

## Self-Reported Outcomes of Mexican Multiple Sclerosis Outpatients and their Impact on Quality of Life Status

**Brenda Bertado-Cortés<sup>1\*</sup> and Luis Enrique Molina-Carrión<sup>2</sup>**

<sup>1</sup>Centro Médico Nacional "Siglo XXI" Instituto Mexicano del Seguro Social, Mexico City, Mexico

<sup>2</sup>Centro Médico Nacional "La Raza", Instituto Mexicano del Seguro Social, Mexico City, Mexico

**\*Corresponding Author:** Brenda Bertado-Cortés, Centro Médico Nacional Siglo XXI, Instituto Mexicano del Seguro Social, Mexico City, Mexico.

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### Abstract

**Introduction:** Multiple sclerosis is a frequent cause of disability that produces physical and psychological disorders in young people. This demyelinating disease significantly impacts on quality of life of patients attenuating their daily life activities. There are few reports focused on correlating physical and psychological comorbidities and pharmacotherapy with quality of life status in the Mexican population. We aimed to describe major clinical, physical, and psychosocial characteristics of MS, which attenuate the quality of life of outpatients from two Mexican third-level medical centers.

**Materials and Methods:** An observational, cross-sectional, retrospective study was performed by applying a self-reported QoL assessment survey (FAMS) in Mexican MS outpatients. A correlation analysis for determining the association between different physical, emotional, clinical, and treatment aspects of MS and quality of life was made.

**Results:** Ninety-six questionnaires from both medical centers were collected. Of the total population, 64% were female patients with a mean age of 38 ( $\pm 12$ ) years old. The median time of diagnosis (years) and the first disease-modifying therapy onset was 7.5 ( $\pm 5.0$ ) years. Dimensions with highest impact on quality of life were emotional well-being ( $r_p = -0.829$ ,  $p < 0.0001$ ), fatigue ( $r_p = -0.807$ ,  $p < 0.0001$ ), symptoms ( $r_p = -0.774$ ,  $p < 0.0001$ ), and additional concerns ( $r_p = -0.861$ ,  $p < 0.0001$ ), such as urinary symptoms, polyuria, depression, and drug-associated adverse events.

**Conclusion:** MS significantly affects the quality of life of sufferers. Depression, urinary symptoms, sleep disorder, and adverse events were the most attenuating conditions for these patients.

**Keywords:** Multiple Sclerosis; FAMS; Quality of Life; Cross-Sectional Studies; Health Surveys

### Abbreviations

MS: Multiple Sclerosis; QoL: Quality of Life; MSFI: Multiple Sclerosis International Federation; FAMS: Functional Assessment of Multiple Sclerosis; EDSS: Expanded Disability Status Scale; NEDA: No Evidence of Disease Activity; DMT: Disease-Modifying Therapy; HRQoL: Health-Related QoL

### Introduction

Multiple Sclerosis (MS) is the first cause of non-traumatic disability in young adults affecting twice more females than males. This condition commonly arises between 20 and 40 years old [1]. A little about the clinical evolution of MS could be predicted. Several patients show remarkable physical and psychological disorders affecting the quality of life [2,3]. Multiple Sclerosis International Federation (MSIF) reported a global prevalence of 30-33 out of 100,000 individuals, which increased from 2008 to 2013 [4]. In Mexico, available epidemiological reports have shown an estimated prevalence of 11 - 13 out of 100,000 individuals. However, this estimation does not reflect a real scenario since it was calculated in a limited region across Mexico [5-7].

Since 1996, World Health Organization has defined quality of life (QoL) as “an individual’s perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns”. This perception might be modified by the physical and psychological health status, degree of independence, and social relationships of the patient [8]. MS is characterized by a broad diversity of signs and symptoms associated with QoL, such as cognitive disorders, fatigue, spasticity, gait alterations, weakness, depression, and anxiety [2].

