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ORIGINAL ARTICLE

# The Experiences and Challenges of Mothers of Adult Patients with Mucopolysaccharidosis; Mothers of Adults with Severe Mucopolysaccharidosis

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## ABSTRACT

Although many studies have examined the treatment and symptoms of children with MPS, very few studies have focused on adults with MPS. This study aimed to clarify the experiences and challenges of mothers of adult patients with severe mucopolysaccharidosis (MPS) who live at home. The data from semi-structured interviews with twelve mothers (patients' ages ranged 19-44 years) were analyzed. The following six categories were extracted: fear that the disease will continue to progress despite treatment, tired of shifting gears in care and healing, fatigue due to multi-department visits to control the progression of the disease, the pain of not being able to see a bright future, desperate for new treatment methods for MPS, and developing care and a place to stay after parental support is gone. A unique issue of patients with MPS is that enzyme replacement therapy must be continued throughout life, and there is an urgent need to create a system that allows patients with severe MPS to receive enzyme replacement therapy for the rest of their lives, even after their parents pass away.

*Keywords*: Pediatric Home Care, family nursing, rare disease support, transitional care, mucopolysaccharidosis

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## 1. Introduction

Mucopolysaccharidosis (MPS) is a rare, hereditary, and intractable disease in which mucopolysaccharide progressively accumulates in systemic organs and tissues due to congenital deficiency or reduced activity of mucopolysaccharidoses, resulting in a variety of symptoms. In Japan, 467 cases have been diagnosed in 27 years, and the incidence of MPS is approximately 1 per 59,000 people[1].

MPS is classified into seven disease types according to the defective enzymes, clinical symptoms, and accumulated substances: Hurler (IH type), Scheie (IS type), Hunter (Type II), Sanfilippo (Type III), Morquio A (Type IV A), Morquio B (Type IV B), Moroteaux-Lamy (Type VI, and Sly (Type VII) (Types V and VIII are missing numbers). When left untreated, patients with this disease become bedridden in their teens and eventually die by age 20[2,3]. However, at present, due to early detection through prenatal diagnosis and optional screening, early initiation of enzyme replacement therapy, and reforms in medical welfare, the number of patients who reach adulthood and are able to live in the community is increasing. Enzyme replacement therapy is a therapeutic method in which the deficient enzyme is replenished from outside the body in the form of preparations, and the symptoms are improved by decomposing glucosaminoglycans accumulated in lysosomes. Since the administered enzyme decomposes and disappears in a relatively short period of time in vivo, patients need to go to a specialized hospital once a week and continue intravenous administration for four to six hours for the rest of their lives[4]. Therefore, most families of patients wish to implement enzyme replacement therapy at home[5].

Several studies have reported on this disease. Muenzer et al. reported that enzyme replacement therapy reduces hepatomegaly and macroglossia, thus improving dyspnea, while Simon et al. reported that it reduces joint contracture and improves joint mobility[6,7]. Giugliani et al. also reported that although the patient survival rates and quality of life have significantly improved, even with enzyme replacement therapy, intravenously administered enzymes cannot cross the blood-brain barrier; thus, they have no effect on the central nervous system[8]. Doherty et al. reported that enzyme replacement therapy has limited effects on the skeletal system[9]. Fabiano et al. noted that the therapy has limited effects on valvular heart disease and is ineffective in enlarging the aortic root of the heart[10]. Tsurusaki et al. claimed that long-term enzyme replacement therapy (up to nine years) resulted in 40% of adverse events and 25.6% improvement in symptoms [11]. Francisco et al. reported that the relief of symptoms did not reduce disease progression or mortality[12]. In 2021, an enzyme preparation that can cross the blood-brain barrier and a reservoir-mediated intracerebroventricular drug was approved for MPS II [13,14]. Sustained increases in the developmental index were also observed in three cases in which intracerebroventricular administration was started before the age of three[15]. Currently, the development of chaperone and gene therapies is progressing, and further improvements in activities of daily living (ADL) and extension of life expectancy can be expected in the future.

