

Quality of Life among Adults with Confirmed Dengue in Brazil

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Abstract. The main objective of this study was to measure the quality of life (QoL) during a dengue episode. We conducted a facility-based survey in central Brazil in 2005 and recruited 372 laboratory-confirmed dengue patients greater than 12 years of age in hospital and ambulatory settings. We administered the World Health Organization QoL instrument approximately 15 days after the onset of symptoms. We used principal component analysis with varimax rotation to identify domains related to QoL. The median age of interviewees was 36 years. Most (85%) reported their general health status as very good or good before the dengue episode. Although ambulatory patients were mainly classified as having dengue fever, 44.8% of hospitalized patients had dengue hemorrhagic fever or intermediate dengue. Principal component analysis identified five principal components related to cognition, sleep and energy, mobility, self-care, pain, and discomfort, which explained 73% of the variability of the data matrix. Hospitalized patients had significantly lower mean scores for dimensions cognition, self-care, and pain than ambulatory patients. This investigation documented the generally poor QoL during a dengue episode caused by the large number of domains affected and significant differences between health care settings.

INTRODUCTION

Dengue is an important vector-borne viral infection. Approximately two-fifths of the world's population is susceptible to this disease.¹ Most of these persons live in tropical regions and several developing countries.^{2,3} Brazil has contributed to the global burden of dengue in the Western Hemisphere in the past decade.^{4–7} The Brazilian Surveillance System reported two-thirds (approximately 560,000 cases) of worldwide dengue cases (approximately 850,000) reported to the World Health Organization (WHO) in 2007.^{8,9} Despite large investments to control the mosquito vectors and reduce dengue transmission, dengue has become endemic throughout Brazil, and outbreaks have occurred in several regions.^{10,11} The increasing trend of hospitalization of patients with dengue and reports of dengue hemorrhagic fever (DHF), which is the severe and life-threatening form of the disease, have made this a serious public health problem.^{11–13}

Several studies conducted in dengue-endemic countries of Asia and the Western Hemisphere have quantified the burden of dengue.^{14–19} In addition, indirect costs (related to work absenteeism and impairment) surpass the direct medical cost during dengue.^{20–24} In addition to morbidity, mortality, and costs, quality of life (QoL) measurements have been increasingly recognized as an important metric in the public health context. Quality of life research has been performed to evaluate the health impact of chronic diseases,^{25,26} infectious diseases,²⁷ and the health state of the general population.^{28–30} These studies are considered valuable tools in guiding health policies in terms of investments in new treatments, diagnostic developments, prevention strategies, and research priorities.²³ Nevertheless, little is known about the impact on QoL during dengue and its relationship to disease severity in various settings.

A multicountry study to evaluate the dengue burden and the impact of the patient's QoL was launched in 2005. It was sponsored initially by the Pediatric Vaccine Dengue Initiative. The main economic findings compared five countries in the Western Hemisphere (Brazil, El Salvador, Guatemala, Panama, and Venezuela) and three in Asia (Cambodia, Malaysia, and Thailand). The results showed high costs imposed by dengue in all settings and suggested a large loss in QoL of dengue patients in Malaysia.^{22,24} As part of this international initiative, we explored the impact of dengue on health status among adolescents and adults treated in hospital and ambulatory settings in a dengue-endemic region in central Brazil.

METHODS

Participants and setting. We conducted a health facility-based study on QoL of dengue patients as part of a multicountry dengue initiative. This investigation was conducted in the city of Goiânia in central Brazil (1.2 million inhabitants) during 2005. The first outbreak in this region occurred in 1994 (dengue virus type 1 [DENV-1]), followed by introduction of DENV-2 and DENV-3 in 2002. At the time of the study, the predominant circulating serotype was DENV-3; DENV-1 and DENV-2 were simultaneously co-circulating. In 2005, approximately 9,000 dengue cases were reported, of which 85% were among adults.²⁴

