



## Disease burden, management patterns and multidisciplinary clinical approaches for patients with MPS IVA and VI in selected Latin American Countries

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### ABSTRACT

**Background:** There is a paucity of real-world epidemiological data on patients with mucopolysaccharidoses (MPS) in Latin America. This real-world study assessed the disease burden, management patterns and multidisciplinary clinical approaches for MPS-IVA and MPS-VI patients in Latin America (Colombia, Ecuador, Mexico, Peru).

**Methods:** Data were collected from physicians/specialists experienced in treating MPS patients between April–June 2020, via an online patient-diary survey.

**Results:** Overall, 29 physicians/specialists participated in this study. Data from 98 patients were analyzed (MPS-IVA, 71 patients and MPS-VI, 27 patients). Mean age for MPS-IVA patients was 17.5 years and for MPS-VI patients was 11.6 years, and the majority were females (52% and 78%, respectively). MPS-IVA and VI patients presented a high absenteeism from school (55% and 37%, respectively; <18 years age) and workplace (78% and 100%, respectively; >18 years age), indicating an impact of the disease on some aspects of the patients' quality of life. The onset of the first symptom occurred at the age of 3.1 years for MPS-IVA patients and at 1 year for MPS-VI, with delay in diagnosis (3.5–3.9 years from symptom onset) and enzyme replacement therapy (ERT) initiation (1.1–3.6 years from diagnosis). ERT interruptions were observed for MPS-IVA (48%) and MPS-VI patients (44%), with non-availability of medication recorded as the main reason for non-adherence (46% and 60% patients, respectively). ERT showed noticeable treatment benefits in MPS-IVA/VI patients, with stabilization/reduction in complications or the number of surgeries. A multidisciplinary clinical team approach was used for patient management.

**Conclusion:** The disease burden for MPS-IVA/VI was high in Latin America, with consistent management, treatment and socio-demographic trends throughout the region.

### 1. Introduction

Mucopolysaccharidoses (MPS) are a group of inherited, progressive metabolic disorders, caused by the deficiency of lysosomal enzymes, which are needed for glycosaminoglycan (GAG) breakdown [1]. Although the global prevalence of MPS is low (1/16,000–30,000 births), the disease is a major public health issue, due to the life-threatening

complications and associated premature deaths [1]. MPS pathophysiology is marked by a progressive accumulation of undegraded GAGs in the organs, resulting in cellular damage and deterioration of vital functions [2,3]. Mucopolysaccharidosis type IVA (OMIM # 253000; also known as Morquio syndrome A [MPS-IVA]) and mucopolysaccharidosis type VI (OMIM # 253200; also known as Maroteaux–Lamy syndrome [MPS-VI]) are subtypes of MPS, which manifest as somatic symptoms

**Abbreviations:** ERT, Enzyme replacement therapy; GAGs, glycosaminoglycans; MPS, Mucopolysaccharidoses; MPS-IVA, Mucopolysaccharidosis type IVA or Morquio syndrome A; MPS-VI, mucopolysaccharidosis type VI or Maroteaux–Lamy syndrome; QoL, quality of life.

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with normal cognitive development [4,5]. MPS-IVA and VI are caused by the lack of enzymes, *N*-acetylgalactosamine-6-sulfatase and *N*-acetylgalactosamine-4-sulfatase, respectively. Both MPS-IVA and VI are associated with a severely compromised quality of life (QoL), reducing the patients' ability to perform their normal day-to-day activities [6].

The onset of MPS symptoms may occur at any age, from early childhood to adolescence or sometimes, even in the second decade of life, depending on the phenotypes (rapidly or slowly progressing). Patients with severe phenotypes usually live only up to their second/third decade of life [7,8]. Symptoms typically include, severe joint pain, skeletal abnormalities, restricted range of motion, spinal cord compression, and increased intracranial pressure. MPS patients develop severe complications, such as impaired vision/hearing, cardiorespiratory disease, pulmonary impairment, and degenerative joint disease. They may also require frequent surgical procedures. Apart from the symptoms stated above, patients with MPS-IVA/VI also manifest psychological and behavioral changes, which may negatively impact their interpersonal functioning, emotional status, self-esteem, social life, school attendance and employment [6,9,10].

Early identification of signs/symptoms is critical in the management of degenerative disorders like MPS, especially to facilitate an early diagnosis and initiate appropriate treatment paradigms. Health-related QoL tools should be used to capture the symptoms, functioning or QoL, which would help identify the early signals and thereby control the negative effects of the disease [6]. According to the MPS guidelines, a multidisciplinary management approach, involving regular follow ups, is effective in managing or avoiding complications [9,10].

Although newer therapeutic approaches like hematopoietic stem cell transplantation (HSCT) are available for some types of MPS, they are not frequently used in Latin America [11–18]. Also, the benefit-to-risk profile of HSCT is less evident in MPS-IVA/VI patients compared with that in patients with other types of MPS [9,10]. Currently, HSCT is the preferred treatment option in patients with MPS 1H because of its potential to improve cognitive symptoms, which are not successfully managed by enzyme replacement therapy (ERT). However, unlike MPS 1H, cognitive deficits are uncommon in patients with MPS-IVA/VI, and hence, ERT is the treatment of choice in MPS-IVA/VI patients [9,10].

