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Quality of Life Among Individuals with HIV Starting Antiretroviral Therapy in Diverse Resource-Limited Areas of the World

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Abstract

As Antiretroviral Therapy (ART) is scaled up in low- and middle-income countries, it is important to understand Quality of Life (QOL) correlates including disease severity and person characteristics and to determine the extent of between-country differences among those with HIV. QOL and medical data were collected from 1,563 of the 1,571 participants at entry into a randomized clinical trial of ART conducted in the U.S. (n = 203) and 8 resource-limited countries (n = 1,360) in the Caribbean, South America, Asia, and Africa. Participants were interviewed prior to initiation of ART using a modified version of the ACTG SF-21, a health-related QOL measure

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including 8 subscales: general health perception, physical functioning, role functioning, social functioning, cognitive functioning, pain, mental health, and energy/fatigue. Other measures included demographics, CD4+ lymphocyte count, plasma HIV-1 RNA viral load. Higher quality of life in each of the 8 QOL subscales was associated with higher CD4+ lymphocyte category. General health perception, physical functioning, role functioning, and energy/fatigue varied by plasma HIV-1 RNA viral load categories. Each QOL subscale included significant variation by country. Only the social functioning subscale varied by sex, with men having greater impairments than women, and only the physical functioning subscale varied by age category. This was the first large-scale international ART trial to conduct a standardized assessment of QOL in diverse international settings, thus demonstrating that implementation of the behavioral assessment was feasible. QOL indicators at study entry varied with disease severity, demographics, and country. The relationship of these measures to treatment outcomes can and should be examined in clinical trials of ART in resource-limited settings using similar methodologies.

Keywords

Quality of life (QOL); Highly active antiretroviral therapy (HAART); HIV

Introduction

In resource-rich countries, antiretroviral therapy (ART) is widely available and HIV is now seen as a manageable chronic illness rather than a terminal disease. Accordingly, ART treatment outcomes now also focus on quality of life [1–6] in addition to disease severity and response to antiretroviral therapy.

Quality of life is a broad construct and can be influenced by many factors such as income, housing, social support, and life situation. Health-related quality of life, in particular, encompasses the impact of disease and treatment on a person's ability to carry out daily activities and affects well-being. It includes physical, social, cognitive, and psychological functioning, as well as subjective sense of health, comfort, and well-being [7].

ART availability is now being scaled up in diverse parts of the world, including low- and middle-income countries, through clinical trials, non-governmental organizations, and government initiatives such as PEPFAR [8]. HIV clinical trials that seek to assess quality of life as a secondary trial outcome require pre-treatment data for HIV-infected individuals in diverse settings. It is well established that quality of life varies with CD4 count and HIV-1 RNA viral load [9–11]. In addition, in various U.S. samples, the AIDS Clinical Trials Group (ACTG) quality of life measures [12, 13] have been shown to vary with person characteristics such as gender [14], race [15], and physical ability [16]. However, the degree to which these associations exist across more diverse settings remains unknown. With the growth of HIV clinical treatment and prevention trials internationally, examining such associations using a standard measure can allow quality of life to be used as an outcome in monitoring HIV treatments.

ACTG A5175, "A Phase IV, Prospective, Randomized, Open Label Evaluation of the Efficacy of Once-Daily Protease Inhibitor and Once-Daily Non-Nucleoside Reverse Transcriptase Inhibitor-Containing Therapy Combinations for Initial Treatment of HIV-Infected Individuals from Resource-Limited Settings (PEARLS) Trial," enrolled 1,571 patients with HIV from 46 study locations in nine countries. Participants were from Africa (Malawi, South Africa, Zimbabwe), Asia (India, Thailand), South America (Brazil, Peru), Haiti, and the United States. It is one of the first large-scale multi-country HIV treatment trials, comparing the effectiveness of 3 three-drug combinations in treatment-naïve HIV-

infected individuals. The diversity of patients and settings allows for a unique opportunity to examine quality of life data from participants when entering the trial and its correlates to disease severity and person characteristics. The analysis examined quality of life indicators from the baseline assessment prior to initiating ART across diverse settings.