Regarding previous Japanese and international research on children/persons with MPS and their families, Kubo et al. reported that 63% of the parents of MPS patients are stressed, resulting from the inability to communicate with the sick child/person and bathing assistance[16]. Furthermore, Kubo reported that parents, especially mothers, feel remorse and pity for their sick children[17]. Kubo also noted that along with the development of therapeutic methods, parents request specialists to reduce symptoms and improve quality of life as treatment methods[17]. Moreover, Kubo et al. also reported that, while feeling joy and satisfaction with enzyme replacement therapy, parents are dissatisfied with the side effects and think that its effects are limited[18]. According to our previous study, in many cases, parents perceive that the sick child/person will not live long enough to reach adulthood, and as such, mothers do not prepare measures to address the

disease should their child reach adulthood. We reported that the indifference of others and the lack of a place to share information about death and heredity hindered parents' grief work when their children died[19]. Somanadhan et al. revealed that the experience of living with MPS, a rare inherited disease, poses problems of stigma and isolation[20]. Meanwhile, Zengin et al. noted that parents of MPS patients have many difficulties related to the multilineage problems brought on by MPS [21]. Finally, Kang clarified that the MPS II parenting process is a "maze-navigating experience" and has three stages, namely, entering the unknown, struggling to escape from the unknown, and settling in the unknown[22].

Many of these surveys targeting MPS in Japan and overseas focused on people who have not reached adulthood. We did not find any studies limited to adults with MPS or their families, which means that there are many uncertainties about the condition and home life of adult patients.

According to our survey, many adult MPS patients experience a decline in ADL as the disease progresses and become severely mentally and physically disabled (hereafter referred to as patients with severe MPS), and efforts are underway to improve patients' home life by gradually increasing outpatient support and home visit support[23]. Previous studies on home-dwelling children/people with severe mental and physical disabilities revealed that their lives depend on the care of their parents as well as community support, but sibling support is inadequate[24,25]. These studies also delved into their satisfaction and anxiety with home-based support, and investigated transitional support from hospital to home/facility, and needs for home care[26-32]. Many caregivers are mothers and do not receive the cooperation of other people[33]. Furthermore, the mothers' sense of the burden of childcare consists of "difficulty in daily life," "anxiety about childcare," and "restrictions on social roles." It has been clarified that the severity of the disability, the mother's perception of the child, the husband's cooperation, and support from the surroundings greatly affect the burden of childcare[34].

In the case of children/people with severe mental and physical disabilities, many are living at home centered on nursing care, but patients with severe MPS in adulthood are characterized by living at home while receiving enzyme replacement therapy and requiring medical care such as ventilators, gastrostomy, and urinary catheterization[23].

Normally, after graduating from high school, children go through a developmental process of becoming independent from their parents. In Japan, mothers of children and persons with severe mental and physical disabilities who require medical care are constrained both externally and internally by the role of care, and the mother and child are in a state of oneness[35,36].

Therefore, in this study, we conducted interviews with mothers, who are the patients' advocates, to clarify the experiences and challenges of mothers living at home with adults with severe MPS. We aim to further improve the quality of life of adult patients with MPS and their families, and we wish to elucidate ways to promote patients' independence.

## 2. Objectives and significance

### 2.1. Objectives

This study aims to clarify the experiences and challenges of mothers living at home with adults with severe MPS.

### 2.2. Significance

Due to recent advances in medical health and welfare and the development of treatment methods, it is speculated that adult patients with severe MPS will be able to live at home for a longer period. However, it is certain that the disease progresses, and by clarifying the experiences and challenges of mothers living at home with adults with severe MPS and

their preparations after a parent's death, the results of this story will become material for considering the life support that they and their families want. Furthermore, there is a rapid increase in the number of children requiring medical care and children dependent on advanced medical care. We believe that the results of this survey can also provide suggestions regarding support for their adulthood.

