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Poor quality of life among untreated Thai and Cambodian children without severe HIV symptoms

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Abstract

There are limited data on quality of life (QOL) in untreated HIV-infected children who do not have severe HIV symptoms. Moreover, such data do not exist for Asian children. Poor QOL could be a factor in deciding if antiretroviral therapy (ART) should be initiated. Thai and Cambodian children (n=294), aged 1–11 years, naïve to ART, with mild to moderate HIV symptoms and CD4 15–24% were enrolled. Their caregivers completed the Pediatric AIDS Clinical Trials Group QOL questionnaire prior to ART commencement. Six QOL domains were assessed using transformed scores that ranged from 0 to 100. Higher QOL scores indicated better health. Mean age was 6.1 (SD 2.8) years, mean CD4 was 723 (SD 369) cells/mm^3, 57% was female, and % CDC N:A:B was 2:63:35%. One-third knew their HIV diagnosis. Mean (SD) scores were 69.9 (17.6) for health perception, 64.5 (16.2) for physical resilience, 84.2 (15.6) for physical functioning, 77.9 (16.3) for psychosocial well-being, 74.7 (28.7) for social and role functioning, 90.0 (12.1) for health care utilization, and 87.4 (11.3) for symptoms domains. Children with CD4 counts above the 2008 World Health Organization (WHO) ART-initiation criteria (n=53) had higher scores in health perception and health care utilization than those with lower CD4 values. Younger children had poorer QOL than older children despite having similar mean CD4%. In conclusion, untreated Asian children without severe HIV symptoms had relatively low QOL scores compared to published reports in Western countries. Therapy initiation criteria by the WHO identified children with lower QOL scores to start ART; however, children who did not fit ART-initiation criteria and those who were younger also displayed poor QOL. QOL assessment should be considered in untreated children to inform decisions about when to initiate ART.

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Note

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Keywords

children; ART-naïve; HIV; quality of life; Asian

Introduction

Quality of life (QOL) is a multi-dimensional measure of general health condition. Chronic illness can worsen QOL in children, but the extent of this worsening may vary across cultures and countries (Bullinger & von Mackensen, 2008). HIV infection is a chronic illness that left untreated results in high morbidity and mortality as well as poor QOL in children (Bong et al., 2007). Standard QOL questionnaires have been used to assess QOL in HIV-infected individuals; however, this has mainly been done in resource-rich settings and in antiretroviral therapy (ART)-treated individuals (Bomba et al., 2010; Butler et al., 2009; Lee, Gortmaker, McIntosh, Hughes, & Oleske, 2006; Potard, Chassany, Lavignon, Costagliola, & Spire, 2010). Lee et al. reported that HIV-infected children had significantly lower mean adjusted QOL scores compared to HIV-exposed but uninfected children (Lee et al., 2006). As the important indicator of physical health in HIV is CD4 level (Cross Continents Collaboration for Kids (3Cs4kids) Analysis and Writing Committee, 2008), its correlation with QOL has been explored (Butler et al., 2009; Cross Continents Collaboration for Kids (3Cs4kids) Analysis and Writing Committee, 2008; Oberdorfer, Louthrenoo, Puthanakit, Sirisanthana, & Sirisanthana, 2008). Among the few reports from resource-limited settings, Oberdorfer et al. found that a CD4% of B25 was associated with poorer QOL in Thai children treated with ART (Oberdorfer et al., 2008). Factors affecting QOL are complex. Family structure is important: children living in HIV/AIDS-affected families reported lower QOL than those from unaffected families (Xu, Wu, Rou, Duan, & Wang, 2010). Although QOL is a good measure of health and well-being, its assessment is not done routinely and results have not been systematically used to inform decisions about initiating ART in children.

There are no reports on QOL in ART-naïve children from resource-limited settings who do not have significant physical ailments from HIV. We aimed to evaluate QOL in untreated Thai and Cambodian children with HIV who do not have severe HIV symptoms and immune suppression. We also aimed to assess factors associated with QOL such as HIV clinical staging and CD4 levels. The information gained from this study could be important in understanding the effects of mild to moderate HIV disease on QOL in untreated children. Significant negative effects on QOL may support the need to assess QOL to inform treatment decisions in such children.