The design and methods of this study have been described.²⁴ Briefly, 550 dengue patients were recruited consecutively in the major public reference hospital, in one large private hospital, and in ambulatory settings linked to these selected hospitals. The eligibility criteria were laboratory-confirmed symptomatic dengue cases and an age greater than 12 years. Patients were enrolled after signing an informed consent, and a home visit was scheduled approximately 15 days after the onset of symptoms. This period of approximately two weeks was considered the length of the acute dengue episode and as the reference period for the QoL evaluation. Dengue hemorrhagic fever and dengue fever (DF) were defined according to WHO criteria. The case definition of a dengue episode

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was high fever with at least two of the associated symptoms or signs (headache, retro-orbital pain, myalgia, arthralgia, rash, vomiting, and bleeding). The intermediate DF/DHF category, which follows the current case definition for clinical management in Brazil,³¹ was defined as dengue with severe clinical manifestation caused by internal hemorrhage, plasma leakage, and shock or thrombocytopenia (defined by a platelet count $\leq 50,000$ platelets/mm³). Patients with laboratory-confirmed dengue were classified by two study clinicians as having DF, DHF, or intermediate DF/DHF.

Blood samples were obtained from all enrolled patients at the first visit for virus detection and/or seven days after the onset of the symptoms for serologic tests. Dengue was confirmed by detection of IgM against dengue (IgM antigen capture enzyme-linked immunosorbent assay or immunochromatographic test), virus detection by cell culture, nucleic acid detection, or multiplex polymerase chain reaction amplification (Qiagen, Hilden Germany and Pan Bio Pty., Ltd. Brisbane, Queensland, Australia).

From the initial patient screening, we excluded 140 cases that could not be laboratory confirmed. Thirty-eight patients ≤ 12 years of age were also excluded from this analysis because the questionnaire was not validated for this age group in our setting. For the remaining 372 laboratory-confirmed dengue patients > 12 years of age, we assessed their general health and QoL during the acute dengue episode.

Research instruments. The questionnaire used was based on the World Health Survey individual questionnaire (WHOQOL-BREF).³² It contains questions related to mobility, self-care, pain and discomfort, cognition, interpersonal activities, vision, sleep, energy, and affect. This questionnaire was validated in Brazil through a nationwide survey³³ and in other countries.^{34,35} The questionnaire was adapted to refer to the duration of the dengue episode instead of the past 30 days. The WHOQOL-BREF is a generic QoL instrument composed of questions measuring general health, social relationships, and physical, psychological, and environmental domains. Each item has scores from 1 (no impairment), 2 (mild), 3 (moderate), 4 (severe), and 5 (extreme impairment), similar to a Likert scale.³⁵ The first question scored general health status before the illness episode as a baseline. We also applied the EuroQol thermometer-like scale (visual analog scale) to evaluate the health status during the dengue episode. Patients were asked to indicate their best and worst health status during the dengue episode (0 corresponded to a state equivalent to worst possible health status and 100 corresponded to perfect health).³⁶ The worst value was used as the patient's health status index (HSI).

Data collection. Patients were interviewed in their homes around the time of their recovery (approximately 15 days after onset of symptoms) by a trained health interviewer. Respondents were asked to answer questions regarding their health status from the onset of the illness until the time of the interview. This time frame, constituting the study reference period, was considered sufficiently long to assess the health profile during the acute dengue episode, but sufficiently short to minimize recall bias. In the dataset, the length of time between the onset of the symptoms and the interviews ranged from 12 to 18 days. The mean duration of the interview addressing health status was approximately 15 minutes.

Demographic characteristics were recorded at study enrollment. In addition, medical records for patients requiring hospitalization were reviewed to extract clinical, laboratory, and

diagnosis information during the study illness episode. All data were double-entered into a customized Microsoft Access database (Microsoft Corp., Redmond, WA) and then transferred for all analyses to SPSS version 17.0 software for Windows (SPSS Inc., Chicago, IL).