Methods

Study Participants

Eligible subjects were men and women ≥18 years with documented HIV-1 infection, CD4+ lymphocytes <300 cells mm^{-3}, Karnofsky performance score ≥70, and ≤7 days of cumulative prior antiretroviral therapy prior to study entry (with the exception of limited prevention of Mother To Child Transmission (pMTCT) therapy). Women of reproductive potential were required to be non-pregnant and, if sexually active, agree to effective contraceptive use. Persons with serious chronic, acute, or recurrent infections must have completed at least 14 days of therapy prior to study entry and be clinically stable. Persons with absolute neutrophil count <750 mm^{-3}, hemoglobin <7.5 g/dL, platelet count <50,000 mm^{-3}, calculated creatinine clearance <60 ml/min, aspartate transaminase (AST), alanine transaminase (ALT) or alkaline phosphatase >fivefold above the upper limit of normal, total bilirubin >2.5-fold above the upper limit of normal, clinical pancreatitis within 3 years, bradycardia (<40 min^{-1}) or a history of untreated active second or third degree heart block were excluded from participation. The study was approved by the institutional review board at each participating institution. Written informed consent was obtained from study participants following the human experimentation guidelines of the U.S. Department of Health and Human Services [17].

Data Collection

At PEARLS study entry, clinical assessments were performed and safety laboratory tests, plasma HIV-1 RNA and CD4+ lymphocyte counts were obtained. Quality of life was measured with the ACTG SF-21, which was adapted from the SF-21 [18] by the ACTG Outcomes Committee with feedback from local community members and site investigators. The ACTG SF-21 was originally adapted from the Medical Outcomes Study HIV Health Survey (MOS-HIV), a measure with well-established reliability and validity [19].

Modifications included removing one item (a visual 0–100 analog scale assessing overall health perceptions), simplifying items, and re-wording items for clarity. The measure consists of 20 items that assessed 8 domains: general health perceptions, physical functioning, role functioning, pain, social functioning, mental health, energy/fatigue, and cognitive functioning. Across all domains, higher scores indicated better quality of life. For example, a low score in the physical functioning domain indicates poor physical functioning, a high score in the energy/fatigue domain indicates high vitality, and a high score in the pain domain indicates less pain. All questions covered the previous 4 weeks. At all sites, the measure was translated and back-translated to ensure accuracy. The measure was administered in a face-to-face interview by study nurses in the local language.

General Health Perceptions

This three-item subscale asks patients to rate their general health, resistance to illnesses, and health outlook. This subscale has been validated by Davis and Ware [20] and Stewart and Ware [21].

Physical Functioning

This is a subscale with four items inquiring about physical limitations that range from minor to severe, including lifting heavy objects or participating in strenuous sports, walking uphill

or climbing a few flights of stairs, and being able to eat, dress, bathe and use the toilet by oneself.

Role Functioning

Using two questions, this subscale asks participants if their health negatively impacts their ability to perform at a job/ school, or to work around the house.

Pain

The two items of this subscale assess intensity of physical pain and degree of interference with daily activities [22].

Social Functioning

This subscale consists of two items that ask participants to what extent their social activities have been limited by their health [23].

Mental Health

The three items in this subscale assess anxiety, depression, and overall psychological well-being [24]. Two questions are reverse coded to control for response set effects.

Energy/Fatigue

This subscale assesses vitality; one item is reverse coded to control for response set effects.

Cognitive Functioning

Consisting of three items, this subscale assesses a participant's level of difficulty with reasoning/solving problems, being attentive, and remembering.

Data Analysis

Means and standard deviations summarized outcome measurements overall and within subgroups. Differences among categories of CD4+ lymphocyte counts and plasma HIV-1 viral load for each quality of life domain were compared using both the Kruskal–Wallis test for unordered alternatives among subgroups and the Jonckheere–Terpstra test for ordered alternatives among ordinal subgroups. Significance for these tests was assessed at a nominal 0.05 level without adjustment for multiple comparisons.

To compare quality of life domains by country, permutation testing was used to account for the multiplicity issue of 36 pair-wise comparisons among 9 countries. As there is no natural referent country, elucidating how countries differ requires an omnibus (8 degree of freedom) test comparing across all countries to reject equanimity. Alternatively, Monte Carlo samples (size 10,000) of the null distribution (i.e., no differences between the two countries being compared) were assembled by randomly permuting country assignment among participants. The normalized difference (*T*-statistic) of the observed pair-wise comparison was compared to the simulated null distribution; a 2-sided *P* value was calculated by the number of times the observed difference was more extreme than the critical value of the largest pair-wise difference from the simulated null distribution.