Methods

Study design and population

This report includes baseline data collected between March 2006 and September 2008 on children who enrolled in the PREDICT study (clinicaltrials.gov identification number NCT00234091). PREDICT is an ongoing randomized study to compare the timing of ART initiation in ART-naïve HIV-infected children. The inclusion criteria are HIV-infected children aged 1–11 years who are ART naïve. They had to meet the Center for Disease Control and Prevention (CDC) clinical category N (no HIV symptoms), A (mild HIV symptoms), or B (moderate HIV symptoms) (Centers for Disease Control and Prevention, 1992, 1994), and have CD4 15–24% and no active opportunistic infections. The study was approved by national and local institutional review boards. Seven Thai sites and two Cambodian sites participated in this study. The QOL questionnaire was completed at the

baseline visit prior to ART initiation. All caregivers of the HIV-infected children gave consent prior to enrolment.

QOL instruments and data collection

The General Health Assessment for Children (GHAC) QOL questionnaire was used in this study with permission (Gortmaker et al., 1998; Lee et al., 2006). This QOL questionnaire has age-specific versions for children ages six months-four years and 5–11 years. The Thai version of the QOL questionnaire was used and validated in a published study of Thai HIV-infected children and parents (Oberdorfer et al., 2008). The Thai questionnaire had good reliability and validity with average internal consistency by Cronbach's alpha coefficient of 0.84 (Oberdorfer et al., 2008). The internal consistency of each domain as measured with Cronbach's alpha is described in Appendix 1. The English version was used for translation and back translation of the Cambodian version. A language expert reviewed and ensured that the questions conveyed the same meaning between the English, Thai, and Cambodian versions.

Six QOL domains were assessed: (1) general health rating (composed of health perception and physical resilience), (2) physical functioning, (3) psychosocial well-being (children 5–11 years old only), (4) social and role functioning, (5) health care utilization, and (6) symptoms.

The primary caregiver was asked to complete the questionnaire, which took approximately 20–30 minutes. For illiterate caregivers, study nurses read the QOL questions to the caregivers and filled in their responses. For orphans, the primary caretaker responsible for each child completed the questionnaire.

During the same visit, the children also had a medical history taken and a physical examination. Body weight and height were measured. Complete blood count, CD4%, CD4 cell counts, and plasma HIV-RNA by Roche Amplicor assay (Palo Alto, USA) were performed. Information about the family, including education level of primary caregivers and biological parents and monthly income (below average, average, or above average), was recorded.

Transforming QOL raw scores

The outcome measures of this study were age-specific domain scores of QOL. Since the raw scores in the six domains had different minimum and maximum values, we transformed the raw scores to simple transformed scores of 0–100 with the following formula: transformed score=[(actual raw score − lowest possible raw score)/(highest possible raw score − lowest possible raw score) × 100], an approach that has been used by other groups (Butler et al., 2009; Lee et al., 2006). In the case of domains with negative scores, the raw scores were "flipped" before calculating the transformed scores so that the higher transformed scores consistently indicated better health in that domain (Butler et al., 2009; Lee et al., 2006).

Statistical analysis

Descriptive statistics (medians, inter-quartile ranges, means, standard deviations, and percentages) were used to summarize demographic and clinical characteristics of the infected children at baseline. Comparison between the demographic characteristics of older and younger children was performed by a chi-square test or t-test as appropriate. We used linear regression models to examine the influence of the following factors on QOL: age, gender, recent negative life events (e.g., parental job loss, separation of caregiver, very ill family member, and death in family; scores ranged from 0 to 18), primary caregivers

(biological or non-biological), living in an orphanage, HIV status disclosure, weight for age Z-score, HIV RNA, and CD4 group.

In this cross-sectional study, we aimed to investigate the effect of CD4 level on the QOL of ART-naïve children; we therefore categorized the children into two groups using the CD4 criteria outlined in the 2008 WHO Antiretroviral Therapy Initiation Criteria for Infants and Children (WHO Antiretroviral Therapy for Infants and Children, 2008). Children with CD4 % and/or CD4 count who met criteria for ART initiation (CD4 % <20% and/or CD4 count <750 cells/mm^3 in children aged one-three years, CD4 % <20% and/or CD4 count <350 cells/mm^3 in children aged three-five years, and CD4 % <15% and/or CD4 count <200 cells/mm^3 in children <5 years of age) were classified as the "lower CD4 group" and vice versa for the "higher CD4 group".

All variables associated with QOL at the level of pB0.10 in the univariate analysis were used to build the multivariate models. A backwards stepwise selection method was used and covariates with pB0.05 were retained in final model. The significance of each variable was assessed with Wald test statistic. Separate analyses were carried out to examine predictors of health perception, physical resilience, physical functioning, psychosocial well-being, social and role functioning, and health care utilization and symptoms. Datasets were organized using SAS 9.13 (SAS Institute, Cary, NC, USA) and statistical analyses were performed using STATA, version 10.0 (StataCorp, College Station, TX, USA).

