Family Experiences with Pediatric Antiretroviral Therapy: Responsibilities, Barriers, and Strategies for Remembering Medications

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Abstract

This study examines the relationship between adherence to pediatric HIV regimens and three family experience factors: (1) regimen responsibility; (2) barriers to adherence; and (3) strategies for remembering to give medications. Caregivers of 127 children ages 2–15 years in the PACTS-HOPE multisite study were interviewed. Seventy-six percent of caregivers reported that their children were adherent (taking $\geq 90\%$ of prescribed doses within the prior 6 months). Most caregivers reported taking primary responsibility for medication-related activities (72%–95% across activities); caregivers with primary responsibility for calling to obtain refills (95%) were more likely to have adherent children. More than half of caregivers reported experiencing one or more adherence barriers (59%). Caregivers who reported more barriers were also more likely to report having non-adherent children. Individual barriers associated with nonadherence included forgetting, changes in routine, being too busy, and child refusal. Most reported using one or more memory strategies (86%). Strategy use was not associated with adherence. Using more strategies was associated with a greater likelihood of reporting that forgetting was a barrier. For some families with adherence-related organizational or motivational difficulties, using numerous memory strategies may be insufficient for mastering adherence. More intensive interventions, such as home-based nurse-administered dosing, may be necessary.

Introduction

ESTIMATES SUGGEST that worldwide, more than 2.5 million children are living with HIV infection.¹ Despite challenges, the widespread availability of antiretroviral therapy (ART) in the United States and other high-resource settings has led to decreased mortality among perinatally HIV-infected children, and many are surviving into adolescence and adulthood.² With recent initiatives to increase the availability of pediatric care and treatment in lower-resource settings,³ many more children with HIV are expected to survive and begin life-long therapy with ART. Research that enhances our understanding of ART adherence will be critical.

Research has generally failed to examine the specific ways in which families manage children's ART regimens and how those family factors relate statistically to adherence. Rather, studies have focused on individual characteristics of a child or caregiver that may indirectly impact adherence, such as depression or substance use,^{4,5} or interpersonal factors, such as a caregiver's perceived social support.^{6,7} While such factors may be important determinants of adherence, they provide little information about families' roles and processes that may affect adherence. Understanding families' experiences—especially who is responsible for regimen-related tasks, what keeps them from accomplishing those tasks, and what helps them succeed—may be critical for developing effective adherence-promoting interventions. For example, it

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may be important to know whether adult caregivers or children are responsible for tasks related to adherence (e.g., refilling prescriptions, remembering to take the medicine, etc.) so that we can both understand how differences in regimen responsibility affect adherence and know to whom interventions should be directed. Research among adolescents with a variety of chronic illnesses suggests that children assume increasing levels of responsibility for disease management as they mature,^{8–11} and at least one study suggests that caregivers may assume less responsibility as children become older.¹² At the same time, adherence problems increase as children get older,^{13–15} especially during adolescence.^{15–18} Thus, children and adolescents may be given responsibility for regimen-related tasks when they may be unlikely to complete them successfully. Studies have reported on some aspects of responsibility for medication-related behaviors within families of children on ART.^{11,19,20} In a study by Boni and colleagues,¹⁹ 86% of 25 caregivers of children on ART reported that they “watched children while they took their therapy.” No additional information about regimen responsibility was provided.¹⁹ Wrubel and colleagues,²⁰ in a qualitative interview study, reported on experiences of 71 mothers of children (ages 1–18 years) on ART; while 89% of mothers reported taking responsibility for their children’s adherence on at least one occasion, 21% indicated that they shared the responsibility with their children at least part of the time, and nearly 25% of mothers indicated a desire for their children to be responsible for ART adherence. Only 2 mothers recognized that their adolescents may not be able to take their medications consistently without maternal reminders.

Only one known study has directly assessed the relationship between regimen responsibility and ART adherence. Martin and colleagues¹¹ studied ART adherence among 24 children ages 8 to 18 years and used both child and caregiver report to assess the extent to which the caregiver, child, or both assumed responsibility for regimen-related tasks. From their report, it was not clear what percentage of children and caregivers were solely responsible for regimen-related tasks. Neither child nor caregiver reports of regimen responsibility were directly associated with adherence, although greater caregiver–child discrepancies about regimen responsibility were associated with worse adherence at the second time-point. Also, children’s regimen responsibility increased significantly with child age.

