarily Spoken at Home	English	208 (82.2%)
	Bilingual or other Language	45 (17.8%)
	Missing[1] (n)	3
Child Full Scale IQ	Mean (SD)	85 (15.4)
Child Word Reading Standard Score	Mean (SD)	86 (18.2)
Caregiver Income	<= $20k	108 (45.4%)
	> $20k	130 (54.6%)
	Missing[1] (n)	18
Caregiver Education Level	< High School Completion	67 (26.5%)
	≥ High School Diploma	186 (73.5%)
	Missing[1] (n)	3
Caregiver is Biological Parent	No	144 (56.9%)
	Yes	109 (43.1%)
	Missing[1] (n)	3
Caregiver HIV Status	HIV+	91 (43.5%)
	HIV-	118 (56.5%)
	Missing[1] (n)	47
Caregiver Race	White	73 (30.4%)
	Black	166 (69.2%)
	Other	1 (0.4%)
	Missing[1] (n)	16
Caregiver Ethnicity	Non-Hispanic	198 (79.5%)
	Hispanic	51 (20.5%)
	Missing[1] (n)	7

Characteristic		Total (N=256) n (%)
Caregiver Full Scale IQ	Mean (SD)	89 (15.2)

Note: IQ = Intelligence Quotient; SD = Standard deviation

[1] Missing n not included in denominator to calculate characteristic percentages.

Table 2

Child HIV Disease Characteristics

Characteristic		Total (N=256) n (%)
Youth Knows HIV Status	Yes	163 (64.7%)
	No	89 (35.3%)
	Missing[1] (n)	4
CDC Class C (at study entry)		68 (26.6%)
History of Encephalopathy		33 (12.9%)
Nadir CD4%	Mean (SD)	17.6 (9.0)
Age at Nadir CD4%	Mean (SD)	5.2 (4.0)
CD4% at Study Entry	Mean (SD)	32.0 (9.6)
Peak log RNA VL	Mean (SD)	5.4 (0.7)
Age at Peak RNA VL	Mean (SD)	4.2 (4.1)
log RNA VL at Study Entry	Mean (SD)	2.6 (0.9)
VL at Study Entry	<400	181 (71.3%)
	≥400	73 (28.7%)
	Missing[1] (n)	2
HAART Lifetime Duration (years)	Mean (SD)	7.75 (2.7)

Note: CDC – Centers for Disease Control and Prevention; RNA – ribonucleic acid;

VL – Viral load; HAART – Highly active antiretroviral therapy.

[1]Missing n not included in denominator to calculate characteristic percentages.

Table 3

Adjusted and Unadjusted Logistic Regression Analyses Modeling the Odds of 7-day Adherence

Adherence Predictor	Measurement	Unadjusted Odds Ratios (95% CI)	P-value	Adjusted [2] Odds Ratios (95% CI)	P-value
Adaptive Behavior (ABAS-II)					
General Adaptive Composite (GAC)	Standard Score [1]	0.78 (0.59, 1.05)	0.105	0.76 (0.56, 1.05)	0.100
Conceptual composite	Standard Score [1]	0.84 (0.63, 1.12)	0.233	0.83 (0.61, 1.13)	0.244
Social Composite	Standard Score [1]	0.89 (0.67, 1.18)	0.412	0.82 (0.60, 1.13)	0.221
Practical Composite	Standard Score [1]	0.71 (0.52, 0.96)	**0.029**	0.71 (0.50, 1.00)	**0.053**
Executive Function BRIEF					
Caregiver Report					
Global Executive Composite (GEC)	T Score[1]	1.03 (0.76, 1.40)	0.853	1.06 (0.76, 1.49)	0.721
Behavioral Regulation Index (BRI)	T Score[1]	1.04 (0.76, 1.42)	0.811	1.03 (0.73, 1.46)	0.853
Metacognition Index (MI)	T Score[1]	1.02 (0.75, 1.39)	0.900	1.08 (0.78, 1.51)	0.645
Child Report					
Global Executive Composite (GEC)	T Score[1]	0.72 (0.50, 1.02)	0.061	0.73 (0.49, 1.08)	0.111
Behavioral Regulation Index (BRI)	T Score[1]	0.65 (0.46, 0.93)	**0.018**	0.65 (0.44, 0.96)	**0.029**
Metacognition Index (MI)	T Score[1]	0.80 (0.57, 1.14)	0.216	0.83 (0.56, 1.23)	0.363
Children Color Trails Test (CCTT)					
CCTT Trial 1	T Score[1]	0.53 (0.38, 0.73)	**<.001**	0.54 (0.38, 0.77)	**<.001**
CCTT Trial 2	T Score[1]	0.72 (0.53,0.98)	**0.037**	0.75 (0.54, 1.05)	0.095
CCTT Interference Index	< 6th percentile	Reference		Reference	
	6–16 percentile	1.09 (0.34, 3.54)	0.881	0.98 (0.27, 3.55)	0.975
	>16th percentile	1.73 (0.73, 4.10)	0.211	1.36 (0.52, 3.58)	0.535
Processing Speed					
WISC-IV Processing Speed Index (PSI)	Composite Score [1]	0.63 (0.46,0.87)	**0.004**	0.63 (0.44, 0.89)	**0.009**

