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# Temporal dynamics of the Scale for the Assessment and Rating of Ataxia in autosomal dominant cerebellar ataxias patients



## Ataxia in autosomal dominant cerebellar ataxias patients



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### Introduction

In 2006, the Scale for the Assessment and Rating of Ataxia (SARA) was developed to assess the presence and the severity of ataxia. SARA was validated for participants with spinocerebellar ataxia, translated in several languages, and validated in related diseases such as Friedreich ataxia. It is nowadays the reference scale for the clinical evaluation of ataxia.

In this study we aimed to:

- 1) Assess the temporal dynamic of each of the eight items composing the scale.
- 2) Study the global progression of the sum score.
- 3) Define the most reliable part of the scale
- 4) Asses the number of required participants for therapeutic trials with different scenarios

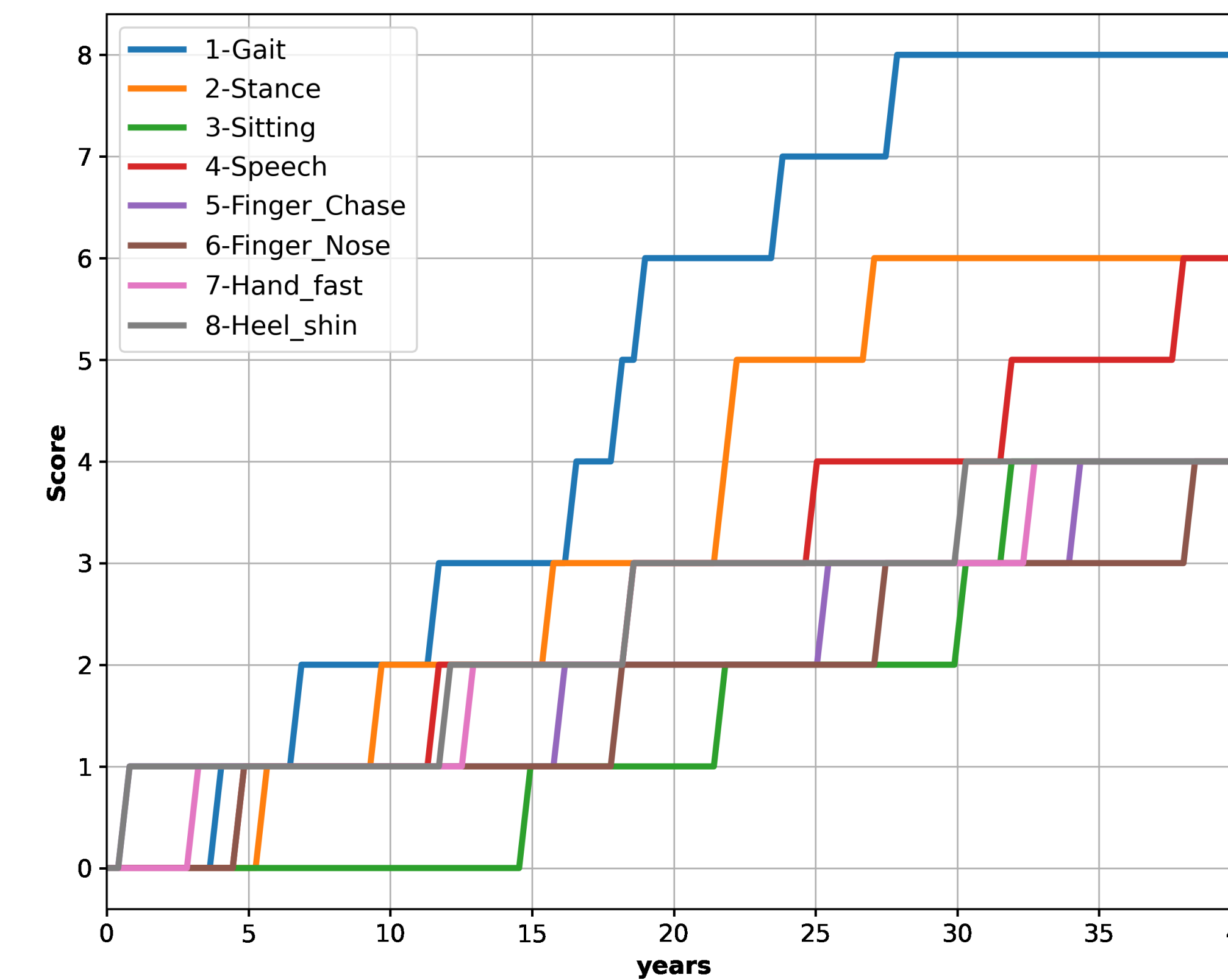
### Methods

Data from four international cohorts (EUROSCA, RISCA, CRC-SCA, SPATAX) were pooled together for a total of 1210 SCA1, SCA2, SCA3 and SCA6 participants and 4092 visits from 2006 to 2020.

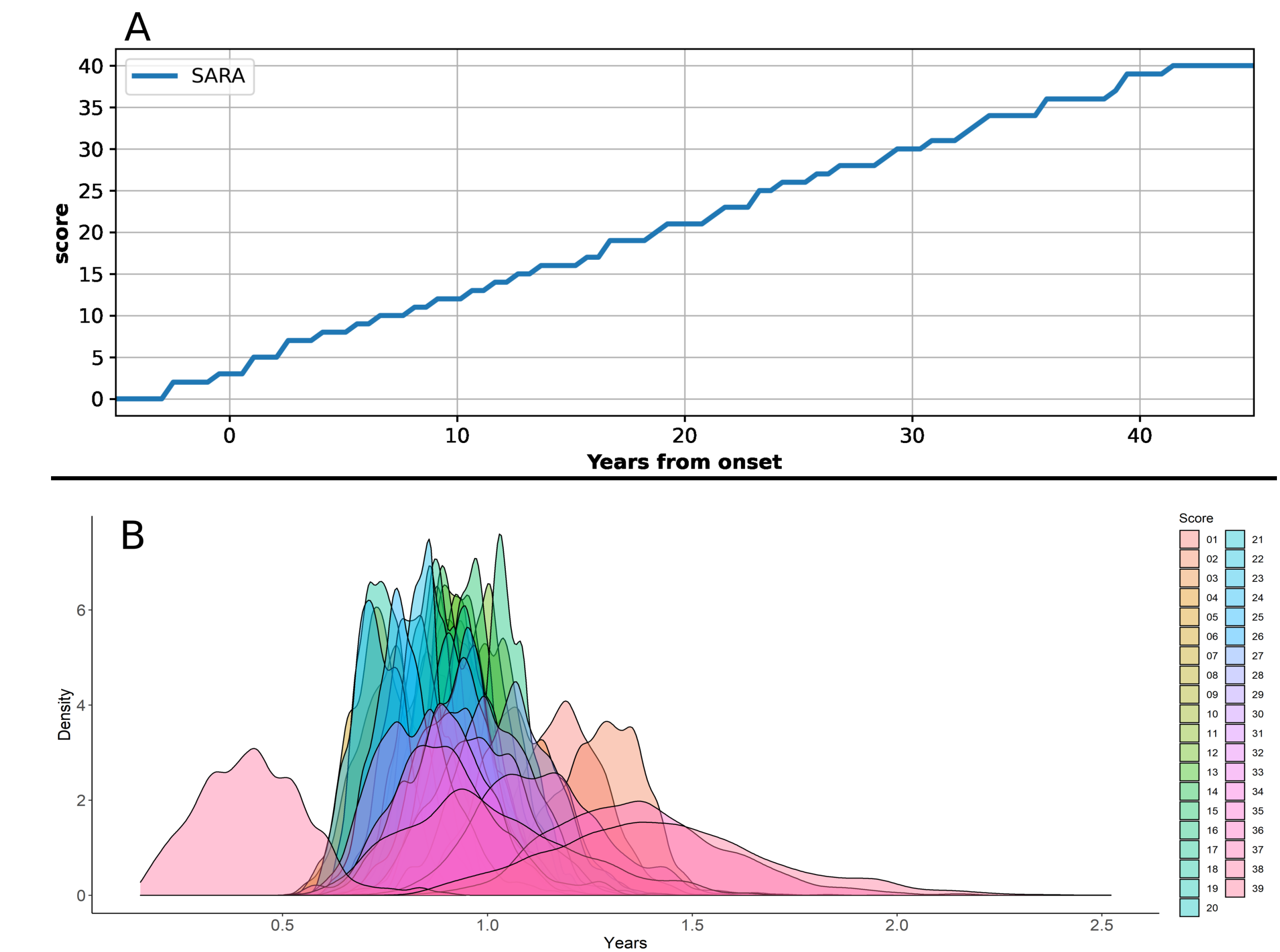
A Bayesian ordinal mixed effect model (Leaspy) was used to estimate:

- 1) The time (in years) spent at each level of each of the eight items composing SARA scale.
- 2) The average time for a one-point increase of each items.
- 3) The average time for a one point-increase of each of the SARA score and the associated variability.
- 4) The linearity of progression of different items and SARA scale.

Sample size calculations for therapeutics trials was done with different scenarios.



**Figure 1:** Average score progression as a function of years from start of progression. Average trajectory of progression of each of the eight item composing the SARA scale.



**Figure 2:** Global temporal dynamic of the SARA scale.

- A:** Average score progression as a function of years from start of progression  
**B:** Posterior distribution of the time spent in each level of the SARA scale.

### Results

Seven of the eight different items had a non-linear progression (Figure 1 and Figure 3B).

The speed of progression was different between most of the items with an average time for a one-point increase from 3.5 years [3.4;3.6] (median, 95% credible interval) for the fastest item to 11.4 [10.9;12.0] years (Figure 3A).

The total SARA score had a linear progression with an average time for a one-point increase of 0.95 [0.92; 0.98] years (Figure 2). The most reliable part of the scale, (with high overlap between the different steps) was between SARA score 4 and 36 (figure 2).

Selecting this range as an inclusion criterion reduced the required sample size from 234 to 218 in an heterogeneous group of SCA participants. (Figure 4).