Multiple regimen-related tasks must be completed in order to achieve adherence, including: (1) remembering that it is time to take the medications; (2) opening the bottles and retrieving the medication; (3) swallowing the medication; (4) noticing when refills are needed; and (5) calling to arrange for refills. It is possible that responsibility for some of these tasks could be allocated to children or youth without detrimental effects on adherence. For example, it may be that adherence could be achieved easily if a child is responsible for opening the bottles and retrieving the medication, as long as an adult ensures that the medications are swallowed. The importance of children versus caregivers assuming responsibility for these specific tasks has not been well studied.

As suggested by the Health Belief Model,^{21,22} identifying barriers to adherence may also help to inform intervention efforts, especially to the extent that barriers are associated with adherence outcomes. Studies have examined families’

barriers to pediatric ART adherence regimens,^{19,20,23–34} but only three small studies have examined the statistical association between reported barriers and adherence, and those have produced conflicting results. When a checklist was used to assess barriers to adherence, more barriers were associated with lower levels of caregiver-reported adherence^{29,30}; yet when 10 barriers were rated on a Likert-type scale, the mean barrier frequency score was not associated with adherence measured by caregiver report, pill counts, or electronic monitoring.³³ Studies with larger sample sizes are needed to clarify the relationship between barrier reporting and adherence, as well as to identify which specific barriers statistically account for adherence difficulties.

Once we identify the critical barriers, it is then important to identify strategies for overcoming those barriers. Understanding which strategies help families successfully manage ART regimens is important for helping other families improve adherence behavior. Some such strategies have been enumerated, including: using reminder devices (e.g., calendars, timers, beepers), using physical reminders such as putting bottles in an obvious location or posting reminder notes, asking other family members to help with reminding, incorporating medication-taking into daily routines, and improving or masking unpleasant tastes.^{24,35,36}

Studies have generally not supported the effectiveness of several commonly recommended strategies for improving adherence among adults. A recent meta-analytic review showed that three interventions using electronic reminder devices (i.e., beepers or pagers) failed to increase the likelihood of participants obtaining >95% adherence relative to controls.³⁷ One of those studies found more one-log decreases in plasma HIV RNA loads among intervention versus control participants, suggesting that electronic reminders may have some adherence-enhancing effects.³⁸ Another controlled study found improvements with the use of an online pager system, but adherence was still low in the intervention group (64%).³⁹ Other interventions have included teaching patients to use cues as reminder of medication times. One controlled study found that using electronic medication monitoring feedback and having participants identify cues that would help them remember to take their ART medications was not effective in improving adherence or plasma HIV RNA loads unless it was paired with a monetary reward.⁴⁰ Another study tested a single-session and follow-up phone call “Life-Steps” intervention that included assistance identifying cues for medication-taking and guided imagery review of medication-taking in response to identified cues. Compared to participants who used daily dairies to monitor their adherence, Life Steps participants showed better adherence outcomes after two weeks but no difference at 12-week follow-up.⁷⁵

Few studies have examined the use of memory strategies for increasing adherence among children on ART. A recent cross-sectional study of children and adolescents found increased odds of adherence among those who used a buddy system to help them remember to take medications, although they found no greater likelihood of adherence among those who tied medication-taking into other activities or used pill boxes to remember doses versus those who did not.¹⁵ An intervention pilot study with youth ages 15–22 provided participants with two reminder devices: a beeper that vibrates and can hold pills, and an alarm watch; provision of these

devices did not significantly improve adherence or reduce the problem of youth forgetting doses, although youth believed that the multiple alarm watch was helpful.⁴¹ These studies provide little support for using cue-based strategies to improve adherence among children and adolescents with HIV. Nevertheless, the literature in this area is too sparse to be conclusive. While the adult literature suggests that memory strategies are of limited effectiveness for improving adherence to ART, it is important to examine the value of cue-based strategies for facilitating adherence among children, as pediatric clinicians continue to recommend these strategies with very limited pediatric data regarding how the use of such strategies impacts adherence.

Using data from the Pediatric AIDS Collaborative Transmission HIV Follow-up of Exposed Children (PACTS-HOPE) study, we aim to further understanding of adherence to pediatric ART by examining three family experience factors and their relationship to adherence. Those family experience factors include: (1) division of regimen responsibility; (2) barriers to adherence; and (3) strategies for remembering medication. Briefly we describe medication regimens and adherence rates for the sample. Based on the extant literature, we test hypotheses that caregivers who report sole responsibility for each regimen-related tasks have younger children than those who report caregiver-child shared responsibility, and that adherence is more likely when caregivers (versus children) assume responsibility for each medication-related task, report fewer barriers, report more memory strategies overall, and report at least one (versus no) cue-based strategy (defined as a visual, auditory, or behavioral cue that serves as a reminder of dosing times).