ERT has proven to be clinically effective in MPS patients, demonstrating an improvement in their range of motion, respiratory functions, cardiac functions, hearing, visual acuity, pain control and QoL [19–21]. Currently, elosulfase alfa and galsulfase are the only licensed ERT for patients with MPS-IVA and MPS-VI, respectively [22–26].

This study was performed to assess the real-world clinical approach in the management of patients with MPS-IVA and MPS-VI under ERT in Latin America (Colombia, Mexico, Ecuador and Peru). The study objectives were to assess (i) the disease burden and management patterns, (ii) multidisciplinary clinical approaches, (iii) socio-demographics and characteristics, and (iv) treatment outcomes. Data were collected via an online patient-diary survey, which is a relevant tool to leverage the real-world evidence, especially during the current COVID-19 pandemic.

## 2. Material and methods

### 2.1. Subjects and study design

Data were collected from the physicians/specialists experienced in treating patients with MPS-IVA/VI, via a patient-diary survey (MPS-IVA/VI specific). Due to the current COVID-19 scenario, physicians/specialists were recruited either via telephonic or web-based interviews. Online interviews were conducted between April and June 2020. The physicians/specialists randomly selected a pre-defined number of patients undergoing ERT. A multiple-choice survey questionnaire was circulated among physicians, to collect data on physicians' and patients' socio-demographic profiles, and patients' clinical profiles, treatment journey i.e., time from birth to the first symptom, diagnosis and ERT treatment in the previous year. Furthermore, data on patients' schooling

or working status, adherence to or interruptions in ERT treatment (in rural and urban areas) and treatment outcomes in terms of occurrences of complications and surgeries (age stratified), and multidisciplinary approaches used, were also assessed. The physicians reported a questionnaire-based report for each patient in an anonymous patient chart, placed on the web-based portal protected by IQVIA.

### 2.2. Statistical analysis

Data were summarized descriptively as absolute numbers and percentages (%) for categorical variables, and by measures of central tendency for continuous variables. Percentages were calculated over the number of patients with available (non-missing) data.

## 3. Results

### 3.1. Socio-demographics

Twenty-nine physicians/specialists participated in the study. The data were collected for 98 patients, of which, 71 had MPS-IVA (Colombia = 58; Mexico = 13) and 27 had MPS-VI (Colombia = 15; Mexico = 9; Ecuador = 2; Peru = 1) (Table 1A, B; Suppl. Table 1). On an average, the participating physicians had treated at least 3 MPS-IVA patients and 1.1 MPS-VI patients in the previous year. Here, we present overall data from the four Latin American countries, as well as specific trends from Colombia and Mexico. Since the data from Ecuador and Peru were insufficient, the country-specific clinical patterns in those countries could not be evaluated.

The overall mean age of MPS-IVA and MPS-VI patients was 17.5 years and 11.6 years, respectively. The patients from Mexico were comparatively younger than those from Colombia (MPS-IVA: 9.69 versus 19.3 years; MPS-VI: 9 versus 13.9 years) (Table 1B; Suppl. Table 2). In total, 38% of MPS-IVA and 19% of MPS-VI patients had siblings who had the same illness (most had 1 affected sibling). Most of the patients lived in urban areas (71%, MPS-IVA; 56%, MPS-VI). The two disease groups had similar socio-demographic profiles in general (Table 1B; Suppl. Table 2).

### 3.2. MPS-IVA

#### 3.2.1. Life in society

Of the total patients with MPS-IVA ( $N = 71$ ), 45% attended regular school. Among those, 59% were in the elementary grade (Table 2A; Fig. 1A). Colombia had a higher rate of school nonattendance than Mexico (62% versus 23%) (Suppl. Table 3). The common reasons for nonattendance were 'personal decision' (54%), and 'disease burden' (33%). Only 5% went to schools for students with special needs (all from Colombia). Among the 28 patients aged  $\geq 18$  years (all from Colombia), 22 did not attend work, owing to their 'disease burden' (64%). Among the 6 patients who attended work, one-third required workplace adaptations (Table 2A).

#### 3.2.2. Patients journey, treatment and multidisciplinary approach

The onset of the first symptom occurred at a mean age of 3.1 years and diagnosis occurred at a mean age of 7.0 years. The mean time from diagnosis until the first ERT infusion was 3.6 years (Table 2A). The average time from symptom to diagnosis and from diagnosis to the first ERT infusion was longer for patients in Colombia than for those in Mexico (4.2 and 3.7 years versus 2.6 and 3.4 years, respectively) (Suppl. Table 3). However, the stratified analysis showed that the mean time from MPS IV-A diagnosis until the first ERT infusion decreased after the commercial availability of ERT (0.7 years and 1.8 years for patients from Colombia and Mexico, respectively) (Suppl. Table 3).

