

# Grip Strength is More Than a Number: The Relationship Between Grip Strength and Fine Motor and Arm Function in FORTITUDE-ALS

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## BACKGROUND

### Grip Strength and Other Measures of ALS Disease Progression

- Grip strength is frequently performed as an outcome measure in amyotrophic lateral sclerosis (ALS) clinical trials, and may also be assessed as part of routine ALS care
- The relationships of declining grip strength with fine motor function, as measured by the ALS Functional Rating Scale-Revised (ALSFRS-R) and with health-related quality of life for arm function, as measured by questions from the 5-item ALS Assessment Questionnaire (ALSAQ-5), however, have not been fully described

### FORTITUDE-ALS

- FORTITUDE-ALS was a 12-week, Phase 2, double-blind trial in 458 patients with ALS, who were randomized to 1 of 3 doses of the selective fast skeletal muscle troponin activator, *reldesemtiv*, or placebo<sup>1</sup>
- Outcome measures included:
  - Grip strength
  - ALSFRS-R: fine motor domain; i.e., handwriting, cutting food, dressing/hygiene
  - ALSAQ-5: Question 2 assesses the patients' perception of difficulty using their arms and hands

## OBJECTIVES

- To investigate the relationship between grip strength and fine motor function as measured by:
  - The fine motor domain sub-score of the ALSFRS-R (lower values reflect worse function)
  - Patients' perception of difficulty using their arms and hands as measured by responses to Question 2 of the ALSAQ-5 (higher values reflect worse function)

## METHODS

- In FORTITUDE-ALS (NCT03160898), ALSFRS-R, bilateral grip strength, and the ALSAQ-5 were collected at Screening, Day 1, Weeks 2, 4, 8, 12, and follow-up
- The average grip strength combined for both hands was summarized for men, women, and both sexes combined using descriptive statistics for:
  - The ranges of the fine motor domain sub-score (combined for all collection times)
  - The change in the fine motor domain sub-score (changes from baseline to each of the later time points)
- For all 7 time points pooled, Spearman's correlation coefficients were calculated between average grip strength combined for both hands and:
  - The ALSFRS-R fine motor domain sub-score
  - Question 2 of the ALSAQ-5
- We defined coefficients <0.3 as very weak correlation, 0.3–0.49 as weak, 0.5–0.69 as moderate, 0.7–0.8 as strong, and >0.8 as very strong

## RESULTS

Table 1. Average grip strength by ranges of ALSFRS-R fine motor domain sub-score

Sub-score range	0–2	3–5	6–8	9–12
<b>Grip strength, lbs, mean ± SD</b>				
All patients	4.97 ± 7.02	14.9 ± 11.4	31.9 ± 17.5	53.2 ± 23.1
Men only	6.27 ± 7.78	15.32 ± 11.59	35.60 ± 19.48	63.21 ± 24.47
Women only	2.53 ± 4.39	14.22 ± 11.03	25.54 ± 10.58	40.29 ± 12.25