Method

Study population

From October 1985 until September 1999, the U.S. Centers for Disease Control and Prevention (CDC) funded the Perinatal AIDS Collaborative Transmission Study (PACTS), which enrolled HIV-infected pregnant and peripartum women and their newborns. The primary purpose of PACTS was to examine the rate of and risk factors for perinatal HIV transmission and early childhood survival in four U.S. HIV/AIDS epicenters (Atlanta, Georgia; Baltimore, Maryland; Newark, New Jersey; New York, New York).⁴²⁻⁴⁴ From March 2001 to March 2003, children formerly enrolled in PACTS were recruited into the PACTS HIV Follow-up of Perinatally Exposed Children (PACTS-HOPE) study, which was designed to examine markers of disease progression, medication adherence, and psychosocial adjustment over time. Procedures have been previously described.⁴⁵ Included in the source population were all living HIV-infected children not lost to follow-up during PACTS ($n = 196$) plus 8 children who had been lost to follow-up and were subsequently found. In total there were 204 potential participants. Of these 204, 7 refused to participate, 12 had relocated, and 3 were ineligible because in some states children in foster care were not allowed to participate. Altogether, 182 children were enrolled.

For the present analyses, children had to be prescribed ART at the time of enrollment and had to have a caregiver-completed interview. Eighteen children were not receiving ART at the time of enrollment. Thirty-seven others did not

have a fully completed caregiver adherence interview. Six of those were missing the adherence interview and are presumed to have not been prescribed ART, although because their baseline medical record review was missing this could not be confirmed. Two participants had begun or changed their medication during the time period assessed, and thus did not have an adherence interview. Six children were prescribed ART, yet their adherence interview was missing. Adherence interviews were available for the remaining 23 participants but data were missing for the primary outcome of this investigation (i.e., adherence, based on reports of the percent of doses taken in the past 6 months). Ultimately, 127 children were included in the present analyses. Children who were excluded from these analyses did not differ significantly from those included in terms of age, gender, race, or ethnicity.

Participants. Child and caregiver demographics were obtained via caregiver report. Children ranged from 2 to 15 years of age ($M = 7.8$, standard deviation [SD] = 2.7). Children were 61% female and most were African American (82% versus 17% Caucasian; 1% marked "other"; 1% refused to answer) and non-Hispanic ethnicity (84%). Caregivers ranged in age from 22 to 73 years ($M = 45$, $SD = 11.7$); most were female (88%) and of African American race (80% vs. 9% Caucasian; 1% Alaskan; 1% marked "other"; and 9% refused to answer) and non-Hispanic ethnicity (79%). Caregivers' relationship to the child varied (42% biologic parent; 21% adoptive; 7% foster; 27% other kin; 2% other; 2% missing).

Procedures

Institutional Review Board (IRB) approval was obtained from the CDC and all study sites. Following receipt of written informed consent from caregivers or legal guardians, and assent from children who were 7 years of age or older, caregivers were interviewed by research assistants not directly involved in their care. Research assistants recorded caregivers' responses to the interview questions. Data were also derived from medical chart abstraction, including children's HIV viral load drawn up to 90 days before or after the adherence assessment.

Self-report measures. Adherence was assessed during a structured face-to-face interview designed for the present study. Previous research among adults supports the validity of a global, 6-month recall of ART adherence, based on a significant relationship with viral load.⁴⁶ In this study, caregivers were asked to recall the proportion of doses the child took over the previous 6 months, and select one item from a 5-point Likert-type scale. Options were: "almost all (or at least 9 out of 10);" "most (or at least 8 out of 10);" "more than half (or more than 5 out of 10);" "less than half (or less than 4 out of 10);" and "none." Due to extreme skewness and small cell size in the latter three categories, adherence was dichotomized to reflect those who were 90% or more adherent (henceforth "Adherent") versus those who were less adherent (<90% adherent; henceforth "Nonadherent"). As previously reported from this dataset, significantly lower $\log_{10}$ viral loads were found among children categorized as Adherent on this measure (odds ratio [OR] = 0.71, 95% confidence interval [CI]: 0.51, 0.97).⁴⁷

Barriers to adherence were assessed with the following question, based on the Pediatric AIDS Clinical Trials Group Adherence Module 2,⁴⁸ a modification of the Adult AIDS Clinical Trials Group Adherence tool.⁴⁹ "When a dose of your child's medication is missed, what are the reasons for the missed dose?" Nine barriers were listed (e.g., "forgot to give"; "change in daily routine"; "afraid of side effects"; etc.), as well as the option of "never missed a dose"; caregivers were instructed to identify all applicable responses.