## 3. Research methods

### 3.1. Definition of terms in this study

#### 3.1.1. Genetic, rare, and intractable diseases

There are many intractable and genetic diseases. Hereditary, rare, and intractable diseases in this study are defined as those with autosomal or sex chromosome inheritance, and among extremely rare diseases, progressive diseases for which no curative therapies have been established.

#### 3.1.2. Adult MPS patients

This study included MPS patients aged 18 years or older.

#### 3.1.3. Experiences

With reference to the definition of a previous study, experience is defined as "an event that leaves a lasting impression when humans (i.e., mothers of patients with MPS), who are social beings with physicality, encounter an uncertain situation, and their mental and physical states at that time, especially their physical sensations and reactions during a limited period. As a result, developmental changes, self-acceptance, positive emotions, negative emotions, discovering the meaning of one's existence, restructuring of relationships, and phenomena indicating acquisition and mastery are found"[37].

### 3.2. Design

This was a qualitative descriptive study. Qualitative descriptive research is a research method that discovers and understands phenomena, processes, or the perspectives and worldviews of those involved[38]. The aim is then to use the target language to create a clear explanation and comprehensive concept of the target phenomenon[39]. This study utilized qualitative descriptive research to explore the experiences and daily challenges of mothers of adult children with severe MPS—a progressive and incurable disease.

### 3.3. Survey method

According to an interview guide, semi-structured interviews were conducted with mothers of adults with severe MPS.

#### 3.3.1. Participants

Participants (N = 12) were mothers of adults with severe MPS. They were members (or friends of members) of the Japan Mucopolysaccharidosis Patient Family Association. All mothers consented to participate in this study. The number of interviews was one to three per person, and each interview lasted 60 to 120 minutes.

The disease types of the interviewees were type II (Hunter), type III (Sanfilipo), and type IV (Morquio). Type I (Hurler, Scheie) and type VI (Marrow-Lamy) were outside the definition of severe adult MPS patients and were excluded from the

study. There are currently 174 members of The Japanese Society of the Patients and the Families with Mucopolysaccharidoses, and since it is a rare and intractable disease affecting only approximately 300 people nationwide, we believe that even 12 members will deliver valuable data. It was determined that the data were saturated because no new information appeared during data collection[40].

### 3.3.2. Interview details

The interview includes basic attributes, current health problems, treatment, life and anguish, support received and reasons, hopes for future treatment and support, thoughts, actions, preparations, and what they felt at that time.

### 3.3.3. Survey period

April–October 2022

## 3.4. Data analysis and description

Interviews were transcribed verbatim. From the verbatim record, narratives related to the research purpose were coded by dividing them into “phrases,” comparatively analyzed based on similarities and differences, and classified into subcategories and categories by increasing the degree of abstraction. A storyline was created from the relationships between categories. The subcategories and categories of the analysis results were presented to the supervisor of this research and to a research advisor who is qualified as a nurse, and they were judged for their validity.

## 3.5. Ethical considerations

This study was conducted with the approval of the ethics review committee of the affiliated university (Institutional Review Board of Tokyo Medical and Health University Kyo-32-38D, Daito Bunka University Human Life Science and Medical Research Institutional Review Board DHR21-011). We explained in writing that the subject’s free will was guaranteed, that there would be no benefit or disadvantage due to the presence or absence of cooperation, the method of publishing the survey results, and voice recording during the interview, and so on, and consent was obtained. At the time of the interview, the purpose and method of the study were explained again, and the interview was started after written consent was obtained. Since interviews can be traumatic for some subjects, we explained that the interview could be stopped at any point should they feel uncomfortable. Furthermore, the interviewer had learned counseling techniques. To protect personal information and privacy, the data were anonymized.

# 4. Results

## 4.1. Background of subjects

Patients' ages ranged 19–44 years at the time of the interview, and eight of them had siblings. All participants were born before enzyme replacement therapy was approved, and their doctors told them at the time of their diagnosis that their life expectancy would be short. At the time of the interview, nine patients were being fed by tube, seven had a tracheostomy, and seven were using a ventilator. In addition, all patients required suction from time to time and were severely mentally and physically disabled. To protect personal information and privacy, we anonymized the data so that individuals cannot be identified by abstracting descriptions that can identify proper nouns or subjects in the data.