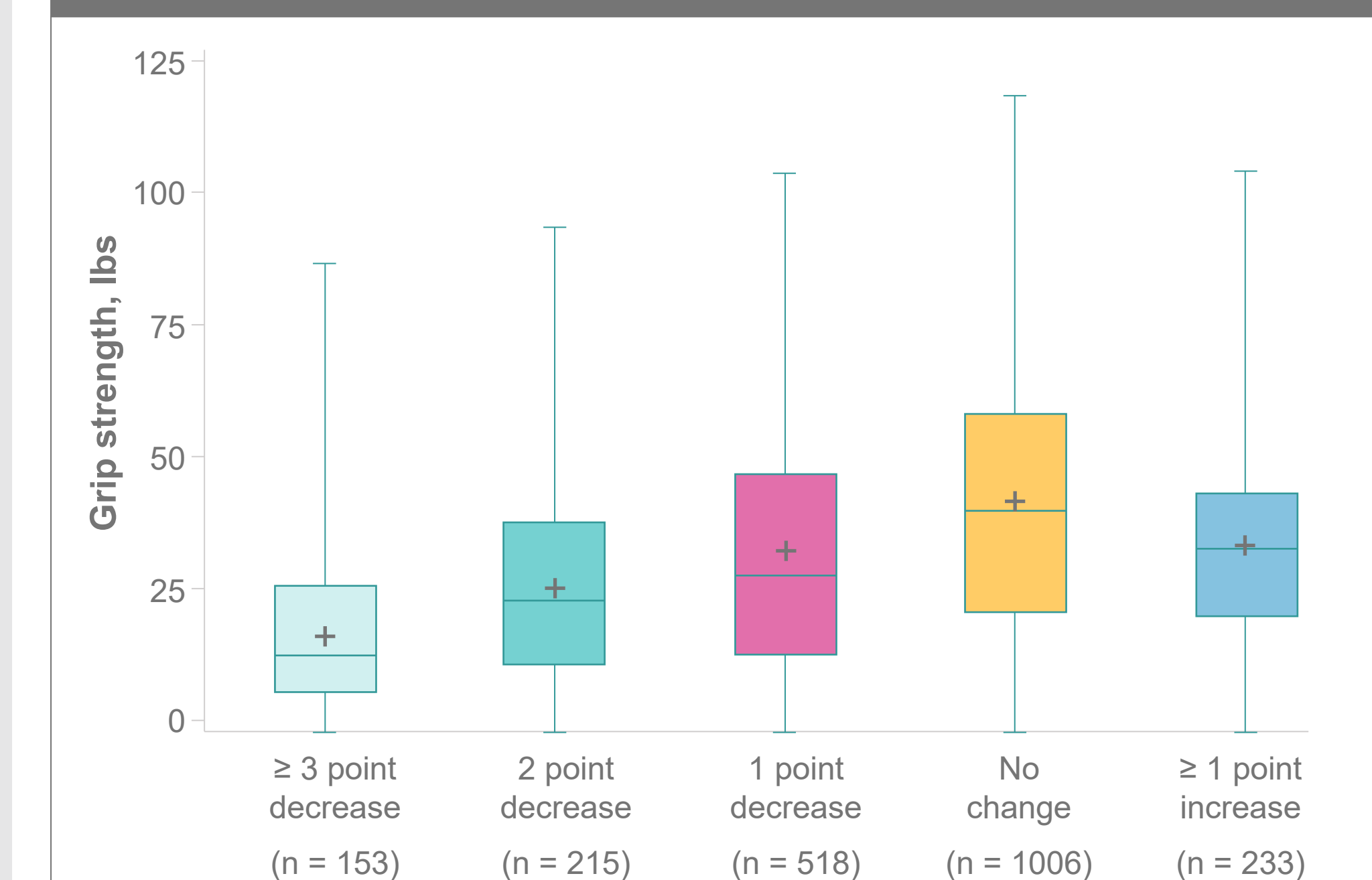
Based on data points at all visits combined. ALSFRS-R, ALS Functional Rating Scale-Revised; lbs, pounds; SD, standard deviation

Table 2. Average grip strength by change in ALSFRS-R fine motor domain sub-score

Sub-score change	≥ 3 point decrease (n = 153)	2 point decrease (n = 215)	1 point decrease (n = 518)	No change (n = 1006)	≥ 1 point increase (n = 233)
Grip strength, lbs, mean ± SD	18.49 ± 15.49	27.27 ± 19.94	34.39 ± 25.52	43.71 ± 26.49	35.03 ± 18.85