Recently, there have been many advances in MS diagnosis and treatment strategies. Therefore, treatment goals need to be assessed considering the reduction of relapses and the risk of disease worsening [1]. In this context, one of the composite clinical outcomes which assess disease progression rate considering relapses, disease progression by Expanded Disability Status Scale (EDSS), and magnetic resonance imaging (T2 and gadolinium-enhancing lesions) is called “no evidence of disease activity” or NEDA [9]. As we can see, this parameter only considers clinical and imaging aspects by definition. However, these criteria should be expanded since QoL is essential to ascertain whether a patient achieved NEDA as possible [10].

It should be noted that clinical trials of many disease-modifying therapies (DMT) have included patient-reported clinical outcomes. These results are perceived as factors that directly affect QoL measurement, so making a better understanding of the health-related impact of MS and new therapies [1,11].

One of the most common symptoms of MS is fatigue, which affects up to 90% of patients and their daily activities [3]. Moreover, fatigue is considered the most disabling symptom of MS [12]. The Multiple Sclerosis Society of Great Britain defines it as “an overwhelming sensation of tiredness for no apparent reason” [13]. Fatigue seems to be different in healthy than sick people. This condition may limit interpersonal relationships and even affect working performance. It has been estimated that up to 50% of MS patients have lost their jobs within 3 years due to fatigue [14]. A recent retrospective study of a large MS population (n = 10,849) showed that the employment rate could be affected up to 8 years before diagnosis. This value could be increased after diagnosis confirmation [15].

Other conditions as cognitive disorders (affecting memory, sustained attention, verbal fluency, conceptual reasoning, and visual-spatial perception) are also common in MS patients. It has been estimated that 40-70% of the MS population suffers cognitive alterations [16]. Several studies suggested that these alterations are associated with depression, and depression itself is associated with working memory, executive function, and information-processing speed [17-19]. However, evidence of the association between psychiatric comorbidities as depression and anxiety is scarce [16].

Finally, sleep disorders are also prevalent in MS patients. It has been mentioned that these alterations should be considered as significant factors on QoL assessment, particularly among economically active patients. Despite clinical trials, commonly do not take into account sleep disorders [20].

### Aim of the Study

The study aimed to characterize QoL-associated conditions in MS outpatients attended in two third-level medical centers (Siglo XXI and La Raza) to understand how MS impacts the psychological and physical features of this population.