## 4.2. The experiences of mothers caring for adult patients with severe MPS at home and preparations for life after the death of a parent

As a result of the analysis, six categories and 21 subcategories were extracted. The categories are written in **bold**, subcategories are *italicized*, remarks by the subjects are in quotation marks, and supplementary comments by the author are written inside parentheses. The description of each category is as follows.

### 4.2.1. Category 1: Fear that the disease will continue to progress despite treatment

As the disease progressed, mothers became *discouraged by the disease progression*.

“I was losing my child more and more and thought that they were becoming a mere spectacle as they felt alienated after having been confined to a wheelchair and losing their ability to speak.”

“I was told (by the attending physician) that, considering the future progression of this disease, it would be easier for my child if they underwent laryngotracheal separation. I have been thinking about it for a long time, but my child would lose their voice and even though they cannot talk, they can still make sounds, so I hate the thought of them being unable to cry.”

When one mother’s child became an adult, she discovered that she had valvular heart disease and retinitis pigmentosa, which had been asymptomatic when she was a minor, and she was *confused by her unexpected condition*.

“My child has glaucoma and is taking medication to lower my intraocular pressure, but their eyesight is getting worse and worse. I’m worried because there is no treatment for their eyes (retina),”

“He was diagnosed with valvular heart disease during a medical examination.”

### 4.4.2. Category 2: Tired of shifting gears in care and healing

Mothers were *disappointed in the effectiveness of enzyme replacement therapy* as the disease continued to progress.

“I can't deny my disappointment with the enzyme.”

“Everyone expected that they might (get better) and I thought that their (bodily functions) would never decline, but they did a little.”

Because the effects of enzyme replacement therapy are unclear, there was a *fear that halving the treatment would lead to progression of the disease.*

“I have been told (by the attending physician) that it is now possible to do the therapy every two weeks. But perhaps this may accelerate the current rate of progression. When I was told that, I really felt like I had to do my best.”

### 4.2.3. Category 3: Fatigue due to multi-department visits to control the progression of the disease

Mothers said that *taking the children to the hospital is hard work* because the hospitals where they can receive enzyme replacement therapy are far away, and because the children are larger than when they were minors, more supplies are needed.

“[Moving to the hospital] is long and causes a lot of fatigue to the child”

“It is difficult to prepare to go to the hospital. Preparing welfare taxis, preparing for aspiration and injection, and arranging goods and people are difficult.”

Mothers said they felt pressured to undergo enzyme replacement therapy once a week, and that they felt *physical*

*exhaustion due to frequent and long hospital visits*.

"My child has an intravenous drip once a week, and it's a lot of pressure, so I'm worried that it would break their body even though it won't."

"We do (enzyme replacement therapy) once a week. Moreover, we spend a day in the hospital because we must do enzyme replacement therapy plus albumin. Enzyme replacement therapy takes about three hours, and plus the albumin, it takes an additional two hours, which brings the total to five hours. That's why we come home very tired."

Hospital visits are a burden not only for parents but also for children, and were *concerns that visits to the hospital will worsen patients' condition.*

"My child has [a] fever every time they come home from the hospital,"

"If my child goes to enzyme replacement therapy and gets sick repeatedly, they will become bedridden."

Since they visit the hospital during weekdays, there are *restrictions on the social life of children and parents accompanying them on hospital visits.*

"Parents themselves have to take time off from work to take their children to the hospital."

"He has to miss school or leave early, and my child's enjoyment decreases."

In cases in which patients are transitioning from pediatrics to adult medicine, they receive consultations at multiple departments and hospitals. This led to *mental and physical fatigue from visiting multiple departments and hospitals* and a *desire for a single department*.

"It's a pattern of going to a hospital to receive enzyme replacement therapy after going to a rehabilitation specialist for an hour in the morning."