Regimen responsibility was assessed with a modified version of Anderson and colleague's regimen.⁵⁰ Diabetes Regimen Responsibility Inventory. The authors revised items to reflect tasks required for adherence to ART. For example, one item on the diabetes version, "Remembering to take morning or evening injection" was revised to, "Remembering to take medications on time." Caregivers were given the list of regimen-related tasks and asked to indicate whether an adult, the child, or both an adult and child are responsible for each task. Most responses indicated that an adult was responsible; therefore, responses were scored as "yes" or "no" based on whether an adult assumed sole responsibility or shared responsibility with the child.

Strategies for medication-taking were assessed with a question designed by the study team. Based on research suggesting that families use a variety of strategies to enhance medication administration³²; caregivers were asked to list "the three most helpful things that [they] use or do to help [them] to remember to take/give medication." Caregivers provided up to three strategies. Responses were examined for content themes, and a coding scheme was developed by the first author and a graduate assistant, who then coded each response by hand⁵¹; coding agreement was high ($\kappa = 0.86$, $p < 0.001$). Discrepancies were resolved following code clarification. Responses were categorized as cue-based strategies if they involved pairing medication-taking with other daily activities or routines, or using specific reminder devices (e.g., pill boxes, calendars, beepers, other visual cues). A variable was created to reflect the number of unique strategies for medication-taking reported by each caregiver.

Statistical analyses. Descriptive statistics were generated to describe regimen characteristics, the proportion of children categorized as Adherent versus Nonadherent, virologic findings, and the three family experience factors (regimen responsibility, barriers, and strategies). We also explored the relationship between adherence and child demographics, including age, gender, race, and ethnicity to provide contextual information for interpreting study findings. Next, Student's *t* tests were conducted to test for age differences between children of caregivers who reported sole responsibility (versus shared responsibility with the child) for regimen tasks (Hypothesis 1). Logistic regression analyses were conducted to test the hypothesis that caregivers are more likely to be categorized as Adherent (versus Nonadherent) when they report sole responsibility (Hypothesis 2), fewer barriers (Hypothesis 3), more memory strategies (Hypothesis 4), and at least one cue-based strategy (Hypothesis 5).

Results

Descriptive findings

Medication regimens. As previously reported,⁴⁷ many children (83%) were prescribed three or more different anti-

retroviral medications (range = 1–6). The most frequent combination included both liquid and pill formulations (37.6%); other common regimens included liquids only (28.9%) and pills only (26.8%). Most children (94.0%) were expected to take ART at least two times per day.

Adherence rates. Seventy-six percent of caregivers indicated that "almost all (at least 90%)" of their child's medication doses were taken in the previous 6 months. Girls were less likely to be categorized as Adherent than boys (OR = 0.34, 95% CI: 0.13, 0.90). Adherence was not significantly associated with child age, Hispanic ethnicity, or African American race.

Virologic findings. Viral RNA tests were available for 83% of the sample and results ranged from less than 50 to 446,000 cells per milliliter. The median viral RNA was 1453 cells per milliliter. Sixty-five participants (62% of those with virologic data) had viral RNA in the undetectable range, defined as less than 400 cells per milliliter.

Regimen responsibility. Table 1 shows the proportion of caregivers reporting sole regimen responsibility for each task. Over half of all caregivers (65%) reported taking sole responsibility for all tasks related to their child's medication adherence.

Barriers to adherence. Table 2 shows the proportion of caregivers selecting each barrier to adherence. Among 127 caregivers, 75 (59.1%) selected at least 1 of 9 listed reasons that their child missed medications, 27 (21.3%) reported another reason that was not listed, and 31 (24.4%) marked that they, "never missed a dose." "Change in daily routine" was the barrier most commonly selected (28.3%), followed by "forgot to give" (16.5%). Caregivers who indicated "another reason" for missing doses were asked to state that reason; those were examined qualitatively by the primary author. Of those responses, 4 indicated that doses were never or rarely missed, and thus did not reflect actual barriers; 12 pertained to being away from home during the dosing time; 2 responses reflected disorganization and difficulty fitting the medication-taking into a busy day; 8 responses were idiosyncratic; and 1 participant did not provide the other reason.

Strategies for remembering medication. One hundred twenty-six caregivers provided 201 responses to a question about strategies (one had missing data; Table 3). Most (85.8%) reported using at least one strategy for remembering medication. Pairing medication-taking with another activity, such as eating meals, was the most commonly employed strategy ($n = 77$), followed by keeping a daily schedule or routine that involves taking the medication at the same time every day ($n = 45$). Other common reports ($n = 25$) included using pill boxes, calendars, beepers, or additional cues as reminders.