The use of concomitant medications was minimal (18%) in MPS-IVA patients. The most frequently prescribed drugs were respiratory (46.2%), analgesic (38.5%) and cardiovascular medications (30.8%)

**Table 1**  
Physician profile and patient characteristics.

A. Physician profile		
	Total number of physicians	
	N = 29	
Specialty		
Geneticists	86.2%	
Pediatricians	6.9%	
Pediatric Neurologist	3.4%	
Pediatric Orthopedic	3.4%	
Years of experience (excluding residency)		
Average years of experience	17.4	
<10 years	24%	
10–<20 years	37%	
20–<30 years	17%	
30–<40 years	17%	
>40 years	3%	
Place of attendance	Private	Public
Overall	67%	33%
Office	16%	2%
Hospital	35%	27%
Reference center	17%	3%
B. Patients characteristics		
	Patients with MPS-IVA	Patients with MPS-VI
	N = 71	N = 27
Gender		
Male/female (%)	48/52	22/78
Age, years (average)	17.5	11.6
% of patients stratified by age, years		
<5	9%	7%
5–12	39%	59%
13–17	11%	11%
18–24	13%	19%
25–29	17%	4%
>30	11%	—
Height, cm (average)	104 <sup>a</sup>	103
% of patients stratified by height, cm		
<80	1%	7%
80 to <100	47%	37%
100 to <120	34%	44%
>120	17%	11%
Weight, Kg (average)	24.2	21.7
% of patients stratified by weight, Kg		
<10	1%	4%
10 to <20	34%	52%
20 to <30	39%	26%
30 to <40	16%	15%
>40	10%	4%
Head Circumference (average)	53.4 <sup>b</sup>	52.5
% of patients by stratified by head circumference, cm		
<50	4%	15%
50 to <55	73%	59%
55 to <60	20%	26%
60 to <65	3%	—
Patients with siblings affected by same disease	38% <sup>c</sup>	19% <sup>d</sup>
Mean number of siblings	1.1	1.2
Patients having 1 sibling	89%	80%
Patients having 2 siblings	11%	20%
House location		
Urban	71%	56%
Rural	29%	44%

<sup>a</sup> MPS-IVA: N = 70.<sup>b</sup> MPS-IVA: N = 69.<sup>c</sup> MPS-IVA: N = 27.<sup>d</sup> MPS-VI: N = 5.

(Fig. 1B; Suppl. Fig. 1A). The number of emergency room (ER) visits was low (average: 0.52 visits/patient in the previous year). In all, 27% patients required wheelchair or ambulant support. Majority of the patients (~70–85%) underwent cardiac, ophthalmological, and pulmonary function examinations in the previous year (Suppl. Fig. 1B). The geneticists and orthopedists were the commonly involved specialties in the management of MPS-IVA patients (average: 2.25 and 1.51 patients treated in the previous year, respectively; Fig. 1C; Suppl. Fig. 1 C).

The overall annual ERT compliance rate was 48% (in the previous year). On average, the patients missed 9 ERT infusions over a period of one year. The interruptions were more frequent in rural than in urban areas (71% versus 44%). The most common reasons for missed infusions were 'availability of medication' (46% patients) and 'treatment access limitation' (30% patients) (Table 2B; Suppl. Table 4A, 4B). Patients in the rural areas took almost twice as long to reach the infusion center than those in cities. (average time: 2.1 versus 0.9 h). Similar trends were observed in Colombia. The patients living in the rural areas of Mexico took ~2–>4 h to reach the infusion center (Suppl. Table 4 A, 4B).

The burden of illness reduced following ERT treatment, per physician's report. The number of complications/surgeries declined or stabilized after the treatment. (Fig. 1D). There were no age-specific trends observed (Suppl. Table 5). The treatment patterns were consistent across Colombia and Mexico (Suppl. Fig. 1D). In Mexico, treatment with elosulfase alfa in patients with MPS-IVA was supported mainly by the public setting (85%). In Colombia, 43% used contributory and 57% used subsidized regimens.

### 3.3. MPS-VI

#### 3.3.1. Life in society

Of the total patients with MPS-VI (N = 27), 63% attended regular school (76% were in the elementary grade) (Table 2A; Fig. 1A). 'Family decision' and 'disease progression' were the main reasons for nonattendance. In Colombia, the rate of nonattendance was comparatively higher than that in Mexico (53% versus 22%) (Suppl. Table 3). None of the five patients aged ≥18 years (all from Colombia) attended work, justifying it as 'personal decision' (60%) or 'family decision' (40%) (Table 2A).

#### 3.3.2. Patients journey, treatment and multidisciplinary approach

The onset of the first symptom occurred at a mean age of 1.0 year and diagnosis occurred at a mean age of 4.5 years. The mean time from diagnosis to the first ERT infusion was 1.1 years (Table 2A). The average time from symptom to diagnosis and from diagnosis to the first ERT infusion were longer for patients in Colombia than those in Mexico (4.4 and 1.5 years versus 2.7 and 0.3 years, respectively) (Suppl. Table 3).