### Materials and Methods

#### Design and subjects

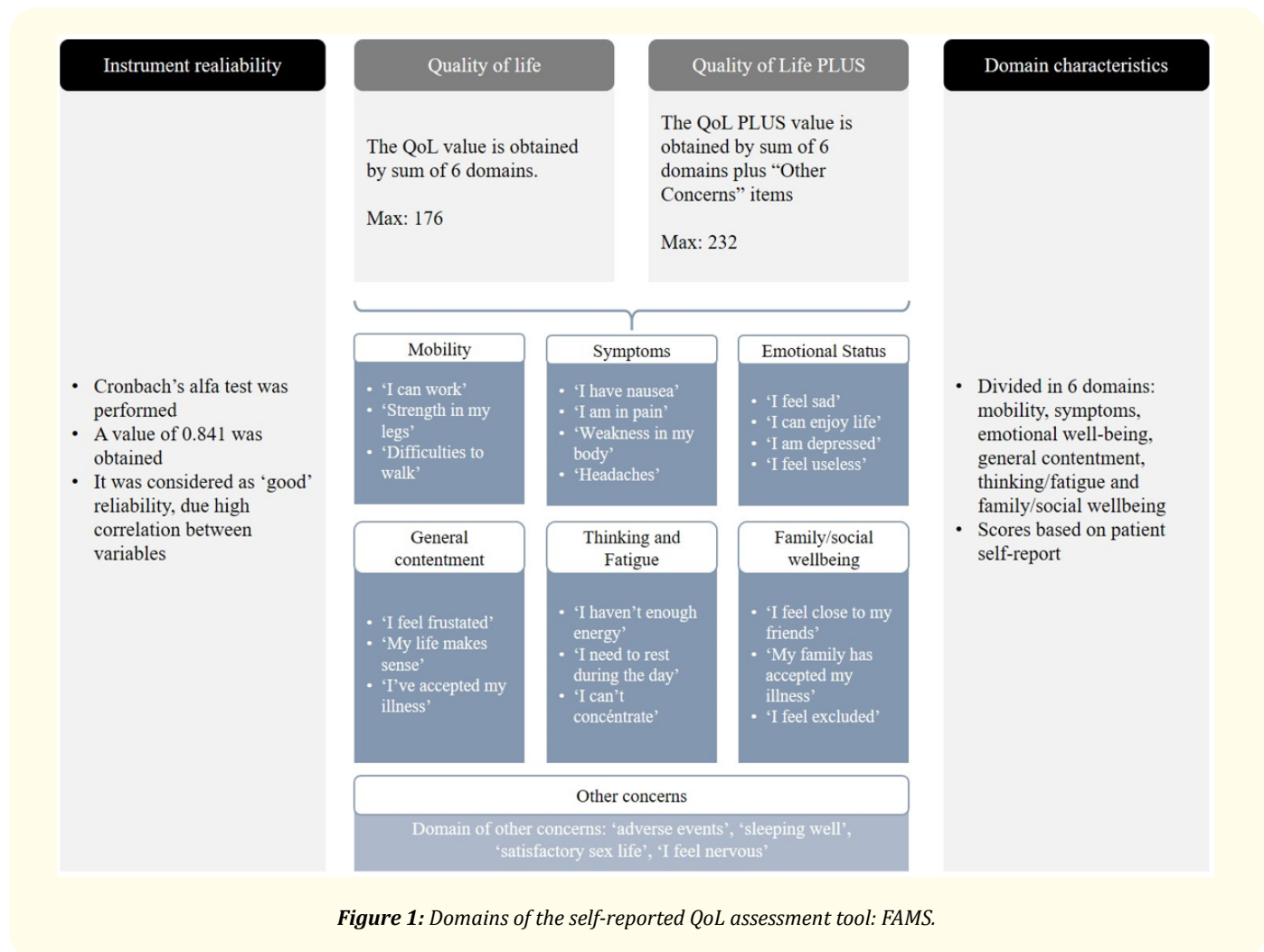
This study was an observational, cross-sectional, retrospective study performed by a self-report survey on outpatients diagnosed with MS. When the survey was applied to participants, all these patients had an effective registration number at any of these two Mexican medical centers.

The subjects included in this study were MS-diagnosed outpatients treated in any of these medical centers, at least one ongoing DMT, and literates. Patients with some physical or neurological disability that completely counteracted the survey were excluded. Any questionnaire with less than 50% answered items were discarded.

**Assessment instrument**

The instrument used to evaluate outpatients’ QoL was the FAMS survey (use permissions were granted), a questionnaire designed to generate MS patient self-reports. This tool allows us to assess health-related QoL (HRQoL) by 44 questions organized into 6 domains related to QoL: mobility (6 items), symptoms (7 items), emotional wellbeing (7 items), general contentment (7 items), thinking/fatigue (9 items), and family/social wellbeing (7 items). This survey also includes 15 additional items that fall outside of the six domains but may provide valuable information to the clinician [21].

A Cronbach’s alpha test was performed to determine the instrument’s reliability. This parameter’s value was 0.841, corresponding to ‘good’ reliability due to the high correlation between the studied variables (Figure 1).



## Participants

All survey participants were MS diagnosed outpatients who participated in the World Multiple Sclerosis Day event performed in Siglo XXI National Medical Center (CMSXXI) and La Raza National Medical Center (CMLR). The questionnaire was given to each assistant when arriving at the event and collected at the end. When the event was taking place, a time interval was scheduled for answering the survey. Finally, both researchers pooled the questionnaires to qualify and analyze data.

## Statistical analysis

A descriptive statistical analysis of collected and analyzed questionnaire data was performed. All FAMS scores of each assessed domain were reported as mean  $\pm$  standard deviation (SD) with a 95% confidence interval.