Hypothesis testing

Hypothesis 1: Caregivers who report sole responsibility for each regimen-related task have younger children than those who report caregiver-child shared responsibility. For each task, children's mean age differed significantly based on

TABLE 1. AGE DIFFERENCES IN FAMILY RESPONSIBILITY FOR REGIMEN-RELATED TASKS: PERINATAL AIDS COLLABORATIVE TRANSMISSION-HIV FOLLOW-UP OF PERINATALLY EXPOSED CHILDREN (PACTS-HOPE) STUDY, 2001–2004

<i>Responsibility item</i>	<i>n (%)</i>	<i>Mean child age in years</i>	<i>Student's t (df)</i>	<i>p value</i>
Remembering to take medications on time			3.93 (124)	0.000
Caregiver solely responsible	99 (78.0)	7.38 (2.46)		
Caregiver and child both responsible	27 (21.3)	9.54 (2.81)		
Opening the containers and taking out the medications			5.08 (125)	0.000
Caregiver solely responsible	91 (71.7)	7.17 (2.34)		
Caregiver and child both responsible	36 (28.3)	9.64 (2.75)		
Assuring that medications have been taken (swallowed)			4.46 (124)	0.000
Caregiver solely responsible	104 (81.9)	7.43 (3.16)		
Caregiver and child both responsible	22 (17.3)	10.06 (3.16)		
Noticing when medicines need to be refilled			2.62 (124)	0.010
Caregiver solely responsible	117 (92.1)	7.69 (2.65)		
Caregiver and child both responsible	10 (7.9)	9.97 (2.43)		
Remembering to call the doctor or pharmacy for refills			2.97 (125)	0.004
Caregiver solely responsible	121 (95.2)	7.72 (2.59)		
Caregiver and child both responsible	6 (4.7)	10.96 (3.02)		

whether their caregiver reported sole or shared responsibility; caregivers who reported sole responsibility had children who were younger (test statistics shown in Table 1).

Hypothesis 2: Caregivers who assume sole responsibility (versus shared responsibility with the child) for each medication-related task are more likely to have Adherent (versus Nonadherent) children. Results provide partial support for this hypothesis. Caregivers who reported sole responsibility for remembering to call the doctor for pharmacy refills ($n = 121$) were more likely to have children characterized as adherent (test statistics shown in Table 4). No other responsi-

bility item was significantly associated with adherence. We explored the possibility that caregivers who reported shared responsibility for remembering to call for pharmacy refills also reported shared responsibility for each of the other four adherence-related tasks. Of those six participants who reported shared responsibility for remembering to call for refills, all reported shared responsibility for opening the containers and taking out the medications; five reported shared responsibility for remembering to take medications on time and for assuring that medications have been swallowed; and three reported shared responsibility for noticing that medications need to be refilled.

TABLE 2. ODDS OF CHILD ADHERENCE IF BARRIERS WERE REPORTED: PERINATAL AIDS COLLABORATIVE TRANSMISSION-HIV FOLLOW-UP OF PERINATALLY EXPOSED CHILDREN (PACTS-HOPE) STUDY, 2001–2004

	<i>Caregivers indicated this is a barrier n (%)^a</i>	<i>Odds ratio of child adherence if barrier was reported (95% CI)^d</i>
Any barrier (not including "Other")	75 (59.1)	0.20 (0.07, 0.57)**
Forgot to give	21 (16.5)	0.35 (0.13, 0.93)*
Change in daily routine	36 (28.3)	0.25 (0.10, 0.58)**
Can't get drug (drug store doesn't supply)	2 (1.6)	— ^b
Busy with other things	15 (11.8)	0.23 (0.07, 0.69)**
Child refused	6 (4.7)	0.06 (0.01, 0.49)**
Afraid of side effects	1 (0.8)	—
Ran out of medicine	14 (1)	0.54 (0.17, 1.75)
Couldn't give at school or other situation because of lack of privacy	3 (2.4)	0.15 (0.01, 1.75)
Another caregiver missed the dose	4 (3.1)	0.97 (0.10, 9.66)
Never missed a dose	31 (24.4)	6.28 (1.40, 28.06)*
Don't know	3 (2.4)	— ^b
Other	27 (21.3)	— ^c

^aPercentages based on $n = 127$.

^bNot calculated due to insufficient sample size in a given cell.

^cNot calculated because some responses to this item did not reflect actual barriers (e.g., "does not miss").

^dCI, confidence interval.

