

Table S1. Alcohol and smoking status overall and according to the tertiles of Δ FS distribution among patients in Apulia region.

| Variable | Category | All (N = 57) | I: Slow progres- sion rate of dis- ease (N = 21) | II: Medium pro- gression rate of disease (N = 13) | III: Fast progres- sion rate of dis- ease (N = 23) | <i>p</i> -value | SMD |
|---------------------------------------|-----------------|-----------------|--|---|--|--------------------|-------|
| Alcoholic drink- ing status - N(%) | Current drinker | 35 (61.4) | 12 (57.1) | 9 (69.2) | 14 (60.9) | 0.453 [#] | 0.385 |
| | Former drinker | 1 (1.8) | 0 (0.0) | 1 (7.7) | 0 (0.0) | | |
| | Non-drinker | 21 (36.8) | 9 (42.9) | 3 (23.1) | 9 (39.1) | | |
| Wine drinking status - N(%) | Current drinker | 33 (57.9) | 12 (57.1) | 8 (61.5) | 13 (56.5) | 0.194 [#] | 0.469 |
| | Former drinker | 2 (3.5) | 0 (0.0) | 2 (15.4) | 0 (0.0) | | |
| | Non-drinker | 22 (38.6) | 9 (42.9) | 3 (23.1) | 10 (43.5) | | |
| Smoking habits - N(%) | Current smoker | 10 (17.5) | 4 (19.0) | 4 (30.8) | 2 (8.7) | 0.241 [#] | 0.524 |
| | Former smoker | 2 (3.5) | 0 (0.0) | 1 (7.7) | 1 (4.3) | | |
| | Non-smoker | 45 (78.9) | 17 (81.0) | 8 (61.5) | 20 (87.0) | | |

Patients represent a subgroup of all 241 ALS patients, with residency in Apulia. Tertiles of Δ FS distribution were ≤ 0.333 (I); $0.334 - 0.875$ (II); >0.875 (III)

Table S2. ΔFS distribution according to alcohol load (during lifetime) in Apulia ALS patients. Former drinkers were excluded from the analysis.

| Variable | Statistic | All (N=56) | I: Non-drink- ers (N=21) | II: ≤1° drinks per day* (N=14) | III: >1° drinks per day* (N=21) | II vs. I (p-value) | III vs. I (p-value) | III vs. II (p-value) |
|------------------|-------------------|----------------------|-----------------------------------|---|--|-----------------------|------------------------|-------------------------|
| ΔFS [#] | Median (range) | 0.68 [0.00- 5.33] | 0.64 [0.02- 5.33] | 0.65 [0.00- 4.33] | 0.72 [0.08- 4.20] | 0.921 | 0.781 | 0.881 |

Patients represent a subgroup of all 241 ALS patients, with residency in Apulia.
SD: standard deviation; p-values were reported from pairwise contrasts defined in ANOVA models; [#]log-transformed variable was used in the ANOVA model (because of skewed distribution); °Median cut-off; *The drinking intensity was computed as the weighted mean number of standard alcoholic units per day at different age periods with weights equal to the number of years spent drinking (i.e. drinking duration) within each age period for all type of beverages

Table S3. Details for power calculation to detect a statistically significant ($p < 0.05$) difference of log- Δ FS means among smoke groups (i.e. non-smokers vs. light vs. heavy smokers) using a one-way ANOVA model. Former smokers are not considered in the present analysis.

| Smoke groups | N | log- Δ FS | |
|------------------------------|-----|------------------|-------|
| | | Mean | SD |
| Non-smokers | 187 | -0.714 | 1.067 |
| ≤ 14 cigarettes per day | 21 | -0.717 | 1.344 |
| > 14 cigarettes per day | 23 | -0.349 | 0.991 |
| Overall | 231 | -0.678 | 1.088 |

$$SD_m = \sqrt{\frac{[(-0.714) - (-0.678)]^2}{3} + \frac{[(-0.717) - (-0.678)]^2}{3} + \frac{[(-0.349) - (-0.678)]^2}{3}} \approx 0.19$$

Given the groups sample size of 187, 21 and 23 subjects and under the assumption that the log- Δ FS's SD of 1.1 was the same within each group, this sample achieved 80% of statistical power (i.e. 1- type II error) to detect a SD_m of 0.23 as statistically significant, using a one-way ANOVA model, having fixed a type I error of 5%. Because the observed SD_m was lower than the expected, we found that the actual statistical power was 64%.

N: number of subjects; SD: standard deviation of log- Δ FS; SD_m: standard deviation of log- Δ FS means