Results

Demographics

The observed sample consisted of 1,563 of 1,571 participants (8 missing baseline quality of life data) enrolled between May 2005 and August 2007 from the United States and eight

countries in resource-limited areas of the world (Table 1). Overall, the sample contained slightly more men (52.7%) than women (47.3%) and was predominately young.

Plasma HIV-1 RNA Viral Load and CD4+ Lymphocyte Counts

Baseline quality of life was associated with both plasma HIV-1 RNA and CD4+ lymphocyte count categories as shown in Tables 2 and 3. Although viral load and CD4 varied by category at baseline, quality of life in each of the domains was relatively high, indicating low levels of limitations and distress.

Four quality of life domains varied significantly across viral load categories: general health perception ($P = 0.002$), physical functioning ($P < 0.001$), role functioning ($P = 0.015$), and energy/fatigue ($P < 0.001$). More specifically, a trend of decreasing quality of life was observed for increasing plasma HIV-1 RNA viral load category for three quality of life domains: physical functioning ($P = 0.004$), role functioning ($P = 0.019$), and energy/fatigue ($P = 0.044$).

All quality of life domains varied significantly across CD4+ lymphocyte count categories (all $P \leq 002$). Trend tests revealed significantly increasing quality of life scores across increasing CD4+ lymphocyte count categories for each of the quality of life domains (all $P \leq 0.005$).

Associations of Quality of Life Domains to Sex and Age

Only the social functioning subscale varied by sex, with men having greater impairments than women ($P < 0.002$), and only the physical functioning subscale varied by age category ($P < 0.002$), with physical functioning decreasing as age increased (data not shown).

Quality of Life Domains by Country

Quality of life domains varied significantly by country; rankings of quality of life domains by country and significant differences between countries are shown in Table 4. For general health perceptions, India's and South Africa's mean scores were significantly higher than 6 other countries. Haiti's mean general health perception was significantly lower than the 3 top-ranked countries, and Malawi's mean was significantly lower than all countries in the top 5. In the domain of physical functioning, Peru's and India's mean scores were highest, while Brazil and the U.S. ranked significantly lower than all 5 of the top-ranked countries. For role functioning, Zimbabwe's, Thailand's, and India's mean scores were highest, while Peru had significantly lower role functioning scores than all other countries. For pain, Zimbabwe's mean score was highest (least pain) while Peru, India, South Africa, Haiti, and Thailand also scored significantly higher (less pain) than the countries with the lowest-ranked mean scores. In the domain of social functioning, India, Zimbabwe, and South Africa ranked significantly higher than the four lowest-rated countries, while the U.S. ranked significantly lower than every other country. In terms of mental health, Zimbabwe, South Africa, India, Thailand, and Malawi ranked significantly higher than the four countries with the lowest-ranked mean scores. For energy, Zimbabwe's and Thailand's means were highest; the U.S. had significantly lower energy scores than every other country. Finally, for cognitive functioning, India, South Africa, and Zimbabwe ranked significantly higher than the four lowest-ranked countries. In addition, Haiti and Peru had significantly higher scores than the lowest-ranked country, the U.S.

Discussion

In the first study evaluating established quality of life measures among clinical trial participants from diverse international settings, we found marked variability in the measure

across countries. For all measures of quality of life, higher CD4+ lymphocyte count category was associated with higher quality of life performance scores. For several quality of life domains (general health perception, physical functioning, role functioning, and energy/ fatigue), higher viral load was associated with lower scores. The more consistent association with CD4 than viral load is expected because CD4 is an overall indicator of immune function and more of an indicator of disease progression, whereas viral load is an indicator of the amount of virus in the system, not an indicator of the effects of the virus [25, 26]. These data provide preliminary evidence for the utility of this quality of life assessment across diverse settings.

