

Adherence to ART in HIV-infected children in Kenya, South Africa, and Thailand



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Background



ICAMP ADHERENCE QUESTIONNAIRE

1. Who gives [name] his/her medicines? (tick all that apply) □ Mother □ Father □ Grandparent □ Auntie/Uncle □ Guardian □ Relative who lives in home □ Relative who lives outside of home □ Neighbor □ Sibling □ House help □ Child takes meds themselves □ Other (specify)

2. Does the child know that he/she is taking the medicines for HIV? □ Yes □ No □ Don't Know	3. How many people in your household take medicines for HIV? □ Don't know
4. Do you ever have problems keeping time with the medicines?	5. Do you ever have problems with getting your child to take the medicines?
When? Mornings Veekends Weekdays Other:	□ Yes □ No What problems does child raise? (explain)

6. Some families tell us that their child worries them or makes it difficult to give them the medicines. Has your child [name] not taken medicines for any of these reasons:

He/she does not know why taking the medicines	or keeps asking questions about the medicines
He/she forgot to take medicine	He/she felt ill or was vomiting
He/she was playing or at school or work	He/she refused to take medicine
 Has problems with 1 formulation (tablets, liquids) 	Finds medicines too bitter
Can't take without food	None of the above
	Other (specify):

7. Sometimes, a child does not take their medicines every day or at the same time every day because of difficulties for the caregiver. I am going to read a list of issues that may be problems for you as a caregiver in having the child take the medicines. Tell me when you hear a problem mentioned that applies to you or the child's caregiver:

None of the above	Other (specify)
	on time
I did not want others to see	I had trouble with timing or giving the doses
I was not always around with the child	I was too busy and forgot
	medicines
I was away from home (work, field, etc.)	I had difficulty with the instructions for the

8. Sometimes, problems at the clinic make it difficult for families to give these medicines every day. Have any of these things been a problem for you:

We finished or ran out of the medicines None of the above	Other (specify)
 The medicine was not available in the pharmacy. (include abx) 	Which medicine? ARVs Septrin Other
There was no money to purchase medicine (if not offered	at RMMCH)

9. In the past week.

a. On how many days did the child miss at least one dose? DO 1 2 3 04 05 06 07 DOn't know b. On how many days did the child take a dose more than an hour late? DO 1 2 3 04 05 06 07 DOn't know c. How many <u>extra</u> doses or syringes of medicine did the child take? DOn't know

10. How many doses of medicine has your child missed in the last month?

- Few low-cost, validated instruments to measure adherence to ART for children and adolescents, especially in low- and middleincome countries
- Initially developed and validated questionnaire in Kenya using electronic dose monitoring, plasma drug levels for validation standard
- CAMP: 10-item pediatric adherence questionnaire with caregiver and child respondent versions
- Unclear how questionnaire would perform outside of Kenya

Objective



ICAMP ADHERENCE QUESTIONNAIRE

1. Who gives [name] his/her medicines? (tick all that apply)

Mother
Father
Grandparent
Auntie/Uncle
Guardian
Relative who lives in home
Relative who lives
outside of home
Neighbor
Sibling
House help
Child takes meds themselves
Other
(specify)

2. Does the child know that he/she is taking the	3. How many people in your
medicines for HIV? Yes No Don't	household take medicines for
Know	HIV? Don't
	know
4. Do you ever have problems keeping time with	5. Do you ever have problems
the medicines?	with getting your child to
🗆 Yes 🗆 No	take the medicines?
Yes No When? Mornings Evenings Weekends	ake the medicines? □ Yes □ No

6. Some families tell us that their child worries them or makes it difficult to give them the medicines. Has your child [name] not taken medicines for any of these reasons:

He/she does not know why taking	the medicines	or keeps	asking questio	ns about	the medicines
He/she forgot to take medicine			He/she felt	till or was	vomiting

He/she was playing or at school	or work
Has problems with 1 formulation	n (tablets, liquids)
Can't take without food	

7. Sometimes, a child does not take their medicines every day or at the same time every day because of difficulties for the caregiver. I am going to read a list of issues that may be problems for you as a caregiver in having the child take the medicines. Tell me when you hear a problem mentioned that applies to you or the child's caregiver:

I was away from home (work, field, etc.)	I had difficulty with the instructions for the
	medicines
I was not always around with the child	I was too busy and forgot
I did not want others to see	I had trouble with timing or giving the doses
	on time
None of the above	Other (specify)

8. Sometimes, problems at the clinic make it difficult for families to give these medicines every day. Have any of these things been a problem for you:

There was no money to purchase medicine (if not offered at RMMCH)
 The medicine was not available in the pharmacy.
 Which medicine?
 ARVs
 Septrin
 Other
 (include abx)
 Which medicine?
 Other (specify)
 Other (specify)

9. In the past

week.

a. On how many days did the child miss at least one dose? $\Box 0$ $\Box 1$ $\Box 2$ $\Box 3$ $\Box 4$ $\Box 5$ $\Box 6$ $\Box 7$ \Box Don't know b. On how many days did the child take a dose more than an hour late? $\Box 0$ $\Box 1$ $\Box 2$ $\Box 3$ $\Box 4$ $\Box 5$ $\Box 6$ $\Box 7$ \Box Don't know c. How many <u>extra</u> doses or syringes of medicine did the child take? D DOn't know

10. How many doses of medicine has your child missed in the last month?

To test how the 10-item adherence questionnaire (CAMP = Comprehensive Adherence Measure for Pediatrics) performed among HIV-infected children and adolescents in Kenya, South Africa, and Thailand