Approximately, 30% of the patients required concomitant treatments. The cardiovascular (62.5%) and respiratory (38.5%) medications were the most widely used drugs (Fig. 1B; Suppl. Fig. 1A). The number of visits to the ER was few (0.7/patient in the previous year). Few patients required wheelchair or ambulant support (7%). Most patients (~70–85%) underwent cardiac examinations, ophthalmological assessments and O<sub>2</sub> saturation in the previous year (Suppl. Fig. 1B). The geneticists, pediatricians, cardiologists and pneumonologists were the frequently involved specialties in the management of patients with MPS-VI (average: 2.04; 1.67; 1.52; 1.52 patients treated in the previous year, respectively; Fig. 1C; Suppl. Fig. 1C).

Overall, annual ERT compliance rate for MPS-VI patients was 44% in the last 12 months, with approximately 10 infusions missed on average in the past 1 year. The interruption rates were higher among patients in urban areas versus rural. 'Availability of medications' (60% patients) and 'personal decision' (20% patients) were the primary reasons cited by patients for missed infusions (Table 2A; Suppl. Table 4A, 4B). The time required to reach the infusion center was similar for patients who lived in rural and urban areas (1.5–1.7 h) (Table 2B). Both, in Colombia and Mexico, the patients took ~1–2 h to get to the infusion center (Suppl.

**Table 2**  
MPS-IVA and MPS-VI patients.

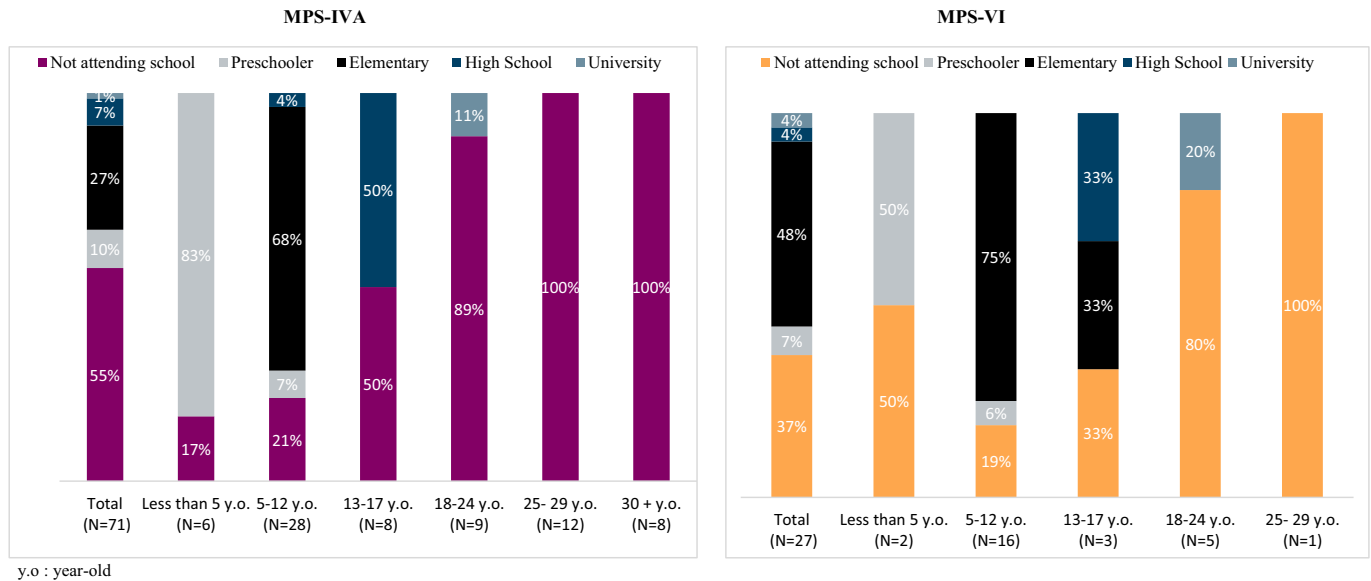
A. Personal profile, life in society and disease journey		
	Patients with MPS-IVA N = 71	Patients with MPS-VI N = 27
<b>School attendance</b>		
Patients attending school	45% <sup>a</sup>	63% <sup>a</sup>
Preschooler	22%	12%
Elementary	59%	76%
High school	16%	6%
University	3%	6%
Patients not attending school	55% <sup>b</sup>	37% <sup>b</sup>
Disease burden	33%	20%
Personal decision	54%	20%
Family decision	10%	60%
Economic reasons	3%	—
<b>Work attendance<sup>c</sup></b>		
Patients attending work	22% <sup>d</sup>	0%
Requiring workplace adaptation	33%	0%
Patients unable to attend work	78% <sup>e</sup>	100% <sup>e</sup>
Disease burden	64%	—
Personal decision	18%	60%
Family decision	18%	40%
Patients requiring caregiver assistance	49%	48%
Patients under national disability registry	68%	78%
<b>Patients journey</b>		
Total time of patient journey from birth to treatment, years	10.6	5.6
Average age at first symptom, years	3.1 <sup>f</sup>	1
Average age at diagnosis, years	3.9 <sup>g</sup>	3.5 <sup>g</sup>
Average time from diagnosis to first ERT infusion, years	3.6 <sup>h</sup>	1.1 <sup>h</sup>
Before ERT commercial availability	5.1 <sup>i, j</sup>	1.1 <sup>j, k</sup>
After ERT commercial availability	1.2 <sup>i, l</sup>	0.7 <sup>k, l</sup>