Comparisons of the quality of life subscales by country, however, provided a complex set of findings, which differed across the quality of life domains. There was no single country consistently showing the highest quality of life subscale scores across domains, though, with one exception, India was consistently in the top 3. U.S. quality of life scores were not significantly higher than other countries, and for many domains, were ranked lowest. This may be partially attributable to selection bias regarding disease stage. Twenty-two percent (22%) of U.S. subjects had CD4+ lymphocyte counts <50 compared to an average of 13% overall and 19% of U.S. subjects had been diagnosed with AIDS compared to 8% overall. Treatment-naïve subjects consisted mostly of late presenters in the U.S., whereas at other sites, the pool of treatment-naïve potential subjects was more diverse in terms of disease progression. Within-country studies of the quality of life measure may further identify contributors to the various domains of quality of life within a given culture. In addition, future research may wish to address the clinical significance and magnitude of differences by country or across quality of life subscales.

There are several limitations of the present study. First, this analysis was cross-sectional. Longitudinal follow-up data from the PEARLS trial will allow for determining the timing of CD4 and viral load changes with respect to improvements or decrements in quality of life as measured by the ACTG SF. Second, individuals with Karnofsky scores <70 were excluded, thereby limiting generalizability of the study. Additionally, the study sample was not a representative sample of HIV-infected persons in participating countries, thereby also limiting the generalizability of the between-country variations in quality of life. Third, the process of adapting the ACTG-SF measure of quality of life occurred through consensus meetings across site investigators and ACTG behavioral scientists, but pilot testing and an iterative process of scale development was not possible in the context of a clinical trial. Finally, the ACT-SF measure has not been formally validated in many of the local languages used in this study. However, the reliability and validity of MOS-HIV, the measure upon which the ACTC-SF was based, has been assessed and found to be comparable to the original measure in French, German, Italian, Dutch, UK English translations [27], Thai [28], Chinese [29], and most recently Greek [30], implying that the measure remains reliable and valid across a variety of languages. Regardless, future studies should address measure validation across languages.

This report provides initial evidence for the ability of the ACTG SF-21 scale to be used in multi-national studies, as well as potential for use as a baseline to compare to current and future cohorts. Because of the associations of subscales to CD4 and viral load, further investigations of the measure may provide supporting evidence that provision of ART not only reduces the medical effects of HIV but also improves functioning and quality of life.

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Table 1

Demographic information for the sample

	Percentage (N = 1,563)
Gender	
Male	52.7
Female	47.3
Age	
<20	<1
20–29	27
30–39	44
40–49	22
50–59	6
60+	1
Country of origin	
Brazil	14.8
Haiti	6.4
India	16.3
Malawi	14.1
Peru	8.6
Thailand	6.4
South Africa	13.4
United States	13.4
Zimbabwe	7.0

Table 2

Means (standard deviation), Kruskal–Wallis tests, and Jonckheere–Terpstra trend tests of QOL scores (range 0–100) by plasma HIV-1 RNA viral load category

	Overall	≤4,000	4,001–0,000	40,001–00,000	400,001–749,999	≥750,000	Kruska-–Wallis test	Jonckheere–Terpstra test
	N = 1,560	N = 65	N = 345	N = 871	N= 158	N= 121	*P* value	*P* value
General health perception	59.96 (24.50)	58.21 (26.45)	63.91 (22.95)	59.61 (23.95)	59.12 (26.60)	53.24 (27.22)	0.002*	0.367
Physical functioning	88.21 (19.38)	86.73 (22.19)	91.36 (16.98)	89.01 (17.97)	84.97 (23.04)	78.62 (24.71)	<0.001*	0.004*
Role functioning	84.07 (28.34)	89.62 (22.92)	85.79 (27.78)	84.54 (27.45)	80.70 (32.04)	77.27 (32.44)	0.015*	0.019*
Social functioning	89.33 (20.57)	89.23 (21.87)	91.40 (17.75)	89.39 (19.69)	89.03 (23.59)	83.47 (27.37)	0.195	0.860
Cognitive functioning	87.26 (17.88)	86.67 (15.94)	87.79 (17.95)	87.22 (17.63)	86.75 (19.08)	87.05 (19.04)	0.609	0.494
Pain	80.60 (22.34)	79.83 (23.15)	83.67 (20.26)	80.13 (21.89)	78.76 (25.65)	78.15 (25.38)	0.134	0.600
Mental health	76.24 (21.36)	77.03 (19.04)	77.11 (20.20)	76.09 (21.66)	76.16 (21.63)	74.44 (23.32)	0.973	0.760
Energy/fatigue	73.51 (24.77)	76.15 (20.89)	78.38 (22.30)	74.02 (23.85)	67.66 (28.87)	62.23 (29.17)	<0.001*	0.044*