Study design



- 6-month prospective cohort study with children (ages 0-16) and caregivers from 3 IeDEAparticipating sites:
 - AMPATH clinic in Busia, Kenya (n=110)
 - Empilweni clinic at Rahima Moosa Mother and Child Hospital in Johannesburg, South Africa (n=109)
 - HIV-NAT clinic at Thai Red Cross HIV Research Centre in Bangkok, **Thailand** (n=100)
 - All have rich clinical data in EMR
- Administered 10-item adherence questionnaire to children and/or caregivers at 3 time points (baseline, month 3, month 6)
- ART in MEMS® electronic dose monitors
- Viral load samples taken at month 3

IeDEA Regional Cohorts







- Used 3 external adherence criteria for validity testing of the questionnaire:
 - **Dichotomized adherence** (>90% vs. <90%) by MEMS
 - **48-hour treatment interruptions** (yes vs. no) by MEMS
 - Viral suppression (<1,000 copies/mL)
- Two approaches to create an "adherence score" on questionnaire:
 - 1. Simple summation adherence score
 - 2. Weighted approach adherence score
- Repeated measures negative binomial GEE models to test association between adherence score and 3 external adherence criteria
- By-site and across-site models presented

Results



- Child participants: 54% female, mean age 10.4 years
 - Thai children older (12.5yrs) compared to Kenyan (9.5) and South African (9.3) (p<.0001)
- Only 48% of children were "adherent" at month 3 (>90% doses by MEMS) and 51% at month 6
- Treatment interruptions: 40% (month 3) and 35% (month 6)
- 82% of children were virally suppressed at month 3

Participants' Adherence by MEMS by site

	Median MEMS® Adherence (% doses taken)				
	Month 3 Month 6				
Kenya	85%	84%			
South Africa	87%	93%			
Thailand	92%	93%			
	Dichotomized MEMS® Adherence ≥90% (Frequency, %)				
	Month 3 Month 6				
Kenya	48 (44%)	43 (40%)			
Kenya South Africa	48 (44%) 48 (49%)	43 (40%) 45 (58%)			





• Across sites, child CAMP adherence questionnaire reports significantly associated with external adherence criteria

	Simple Summation Adherence Score		Weighted Adh	erence Score	
	Odds ratio (95%	ό CI), p-value	Odds ratio (95% CI), p-value		
	Dich	otomized MEMS®	© adherence ≥90%		
Child form	1.16 (1.08, 1.26)	.0002*	1.85 (1.41, 2.42)	<.0001*	
Caregiver form	1.08 (1.01, 1.15)	.0348*	1.08 (0.83, 1.41)	.5492	
	MEMS	S® 48-hour treatme	ent interruption (yes)		
Child form	0.81 (0.73, 0.91)	.0005*	0.41 (0.27, 0.62)	<.0001*	
Caregiver form	0.86 (0.77, 0.95)	.0026*	0.73 (0.50, 1.06)	.0987	
	Virally suppressed (yes)				
Child form	1.16 (0.97, 1.38)	.1038	3.39 (1.72, 6.71)	.0004*	
Caregiver form	1.03 (0.88, 1.20)	.7534	1.56 (0.95, 2.57)	.0792	





• By site, some variation in association of simple summation scores

	Kenya		South Africa		Thailand	
	Odds ratio (95% CI), p-value		Odds ratio (95% CI), p-value		Odds ratio (95% CI), p-value	
	Dichotomized MEMS® adherence ≥90			90%		
Child form	1.09 (0.92, 1.30)	.3125	1.07 (0.96, 1.19)	.2144	1.37 (1.22, 1.54)	<.0001*
Caregiver form	1.03 (0.93, 1.14)	.5825	1.13 (1.01, 1.28)	.0409*	1.13 (1.02, 1.25)	.0162*
	MEMS® 48-hour treatment interruption (yes)					
Child form	0.86 (0.69, 1.08)	.1872	0.78 (0.64, 0.96)	.0184*	0.83 (0.70, 0.98)	.0315*
Caregiver form	0.90 (0.77, 1.04)	.1530	0.78 (0.64, 0.96)	.0176*	0.82 (0.70, 0.96)	.0161*
	Virally suppressed (yes)					
Child form	1.31 (1.03, 1.66)	.0283*	0.92 (0.67, 1.27)	.6173	1.34 (0.71, 2.54)	.3735
Caregiver form	0.99 (0.82, 1.18)	.8768	1.09 (0.78, 1.52)	.6245	1.43 (0.74, 2.76)	.2847

Results



• By site, sensitivity fairly good for Kenya site and child form (~.85) and lower for other sites (.48-.54)

	Kenya		South Africa		Thailand	
	Sensitivity, Specificity		Sensitivity, Specificity		Sensitivity, Specificity	
		D	vichotomized MEMS® Adherence ≥90%			
Child form	.84	.20	.48	.65	.54	.70
Caregiver form	.64	.42	.61	.56	.68	.59
	MEMS® 48-hour Treatment Interruption (yes)					
Child form	.84 .21 .49		.68	.48	.67	
Caregiver form	.63	.44	.61	.58	.62	.60
	Virally Suppressed (yes)					
Child form	.85	.33	.39	.53	.46	.67
Caregiver form	.50	.52	.51	.59	.59	1.00

Conclusions



- Non-adherence common in this multi-national cohort
- CAMP pediatric adherence questionnaire performed well overall, validated as pediatric screening tool globally
- Importance of asking children about adherence
- Variation by site, especially higher sensitivity in Kenya, suggests importance of adaptation for culture, context, and population



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