"Plastic surgery, ophthalmology, cardiology, ERT (enzyme replacement therapy), regular checkups, all of them are different, which makes it hard to go to the doctor."

"I wished the departments were in one place."

### 4.2.4. Category 4: The pain of not being able to see a bright future

Enzyme replacement therapy was the only treatment available even as the disease progressed, and mothers expressed *a sense of obligation to continue treatment for the child's life*.

"It's a long-term battle. It's going to be a long battle. I still can't see ahead. Using enzymes has only made it more difficult to see what's ahead."

"It's tough to think that I can get away with this condition because I'm doing enzyme therapy, but I have no choice but to continue doing it for the rest of my life."

As the condition progressed and medical care was introduced, mothers were left alone to take on the role of an ICU nurse, feeling *nervous and anxious about providing care to protect their children's lives.*

"Just by changing the child's position, the oxygen suddenly drops; so, every day was like being an emergency rescue worker. I had to suction, evacuate, aspirate, evacuate over and over again."

"I get inhaled at night; so, I wake up in the middle of the night, and it's getting hard to wake up, and I wake up thinking it's dangerous.'"

Additionally, as mothers aged, they faced challenges such as *the transition from childcare to nursing care* and *their own limitations*.

"What I'm doing now is not childcare, but nursing care. Until my child enters the facility, I wonder if it will stay like this unless he goes to the facility."

"I haven't been able to sleep properly for 10 years."

When the welfare system was being changed, even though their condition had not changed, they felt *confused about the disparity in public support based on their children's ages.*

"There is a wall between specific childhood chronic diseases (medical cost subsidies for specific childhood chronic diseases) and specific diseases (support for intractable diseases). …Does it cost that much? I was prepared, but eh, this much?"

"You can rent lifts if you have elderly care (long-term care insurance), but children of this age have to buy everything because there are no rentals."

"It would be nice if we could create a system for intractable disease welfare, similar to welfare for the elderly and people with disabilities."

Adult patients with severe MPS require medical care; thus, mothers talked about the *difficulty using facilities owing to a lack of medical personnel.*

"Especially around here, there are no facilities to look after medical care."

"There are few facilities for the center of gravity (severely mentally and physically disabled), and there are no facilities that provide medical care."

When the siblings of the affected children reached marriageable age, they *experienced not being able to tell their relatives about the genetic disease*.

"I haven't told my parents (my parents) about my siblings or my genetics, and I don't have anything to say."

"When I got married, I honestly wondered what would happen. (My siblings and spouse) go to the same junior high school, so I must tell them about their sibling (MPS patient). It seems like they thought the patient had some kind of disability or an illness, but they choose to not ask too much about it, so I think I have to say it."

### 4.2.5. Category5: Desperate for new treatment methods for MPS

Those who could not use home-based enzyme replacement therapy said that *home-based enzyme replacement therapy was psychologically relaxing*.

"We can have it at home, and I have had COVID-19, so I feel a little better mentally."

Additionally, there was a *desire to try a new drug, even if it was through a clinical trial*, and discontinuing enzyme replacement therapy became less and less of an option.

"[After using the new drug], my child was able to recall a song and sing along to the music. "

"What about those who are undergoing clinical trials? I wonder if things are getting better. If things are getting better, I would like to have my child undergo a clinical trial."

Mothers had been *hoping for gene therapy* ever since their children were diagnosed with a rare and incurable disease.

"If gene therapy is successful, it will be possible to treat mucopolysaccharidosis. Gene therapy is 10 to 20 years away."

"Right now, drug development seems to be progressing, so if we work hard now, it might be a little easier in the future."

### 4.2.6. Category 6: Developing care and a place to stay after parental support is gone

Mothers *wanted a place where their children could have fun and feel safe* after losing parental support.

"A child's purpose is to have fun."

"I am looking for a comfortable place for my child while using respite services."

One mother was worried about what will happen to her child after she dies. She was *searching for financial independence and guardianship*.