*$P \leq 0.05$

Table 3

Means (standard deviation), Kruskal–Wallis tests, and Jonckheere–Terpstra trend tests of QOL scores (range 0–100) by CD4+ lymphocyte count category

	Overall N = 1,563	<50 N= 198	50–99 N = 229	100–199 N = 526	200–249 N = 336	250–299 N = 274	Kruskal–Wallis test *P* value	Jonckheere–Terpstra test *P* value
General health perception	59.97 (24.49)	48.27 (26.02)	54.00 (24.71)	62.20 (23.44)	63.37 (22.66)	64.98 (23.87)	<0.001*	<0.001*
Physical functioning	88.24 (19.37)	77.21 (25.76)	84.06 (20.87)	90.45 (17.41)	91.21 (15.88)	91.83 (16.54)	<0.001*	<0.001*
Role functioning	84.10 (28.32)	71.59 (34.69)	79.37 (30.75)	86.57 (26.40)	86.53 (25.96)	89.42 (24.16)	<0.001*	<0.001*
Social functioning	89.34 (20.55)	76.71 (29.78)	88.69 (19.85)	91.11 (19.03)	91.20 (18.00)	93.35 (14.51)	<0.001*	<0.001*
Cognitive functioning	87.29 (17.87)	83.20 (20.36)	85.74 (18.41)	87.76 (17.53)	88.93 (15.84)	88.61 (18.05)	0.002*	0.005*
Pain	80.62 (22.32)	71.83 (27.35)	76.95 (22.68)	82.65 (20.36)	83.00 (20.96)	83.25 (21.36)	<0.001*	<0.001*
Mental health	76.24 (21.35)	70.20 (24.08)	73.60 (21.62)	77.13 (20.63)	78.58 (19.91)	78.25 (21.23)	<0.001*	0.001*
Energy/fatigue	73.55 (24.77)	60.30 (29.50)	69.52 (24.16)	76.56 (22.94)	76.88 (22.99)	76.64 (23.50)	<0.001*	<0.001*

* $P \leq 0.05$

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Table 4

Means, ranks, and significant differences (*T* statistic) by country and QOL domain

Country	Domain	Mean	Rank	Sig. differences	Mean difference (95% CI)
India	General health perceptions	68.40	1	4 Thailand	7.90 (2.98, 12.81)*
				5 Peru	8.51 (4.11, 12.91)**
				6 Zimbabwe	12.49 (7.37, 17.61)***
				7 USA	12.55 (7.92, 17.18)***
				8 Haiti	15.98 (10.62, 21.35)***
				9 Malawi	18.89 (14.6, 23.19)***
	Social functioning	97.25	1	4 Thailand	5.48 (2.22, 8.73)*
				5 Haiti	8.03 (3.98, 12.09)**
				6 Peru	8.37 (4.95, 11.78)***
				7 Brazil	10.15 (6.77, 13.52)***
				8 Malawi	11.5 (8.54, 14.45)***
				9 USA	21.61 (17.56, 25.66)***
	Cognitive functioning	93.46	1	5 Peru	5.65 (2.95, 8.35)**
				6 Thailand	8.73 (6.12, 11.34)***
				7 Brazil	10.03 (6.66, 13.4)***
				8 Malawi	10.34 (7.45, 13.24)***
				9 USA	11.99 (8.73, 15.24)***
	Physical functioning	93.53	2	6 Malawi	4.78 (1.84, 7.72)*
				7 South Africa	5.14 (2.17, 8.10)*
				8 Brazil	10.74 (7.38, 14.10)***
				9 USA	16.28 (12.27, 20.29)***
	Role functioning	92.35	3	6 Malawi	8.03 (3.89, 12.18)**
				7 Brazil	9.13 (4.83, 13.42)**
				8 USA	16.73 (11.9, 21.55)***