We also performed a correlation analysis between the calculated total QoL and each item score. The Pearson correlation coefficient (rp) was calculated for each questionnaire item.

## Results and Discussion

Ninety-six questionnaires were collected from both study centers. Of the total population, 64% were females with a mean age of 38 ( $\pm$  12) years. The majority of participants were high-school or college graduates (high school: 31.9%, BA: 40.4%, postgraduate: 10.6%). About 91% of the participants did not report smoking behavior (Table 1).

Variables	N (%)
Age, mean (SD)	38 (12)
Gender*	
Female	59 (64)
Male	34 (36)
Study center	
Siglo XXI (CMSXXI)	55 (57.3)
La Raza (CMLR)	41 (42.7)
Educational level	
Elementary	1 (1.06)
Junior high-school	10 (10.63)
High-school	30 (31.94)
BA	37 (40.4)
Post-graduate	10 (10.63)
Other	5 (5.3)
Smoking	
Yes	8 (9)
No	80 (91)

**Table 1:** Demographic data of the outpatient population.

SD: standard deviation, \*Patient gender in three cases (n= 93) was not reported.

Time of diagnosis and time of the first DMT onset was 7.5 years for both parameters. Also, patients reported receiving two therapies in this period (Table 2).

Parameter	Study center	Mean (SD)
Time from start to diagnosis		
How long ago were you diagnosed with MS?	CMSXXI	7 (5)
	CMLR	8 (7)
	Total	7.5 (6)
Time with disease-modifying therapies (DMT)		
How long ago did you start therapy for MS?	CMSXXI	7 (5)
	CMLR	8 (6)
	Total	7.5 (6)
Number of DMTs received		
How many MS therapies have you tried?	CMSXXI	2 (1)
	CMLR	2 (1)
	Total	2 (2)

**Table 2:** Characteristics of disease onset and therapeutic management.

SD: Standard deviation; CMSXXI: Siglo XXI Medical Center; CMLR: La Raza Medical Center; MS: multiple sclerosis.

The calculated scores for each assessed domain show that the mean total QoL of the patients was  $111 \pm 30.3$ , or almost 65 points less than the score’s maximum value. The domains which affected largely the total QoL were: mobility (17.71 of 28, difference = 10.29), general contentment (17.89 of 28, difference = 10.11), family/social wellbeing (17.97 of 28, difference = 10.03), and thinking/fatigue (19.07 of 36) (Table 3).

Parameter	Mean (SD)	Scoring value interval †	Difference*
Mobility	17.71 (5.1)	(0-28)	-10.29
Symptoms	19.04 (6.5)	(0-28)	-8.96
Emotional wellbeing	19.62 (6.7)	(0-28)	-8.38
General contentment	17.89 (6.1)	(0-28)	-10.11
Thinking/fatigue	19.07 (8.4)	(0-36)	-16.93
Family/social wellbeing	17.97 (6.2)	(0-28)	-10.03
Other concerns (additional)	33.31 (8.0)	(0-56)	NA
QoL for MS patients**	111.01 (30.3)	(0-176)	-64.99

**Table 3:** Quality of life levels and their domains in MS patients.

\* The result of the calculated average minus the maximum value of the interval representing the maximum QoL. Negative values represent scores under the maximum value. \*\* Sum of all assessed domains, except Other concerns. † Reference values reported by Yorke and Cohen (21).

Correlation analysis between each FAMS domain and total QoL showed a significant inversely proportional correlation. The domains most affected were emotional wellbeing (rp = -0.829, p < 0.0001, n = 96), fatigue (rp = -0.807, p < 0.0001, n = 94), and symptoms (rp = -0.774, p < 0.0001, n = 96) (Table 4).