Data analysis. Descriptive statistics and exploratory data analyses were performed to evaluate the distribution of variables. The values of the worst health status measured by using the visual analog scale for ambulatory and hospitalized cases were compared by using the Mann-Whitney rank sum test and displayed as a box plot.

We also excluded nine variables because of their lack of suitability or relevance for data analysis. The excluded variables were one baseline question that asked about well-being before the initial symptoms with no parallel to the variables that measured health perception at the end of the dengue episode; five questions related to the duration of the symptoms, which were not categorical variables; one yes/no question; and two questions related to visual impairment, which was missing values on $> 20\%$ of the observations.

Principal components analysis. Principal components analysis (PCA) was performed with varimax rotation to 1) identify patterns and simplify structures underlying the multiple questions regarding patient's health; 2) identify groups of variables that are mainly correlated with each component; and 3) calculate individual scores related to each one of these components. This technique is appropriate for assessing continuous variables and ordinal scales.³⁷ The Kaiser-Meyer-Olkin (KMO) test was used to assess the measure of sampling adequacy, where KMO values > 0.6 were considered acceptable. The Bartlett's test of sphericity was also applied to verify the sufficiency of the correlation between the variables for the PCA analysis, where a non-significant result ($P > 0.05$) would indicate lack of suitability of the variables for identifying underlying components. In the first step of PCA, we retained factors in the model with an Eigen value ≥ 0.9 , aiming to achieve $\geq 70\%$ of the amount of variability. The second step was to identify variables strongly correlated with each component (correlation coefficient ≥ 0.6). These coefficients were the factor loadings generated in the rotated component matrix. The individual factor scores for each component were then added to the dataset for stratified analysis.

Stratified analysis. For stratified analyses, we used factor score means for each component obtained by PCA. First, the difference between ambulatory versus hospitalized patients was tested by using the analysis of variance model. Next, we compared patients with DF versus patients with DHF/intermediate by using analysis of variance. We limited this comparison to the subset of hospitalized patients to control for the effect of setting on QoL.

Ethical considerations. The study protocol was approved by the Institutional Review Board at Brandeis University and Ethical Committee of the Federal University of Goias, Brazil (CEPMHA/HC/UFG) (no. 097/2004). The parent multi-country study was also approved by Brandeis University and the sponsor. All participants or legal guardians for underage participants signed the informed consent form.

RESULTS

Demographic and diagnostic characteristics. Among 372 confirmed cases of dengue in adults and adolescents, 63.4%

were in female patients. The median age of patients was 36 years (range = 13–88 years). Ages of patients were similar for those who attended ambulatory (37 years old) and hospital (34 years old) facilities. Nearly all (99.6%) ambulatory patients were classified as having DF.

The ambulatory patients were almost equally divided by sector: 48.8% from the public sector and 52.2% from private facilities. The duration of fever was calculated from self-reported dates of fever onset and defervescence for all patients (ambulatory and hospitalized). This period (mean \pm SD) was longer for hospitalized patients (5.7 ± 2.6 days) than for ambulatory patients (4.8 ± 2.6 days) (Table 1). This difference was statistically significant ($P = 0.04$, by Kolmogorov-Smirnov test). We used this procedure because the distribution of fever duration in ambulatory patients was skewed to the left (shorter durations).

In the hospital setting, most (55.2%) cases were diagnosed as dengue fever, followed by intermediate DF/DHF (33.3%) and DHF (11.5%). A statistically significant higher percentage of hospitalized cases were classified as intermediate DF/DHF and DHF than among ambulatory patients ($P < 0.001$, by chi-square test). In both health settings, most patients sought medical care within 48 hours of onset of symptoms.

The most frequent clinical characteristics were fever, muscle/joint pain, dizziness, retro-orbital pain, dizziness, and rash among adolescents and adults. Vomiting and bleeding were signs more frequently recorded among hospitalized dengue patients than among ambulatory patients ($P < 0.001$) (Table 2).

