# Harbouring 4 *SMN2* gene copies does not guarantee a milder phenotype: data from the Spanish Self-reported SMA Registry (RegistrAME)

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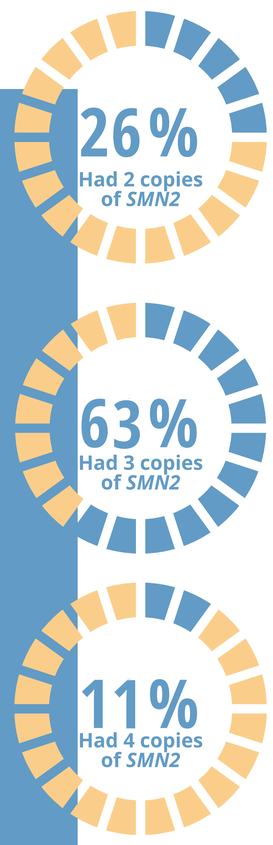
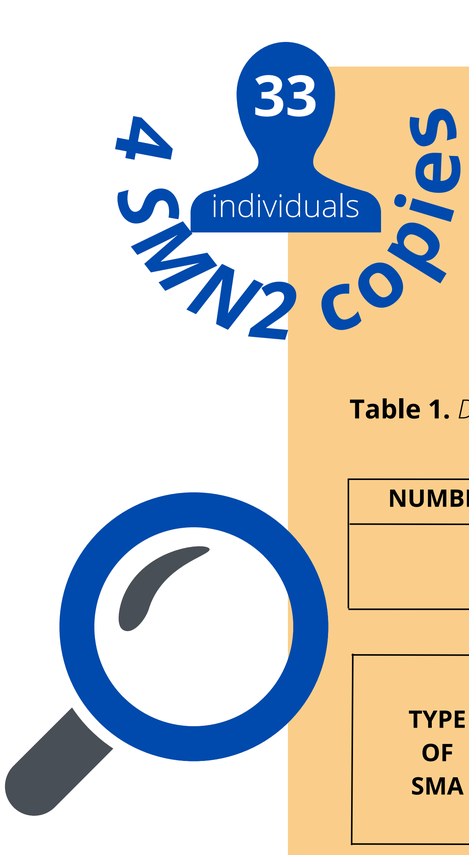
## INTRODUCTION

While a higher *SMN2* gene copy number is generally associated with a milder SMA phenotype, it is an imperfect predictor of disease progression. This study aims to characterize the profile of patients with four *SMN2* copies from RegistrAME

**Method:** All data are from RegistrAME: the Spanish Self-reported SMA Registry.

**294 out of the 325 patients included in RegistrAME, with genetically confirmed SMA (5q), provided a copy number report**


## Clinical Characteristics and Functional Status

of Patients with 4 *SMN2* Gene Copies in Spinal Muscular Atrophy (SMA)

**Table 1.** *Demographic and clinical characteristics*

| | | ALL |
|---|---|---|
| NUMBER OF PATIENTS | | 33 |
| AGE | | 9-66 YEARS OLD (m: 34,36) |
| | | % (n) |
| TYPE OF SMA | SMA 1 | 0 |
| | SMA 2 | 18% (6) |
| | SMA 3 | 79% (26) |
| | SMA 4 | 3% (1) |

**Table 2.** *Functional status, rotation, and hand function*

| | | % (n) |
|---|---|---|
| Functional Status | Non-sitters | 10% (3) |
| | Sitters | 45% (15) |
| | Walkers | 45% (15) |
| Rolling capability | Could not turn | 21% (7) |
| | Could only partially turn | 18% (6) |
| Hand function | Could not reach their mouth | 9% (3) |
| | Could not raise hands above head | 24% (8) |

**Table 3.** *Functional status of Walkers*

| | % (n) |
|---|---|
| Required wheelchair outdoors | 9% (3) |
| Could no longer climb stairs | 6% (2) |
| Had difficulty climbing stairs | 9% (3) |
| Walked short distances | 18% (6) |
| Required assistance to walk | 18% (6) |

**Table 4.** *Health data*

| | % (n) |
|---|---|
| Scoliosis surgery | 21% (7) |
| Used Non-Invasive Ventilation | 18% (6) |
| Receiving Treatment (DMT) | 70% (23) |

## Patients with 4 *SMN2* Copies According to age

Patients with 4 *SMN2* copies experienced the impact of spinal muscular atrophy (SMA) from a young age, with the severity of the disease worsening over time.

**In the group of children**
(Aged 9 to 17 years)


**In the young adult group**
(Aged 20 to 38 years)


**In the adult group**
(Aged 42 to 66 years)


> Individuals with 4 *SMN2* copies bear the profound impact of SMA from a young age

## Conclusion

Patients with four copies of the *SMN2* gene represent a **heterogeneous group**, ranging from non-sitters to walkers across all age groups. Over half of these patients **will either be unable to walk or will eventually loose the ability to walk**. Some may also **loose the capacity to sit up** unassisted or **maintain useful hand function. Motor decline can commence from an early age** and is not exclusive to disease progression in adulthood.

It is crucial to emphasize that the **functional status of a walker is not equivalent to that of a healthy person**, as a significant number of patients in this group may experience limitations in walking quality, difficulty climbing stairs, or the necessity for a wheelchair or other walking assistance.

Harboring four copies of the *SMN2* gene implies that some patients will develop a high degree of disability. **Improved evaluation of the quality of *SMN2* copies**, along with other potential biomarkers or predictive factors, is necessary to assess disease progression in these patients.