Results

The demographic data

Three hundred children were enrolled in PREDICT but six were excluded from this study: one child never returned for the baseline visit and the other five were older than 11 years. The characteristics of 294 children, included in this study, are shown in Table 1. All children were infected with HIV via mother-to-child transmission. The mean (SD) age was 6.1 (2.8) years, 57% were female, and the proportion of children with CDC clinical category N:A:B disease was 2:63:35%, respectively. A total of 59 and 41% of children were enrolled from Thai sites and Cambodian sites, respectively. Overall 83 (28%) children were reported by their caregiver to know their HIV status with a higher proportion in the older age group. Thirty-seven (12%) children were living in orphanages. Demographic characteristics did not differ across age groups, with the exception of higher CD4 cell counts and HIV-RNA, less HIV disclosure (all pB0.0001), and a higher proportion of caregivers being their biological parents (p=0.004) among younger children. Fifty-three children (18%) were assigned to the "lower CD4 group", according to 2008 WHO ART-initiation criteria. Differences in demographic characteristics between the "lower CD4 group" and "higher CD4 group" were younger age (pB0.0001), higher mean (SD) HIV-RNA $\log_{10}$ copies/ml (5.0 [0.4] vs. 4.5 [0.6], p<0.001), and less HIV disclosure (7.6% vs. 32.8%, p<0.0001) in the "lower CD4 group".

Mean (SD) score of QOL domains are presented in Table 2. Comparing age groups, the children aged one-four years had significantly lower scores in all evaluated domains except for physical resilience and symptoms.

Multivariate linear regression analysis results

Linear regression analysis for all 294 children was performed to assess factors thought or known to impact QOL in each of the six domains (Table 3). Children in the "higher CD4 group" had higher QOL scores for health perception [adjusted mean difference=9.5 (95% confidence intervals [95% CI] 4.9–14.3), p<0.0001] and health care utilization (adjusted mean difference=4.0 [95% CI 0.06–8.03], p<0.046) when compared to the lower CD4

group. Having CDC N or A, weight for age Z-score ≥ −1.5, HIV-RNA <5 $\log_{10}$ copies/ml, or being older were associated with better QOL in some domains. Having recent negative life events and having biological parents as caregivers were associated with poorer social and role functioning. Thai children had higher scores in the health perception, physical functioning, and social and role functioning domains (all p<0.0001). No association of gender or living in orphanages with QOL was found in any domain.

Discussion

This is the first report of QOL assessment in ART-naïve HIV-infected children in Asia. Our study showed that having CD4 above the 2008 WHO criteria for initiating ART was clearly associated with better QOL. Similarly, there was a positive association between QOL and having mild or no HIV-related symptoms, better weight for age, and lower HIV-RNA. Younger children aged one-four years had poorer QOL than children aged 5–11 years with similar immunological status. Children who had biological parents as their primary caregivers had poorer social functioning, and those with higher numbers of negative life events in the past year had poorer psychological well-being and social and role functioning.

When we compared the transformed QOL scores in the younger age group in this study to a previous report on ART-naïve HIV-infected children of similar ages in the USA (Lee et al., 2006), we found that our children had significantly lower scores in three domains; −23.1 in health perception (95% CI −44.7 to −1.5; p=0.04), −18.5 in physical functioning (95% CI −34.1 to −2.9; p=0.02), and −32.9 in social and role functioning (95% CI −61.5 to −4.3; p=0.02). However, there were only three children in the younger age group in the American study, with mean (SD) CD4% of 25 (3)%. There was no significant difference in QOL scores in the seven ART-naïve HIV-infected American children aged 5–11 years, mean (SD) CD4% 20 (9)%, compared to the children of similar ages and mean CD4% in our study. When we compared the raw scores of QOL between our study of 294 ART-naïve children and a study from Northern Thailand of 131 ART-experienced children with similar mean CD4% (Oberdorfer et al., 2008) (mean [SD] CD4% 20 [8]%), children in our study had significantly poorer mean (SD) QOL in four domains: health perception 26.8 (7.3) vs. 29.6 (5.5) [mean difference −2.8, 95% CI −4.2 to −1.4], psychological well-being 71.6 (9.1) vs. 74.1 (6.5) [mean difference −2.5, 95% CI −4.3 to −0.7], social and role functioning 9.5 (2.9) vs. 10.5 (2.5) [mean difference −1, 95% CI; −1.6 to −0.4), and symptoms 107.4 (11.3) vs. 113.3 (9.7) [mean difference −5.9, 95% CI −8.1 to −3.7]. They had higher QOL scores only in the physical functioning domain 30.8 (5.3) vs. 28.5 (4.2) [mean difference 2.3, 95% CI 1.3–3.3]. It is possible that the better QOL could be explained by ART use (for a mean duration of 1.6 years) and older age (mean age of 10 years) in the Northern Thailand study (Oberdorfer et al., 2008). The effect of ART on QOL is difficult to interpret in that study as the children did not have baseline QOL assessment prior to ART initiation. Data reflecting the change in QOL after ART initiation from the PREDICT study will be available in late 2011.