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

TABLE 3. CAREGIVER-REPORTED STRATEGIES FOR REMEMBERING MEDICATION: PERINATAL AIDS COLLABORATIVE TRANSMISSION-HIV FOLLOW-UP OF PERINATALLY EXPOSED CHILDREN (PACTS-HOPE) STUDY, 2001–2004

Strategy category	Sample quotes	n (%)
Pair medication-taking with another activity	<i>She takes it just before school and just after dinner. She remembers the time. It is the same time as food.</i>	77 (61%)
Keep a daily schedule or routine that involves taking medication at the same time every day	<i>I just do it at the same time every day. 8 AM and 8 PM every day.</i>	45 (36%)
Use pill boxes, calendars, beepers, or additional cues for reminders	<i>I keep medication out in the open on the kitchen counter. All his medications are set up in a pill box.</i>	30 (20%)
Child and caregiver take medication at the same time	<i>I take medicine, too, so we take them together.</i>	10 (8%)
Child or other person reminds caregiver that it is time for the child to take medication	<i>She also reminds me. The child won't let me forget.</i>	10 (8%)
Other response, does not easily fit into categories.	<i>I use measuring tubes.</i>	10 (8%)
Responded, but did not identify a strategy	<i>I just remember. I just know it's got to be done.</i>	16 (13%)
Said they used no strategies	<i>Nothing</i>	3 (2%)

Note: Percentage based on 126 participants who provided a response.

Hypothesis 3: Caregivers who report fewer barriers (including barriers listed under “another reason”; versus those who report more barriers) are more likely to have Adherent (versus Nonadherent) children. This hypothesis was confirmed (OR = 0.36, 95% CI: 0.20, 0.64), and is consistent with the finding that most caregivers who did not identify a barrier (89%) or who identified only one barrier (78%) also reported that their child took “almost all” of their doses. As shown in Table 2, several barriers were significantly associated with Nonadherent categorization: “forgot to give,” “change in daily routine,” “too busy,” and “child refused.” Conversely, caregiver reports that the child “never missed a dose” were associated with Adherent categorization.

Hypothesis 4: Caregivers who report more (versus less) memory strategies are more likely to have Adherent (versus Nonadherent) children. This hypothesis was not supported, as the number of memory strategies was not significantly associated with adherence (OR: 0.74; 95% CI: 0.38, 1.46). It may be, however, that using memory strategies protects families against experiencing forgetting as a barrier to adherence.

When we conducted a *post hoc* analysis to explore this, we found the opposite: those who used more memory strategies were more likely to have reported forgetting as a barrier than those who used fewer strategies (OR: 3.67; 95% CI: 1.54, 8.75).

Hypothesis 5: Caregivers who report at least one (versus no) cue-based strategy are more likely to have Adherent (versus Nonadherent) children. This hypothesis was not supported, as reports of using cue-based strategies were not significantly associated with adherence (OR: 0.70; 95% CI: 0.31, 1.61).

Discussion

This paper examined family experiences with pediatric ART regimens among participants enrolled in the PACTS-HOPE study, focusing on responsibility for medication-related activities, barriers, and strategies for remembering medication administration. Caregivers who reported taking primary responsibility for calling to refill ART prescriptions (versus giving the responsibility to or sharing the responsi-

TABLE 4. ODDS OF ADHERENCE WHEN CAREGIVERS REPORT SOLE REGIMEN RESPONSIBILITY: PERINATAL AIDS COLLABORATIVE TRANSMISSION-HIV FOLLOW-UP OF PERINATALLY EXPOSED CHILDREN (PACTS-HOPE) STUDY, 2001–2004

	Caregivers reporting sole responsibility n (%) ^a	Adherence odds ratio (95% confidence interval)
Remembering to take medications on time (<i>n</i> = 126)	99 (78.0)	1.47 (0.57, 3.82)
Opening the containers and taking out the medications (<i>n</i> = 127)	91 (71.7)	1.28 (0.53, 3.08)
Assuring that medications have been taken (swallowed) (<i>n</i> = 126)	104 (81.9)	0.67 (0.21, 2.15)
Noticing when medicines need to be refilled (<i>n</i> = 127)	117 (92.1)	1.36 (0.33, 5.62)
Remembering to call the doctor or pharmacy for refills (<i>n</i> = 127)	121 (95.2)	6.93 (1.21, 40.09) ^b

^avs. shared responsibility with the child.

^b*p* < 0.05.

bility with the child) were more likely to have adherent children. This finding differs from that of a previous study,¹¹ which found no relationship between adherence and the sum of scores for nine responsibility items. Ours is an important finding, because it suggests that to achieve adherence caregivers may need to retain responsibility for some regimen tasks, although they may be able to share or allocate responsibility for other tasks without compromising adherence. Adherence may improve if clinicians help caregivers and children identify which tasks can be safely allocated to the child and which tasks are better left to caregivers. However, some caution is warranted in interpreting this finding, as only six caregivers in the study reported sharing responsibility with the child for making refill requests.

