

Impact of Early Intervention on Motor Milestone Achievement in Spinal Muscular Atrophy: Insights from Cure SMA Survey Data

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Supplementary Material

Equation S1. Hierarchical ordinal model expression

The cumulative logit model can be expressed as:

$$\log(P(\text{cur_max_motor}_{it} \leq j)/P(\text{cur_max_motor}_{it} > j)) = \beta_0 + \beta_1(\text{age_first_tx}_{it}) + \beta_2(\text{mono_combo}_{it}) + \beta_3(\text{SMN2}_{it}) + \beta_4(\text{income}_{it}) + \beta_5(\text{sex}_{it}) + \beta_6(\text{age}_{it}) + \beta_7(\text{early_diagnosis}_{it}) + \beta_8(\text{Survey_Year}_{it}) + u_i + \epsilon_{it}$$

Hierarchical Logit Model: Explanation of terms:

- $\log(P(\text{cur_max_motor}_{it} \leq j)/P(\text{cur_max_motor}_{it} > j))$: This represents the cumulative probability that the maximum motor milestone for individual i at time t falls at or below j , where j represents the ordinal motor milestones.
- $\beta_0, \beta_1, \dots, \beta_8$: These are the fixed-effect coefficients for the predictor variables. Each β represents the change in the log odds of achieving a higher motor milestone for a one-unit change in the respective predictor.
- u_i : The random intercept for individual i , which accounts for individual-level variability and captures the within-individual correlation
- t : Denotes the time (i.e. year) at which the survey was completed, representing the longitudinal component of the model. It captures time-dependent variations in motor milestone achievements across repeated measures.
- ϵ_{it} : Residual error term representing within-individual variability at each time point t .

Table S1. Description of variables

Variable	Description	Type
Outcome Variable		
Maximum Motor Milestone	Maximum motor milestone achieved at the time of the survey	Categorical, six levels: (1) no motor milestones, (2) head control, (3) rolling, crawling, or sitting without support, (4) standing with support, (5) standing alone, and (6) walking alone
Predictor Variables		
Age at Initial Treatment	Age when individual received their first SMA treatment	Categorical, four levels: (1) before three weeks of life, (2) three weeks to 59 days, (3) two to four months, and (4) more than four months
Screening Status	Diagnosis approach	Binary: (1) newborn screening or prenatal screening or unspecified screening (0) no screening
Treatment Status ^a	SMA treatment received at the time of survey	Binary: (0) monotherapy (single treatment), (1) polytherapy (more than one SMA treatment)
Biological Sex	Sex of the individual	Binary: (1) male, (2) female.
Survey Year	Year the survey was completed	Categorical, five levels: 2020, 2021, 2022, 2023, and 2024.
Household Income	Household income	Categorical, six levels: (1) under \$40,000, (2) \$41,000–\$70,000, (3) \$71,000–\$100,000, (4) \$101,000–\$200,000, (5) more than \$200,000, and (6) missing income data.
Age	Age of the affected individual at the time of survey (in days).	Continuous
<i>SMN2</i> Copy Number	Number of <i>SMN2</i> copies of the affected individual	Binary: (1) one copy, or (2) two copies.
^a Monotherapy was defined as the use of a single SMA treatment at the time of each survey. Polytherapy was defined as the concurrent or cumulative use of two or more SMA treatments. Due to the irreversible nature of OA, individuals were considered permanently treated with OA once it was reported. This rule did not apply to nusinersen or risdiplam, which may be discontinued over time. Sequential treatment use was not classified as polytherapy unless OA was involved. For example, an individual reporting nusinersen at baseline and risdiplam in a later year was considered to be receiving monotherapy in each survey year. In contrast, an individual reporting OA at baseline and subsequently reporting nusinersen was categorized as receiving polytherapy due to the ongoing effect of OA. Abbreviations: SMA, spinal muscular atrophy; <i>SMN2</i> , <i>survival motor neuron 2</i> ; OA, onasemnogene abeparvovec		

Table S2. Survey participation, 2020-2024

Year	2020	2021	2022	2023	2024	Total
Survey responses	98 (23.7)	73	65 (15.7)	80	98	414
Survey Participation, n (%)						
Total unique individuals						228
One year only	32 (26.9)	14	18 (15.1)	19	36	119 (52.2)
More than one year of survey participation						109 (47.8)
Earliest year	66 (60.6)	18	11 (10.1)	14	-	
Latest year	-	13	14 (12.8)	20	62	
Unique Individuals by Number of Survey Year Participation, n (%)						
Survey participation	One year	Any two	Any	Any four	Any five	Total
	119	63	24 (10.5)	13 (5.7)	9 (3.9)	228