**B. ERT interruptions in the last year among MPS-IVA and MPS-VI patients.**

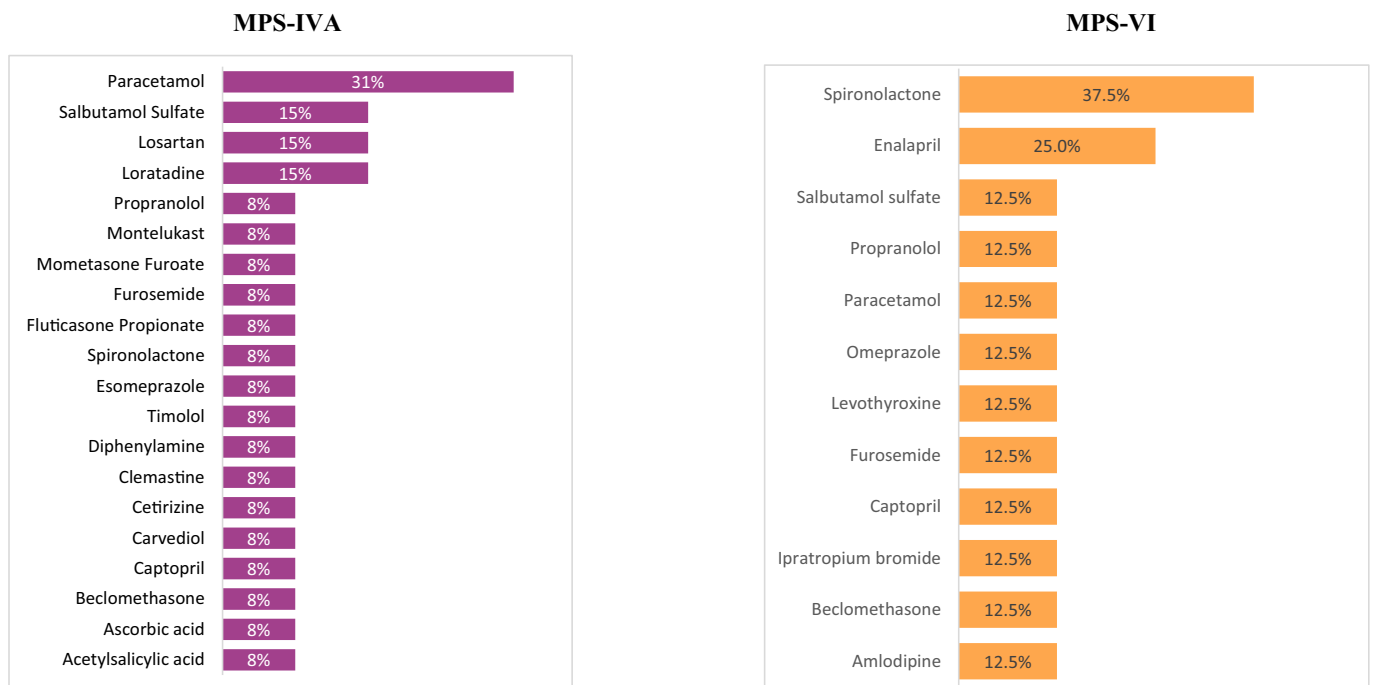
	ERT interruptions overall and stratified by house location (region)					
	MPS-IVA			MPS-VI		
	Overall	Urban	Rural	Overall	Urban	Rural
	N = 71	n = 50	n = 21	N = 27	N = 15	N = 12
% of patients with ERT interruptions in the last year						
Yes/No	52/48	44/56	71/29	55/44	67/33	42/58
Average (min-max) time to infusion center, hours <sup>a</sup>	1.4 (0.3–6.0)	0.9 (0.3–2.0)	2.1 (0.5–6.0)	1.5 (0.17–3.3)	1.5 (0.17–3.0)	1.7 (0.5–3.3)
% of patients stratified based on travel time to infusion center						
<1 h	49%	64%	27%	43% <sup>c</sup>	44%	40%
1 to <2 h	22%	23%	20%	21% <sup>c</sup>	22%	20%
2 to <3 h	19%	14%	27%	7% <sup>c</sup>	0%	20%
3 to <4 h	5%	—	13%	29% <sup>c</sup>	33%	20%
≥4 h	5%	—	13%	—	—	—
Average (min-max) of infusion missed in last 12 months <sup>b</sup>	9.1 (1–36)	8.4 (2–25)	10.1 (1–36)	9.9 (2–32)	8 (2–16)	13.8 (3–32)
Main reason for missing an infusion <sup>b</sup>						
Personal decision	14%	14%	13%	20%	10%	40%
Availability of the medication	46%	41%	53%	60%	60%	60%
Treatment access limitation	30%	27%	33%	7%	10%	—
Limitations in transportation to the center	3%	5%	—	—	—	—
Others	8%	14%	—	13%	20%	—