Confirming our hypotheses as well as a previous finding in the pediatric ART literature,¹¹ children who shared responsibility with their caregivers were older than children who did not share responsibility for each of five regimen tasks. Caregivers often allow children to assume increasing responsibility for medication adherence as they become older and show signs of maturity,^{8–11} which for some may be an appropriate means of preparing children for self-care during adulthood. Children and adolescents may appreciate the opportunity to control whether or not and when they get their medications, leaving them with less anger and greater regimen-specific self-efficacy,⁵² while caregivers may be relieved to relinquish medication responsibilities.⁵³ Unfortunately, across chronic conditions, data consistently show that for many, adolescence—the time when caregivers are most likely to grant their children greater responsibility—is a time of poor adherence to medical regimens.^{15–18} Thus, it may be important for clinicians to offer caregivers anticipatory guidance that stresses the importance of supervising and monitoring their child's completion of regimen-related tasks,^{11,54} even when they allocate primary responsibility for medication-taking to their child or adolescent.

Older age was not significantly associated with nonadherence in this study. Other studies in the pediatric HIV literature have failed to find a direct relationship between age and adherence^{30,32,33,55,56} or have found that caregiver reports of adherence increase with child age.²⁶ Like the present study, most such studies have included primarily children under age 13 years^{30,32,55,56} at least partially excluding adolescents, who may have the greatest difficulty adhering. Therefore, the failure to find an age effect may be due to truncation of the sample. Moreover, the relationship between age and adherence is likely mediated by other factors, including regimen responsibility, in which case identifying and changing those mediators may be the most pertinent objectives.

Consistent with findings of two previous studies, caregivers who reported fewer barriers to adherence were more likely to have adherent children.^{29,30} Several individual barriers were significantly associated with nonadherence, including three barriers that may reflect disorganization (forgot, busy with other things, and change in daily routine), and one barrier associated with parent-child dynamics (child refused). As they are the most commonly reported barriers in this sample, determining whether or not families experience these barriers may be particularly important for identifying adherence problems and creating a dialogue with families about their medication-related experiences.

Once adherence problems are identified, providers may recommend commonly used strategies for remembering medication. Our findings suggest that this approach may not always be effective. Neither using more memory strategies overall nor using at least one (versus no) cue-based strategy was significantly associated with adherence. Although strategies such as tying medication-taking into daily routines and using reminder devices may assist some families with adherence, using such strategies is insufficient for some families to achieve adherence.^{15,40,41,57} In fact, our results show that caregivers who used more strategies (versus less) for remembering medications were more likely to report a problem with forgetting doses. Similarly, Kalichman and colleagues⁵⁸ found that some adults on ART who used pill boxes also used other memory strategies and were more likely than non-pillbox users to report missing medications due to forgetting. It seems unlikely that using memory strategies contributes to problems of forgetting; rather, the problem of forgetting may trigger the use of multiple strategies to address adherence problems. Families who miss doses due to forgetting may try multiple strategies for remembering medication dose times.

Families who struggle with forgetting, multiple demands, or changes in their routine may have difficulties with organization in general. A beeper or other reminder device is only helpful if, upon receiving the reminder, the child takes the medication. The reminder device will be ineffective if the reminder is given but the child does not get the medicine. For example, a child may not get the medicine after a reminder due to a supply problem (e.g., they ran out of medication) or a proximity problem (e.g., they did not take the reminder device or the medication along when they left the house). Families who experience such situations may benefit from assistance in organizing their lives so that they have a dose of medication available at all times. In the case of proximity problems, families may also benefit from learning how to set their reminder devices to alert them later, when they are likely to be at home.

Stigma—anticipated or experienced—is a potential barrier to the success of memory strategies for promoting adherence. It is uncommon for families to disclose a child's HIV status to most people outside of the immediate family; thus, even when families have effective strategies for remembering doses, children may miss doses due to concerns that others will inadvertently learn about the child's HIV status.^{28,53} Yet stigma does not explain the lack of relationship between memory strategies and adherence in this study, given that only 2% of caregivers reported that nonprivacy was a barrier.

