**Supplementary information**

Proposed predictors of ALSFRS slope steepness

1**) Bulbar rather than limb onset**: Gordon 2010 and Qureshi 2006 found that bulbar onset leads to steeper slopes, but not all studies replicated these findings (Magnus 2002).

2) **Age of onset**: Gordon 2010 found that older age at onset is predictive of a steeper slope, but not all studies replicated these findings (Magnus 2002).

3) **A shorter time period between onset of symptoms and diagnosis**: indicated steeper progression (Qureshi 2006).

4) **Having** **served** **active duty as an Army Veteran**: led to a steeper slope of progression (Qureshi 2006).

5) **Level of uric acid**: was predictive in males (Pagnoni 2012).

6) **Size of repeat expansion in the gene C9ORF72:** was predictive of progression (Brettschneider 2012).

Proposed non-predictors of ALSFRS slope steepness include:

Gender, family history, nutrition (fish, milk), infection in last 3 years, head trauma, heart disease, geographical area, history of gum disease, history of hypertension, history of neck trauma, history of pet ownership, history of physical trauma, history of polio vaccination, history of psychiatric illness, history of thyroid disease, history of toxin exposure, marital status, missing teeth, root canal procedure, tooth fillings, use of a cholesterol lowering agent, welding as occupation, number of activities, smoking quit and start age, number of cigarettes smoked per day, weight, height, mean hours of activity, years of education, baseline ALSFRS, age of symptom onset or diagnosis or enrollment.

**However all of these factors were only examined in small studies and none can be considered conclusive.**

**Summary: Predictive factors of steep ALSFRS slope are disputed but include: bulbar onset, older age of onset, short time between onset and diagnosis, active military duty, and low levels of uric acid.**

**Note that ALSFRS slope is predictive of survival time (see below) but factors associated with survival were not necessarily found to be associated with ALFRS slope.**

**Also note that most studies were very small (see table 1) and therefore limited in predictability.**

**Predictors of shorter survival times**

**1) ALSFRS slope:** was repeatedly found to be predictive of survival, with a steeper slope correlated with shorter survival times (Magnus 2002, Traynor 2004, Kollewe 2008, Gordon 2010 and Pagnoni 2012) this was true for various stretches of time over which ALSFRS was measured (Kollewe 2008). Absolute number at measure was predicted; Kaufmann 2005) in one study.

**2) Functional vital capacity (FVC) slope:** was predictive of survival, with a steeper decline correlated with shorter survival times (Magnus 2002, Traynor 2004, Kollewe 2008 and Pagnoni 2012).

**3) Site of onset:** bulbar onset was correlated with shorter survival times (Magnus 2002, Del Aguila 2003, Testa 2004, Czaplinski 2006, Mandiroli 2006, Kihira 2008, Pastula 2009, Gordon 2010 and Pagnoni 2012 ) than limb onset. Early manifestations of bulbar symptoms within the first year were associated with worse survival (Fujimura-kiyono 2011). Patients with simultaneous appearance in 2 sites never survived more then 5 years (Pagnoni 2012).

**4) Time between onset and second affected site/diagnosis:** shorter time was predictive of shorter survival (time until second site Fujimura- kiyono 2011, time to diagnosis Del Aguila 2003, Testa 2004 and Pastula 2009) this is similar to slope of ALSFRS.

**5) Age of onset:** older age of onset was predictive of shorter survival (Magnus 2002, Del Aguila 2003, Testa 2004, Czaplinski 2006, Mandiroli 2006, Pastula 2009, Gordon 2010, Pagnoni 2012, Kihira 2008 and Zoccolella 2012).

**6) BMI:** was correlated with survival (Pagnoni 2012). Also absolute weight: there was a ‘U’-shaped association between BMI and mortality, with the highest survival at 30–35 kg/m2 (Pagnoni 2011).

**7) Baseline uric acid levels:** lower levels predicted shorter survival (Pagnoni 2012).

**8) Marital status:** lack of marital partner is associated with shorter survival (Del Aguila 2003).

**9) Coefficient of variation of heart rate** (Pinto 2012).

**10)** **Microglial pathology in the corticospinal tract** (Brettschneider 2012)

**Summary: Factors predicting survival include ALSFRS and FVC and time between onset and diagnosis, site of onset (bulbar leads to shorter than limb), age of onset (older<younger).**

**Factors predictive but less supported: BMI (there is apparently an optimal BMI), marital status (being married leads to longer survival), uric acid levels, and coefficient of variation of heart rate.**

**Again note the limitation of the small number of patients in most studies.**

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