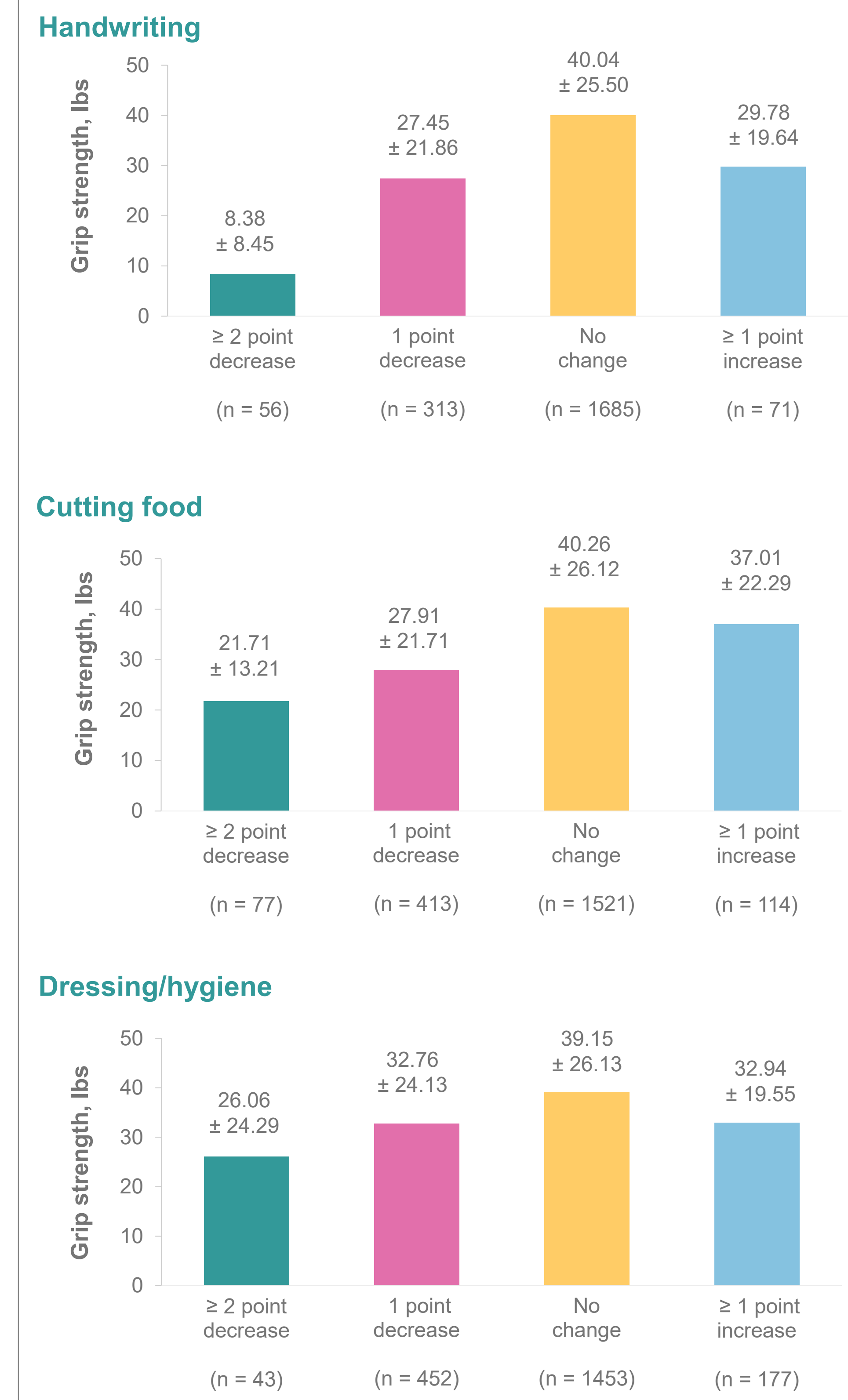
Data for all patients (men and women). Sub-score change is change from baseline to each post-baseline data point that collected data. Grip strength is the average for both hands combined. ALSFRS-R, ALS Functional Rating Scale-Revised; lbs, pounds; SD, standard deviation

Figure 1. Average grip strength by change in ALSFRS-R fine motor domain sub-score