### Conclusion

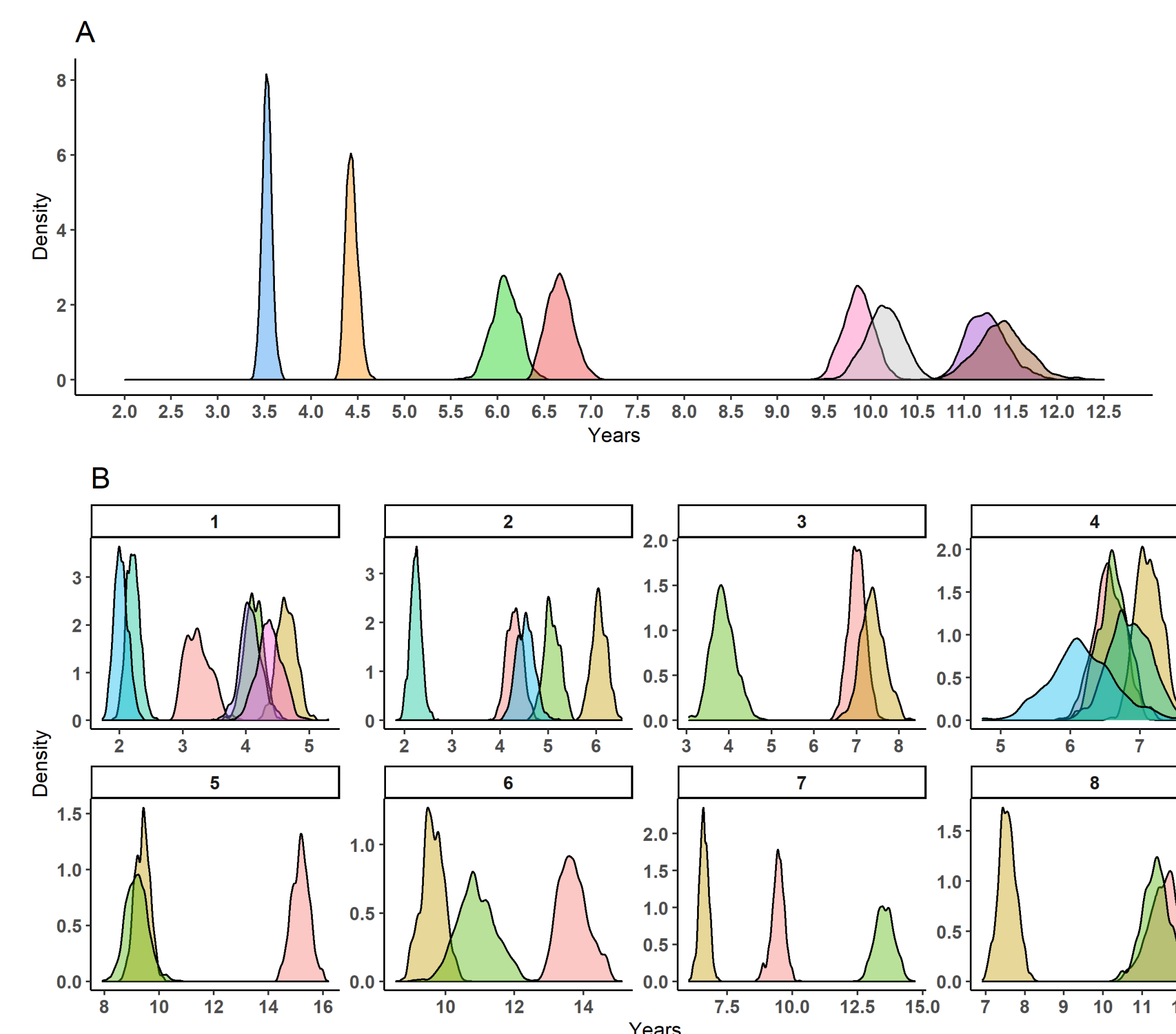
Despite a heterogeneous temporal dynamic at the item level, the global progression of the SARA scale was linear. This important result suggests that all items are complementary and that they each provide specific information at different stages of the disease.

Selecting patients with a baseline SARA score between 4 and 36 reduced the required sample size, reflecting a better performance of the scale on this range. This new information about the temporal dynamic of the scale should help to design outcome of future clinical trials.

As the SARA scale is used in all types of SCAs, and to reach more power, the different SCAs and cohorts were pooled together. This information must be taken into account, and the individual progression at the SCA level could be not linear.