"There is a public hospital, so I would like to have about two beds available and use it in conjunction with the guardianship system. I'll pay the money properly; and when I die, I'll donate my assets to the city, so I want my child to be admitted to the hospital.'"

In addition to aiming to build a place for children to live and improve quality of life, they also *began training supporters to provide the same care as their parents*.

"We are thinking that our children will die after we die, so we have to have various people take care of us and learn how to take care of them."

"It's important that everyone can do the same care."

### 4.2.7. Storyline by categories

As children's condition progressed and they transitioned to adult medical care, mothers experienced **fear that the disease will continue to progress despite treatment** and were **tired of shifting gears in care and healing** regarding whether to continue treatment.

Unable to make the decision to change shifts, the mothers were **fatigued owing to multi-department visits to control the progression of the disease**, and they wondered how long this life would last. They felt **the pain of not being able to see a bright future.** They were **desperate for new treatment methods for MPS**. Simultaneously, they began **planning for when they could no longer provide support**, so that they would have peace of mind concerning their children's futures.

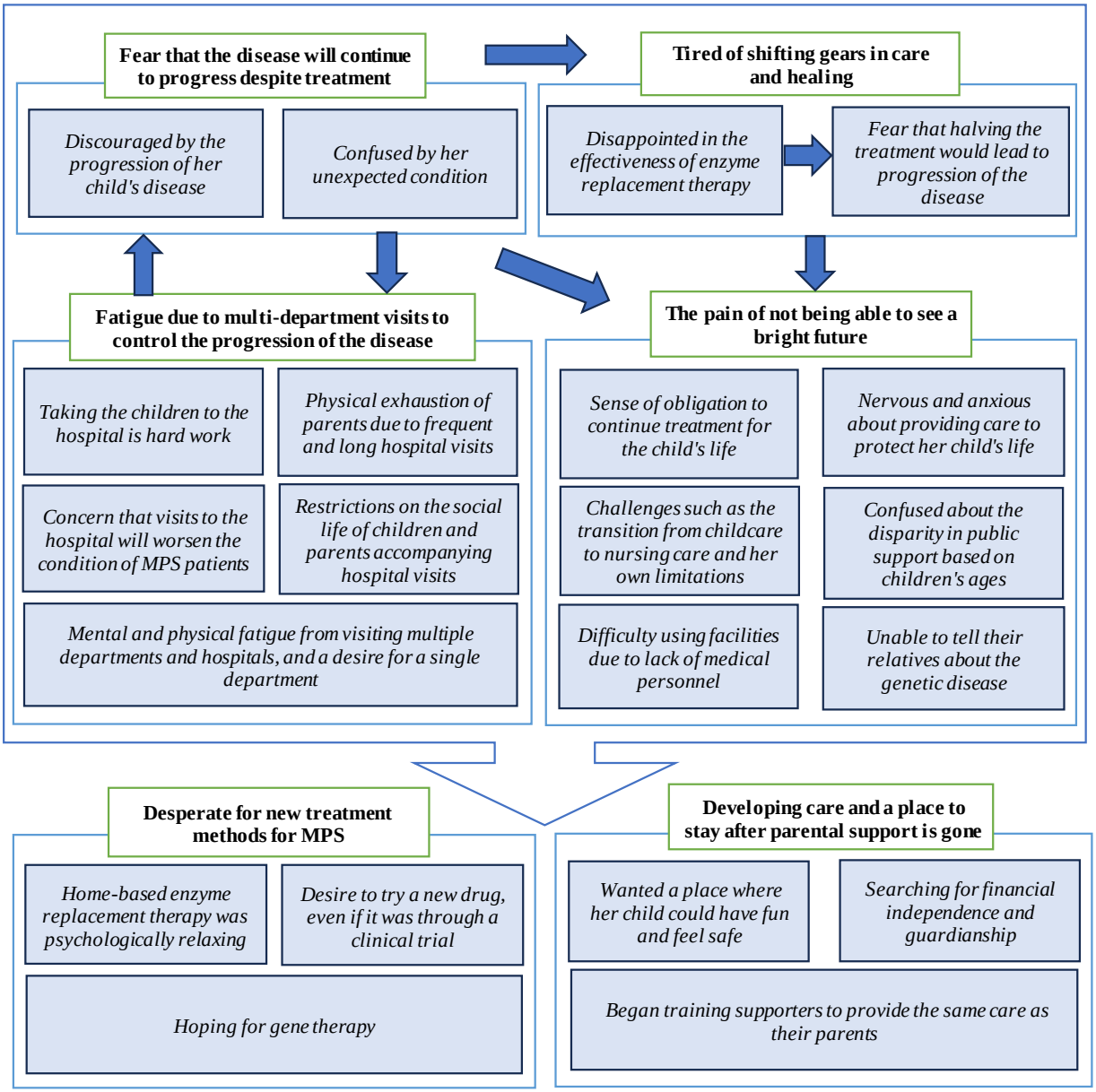


Figure 1. Relationship between categories regarding the experiences and challenges of mothers of adult patients with severe MPS

## 5. Discussion

The following six experiences were raised by mothers of adult patients with severe MPS: fear that the disease will continue to progress despite treatment, feeling tired of the shifting of gears in care and healing, fatigue due to multi-department visits to control the progression of the disease, the pain of not being able to see a bright future, desperation for new treatment methods for MPS, and worries about developing care and a place to stay after parental support is gone. The findings concerning fear that the disease will continue to progress despite treatment and fatigue due to multi-department visits to control the progression of the disease were similar to those found in previous studies[41–44].

Two new findings were that mothers were tired of shifting gears in care and healing and the pain of not being able to see a bright future. MPS is an incurable disease, and the only treatment method is enzyme replacement therapy. It is completely understandable that it is unclear how effective this treatment is, and that there is concern that patients' condition will worsen after years of careful care. Contrastingly, the subcategories "*the transition from childcare to nursing care* and *their own