<sup>a</sup> MPS-IVA: N = 32/71 patients; MPS-VI: N = 17/27 patients.<sup>b</sup> MPS-IVA: N = 39/71 patients; MPS-VI: N = 10/27 patients.<sup>c</sup> Number of patients evaluated: for MPS-IVA: N = 28; MPS-VI: N = 5.<sup>d</sup> MPS-IVA: N = 6/28.<sup>e</sup> MPS-IVA: N = 22/28; MPS VI: N = 5/5.<sup>f</sup> MPS-IVA: N = 65 (outlier values were disregarded for all averages calculations).<sup>g</sup> MPS-IVA: N = 67 (outlier values were disregarded for all averages calculations); MPS VI: N = 25.<sup>h</sup> MPS-IVA: N = 39; MPS VI: N = 23 (outlier values were disregarded for all averages calculations).<sup>i</sup> Elosulfase alfa commercial availability for MPS-IVA in Mexico: May/2016, and in Colombia: Mar/2015.<sup>j</sup> MPS-IVA: N = 24 patients; MPS-VI: N = 12 patients.<sup>k</sup> Galsulfase commercial availability for MPS-VI in Mexico: Nov/2011, and in Colombia: Dec/2011.<sup>l</sup> MPS-IVA: N = 8 patients; MPS VI: N = 15 patients.<sup>a</sup> MPS-IVA: Overall, N = 37; urban, N = 22; rural, N = 15; MPS VI: overall, N = 14, urban, N = 9, rural, N = 5.<sup>b</sup> MPS-IVA: Overall, N = 37; urban, N = 22; rural, N = 15; MPS VI: overall, N = 15, urban, N = 10, rural, N = 5.<sup>c</sup> MPS-VI: N = 15.

**A) School grade by age group**



**B) Concomitant medications**



13/71 patients used concomitant medications  
MPS = mucopolysaccharidosis

8/27 patients used concomitant medications

**Fig. 1.** Patient profile, concomitant medications, ERT treatment and multidisciplinary approaches in MPS-IVA and MPS-VI patients.

Table 4A, 4B).

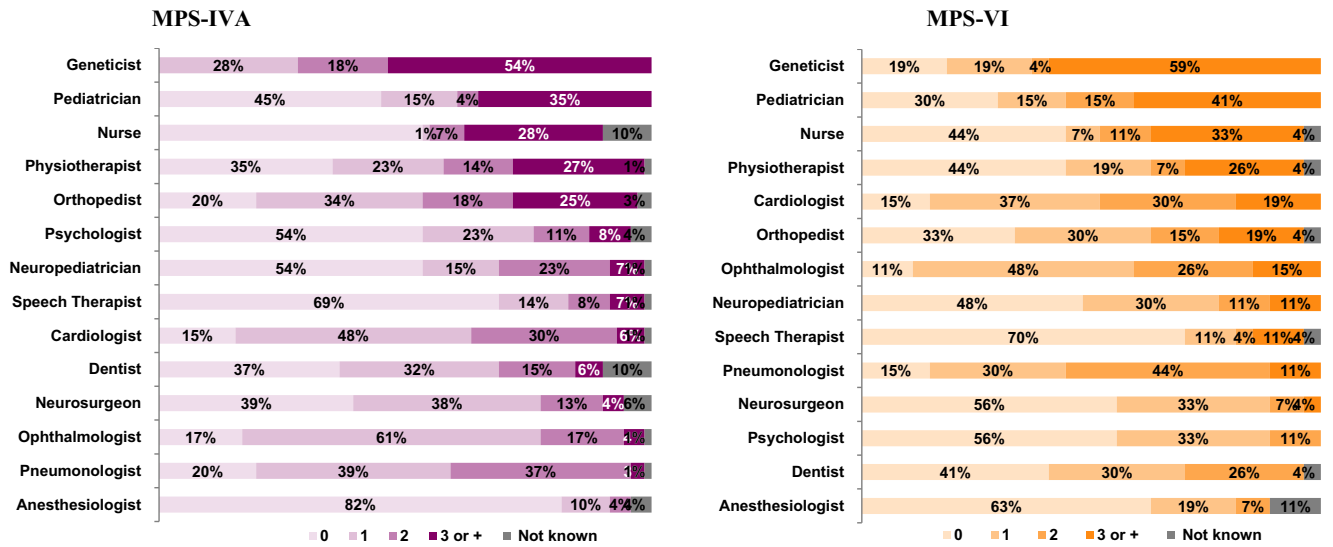
Overall, ERT therapy reduced the occurrences of complications and surgeries, according to physicians' judgment. However, high rates of spinal cord compression, hernia correction and otorhinolaryngologic surgeries were observed (Fig. 1D). There were no age-specific trends noted (Suppl. Table 5). Treatment patterns in patients from Colombia and Mexico were consistent (Suppl. Fig. 1D). Treatment with Galsulfase in MPS VI patients was supported by the public sector in Mexico. In

Colombia, 40% patients used contributory regimens and 60% used subsidized regimens.