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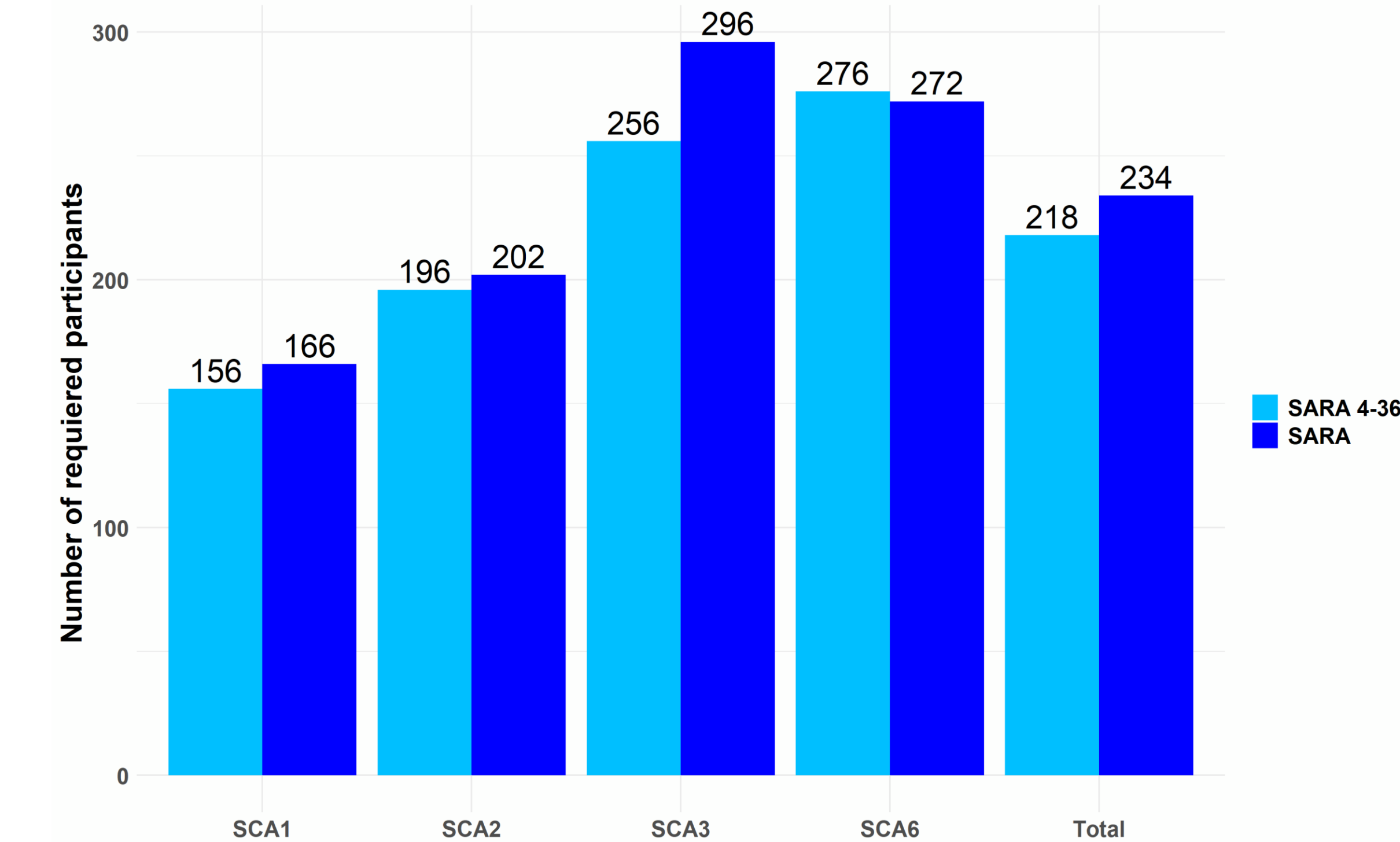
EUROSCA, CRC-SCA and SPATAX consortiums



**Figure 3:** Score progression at the item level

**A:** Posterior distribution of the average time for a one-point increase of the corresponding item. For instance, the blue distribution is the average time for a one point-increase of the item 1-Gait of the SARA scale.

**B:** Each panel corresponds to the progression of one item of the SARA scale. In one panel, each distribution represents the time spent in each level of this item. For instance, for panel B-1-Gait, the red distribution, Score1, is the average time spent at Gait score 1.



**Figure 4:** Total number of participants required for a therapeutic trial. Sample size for a two-group interventional trial (1:1 ratio per group) of 12 months duration with a treatment effect of 50% on the disease progression, a power of 90% and an alpha of 5%. SCA = Spinocerebellar ataxia. Total = Heterogeneous group of SCA. SARA 4-36 = Inclusion criterion: participants between SARA score 4 and 36.