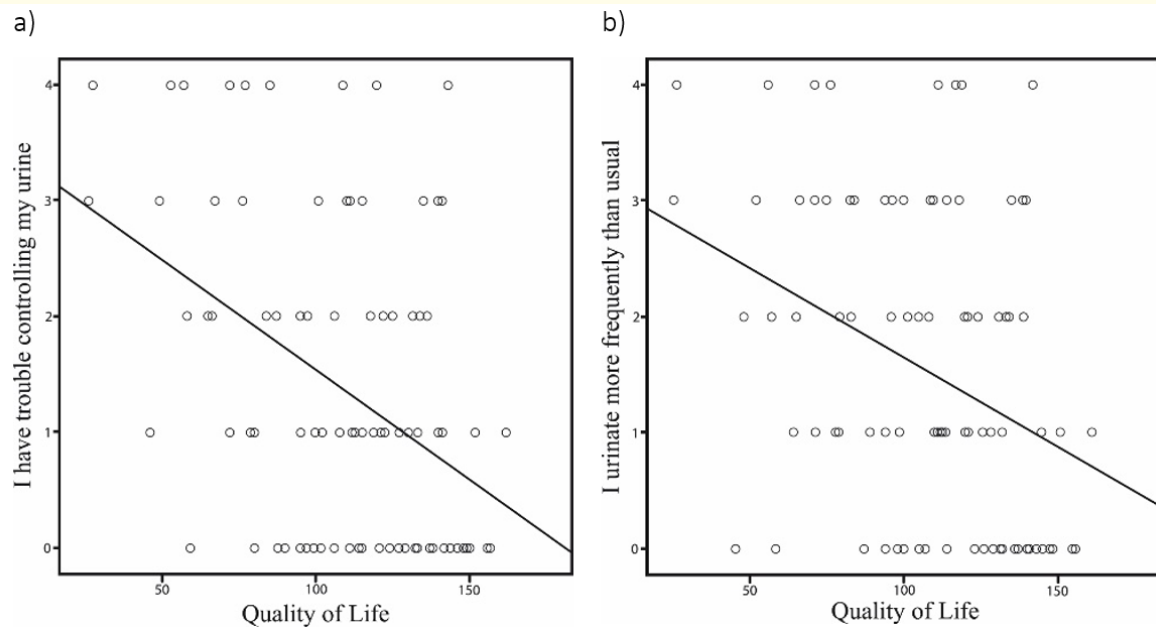
QOL	Mobility	Symptoms	Emotional Wellbeing	General Contentment	Fatigue	Family	Other Concerns
Total	-0.650†	-0.774†	-0.829†	-0.684†	-0.807†	-0.683†	N/A
PLUS	-0.632†	-0.809†	-0.836†	-0.656†	-0.799†	-0.642†	-0.861†