limitations*" indicates that continuing the current care is a heavy burden for mothers. In Japan, home enzyme replacement therapy became possible for MPS I, II, IV, and VI in 2021[45]. The introduction of home medical care may lead to a reduced burden on mothers. In addition, guidelines concerning enzyme replacement therapy are required. Further, mothers were desperate for new treatment methods for MPS, such as gene therapy. In Japan, the medical subsidy system changes dramatically after the age of 20 years, and pediatric medical care is no longer available. Previous research has shown that people are struggling with the reduction in medical subsidies, and it is hoped that financial support will be expanded for people with MPS, among others[46]. Concurrently, it is necessary to provide care and a place to stay for patients after parental support is gone. Several studies have noted the problems faced by people with disabilities after the death of a parent[47–52].

A unique challenge for patients with MPS is the need for lifelong enzyme replacement therapy. There is an urgent need to create a system that allows patients with severe MPS to receive enzyme replacement therapy for the rest of their lives, even after their parents have passed away. It is desirable to expand facilities that provide medical care for seriously ill community-dwelling patients. In addition, it is hoped that coordinators, community health nurses, and consultation support staff will work together to provide continuous support for patients with MPS after the death of a parent to foster patients' independence as much as possible.

## 6. Conclusion

We identified six categories based on the experiences of Japanese mothers of adults with severe MPS. Even without the support of the mother, the patient wanted enzyme replacement therapy for life, and the development of a new treatment was the only hope. We believe that some of these results are a common issue not only for MPS patients but also for patients with progressive rare and intractable diseases that have no established fundamental treatments. Medical and welfare professionals must work together to provide support to patients with advanced rare and incurable diseases so that they do not lose their will to live.

## 6.1. Limitations and future challenges

This study targeted mothers of adults with severe MPS, but the demographics of the subjects were inconsistent, and the overall picture could not be presented. To make a generalization, it is necessary to increase the number of subjects for other rare hereditary diseases, consider family backgrounds, and so on to find commonalities and differences, and obtain suggestions for better support.

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## Conflict of interest

None.

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