Health status. Before the dengue episode, general health status was self-reported as very good or good by 85.4% of the participants; only 14.0% and 0.6% reported moderate or bad/very bad health status, respectively. Distributions of general health status before illness were similar between ambulatory and hospitalized patients ($\chi^2 = 3.2$, degrees of freedom = 4, $P = 0.52$). The box plot distribution for the self-assessed HSI on a scale of 0–100 is shown in Figure 1. The median value of the worst HSI for ambulatory patients (20) was significantly higher ($P < 0.001$) than the value among hospitalized patients (10) (by Mann-Whitney rank test). Similarly, during this reference period, ambulatory patients had a slight, but significantly lower, number of days described as very bad or bad (median = 8 days) than hospitalized patients (median = 9 days) ($P < 0.05$, by Mann-Whitney rank test). In addition, the extreme values and upper quartiles shown in Figure 1 (30 and 21 days for

TABLE 2
Prevalence of symptoms and signs among confirmed dengue patients, by setting, Brazil

Symptoms and signs	Ambulatory (n = 276), %	Hospitalized (n = 96), %	P
Fever	98.2	96.9	0.72
Myalgia or arthralgia	94.9	94.8	0.82
Headache	91.3	91.7	0.91
Retro-orbital pain	82.6	78.1	0.33
Dizziness	81.9	87.5	0.20
Rash	75.0	78.1	0.53
Abdominal pain	62.3	65.6	0.56
Vomiting	50.4	70.0	0.0001
Bleeding	24.3	47.9	0.0001
Diarrhea	41.7	46.9	0.37
Sore throat/running nose	37.3	30.2	0.20

hospitalized and ambulatory patients, respectively) show that dengue affects some patients in both groups for long periods.

Factor structure. Before PCA, the KMO test result was 0.824, which suggested that sampling was appropriate for performing PCA. The result of the Bartlett test was significant ($P < 0.0001$), which indicated a sufficient correlation between the variables to perform the analysis.

For the 15 health questions, a five-factor model emerged from the data reduction when the criteria of Eigen values > 0.9 was applied. This five-factor model accounted for 73% of total variation and was divided among components 1–5 as 19.1%, 14.8%, 13.8%, 12.9%, and 12.3%, respectively. Factor loadings obtained by the PCA are shown in Table 3. For each of the five components, high factor loadings were obtained for specific subsets of variables. Component 1 included issues related to mental status such as difficulty in learning, remembering, and participating in social life in general; component 2 also aggregated a mental evaluation of sleep difficulties, anxiety, and worries; component 3 covered the physical health domains such as performing daily activities, mobility and vigorous activities; component 4 distinguished issues related to the difficulties of personal care; and component 5 aggregated the questions related to pain and suffering.

In stratified analysis, we observed variation between settings for components 4 and 5 at the 5% significance level and for component 1 at the 10% significance level (Table 4). Similarly, in breakdowns by severity within the hospitalized patients, components 1 and 4 showed significant difference between

TABLE 1
Characteristics of confirmed dengue patients by setting, Brazil*

Characteristic	Ambulatory (n = 276)	Hospitalized (n = 96)	P
Female (%)	175 (63.4)	63 (65.6)	0.69
Age years, median (range)	37 (13–88)	34 (13–79)	0.52
Age, years, mean (SD)	39.4 (16.2)	38.1 (17.6)	
Education years, mean (SD)	11.8 (5.2)	10.3 (4.9)	0.12
Classification (%)			
DF	275 (99.6)	53 (55.2)	0.0001
Intermediate DF/DHF	1 (0.4)	33 (33.3)	
DHF	–	11 (11.5)	
Medical care within 48 hours of onset of symptoms (%)	174 (57.8)	75 (68.8)	0.04
Health care system (%)			
Public (SUS)	132 (47.8)	47 (49.0)	0.47
Private (UNIMED)	144 (52.2)	49 (51.0)	
Length of dengue episode, days, mean (SD)	10.9 (4.9)	11.2 (3.7)	0.56
Length of fever, days, mean (SD)	4.8 (2.6)	5.7 (2.6)	0.02