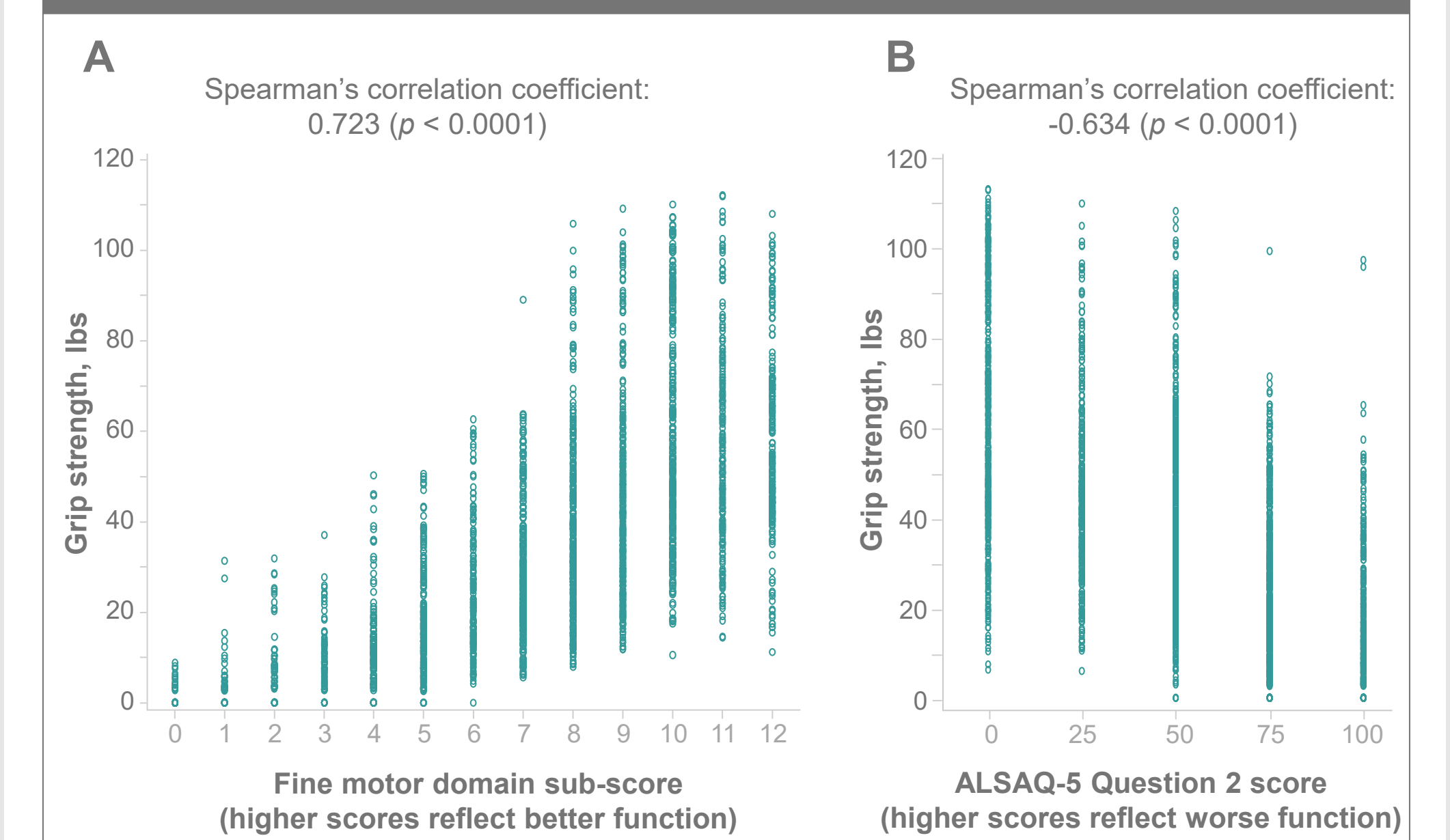
Data for all patients (men and women). Sub-score change is change from baseline to each post-baseline data point that collected data. Horizontal lines show the median values, the boxes the 25th to 75th percentiles, and the whiskers show the minimum to maximum values. Crosses indicate the mean. ALSFRS-R, ALS Functional Rating Scale-Revised; lbs, pounds

Figure 2. Average grip strength by change in ALSFRS-R handwriting, cutting food, and dressing/hygiene



Data for all patients (men and women). Sub-score change is change from baseline to each post-baseline data point that collected data. Average grip strength is for both hands combined. Bars show mean, values above the bar show mean and standard deviation. ALSFRS-R, ALS Functional Rating Scale-Revised; lbs, pounds

Figure 3. Scatter plots between average grip strength and A) ALSFRS-R fine motor domain or B) ALSAQ-5 Question 2



ALSAQ-5, 5-item ALS Assessment Questionnaire; ALSFRS-R, ALS Functional Rating Scale-Revised; lbs, pounds

## CONCLUSIONS

- In this analysis of FORTITUDE-ALS, mean grip strength in both hands combined:
  - Was strongly correlated with the fine motor domain sub-score of the ALSFRS-R
  - Was moderately correlated with ALSAQ-5 Question 2 (perceived difficulty using arms)
- Our results suggest that grip strength has clinical and patient relevance as an outcome measure in ALS clinical trials

### References

1. Shefner JM et al. Amyotroph Lateral Scler Frontotemporal Degener 2021;22:287-99.

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