Our study found that QOL scores among young children (one-four years of age) were lower than those in the older age group (5–11 years of age) in all domains except for physical resilience. This may be explained by the natural history of HIV disease in which for the same CD4 percentage range, younger children are at higher risk for HIV-related morbidity (Storm et al., 2005). Furthermore, more children in the young age group were living with biological parents. It is possible that biological parents also living with HIV themselves have their own health issues, and consequently may be less able to support their children (Ji, Li, Lin, & Sun, 2007). In support of this, a study conducted in China showed that families with both parents being HIV-positive reported a lower level of family sociability and QOL compared to families with only one HIV-positive parent (Li et al., 2009).

The positive correlation between high CD4 and QOL has been reported in other studies albeit in different domains. CD4%]25% has been previously found to be associated with significantly higher QOL scores in four domains, including physical functioning, psychological well-being, social and role functioning, and symptoms (Oberdorfer et al., 2008), while our study saw improvement in health perception and health care utilization. A cross-sectional PACTG 219 study showed that in protease inhibitor-treated children, 62% with CD4%]25%, health perception and physical functioning scores were positively associated with CD4 cell counts (Storm et al., 2005). HIV-infected women in sub-Saharan Africa with higher CD4 counts reported fewer AIDS-related symptoms (Patel et al., 2009).

Our study showed that less severe HIV disease status, higher weight for age, and lower HIV-RNA were positively correlated with QOL. This is not surprising as physical health often directly impacts QOL. For example, lean body mass was associated with better general health perception and physical functioning in HIV-infected adults (Wilson, Roubenoff, Knox, Spiegelman, & Gorbach, 2000). Untreated American HIV-infected children with significantly higher HIV-RNA level and lesser CD4% had significantly worse symptoms compared with those receiving any antiretroviral regimen (Lee et al., 2006). Having negative life events was associated with poorer psychological well-being in our study, and this was also shown in a study in the USA with similar mean incidences of negative life events (Lee et al., 2006).

In terms of the role of family structure and psychosocial factors on QOL, we found that having biological parents as caregivers was associated with poorer QOL in the social and role functioning domain. Almost all of the biological parents of children in our study were HIV-infected. As previously noted, the link may be due to the parents' own negative social and role functioning secondary to their HIV infection. Eighty-three (28.2%) caregivers reported that their children were aware of their own HIV status. This variable was negatively associated with health care utilization. However, this is difficult to interpret as the children may have been too young to understand the implications of HIV/AIDS: 4 out of 83 children reported to be aware of their HIV status were younger than five years of age and the remaining 79 were aged 5–11 years with mean age of 8.5 years. We believe that in our study, the response to the question about HIV disclosure was based on the subjective perception of the caregivers and not a true assessment of disclosure status in the children. In the PACTG219 study in the USA, there were no statistical differences in QOL before and after HIV disclosure (Butler et al., 2009), while Chinese parents living with HIV/AIDS reported HIV disclosure being associated with better overall QOL in their children (Li et al., 2009). In general, the disclosure process should be encouraged when appropriate to allow children to better understand and cope with their HIV disease (Sungkanuparph et al., 2008).

The QOL may be affected by geographical area and cultural differences. All of our sites were located in the urban areas. We did not see significant differences of QOL scores across sites in the same country, but we saw some differences between the Thai and Cambodian sites.