**4. Discussion**

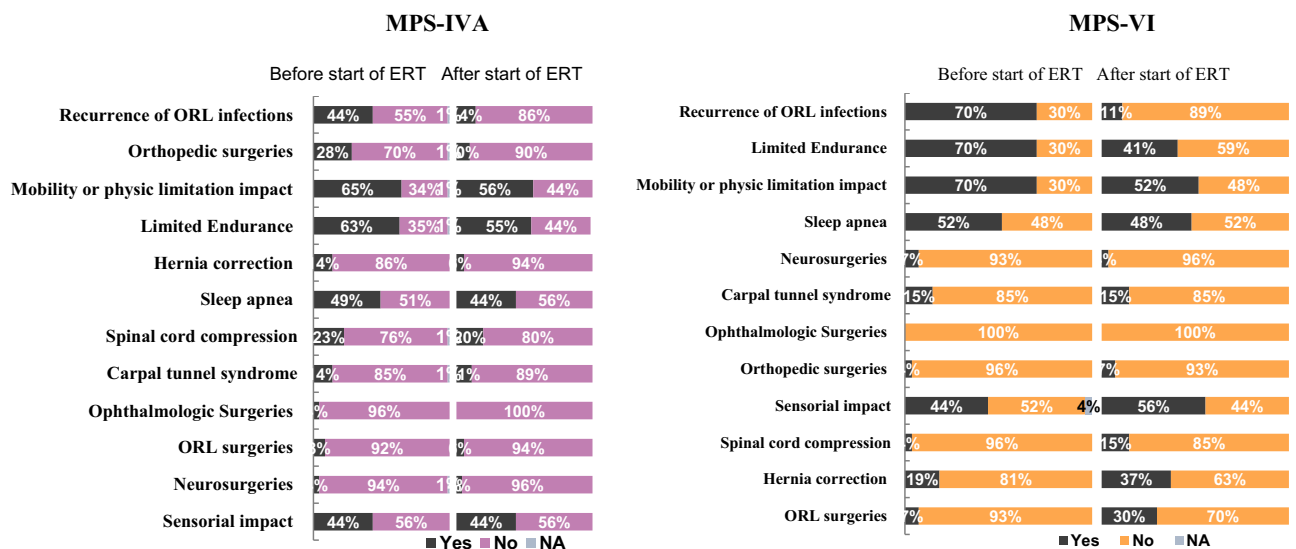
This study showed that MPS-IVA and VI impose a significant burden on patients' life. High rate of absenteeism from school and work was observed in the study population. The school non-attendance rate

**C] Multidisciplinary approach: number of medical appointments by specialties that have evaluated the patient in the last year**



MPS-IVA: N=71; MPS-VI: N=27  
MPS = mucopolysaccharidosis

**D] ERT Treatment**



MPS-IVA: N=71; MPS-VI: N=27  
ERT = enzyme replacement therapy; MPS = mucopolysaccharidosis

Fig. 1. (continued).

increased proportionally with age in both the disease groups. ‘Personal/family decision’ and ‘disease burden’ were the most cited reasons in MPS-IVA and MPA-VI patients, respectively. Similar reasons were cited for absenteeism at work. Further investigations would be needed to better understand the personal reasons for non-attendance at school and work. School attendance is very important for developing many skills, including social abilities, and may help children with MPS feel more accepted by society [27]. Among patients attending school (MPS-IVA/VI), ~50–80% were in elementary grade (regular school). This was consistent with our observation, that a high proportion of the study population was in the age-group between 5 and 12 years. Most patients (MPS-IVA/VI) were registered on the national disability registry and required caregiver assistance, in line with the natural disease course, wherein, the ability to perform their daily-life activities progressively deteriorates. MPS patients generally have a short stature and joint

manifestations, with a slight decrease in the growth velocity that occurs during their early ages (2–4 years) [28]. The growth pattern in this study population was consistent with the published literature [29,30].

Delayed diagnoses or misdiagnoses in MPS are common, especially as the disease progresses slowly with subtle symptoms in some cases, and may be overlooked by the physician [31]. Early diagnosis in the asymptomatic stage helps to preserve the organ-function and improve outcomes [32]. Typically for MPS-IVA/VI, initial symptoms occur in the first 2–3 years of life, with a definitive diagnosis being delayed by an additional ~2 years [33–35]. In our study, the symptom onset occurred at the age of ~1–3 years, suggesting that our MPS population belongs to the classical phenotypes, which are more vulnerable to disease progression. Notably, the formal diagnosis was initiated ~2–4 years following the onset of symptoms and ERT treatment was started after another 3–4 years from diagnosis. Such a delay in diagnosis and

treatment is highly concerning because of the potential to cause irreversible damage. However, for both MPS-IVA and VI patients, the time from diagnosis to ERT treatment reduced after ERT became commercially available (than before). Nonetheless, despite improved accessibility to ERT, MPS-IVA patients in Mexico nearly took 2 years on average to have their first infusion; in Colombia, however, the patient received ERT within a year after diagnosis. This disparity in data could be explained by the variations in regional access to healthcare. Additional investigations would be crucial to verify the causes in this delay [36]. Our data have shown that ERT treatment was initiated earlier in patients with MPS-VI (1–2 years post-diagnosis) than in patients with MPS-IVA (3–4 years). This may be because, galsulfase was approved 9 years earlier than elosulfase alfa, and therefore, the observation period for patients with MPS-VI on ERT was comparatively longer than for those with MPS-IVA.