Untested in this study is the hypothesis that motivational barriers may keep some children from receiving the medication in response to a reminder. The child or caregiver might turn off a medication alarm with some vague intention of taking or administering the medication in the ensuing minutes or hours, and then “forget” to take or give the medication.²⁸ “Forgetting” may be a proxy for psychological processes such as avoidance and denial.⁵⁹ Depression^{5,60} and posttraumatic stress related to the HIV diagnosis,⁶¹ other mental health problems,⁵⁶ and limited adherence-specific or global social support⁵⁶ may fuel this avoidance or otherwise make dose administration difficult if not impossible. Surely most caregivers want to their child to get this critical med-

ication, although some caregivers may avoid dosing either: (1) because the medication reminds them of HIV—a life-threatening, stigmatized chronic illness that burdens their family, and in some cases, which they passed to their child⁵³; (2) out of compassion for their child's reluctance to take the medicine⁵³ or (3) to avoid stressful caregiver-child conflicts around medication-taking.^{28,53} Studies have examined attitudes and beliefs related to ART medication^{62–64} (see Fisher et al.⁶⁵ for a brief review), but these psychological barriers to adherence have not been well explored.

Research is needed to determine families' goals or behavioral intentions for medication-taking and how they relate to adherence.⁶⁶ Although health care providers often have near-perfect adherence as a goal, some families may be content with the child getting their medication most of the time as long as their child appears healthy. Bauman⁶⁷ distinguishes between types of nonadherers: volitional and inadvertent. Volitional non-adherers consciously choose to not follow a regimen. Inadvertent nonadherers make a decision to follow a medical regimen but fail to do so; they may fall into one of three subtypes: (1) those who are nonadherent because they misunderstand the regimen; (2) those who want to adhere but face barriers; and (3) those who miss doses at times, but feel they are adhering sufficiently. In a study of young women with HIV, Kalichman and colleagues⁶⁸ found that intentions to adhere were significantly associated with adherence; similar work is needed to better understand the role of intentions in adherence to pediatric regimens. Such research should attempt to reduce social desirability bias, because women may be concerned about the consequences of reporting socially undesirable intentions for adhering to their child's regimen.⁶⁹

This study has multiple strengths, including a large sample relative to most studies in the literature.⁷⁰ Data were drawn from seven pediatric HIV clinics in four U.S. cities; thus, these findings are likely generalizable to a large portion of children living with HIV in the United States. Moreover, this study is unique in its examination of three family experience factors as they relate to adherence. Several limitations must be noted as well. First, conclusions about causality are limited due to the cross-sectional design. Additionally, this study used a single caregiver self-report question to assess adherence over a 6-month period. Although the association between this measure and virologic outcomes supports its validity, replication of this finding is important, and findings will be enhanced when multiple measures are used.⁷¹ For example, incorporating child as well as caregiver reports may provide a fuller, if more complex, picture of adherence. More objective assessment tools such as electronic monitoring devices, while expensive and imperfect, can provide useful triangulation of data, as well.²⁵

Both the present study and a previous study¹¹ adapted a measure originally used to assess responsibility for diabetes regimen tasks,⁵⁰ which asks caregivers whether the child, caregiver, or both are primarily responsible for regimen tasks. The current study found limited variability in responses to most items, suggesting that a different response set may improve the measure. A similar measure to assess responsibility for asthma management has the respondent rate each task on a 5-point Likert-type scale ranging from 1 (parent is completely responsible) to 5 (child is completely responsible),¹² although only limited support was found for

the relationship between that measure and children's adherence.^{12,72} Another option would have respondents report how frequently over a set period of time a caregiver (versus child) actually completed each task. For some regimen tasks it may be valuable to reframe the construct from responsibility to supervision and monitoring.⁵⁴ Presumably, the child is typically the one who puts the medication in his/her mouth, so the important question may be whether or not a caregiver was present and watched it occur.⁷³ With either modification, efforts to limit response biases due to social desirability will be critical to the future success of this measure.

In conclusion, this multisite study of children's adherence to ART highlights the importance of caregivers taking responsibility for the medication supply and demonstrates the utility of barrier assessments for identifying suboptimal adherence. This study also suggests that for some families, using strategies for remembering medication may be insufficient to address problems with forgetting doses, although this finding warrants replication with a longitudinal, experimental design that can clarify the causal direction of these preliminary findings. Clinicians and researchers working with families may want to investigate how motivating factors account for adherence problems, and how established techniques, such as cognitive-behavioral and motivational interviewing may be useful in addressing these issues. Although some adherence-promoting interventions have been tested among children and youth, their effectiveness has been limited, at best, and their effects on adherence motivations have not been well studied.^{41,70–73} For some struggling families, home-based nurse-administered dosing may be the only viable strategy for ensuring adherence⁷⁴ while we await future studies to identify promising alternative intervention strategies.

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