There are several strong points to this study. First, our population of ART-naïve, HIV-infected children with mild to moderate HIV disease and CD4 15–24% is unique and represents the largest population of Asian children with HIV in whom QOL assessments have been undertaken. Second we studied QOL in a population that has not had severe clinical and immune suppression from HIV. Finding poor QOL in such children, with few physical consequences from HIV, is significant and highlights the need for early assessment for ART and psychosocial support. Our study has some limitations. First, we did not include children older than 11 years, which is a limitation since adolescents may be the most challenging group in terms of psychosocial issues and QOL. Second, this is a cross-sectional

analysis, which by design cannot assess whether the positive and negative associations of different factors with QOL will change overtime. Third, the QOL was assessed via the parents' point of view only; we did not interview the children.

Further studies are needed to assess the QOL of HIV-infected children in the developing countries. Most such publications have not yet assessed the effect of ART beyond the first year so long-term outcomes of ART on QOL are still unknown (Beard, Feeley, & Rosen, 2009). Moreover, effective psychological and psychosocial support should be incorporated in the management of care of people living with HIV/AIDS to improve the QOL. Cognitive-behavioral group therapy and peer support/counseling group therapy have been shown to benefit Chinese adults with symptomatic HIV by decreasing their psychological distress and improving their QOL (Molassiotis et al., 2002). However, the Cochrane database of systematic reviews 2009 did not find any significant benefit of psychological therapy to improve the QOL of HIV-infected children (King, De Silva, Stein, & Patel, 2009). Effective counseling interventions that build coping skills among HIV-infected children and their families need to be investigated (Ji et al., 2007).

In conclusion, this is the first large study to assess QOL in ART-naïve Asian children. Despite having only mild to moderate symptoms, our children had poorer QOL than that reported in American ART-naïve children and in Thai ART-experienced children. Children with CD4 counts below the 2008 WHO threshold for initiating ART had poorer QOL. This illustrates the need for CD4 monitoring to determine when to start ART, which may in turn improve QOL. Having biological parents as caregivers was related to poorer social functioning, suggesting that more education and counseling for children and families are needed to help them cope and live with HIV. QOL assessment should be considered in untreated children to inform decisions about when to initiate ART.

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Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Demographic characteristics of ART-naïve HIV-infected children.

Characteristics	Total (*N*=294)	1–4 years (*N*=103)	5–11 years (*N*=191)
Mean age (SD), years	6.1 (2.8)	3.2 (1.3)	7.7 (1.9)
Female, n (%)	168 (57)	56 (54)	112 (59)
CDC classification N:A:B (%)	2:63:35	2:59:39	2:66:32
Thai:Cambodian (%)	59:41	50:50	64:36
Mean (SD) Z-score			
Weight for age	−0.85 (1.17)	−0.62 (1.27)	−0.97 (1.09)
Height for age	−0.89 (1.49)	−0.54 (1.68)	−1.08 (1.34)
Weight for height	−0.44 (1.04)	−0.43 (1.01)	−0.44 (1.05)
Mean (SD) baseline CD4%	20 (2.9)	20 (2.9)	20 (2.9)
Mean (SD) CD4 count (cells/mm^3)	723 (369)	940 (424)	608 (273)
Mean (SD) HIV-RNA $\log_{10}$ (copies/ml)	4.6 (0.6)	4.8 (0.6)	4.5 (0.6)
HIV status disclosed, n (%)	83 (28)	4 (4)	79 (41)
Mean (SD) negative life event score[a]	1.4 (1.9)	1.5 (2.1)	1.3 (1.8)
Biological parents as primary caregivers, n (%)	187 (63.6)	77 (74.8)[b]	110 (57.6)
Education of primary caregivers			
No education (%)	40 (13.6)	10 (9.7)	30 (15.7)
Elementary school (%)	123 (41.8)	44 (42.7)	79 (41.4)
High school (%)	78 (26.5)	28 (27.2)	50 (26.2)
Higher than high school (%)	35 (12.0)	13 (12.6)	22 (11.5)
No data available (%)	18 (6.1)	8 (7.8)	10 (5.2)
Monthly income [c]			
Below average (%)	155 (52.7)	50 (48.5)	105 (55.0)
Average (%)	76 (25.9)	30 (29.1)	46 (24.1)
Above average (%)	4 (1.4)	2 (1.9)	2 (1.0)
Data not available (%)	59 (20.1)	21 (20.4)	38 (19.9)
Number of children in lower CD4 group, [d] n (%)	53 (18.0)	45 (43.7)[e]	8 (4.2)

[a] Recent negative life events, i.e., parental job loss, separation of caregiver, very ill family member, death in family, and so on. Scores ranged from 0 to 18. Comparisons between two age groups was done by chi-square for categorical covariates or t-test for continuous covariates.