Note: ABAS-II – Adaptive Behavior Assessment System, Second Edition; BRIEF – Behavior Rating Inventory of Executive Function; WISC-IV – Wechsler Intelligence Scale for Children, Fourth Edition.

[1]Estimates are displayed for a one unit change in the observed standard deviation.

[2]Adjusted only for Caregiver Education, Child Race, Nadir CD4%, Age and Medication Responsibility.

Table 4

Adjusted and Unadjusted Logistic Regression Analyses Modeling the Odds That the Child is Solely Responsible for Medication

Adherence Predictor	Measurement	Unadjusted Odds Ratios (95% CI)	P-value	Adjusted [2] Odds Ratios (95% CI)	P-value
Adaptive Behavior (ABAS-II)					
General Adaptive Composite (GAC)	Standard Score [1]	1.06 (0.74, 1.52)	0.765	0.98 (0.63, 1.53)	0.933
Conceptual composite	Standard Score [1]	1.17 (0.81, 1.69)	0.403	0.98 (0.61, 1.58)	0.927
Social Composite	Standard Score [1]	0.96 (0.67, 1.38)	0.843	0.91 (0.58, 1.42)	0.665
Practical Composite	Standard Score [1]	1.07 (0.74, 1.54)	0.728	1.12 (0.72, 1.73)	0.621
Executive Function (BRIEF)					
Caregiver Report					
Global Executive Composite (GEC)	T Score [1]	0.87 (0.59, 1.28)	0.465	0.78 (0.50, 1.20)	0.258
Behavioral Regulation Index (BRI)	T Score [1]	0.89 (0.60, 1.32)	0.560	0.81 (0.52, 1.26)	0.342
Metacognition Index (MI)	T Score [1]	0.86 (0.59, 1.27)	0.456	0.78 (0.51, 1.21)	0.274
Child Self-Report					
Global Executive Composite (GEC)	T Score [1]	0.76 (0.50, 1.15)	0.197	0.82 (0.52, 1.30)	0.404
Behavioral Regulation Index (BRI)	T Score [1]	0.74 (0.49, 1.13)	0.164	0.76 (0.48, 1.21)	0.249
Metacognition Index (MI)	T Score [1]	0.80 (0.53, 1.20)	0.275	0.90 (0.57, 1.42)	0.651
Children Color Trails Test (CCTT)					
Processing Speed					
CCTT Trial 1	T Score [1]	1.13 (0.76, 1.68)	0.536	1.11 (0.70, 1.77)	0.645
CCTT Trial 2	T Score [1]	0.93 (0.63, 1.38)	0.730	0.69 (0.42, 1.13)	0.139
Interference Index	< 6th percentile	Reference		Reference	
	6–16 percentile	0.53 (0.11, 2.41)	0.408	0.65 (0.12, 3.65)	0.628
	>16th percentile	0.45 (0.16, 1.26)	0.131	0.49 (0.15, 1.62)	0.243
WISC-IV Processing Speed Index (PSI)	Composite Score [1]	1.13 (0.78, 1.65)	0.51	1.27 (0.87, 1.83)	0.210

Note: ABAS-II – Adaptive Behavior Assessment System, Second Edition; BRIEF – Behavior Rating Inventory of Executive Function;

WISC-IV – Wechsler Intelligence Scale for Children, Fourth Edition.

[1]Estimates are displayed for a one unit change in the observed standard deviation.

[2]Adjusted only for child age and Full Scale IQ.