Country	Domain	Mean	Rank	Sig. differences	Mean difference (95% CI)
				9 Peru	33.58 (25.91, 41.26)***
	Pain	85.45	3	7 Brazil	8.53 (4.49, 12.58)**
				8 Malawi	10.45 (6.6, 14.29)***
				9 USA	14.28 (10.1, 18.46)***
	Mental health	81.62	3	6 Peru	11.67 (8.05, 15.29)***
				7 Brazil	12.13 (8.05, 16.2)***
				8 Haiti	14.15 (9.96, 18.34)***
				9 USA	14.48 (10.61, 18.35)***
	Energy	76.63	4	9 USA	16.78 (12.28, 21.27)***
South Africa	General health perceptions	68.33	2	4 Thailand	7.83 (3.08, 12.59)*
				5 Peru	8.45 (4.23, 12.66)**
				6 Zimbabwe	12.42 (7.46, 17.39)***
				7 USA	12.48 (8.03, 16.94)***
				8 Haiti	15.92 (10.7, 21.13)***
				9 Malawi	18.83 (14.72, 22.93)***
	Mental health	85.37	2	5 Malawi	7.09 (3.68, 10.5)**
				6 Peru	15.41 (11.67, 19.16)***
				7 Brazil	15.87 (11.69, 20.05)***
				8 Haiti	17.90 (13.61, 22.19)***
				9 USA	18.22 (14.24, 22.2)***
	Cognitive functioning	91.87	2	6 Thailand	7.14 (4.13, 10.15)***
				7 Brazil	8.44 (4.75, 12.13)***
				8 Malawi	8.75 (5.49, 12.02)***
				9 USA	10.40 (6.81, 13.98)***
India	General health perceptions	68.40	1	4 Thailand	7.90 (2.98, 12.81)*
				5 Peru	8.51 (4.11, 12.91)**
				6 Zimbabwe	12.49 (7.37, 17.61)***

Country	Domain	Mean	Rank	Sig. differences	Mean difference (95% CI)
				7 USA	12.55 (7.92, 17.18)***
				8 Haiti	15.98 (10.62, 21.35)***
				9 Malawi	18.89 (14.6, 23.19)***
	Social functioning	97.25	1	4 Thailand	5.48 (2.22, 8.73)*
				5 Haiti	8.03 (3.98, 12.09)**
				6 Peru	8.37 (4.95, 11.78)***
				7 Brazil	10.15 (6.77, 13.52)***
				8 Malawi	11.5 (8.54, 14.45)***
				9 USA	21.61 (17.56, 25.66)***
	Cognitive functioning	93.46	1	5 Peru	5.65 (2.95, 8.35)**
				6 Thailand	8.73 (6.12, 11.34)***
				7 Brazil	10.03 (6.66, 13.4)***
				8 Malawi	10.34 (7.45, 13.24)***
				9 USA	11.99 (8.73, 15.24)***
	Physical functioning	93.53	2	6 Malawi	4.78 (1.84, 7.72)*
				7 South Africa	5.14 (2.17, 8.10)*
				8 Brazil	10.74 (7.38, 14.10)***
				9 USA	16.28 (12.27, 20.29)***
	Role functioning	92.35	3	6 Malawi	8.03 (3.89, 12.18)**
				7 Brazil	9.13 (4.83, 13.42)**
				8 USA	16.73 (11.9, 21.55)***
				9 Peru	33.58 (25.91, 41.26)***
	Pain	85.45	3	7 Brazil	8.53 (4.49, 12.58)**
				8 Malawi	10.45 (6.6, 14.29)***
				9 USA	14.28 (10.1, 18.46)***
	Mental health	81.62	3	6 Peru	11.67 (8.05, 15.29)***
				7 Brazil	12.13 (8.05, 16.2)***