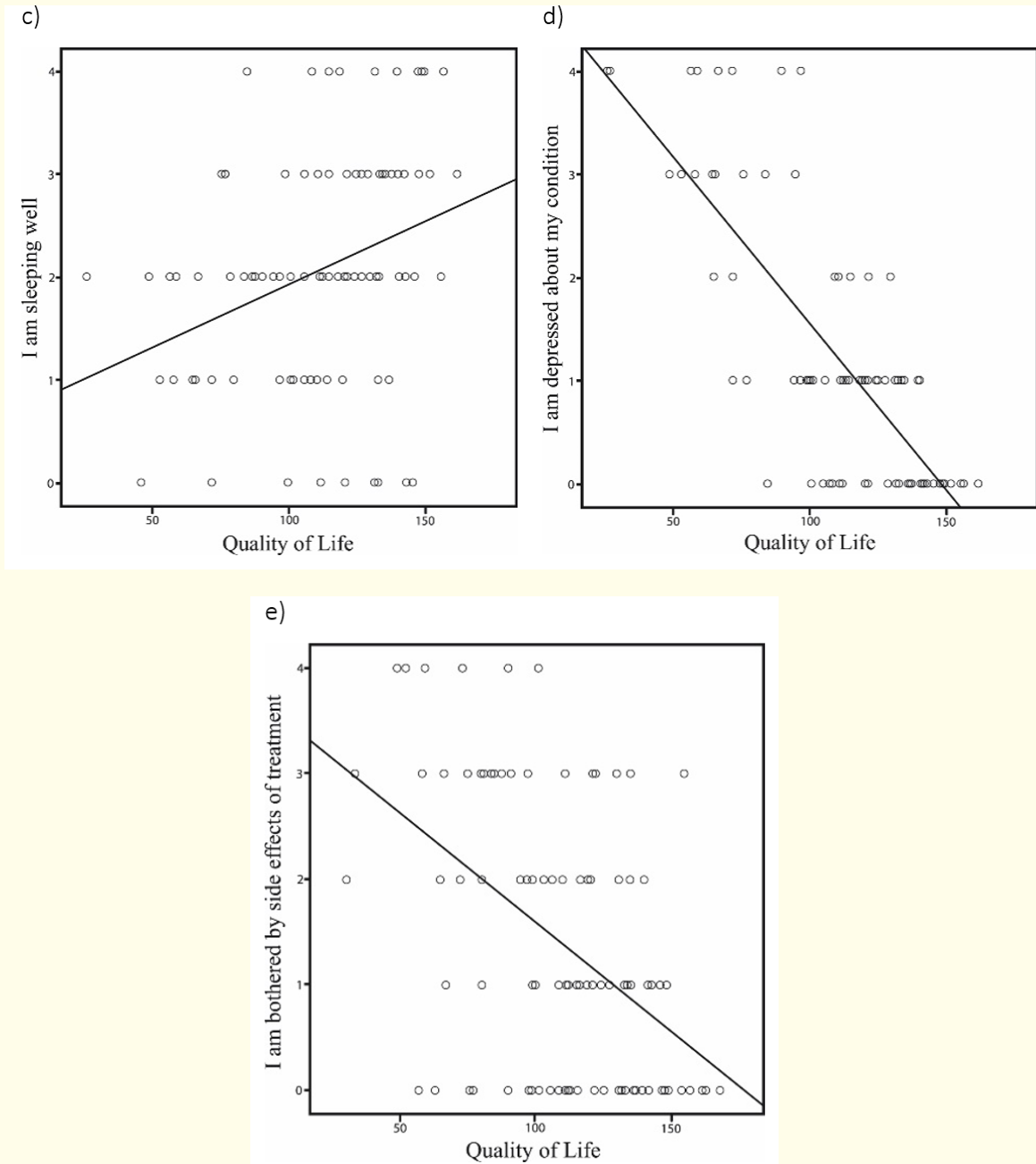
**Table 4:** Pearson’s correlation coefficients of the FAMS domains and QoL (total and PLUS).

Note: N/A, not applicable. \* p<0.05, † p<0.0001.

When considers the “Other concerns” domain (QoL Plus outcome), we found that there is also a significant inversely proportional correlation for QoL (rp = -0.861, p < 0.0001, n = 95). Therefore, a most detailed analysis to identify which single item is inducing this loss of QoL was performed.

It was found that urinary symptoms [urinary incontinence (rp = -0.465, p < 0.0001, n = 94) and polyuria (rp = -0.399, p < 0.0001, n = 93)], depression (rp = -0.785, p < 0.0001, n = 95), and adverse events (rp = -0.485, p < 0.0001, n = 91) were the most correlated items. However, there was a negative correlation between sleep disorders (rp = -0.323, p < 0.01, n = 93) and QoL (Figure 2).





**Figure 2:** Correlation plots for QoL and selected items associated with urinary symptoms (a, b), sleep disorders (c), depression (d), and drug-associated adverse events (e).



To the best of our knowledge, this study is the first one that uses the FAMS survey to measure and correlate physical and psychological characteristics of MS patients with QoL. This questionnaire includes specific questions within the International Classification of Functioning, Disability, Health, Activities, Participation, and Environmental Factors issued by the World Health Organization [21]. One of the most important findings of this study was that domains related to psychological and social status significantly affect QoL. Also, domains associated with daily life activities (thinking, fatigue, and mobility) were involved in less wellness.