* DF = dengue fever; DHF = dengue hemorrhagic fever; SUS = Sistema Único de Saúde; UNIMED = União and Médicos. DHF and DF were defined according to World Health Organization criteria. Intermediate DF/DHF was defined as dengue with severe clinical manifestation caused by internal hemorrhage, plasma leakage, and shock or thrombocytopenia $\leq 50,000$ platelets/mm³.

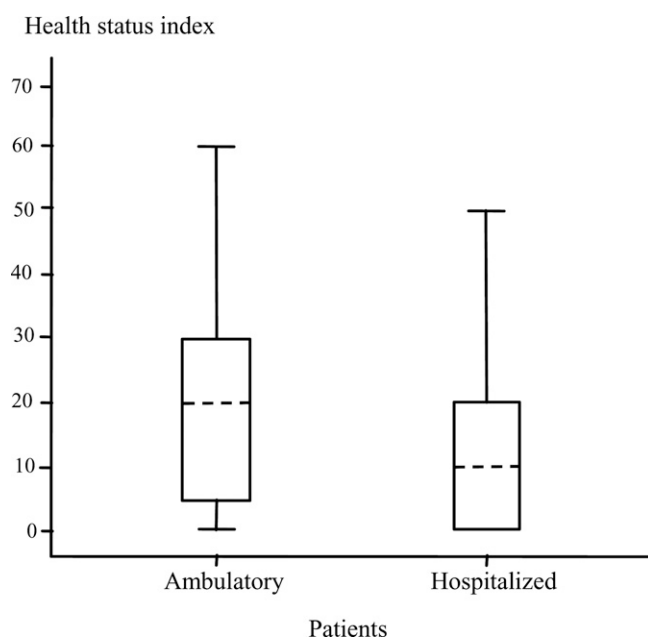


FIGURE 1. Box plot distribution of the self-assessed health status index based on EuroQOL thermometer-like scale during the dengue episode, Brazil. Health status index was the value assigned by the patient to the worst health status during the dengue episode on a 0–100 analog scale.

the DF and the DHF/intermediary groups. This comparison of disease severity showed significantly higher scores related to self-care among DHF/intermediate cases. For the cognition dimension, DF patients had significantly higher scores than DHF/intermediate patients (Table 5).

DISCUSSION

We report results of a health status assessment from the view of the patient with dengue in an urban dengue-endemic area in central Brazil. We used the WHO survey individual questionnaire (WHOQOL-BREF) because it has been validated in Brazil^{33,38,39} and it assesses QoL over a broad range of domains affected by dengue. The QoL concept combines

TABLE 4
Comparison of mean component scores between settings, Brazil

Component	Setting		F	P
	Ambulatory (n = 276) mean (SD)	Hospitalized (n = 96) mean (SD)		
Cognition	-0.0528 (0.97)	0.1519 (1.06)	3.00	0.084
Sleep and energy	-0.0416 (1.02)	0.1198 (0.93)	1.86	0.173
Mobility	-0.0291 (1.02)	0.0838 (0.93)	0.91	0.341
Self-care	-0.1238 (0.95)	0.3559 (1.03)	17.11	< 0.001
Pain and discomfort	-0.0770 (1.00)	0.2215 (0.94)	6.44	0.012

objective features of health and welfare (absence of pain, abilities) and subjective reactions. The PCA identified five principal components that explained 73% of the variability of the data matrix. This method distinguished impairments in several dimensions covered by the WHO survey, which included cognition and interpersonal activities; sleep/energy and affect; mobility; self-care; and pain and discomfort. The factors that emerged from this model seem to capture the physical and mental distress caused by the clinical symptoms of dengue such as fever, severe headache, muscle/joint pain, dizziness, and retro-orbital pain.⁴⁰