Country	Domain	Mean	Rank	Sig. differences	Mean difference (95% CI)
				8 Haiti	14.15 (9.96, 18.34)***
				9 USA	14.48 (10.61, 18.35)***
	Energy	76.63	4	9 USA	16.78 (12.28, 21.27)***
South Africa	General health perceptions	68.33	2	4 Thailand	7.83 (3.08, 12.59)*
				5 Peru	8.45 (4.23, 12.66)**
				6 Zimbabwe	12.42 (7.46, 17.39)***
				7 USA	12.48 (8.03, 16.94)***
				8 Haiti	15.92 (10.7, 21.13)***
				9 Malawi	18.83 (14.72, 22.93)***
	Mental health	85.37	2	5 Malawi	7.09 (3.68, 10.5)**
				6 Peru	15.41 (11.67, 19.16)***
				7 Brazil	15.87 (11.69, 20.05)***
				8 Haiti	17.90 (13.61, 22.19)***
				9 USA	18.22 (14.24, 22.2)***
	Cognitive functioning	91.87	2	6 Thailand	7.14 (4.13, 10.15)***
				7 Brazil	8.44 (4.75, 12.13)***
				8 Malawi	8.75 (5.49, 12.02)***
				9 USA	10.40 (6.81, 13.98)***
	Social functioning	94.92	3	6 Peru	6.03 (2.38, 9.69)*
				7 Brazil	7.81 (4.2, 11.43)**
				8 Malawi	9.16 (5.93, 12.39)***
				9 USA	19.28 (15.02, 23.53)***
	Energy	76.95	3	9 USA	17.10 (12.22, 21.98)***
	Role functioning	88.33	4	8 USA	12.71 (7.38, 18.04)***
				9 Peru	29.56 (21.57, 37.56)***
	Pain	85.24	4	7 Brazil	8.33 (4.02, 12.64)**
				8 Malawi	10.24 (6.11, 14.36)***

Country	Domain	Mean	Rank	Sig. differences	Mean difference (95% CI)
				9 USA	14.07 (9.63, 18.51)***
	Physical functioning	88.39	7	9 USA	11.14 (6.65, 15.63)***
Brazil	General health perceptions	61.83	3	8 Haiti	9.42 (3.61, 15.22)*
				9 Malawi	12.33 (7.49, 17.16)***
	Role functioning	83.23	7	9 Peru	24.46 (16.28, 32.64)***
	Social functioning	87.11	7	9 USA	11.47 (6.4, 16.53)**
	Energy	71.77	7	9 USA	11.92 (6.4, 17.45)**
	Pain	76.91	7		
	Mental health	69.49	7		
	Cognitive functioning	83.43	7		
	Physical functioning	82.79	8		
Thailand	Role functioning	92.50	2	6 Malawi	8.18 (3.4, 12.97)*
				7 Brazil	9.27 (4.36, 14.19)*
				8 USA	16.88 (11.49, 22.26)***
				9 Peru	33.73 (25.69, 41.77)***
	Energy	81.00	2	7 Brazil	9.23 (3.7, 14.75)*
				8 Malawi	9.91 (5.04, 14.78)**
				9 USA	21.15 (15.88, 26.41)***
	Physical functioning	92.63	3	8 Brazil	9.83 (6.07, 13.59)***
				9 USA	15.38 (11.02, 19.73)***
	General healthperceptions	60.50	4	9 Malawi	10.99 (5.71, 16.28)*
	Social functioning	91.78	4	9 USA	16.13 (11.14, 21.12)***
	Mental health	79.20	4	6 Peru	9.25 (4.48, 14.02)**
				7 Brazil	9.71 (4.59, 14.82)**
				8 Haiti	11.73 (6.52, 16.94)***
				9 USA	12.06 (7.1, 17.01)***
	Pain	79.89	6	9 USA	8.72 (3.96, 13.48)*