We observed beneficial effects of ERT in controlling disease progression, and reducing/stabilizing complications in MPS-IVA/VI patients, although this survey was not primarily designed to assess its effectiveness. The percentage of complications/surgeries following ERT was comparatively higher for MPS-VI patients than MPS-IVA patients, which could be due to the longer observation period for MPS-VI patients on galsulfase.

Reported studies have shown a high adherence to ERT in MPS patients, albeit published literature in this regard is limited. [26,37,38]. In our study, ~40–50% of MPS-IVA/VI patients had ERT interruptions (nonadherence), with ‘availability of medication’ being the most common reason for missed infusion, regardless of country (Colombia/Mexico) and region (rural/urban). In 2018, the general population distribution trend showed that most of the people lived in urban areas in Colombia and Mexico (80.8% and 80.2%, respectively) [39]. While only 20% of total country population lived in rural areas, in this study, 29% of MPS-IVA patients and 44% of MPS-VI lived in the rural areas; therefore, higher proportions of patients in the rural areas than total country population [39]. Specific reports on the proportion of MPS-IVA/VI patients living in urban and rural areas in Colombia and Mexico are not available in the literature. The higher percentage of patients in the rural areas could be explained on the basis of the recessive nature of this genetic disease. The high inbreeding in clusters of MPS patients would lead to high prevalence of the disease, corroborating with hypothesis of the founder effect [40,41]. Although MPS is a rare autosomal disease, the study included a sufficient number of patients. The impact of selection bias, however, cannot be completely refuted. Ascertainment bias resulting from the selection of physicians/specialists can also contribute to the disparity in the geographical distribution of the patients.

In general, the accessibility to ERT infusion center was not a concern in either rural or urban regions in both Colombia and Mexico. However, the travel time to the infusion center was long (~2- > 4 h) for some rural patients in Mexico, emphasizing the need for patient support programs. Also, wheelchair dependency might limit accessibility to ERT treatment, not only due to low facilities but also because of the patient’s altered mental status and low willingness to engage in out-of-home activities [42]. Previous studies showed that lack of mobility appears to have a significant impact on QoL [6,19].

Management of MPS-IVA/VI patients involved multidisciplinary clinical teams, consonant with the multiorgan somatic complications associated with these disorders. Overall the trends in Latin America were aligned with the international MPS guidelines and recommendations [9,10,43]. Use of respiratory, cardiovascular and pain medications was prevalent in this region, corroborating with the early symptoms of pain and cardiorespiratory complications in MPS [6,44]. Concomitant medication use was higher in MPS-VI than MPS-IVA patients, due to the higher percentage of complications.

Generally, the lack of multidisciplinary treatment expertise, a need for regular follow-up, limited treatment access, and the lack of appropriate reimbursement policies, are a few major factors impeding the management of MPS [9]. The data collected via the questionnaire/

survey were for the previous 12 months, starting from the time of interview i.e., the period between April/June 2019 and April/June 2020 (start of COVID-19 pandemic). Most of the data collection was conducted before the COVID-19 period. Therefore, questions specific to COVID-19 situation were not included in the survey. Nevertheless, some influence of COVID-19 situation on the data interpretation and results cannot be negated. In the current COVID-19 scenario, patient-diary survey emerges as an effective way to collect data without physical contact or to avoid travel from one place to another.

## 5. Conclusion

In conclusion, MPS IVA/VI disease burden was high in Latin America (Colombia, Ecuador, Mexico, Peru), possibly due to the issues, such as delayed diagnosis and treatment access throughout the region. Also, the patients seemed to have a classical MPS phenotype (vulnerable to disease progression). Overall, ERT treatment was effective in these patients. Socio-demographics and multidisciplinary management patterns were consistent across the region. These findings would aid clinicians in making informed decisions and provide valuable insights for policy makers to reform policies.

## Author contributions

All authors were involved in data analysis and imputed their scientific contribution for the data interpretation, as experts in MPS. All authors meet the International Committee of Medical Journal Editors criteria for authorship for this manuscript, with full access to the study data, and take complete responsibility for the integrity and accuracy of the data. All authors approved this version for publication.

## Ethics approval

The Ethics Committee’s approval was not required for this study since anonymized surveys of personal opinion do not require approval from the ethics committee. The study was done in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki), and with applicable regulatory requirements.

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## Declaration of Competing Interest

Claudia Yazmín Cossío Mandujano and, Carmen Amor Avila-Rejon, have received speaker fees/payments and travel support by BioMarin; Victor Hugo Espin was speaker of Sanofi-Genzyme and travel support by Takeda; Hector Paul Quintero Montaña declares that he has no conflicts of interest; Martha Luz Solano Villarreal have received speaker fees by Takeda, Roche, BioMarin.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ymgmr.2021.100769>.

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