Beyond SMN: What's Next? Broadening the Focus on Spinal Muscular Atrophy

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Introduction

Disease-modifying therapies (DMTs) have significantly altered the natural course of SMA, improving survivaland functional outcomes.

However, numerous unmet needs continueto profoundly affectthe quality of life(QOL) of people with SMA (pwSMA).

While these manifestations may not directlythreaten survival, they place a considerable physical, emotional, financial, and time burden on patients and their families.

The PROfuture & RegistrAME Initiatives

377 individuals

RegistrAME includes 377 genetically confirmed cases of 5q SMA.

In the PROfuture project, pwSMA and their families identified several areasthat significantly impact theirQOL and which,if adequately addressed, could lead to substantial improvements.

These domains are also monitored through the RegistrAME registry .

Key problem areas identified:

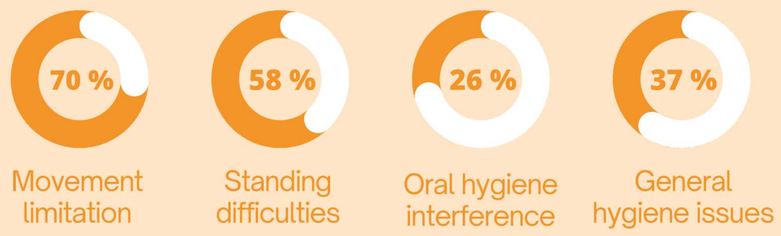
✓Contractures ✓Pain ✓Fatigue

Contractures

44 %

Patients reported Contractures

Functional impact among those affected:



Managing contractures involves daily work often causing discomfort or chronic pain.

Management involves daily:

- Physiotherapy
- Orthoses
- Standing
- Stretching
- Positioning

High burden of general care:

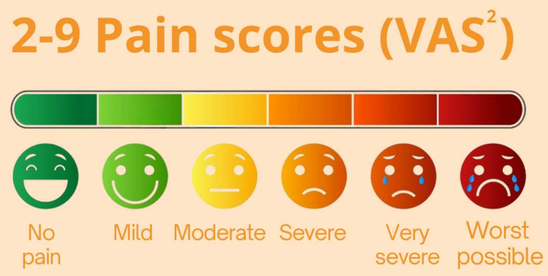
- 14% spend >20 h/week
- 11 patients exceed 30 h/week

Despite how alarming this is, care for a sitter can exceed 20 hours/week according to international standards. This burden forces families to choose between essential care and the child's right to age-appropriate experiences.

Pain

32 %

Patients reported frequent pain



39 %

Patients with pain reported poor sleep quality

Lower limb contractures are a key pain contributor

A study[1] promoted by FundAME found that lower limb contractures significantly contribute to pain perception in pwSMA, highlighting the need for more targeted and effective management.

1 Pain in Children and Adolescents with Spinal Muscular Atrophy: A Longitudinal Study from a Patient Registry
2 Visual Analogue Scale (VAS): https://pmc.ncbi.nlm.nih.gov/articles/PMC6132313/

Fatigue

50 %

Patients reported fatigability

Patients indicated that fatigability had a high prevalence and a functional impact in their lives.

Supportive medications:

27 %

Active registry members use salbutamol or pyridostigmine

However, since these medications are not formally recognized as standard SMA care, their use remains limited, particularly among patients enrolled in clinical trials—forcing several individuals to discontinue them despite the perceived benefit.

Conclusions

SMA is a complex disease characterized by multiple functional challenges that profoundly affect the QOL.

Contractures, pain, and fatigue must be recognized as clinical and research priorities.

Broadening the therapeutic and research focus beyond the *SMN gene* is not only a matter of optimizing efficacy but also a necessary step toward achieving long-term equity and well-being for individuals living with SMA.

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