It is well known that a decrease in QoL of patients with autoimmune diseases is common, independently of the affected site or organ. Recently, Janik, *et al.* reported that the HRQoL assessed with SF-36 was considerably affected in autoimmune hepatitis patients, mostly due to physical fatigue, depression, and anxiety [22]. Another study showed that physical and mental components are significantly more affected in autoimmune diseases than in other conditions [23]. Also, a survey applied to systemic lupus erythematosus patients in the United Kingdom reported that almost two-thirds of the patients had problems limiting their ability to carry out daily activities. Moreover, the survey found that only 15% of this population had a full-time job [24].

For this reason, MSIF established seven principles based on experiences collected from MS patients. Overall, these principles promote the right to access effective treatments, transport services, financial resources, working opportunities, and equity policies, as well as social support (from family, partners, and friends) [25].

The patient self-reported health status is a complex evaluation based on daily and first-hand experience of a disease. One useful tool to evaluate this experience is the 36-Item Short-Form Health Survey (SF-36), a simple instrument that measures two basic concepts of patient health status: physical and mental status. This survey helps identify QoL parameters with simple questions. However, it does not consider other essential parameters in MS patients, such as adverse events, satisfaction in sex life, and sleep disorders [26].

It is pivotal to understand and describe no clinical aspects that impact HRQoL since this information should be a background for healthcare policies, clinical guidelines, etc. Unfortunately, Mexico has lacked comprehensive investigation around QoL outcomes in MS patients. Only one study showed evidence of coping strategies, and QoL applied to MS. Hernández-Ledesma, *et al.* reported a cross-sectional clinical trial ( $n = 26$ ) where assessed QoL, the use of coping strategies, and their relationship with other physical and psychosocial factors. This study showed that coping strategies most commonly used by individuals are problem-solving, hope, social support, and emotions based on positive strategies. It is crucial to notice that stress-coping strategies positively correlate with the patients' physical and psychosocial factors [3]. Based on these outcomes, it could be that the Mexican population has a significant difference between perception and self-management of the disease, as compared with communities in other countries. That could be due to the socio-cultural environment of Mexican people, which overlooks stressful situations or engages in spiritual practices. This situation could help them to endure a current unhealthy situation [27]. Resilience might explain why there is a low correlation between mobility, general contentment, and family domains with QoL (Table 4). It should be noted that some aspects prevail on these people, such as self-sufficiency, acceptance, satisfaction, and perception of daily life.

Our study also evaluated other items that let us know more about the essential aspects of drug-associated adverse events, sex life, sleep disorders, and comorbidities as spasticity and urinary symptoms [21]. Recently, a prospective study showed that more than half of an MS cohort (about 55%) reported low-quality sleep was reported. Therefore, sleep disorders correlate with fatigue and impaired functional health status [28]. However, MS-associated fatigue could be associated with the autonomous nervous system impairments independent



of sleep quality, even early disease [29]. Also, fatigue intensity is negatively associated with low performance in sexually active women, as reported previously [30]. More studies are needed to confirm these findings.

On the other hand, a real-life study (Teri-PRO), which reports patient-reported outcomes changes after treatment switching for 2-year follow-up, showed that treatment switching (injection to oral DMT) could change patient satisfaction [31]. This evidence is related to our findings since QoL measurement decreased when the patient reported drug-associated adverse events during its therapy. However, our study is limited due to insufficient clinical data, the information was only from two public institutions, and it is not a representative cohort.

### Conclusion

This study showed significant evidence on QoL outcomes of Mexican MS patients by the self-reported FAMS survey. Urinary symptoms, sleep disorders, depression, and drug-associated adverse events were the most attenuating factors. Therefore, clinical strategies and practice guidelines for MS should be reformed to attend to all unmet needs since this disease is not controlled only by prescribed medicines. A multidisciplinary healthcare team should be comprised of neurologists and health specialists for any condition described above. This study contributed to generating updated knowledge about the implications of mental and physical features in QoL.

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### Conflict of Interest

The authors declared no conflicts of interest.

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