[b] p=0.004.

[c] Defined by the caregivers' self-report.

[d] Classified by the WHO Criteria for antiretroviral therapy (ART) initiation for Infants and Children 2008 (WHO Antiretroviral Therapy for Infants and Children, 2008); CD4% <20% and/or CD4 count <750 cells/mm^3 in children aged 1–3 years, CD4% <20% and/or CD4 count <350 cells/mm^3 in children aged 3–5 years, and CD4% <15% and/or CD4 count <200 cells/mm^3 in children aged more than five years.

[e] p<0.0001.

Table 2

Quality of life transformed scores of 294 Thai and Cambodian HIV-infected children naïve to antiretroviral therapy.

	Total (*N*=294)	1–4 years (*N*=103)	5–11 years (*N*=191)	p-Value[a]
Health perception	69.9 (17.6)	64.6 (18.7)	72.7 (16.4)	<0.001
Physical resilience	64.5 (16.2)	63.4 (16.5)	65.2 (16.0)	NS
Physical functioning	84.2 (15.6)	71.5 (13.5)	91.1 (12.0)	<0.001
Psychological wellbeing	77.9 (16.3)	NA	77.9 (16.3)	NA
Social and role functioning	74.7 (28.7)	50.4 (24.5)	87.3 (21.8)	<0.001
Health care utilization	90.0 (12.1)	88.1 (13.0)	91.1 (11.4)	<0.05
Symptoms	87.4 (11.3)	86.6 (10.9)	87.9 (11.6)	NS

Notes: Quality of life score assessed by the Pediatric AIDS Clinical Trials Group (PACTG) quality of life questionnaire (Gortmaker et al., 1998; Lee et al., 2006). Scores ranged from 0–100; higher scores indicated better health.

NA, not applicable; NS, not statistically significant.

[a]The comparison was made by t-test.

Table 3

Multivariate linear regression analysis of factors associated with quality of life scores of HIV-infected children.[a]

Domain	N	Predictors factors	Coefficient[b] (95% CI)	p-Value
Health perception	287	CDC N and A vs. CDC B	4.4 (0.8–8.1)	0.02
		Higher CD4 vs. lower CD4[c]	9.5 (4.9–14.3)	<0.0001
		HIV-RNA $\log_{10}$ <5 vs. ≥ 5	5.2 (1.4–9.0)	0.007
		Thai vs. Cambodian	15.4 (11.8–18.9)	0.0001
Physical resilience	290	CDC N and A vs. CDC B	4.3 (0.5–8.2)	0.03
		Weight for age Z-score ≥ −1.5 vs.<1.5	5.7 (1.7–9.8)	0.01
Physical functioning	293	Age (years)	2.6 (2.0–3.2)	<0.0001
		Thai vs. Cambodian	6.9 (3.6–10.3)	<0.0001
Psychological well-being	191	Recent negative life events vs. none	−1.4 (−2.7 to −0.2)	0.03
Social and role functioning	289	Age (years)	5.9 (4.9 −7.0)	<0.0001
		Biological vs. non-biological parents	−8.1 (−14.4 to −1.8)	0.01
		HIV-RNA $\log_{10}$ <5 vs. ≥ 5	6.7 (1.0–12.5)	0.02
		Thai vs. Cambodian	10.5 (4.3–16.7)	<0.0001
Health care utilization	294	Age (years)	0.8 (0.2–1.4)	0.01
		Disclosed vs. non-disclosed of HIV	−6.2 (−9.6 to −2.8)	<0.0001
		Higher CD4 vs. lower CD4[c]	4.0 (0.1–8.0)	0.046
Symptoms	292	Recent negative life events vs. none	−1.2 (−1.9 to −0.6)	<0.0001
		CDC N and A vs. CDC B	3.0 (0.3–5.6)	0.03

[a] Higher score indicated better quality of life. There was no statistically significant association between the gender or orphanage status and QOL domains (data not shown). All variables associated with QOL at the level of p <0.10 in the univariate analysis (data not shown) were used to build the multivariate models.

[b] Represents the coefficient (95% CI) for each parameter in a multiple regression model. Apart from age, these coefficients represent the mean difference in transformed QOL scores between the two groups.

[c] Grouping CD4 by 2008 WHO criteria for initiating antiretroviral therapy (Lower CD4 group was defined as children who met the CD4 criteria for ART initiation while the higher CD4 group was defined as children who did not meet these criteria) (WHO Antiretroviral Therapy for Infants and Children, 2008).