In the present study, most participants perceived their general health status as good/very good before the dengue episode. This finding is in agreement with the fact that dengue is an acute infectious disease, which affects persons independent of their previous health status.^{2,41} Most of the patients in our study were classified as having DF. In a study in Malaysia in which patients were assessed by using the same instrument, patients generally had more severe dengue (DHF or DF with plasma leakage).²² Despite differences in types of respondents and epidemiologic patterns related to peak-age incidence and the dengue severity, both studies identified similar affected domains in hospital and ambulatory settings. For example, a high prevalence of difficulty in performing physical activities and activities related to self-care, body pain and discomfort and feeling depressed/anxious were observed in adult patients with dengue in central Brazil and in Malaysia.²² The lower health status among hospitalized patients compared with ambulatory patients reinforces the validity of our measures because clinicians and patients would be more likely to seek medical care for more severe cases. In our study, prompt action of

TABLE 3
Dimensionality of World Health Organization survey factor loadings from principal components analysis, Brazil*

Variables	Components				
	1	2	3	4	5
Difficulties with schooling or job	0.144	0.146	0.808	0.013	0.155
Difficulties in moving	0.042	0.187	0.726	0.411	0.052
Difficulties in vigorous activities	0.137	0.218	0.777	0.163	0.085
Difficulties with self-care	0.232	0.146	0.204	0.891	0.134
Difficulties in taking care of appearance	0.242	0.172	0.193	0.887	0.113
Body aches or pains	0.137	0.164	0.062	0.118	0.892
Body discomfort	0.182	0.193	0.209	0.100	0.855
Difficulties with concentration	0.728	0.215	0.075	0.195	-0.028
Difficulties in learning a new task	0.830	0.190	0.127	0.174	0.031
Difficulties in participating in the community	0.782	0.165	0.111	0.104	0.215
Difficulties in dealing with personal relationships	0.792	0.143	0.091	0.081	0.254
Difficulties in sleeping	0.169	0.760	0.259	0.062	-0.070
Tired and without energy	0.083	0.729	0.185	0.107	0.202
Feeling sad or depressed	0.312	0.580	0.046	0.112	0.264
Feeling worried or anxious	0.266	0.653	0.128	0.165	0.186

*Numbers are scores by varimax rotation methods with factor loadings > 0.50 shown in bold. Domains related to each component are component 1 = cognition and interpersonal activities; component 2 = sleep and energy and affect; component 3 = mobility; component 4 = self-care; component 5 = pain and discomfort.

TABLE 5
Comparison of mean (SD) domain scores for severity of disease (DF vs. DHF/intermediate) among hospitalized patients, Brazil*

Component	DF fever, mean (SD)	DHF/intermediate, mean (SD)	F	P
Cognition	0.4255 (0.92)	-0.1852 (1.12)	8.55	0.004
Sleep and energy	0.1259 (0.82)	0.1124 (1.06)	0.005	0.944
Mobility	0.1425 (1.02)	0.0115 (0.82)	0.466	0.497
Self-care	0.0183 (1.02)	0.7721 (0.91)	14.245	<0.001
Pain and discomfort	0.2044 (0.99)	0.2426 (0.91)	0.038	0.846

* DF = dengue fever; DHF = dengue hemorrhagic fever. DF (n = 53) vs. DHF/intermediate (n = 43) among hospitalized patients.

households in seeking health care within 48 hours of onset of the symptoms suggests households perceived the worsening health conditions, and/or early recognition of dengue symptoms as a potential life-threatening condition. In the study in Malaysia, QoL measured on a daily basis enabled researchers to follow the decrease in the condition of the patient with dengue from the beginning of symptoms until the third to fifth day of the disease.²² In addition, our results suggested that there is prolonged period of impairment during illness in hospital and ambulatory settings. Patients self-rated their general health status as bad/very bad for a median of 8.0 days for ambulatory patients and 9 days for hospitalized patients.