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Country	Domain	Mean	Rank	Sig. differences	Mean difference (95% CI)
	Cognitive functioning	84.73	6		
Peru	Physical functioning	93.94	1	7 South Africa	5.54 (2.18, 8.91)*
				8 Brazil	11.14 (7.43, 14.86)***
				9 USA	16.69 (12.37, 21.00)***
	Pain	85.66	2	7 Brazil	8.74 (4.2, 13.28)**
				8 Malawi	10.66 (6.29, 15.02)***
				9 USA	14.49 (9.83, 19.15)***
	General health perceptions	59.89	5	9 Malawi	10.38 (5.57, 15.2)**
	Cognitive functioning	87.81	5	9 USA	6.33 (2.53, 10.14)*
	Social functioning	88.89	6	9 USA	13.25 (8.15, 18.34)***
	Energy	75.22	6	9 USA	15.37 (10.11, 20.63)***
	Mental health	69.95	6		
	Role functioning	58.77	9		
Zimbabwe	Role function ing	96.14	1	4 South Africa	7.80 (3.81, 11.8)**
				5 Haiti	11.14 (5.24, 17.03)*
				6 Malawi	11.82 (7.62, 16.02)***
				7 Brazil	12.91 (8.56, 17.26)***
				8 USA	20.51 (15.64, 25.39)***
				9 Peru	37.37 (29.66, 45.07)***
	Pain	88.99	1	6 Thailand	9.10 (4.56, 13.64)**
				7 Brazil	12.08 (7.42, 16.74)***
				8 Malawi	13.99 (9.5, 18.48)***
				9 USA	17.82 (13.05, 22.6)***
	Mental health	86.21	1	5 Malawi	7.94 (4.34, 11.53)***
				6 Peru	16.26 (12.35, 20.17)***
				7 Brazil	16.72 (12.39, 21.05)***
				8 Haiti	18.75 (14.31, 23.19)***

Country	Domain	Mean	Rank	Sig. differences	Mean difference (95% CI)
				9 USA	19.07 (14.93, 23.21)***
	Energy	83.18	1	4 India	6.55 (2.69, 10.42)*
				6 Peru	7.96 (3.23, 12.68)*
				7 Brazil	11.41 (6.39, 16.42)***
				8 Malawi	12.09 (7.8, 16.38)***
				9 USA	23.33 (18.6, 28.06)***
	Social functioning	95.96	2	6 Peru	7.07 (3.03, 11.11)*
				7 Brazil	8.85 (4.84, 12.86)**
				8 Malawi	10.20 (6.54, 13.87)***
				9 USA	20.32 (15.72, 24.91)***
	Cognitive functioning	91.58	3	6 Thailand	6.84 (3.56, 10.12)**
				7 Brazil	8.14 (4.23, 12.05)**
				8 Malawi	8.45 (4.94, 11.97)***
				9 USA	10.10 (6.29, 13.91)***
	Physical functioning	92.61	4	8 Brazil	9.82 (6.03, 13.61)***
				9 USA	15.36 (10.99, 19.74)***
	General health perceptions	55.91	6		
Haiti	Cognitive functioning	88.87	4	9 USA	7.39 (3.27, 11.51)*
	Physical functioning	91.00	5	8 Brazil	8.21 (4.18, 12.23)**
				9 USA	13.75 (9.17, 18.33)***
	Role functioning	85.00	5	9 Peru	26.23 (17.13, 35.33)***
	Pain	83.22	5	8 Malawi	8.22 (3.11, 13.34)*
				9 USA	12.06 (6.68, 17.43)***
	Social functioning	89.22	5	9 USA	13.58 (8.04, 19.12)***
	Energy	75.60	5	9 USA	15.75 (10.29, 21.2)***
	Mental health	67.47	8		
	General health perceptions	52.42	8		

Country	Domain	Mean	Rank	Sig. differences	Mean difference (95% CI)
Malawi	Mental health	78.27	5	6 Peru	8.32 (4.35, 12.29)**
				7 Brazil	8.78 (4.39, 13.16)**
				8 Haiti	10.81 (6.31, 15.3)***
				9 USA	11.13 (6.93, 15.33)***
	Physical functioning	88.75	6	9 USA	11.50 (7.03, 15.97)***
	Role functioning	84.32	6	9 Peru	25.55 (17.45, 33.65)***
	Pain	75.00	8		
	Social functioning	85.76	8	9 USA	10.11 (5.32, 14.91)**
	Energy	71.09	8	9 USA	11.24 (6.37, 16.11)***
	Cognitive functioning	83.12	8		
	General health perceptions	49.51	9		
USA	General health perceptions	55.85	7		
	Role functioning	75.63	8	9 Peru	16.86 (8.38, 25.33)**
	Physical functioning	77.25	9		
	Pain	71.17	9		
	Social functioning	75.64	9		
	Mental health	67.14	9		
	Energy	59.85	9		
	Cognitive functioning	81.48	9		

*≤0.05,

**≤0.01,

***≤0.0001