Similarly, the prolonged duration of symptoms beyond the acute febrile phase (5–6 days) was also reported in patients from Nicaragua,⁴² Panama,²⁰ and Malaysia.²² When using a visual analog scale for health state valuation, we found that mean values during the dengue episode were close to death levels, pointing out the low health state in both settings, and were significantly lower for hospitalized patients (median = 10) than for ambulatory patients (median = 20). These low QoL values are somewhat below the means reported by dengue patients in Malaysia.²² The difference from the study in Malaysia may be related to the methods used. Our study reported the lowest value of each patient, and the study in Malaysia reported mean values by day. Because evolution of illness varies by patient, the lowest point reported in the study in Malaysia does not necessarily represent the lowest point of every patient.

Some methods issues regarding the analytic approach using PCA should be mentioned. First, this method is partly exploratory for finding patterns and scores for data with multiple dimensions such as in this study.^{37,43} Factor analysis has been applied extensively to simplify data on QoL in other fields²⁷ and in the general population.²⁹ In the present study, this type of analysis seems appropriate in evaluating perceptions of dengue patients. The PCA approach used in this study reduced the variables to five principal components that captured diverse dimensions of QoL. The questions related to cognition (concentration and remembering) and interpersonal activities (personal relationship/community participation) were combined as component 1 and questions related to sleep and energy with affect issues (feeling sad, low, and depressed) were combined as component 2. Questions related to visual impairment were not included in the analysis because substantial data were missing. When QoL scores were stratified by recruitment settings, hospitalized patients were more prone to be affected in dimensions related to cognition (component 1), self-care (component 4) and pain and discomfort (component 5) than ambulatory patients. Although there were no statistically significant differences between the two groups for other dimensions, scores were always greater for the hos-

pitalized patients, which suggested a worse health perception in this group.

Worse health perceptions were related to more severe dengue cases when analysis was restricted to the subset of hospitalized patients, except in the domain of cognition. One difficulty in interpreting these findings may be related to a certain degree of misclassification of dengue severity.⁴⁰

Our study included only dengue patients seeking health care. Because this study was not a population-based study, we did not include persons with acute dengue infections who did not seek care because of asymptomatic infections, mild symptoms, or lack of access to care. A previous study in Brazil found that approximately 50% of infected persons had inapparent or subclinical infections.⁴⁴ In Southeast Asia, this proportion ranged from 53%⁴⁵ to 90%.⁴⁶ However, these subclinical infections would not have entailed any substantial loss in QoL. The multiplicity of settings in ambulatory and hospital settings and in the public and private sector in central Brazil indicated that we enrolled participants from diverse socioeconomic and educational levels, as described.²⁴ We are aware that this study is constrained by a convenience sample that was not necessarily representative and that a population-based study would have been more desirable. However, population-based studies are costly and commensurate resources were not available. Despite these limitations, the current study participants parallels the epidemiologic dengue pattern in Brazil, where adults are the most affected age group and classical DF is the predominant form of disease.^{11,17,41}

We acknowledge that the extrapolation of our results to other settings should be made cautiously because the epidemiology of dengue varies across Brazil and other countries. Although outside the scope of the current investigation, a comparison of our results with a QoL evaluation of the general population would further help quantify the net impact of dengue. Our results showed that a dengue episode imposes a prolonged period of physical and mental impairment with an impact on QoL for hospitalized and ambulatory patients. These findings are particularly noteworthy because most participants were classified as having DF, which in clinical practice is considered the more benign spectrum of the disease.

This investigation has documented the generally poor QoL during a dengue episode in adolescents and adults in central Brazil. The factor analysis suggests that a major reason for this finding is the large number of domains affected. The lower QoL among hospitalized patients is consistent with a greater number of domains affected.

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