Supplementary file 1: Variables, data sources and statistical methods

Variables and data sources

Demographic clinical characteristics

The following demographic and clinical characteristics were collected: gender, age of onset, duration of disease, ALS Functional Rating Scale revised (ALS-FRSr), and the King’s clinical staging of ALS.4

Setting

The participating ALS centres were all part of a multicentre case management network. Data were collected on a web-based platform called “APST” (Ambulanzpartner Soziotechnologie APST GmbH, https://www.ambulanzpartner.de/). For the assessment of drugs, the ID MEDICS® software was used, which features a complete compilation of all medicines registered within the German health care system.

ALS-related medicines

Frequency of riluzole use

Data on riluzole prescriptions were recorded. The frequency of riluzole treatment was calculated on the basis of the number of patients receiving riluzole as part of their ALS treatment regimen. Each initiation of riluzole treatment in any one patient was counted only once, irrespective of the number of repeat prescriptions over time and the overall treatment period.

Symptomatic drugs assigned to ALS treatment

ALS-trained neurologists decided which drugs the respective patient was due to receive to alleviate their symptoms. The definition “symptomatic medicine” was assigned to a drug when prescribed for the control of (at least) one of the following ALS-related symptoms: sialorrhea, spasticity, depression, emotional lability, pain, dyspnoea, insomnia, anxiety, restlessness, muscle cramps, fasciculations or constipation. The data on prescription drugs were recorded using the drug’s generic name. As we had no confirmation if the medicines prescribed were ultimately administered, the subject of scrutiny was the patients’ medical need rather than their actual intake of drugs.
**Ranking of symptomatic drugs assigned to ALS treatment**

Symptomatic drugs were ranked according to their frequency of use, i.e. the number of patients receiving the respective drug. Each drug was counted once per patient upon initiation of treatment, irrespective of the number of repeat prescriptions over time and the overall treatment period.

**Assignment of symptomatic drugs to pharmacologic domains**

Symptomatic drugs were allocated to pharmacologic domains and, by this means, to distinct medical indications. The following domains were distinguished: 1) anticholinergic drugs (indication: sialorrhea), 2) antidepressant drugs (indication: emotional lability or depression); 3) spasmyloytic drugs (indication: spasticity); 4) benzodiazepines (indication: anxiety, restlessness, dyspnoea or palliative sedation); 5) non-opioid analgesic drugs (indication: mild to moderate pain); 6) opioid drugs (indication: moderate to severe pain, dyspnoea or palliative sedation); 7) cramp-reducing drugs (indication: muscle cramps); 8) hypnotic drugs (indication: insomnia); 9) anticonvulsant drugs (indication: neuropathic pain, fasciculations); 10) prokinetic and laxative drugs (indication: reflux, flatulence, and constipation).

**Number of symptomatic drugs per patient**

The number of drugs per patient referred to all symptomatic medicines of any given patient that were applied during the course of disease. It is confined to distinct drugs used for symptom control that had previously been defined as ALS-related symptomatic drugs.

**Number of symptomatic drugs per patient in correlation to King´s clinical stage of ALS**

The number of drugs per patient referred to all ALS-related symptomatic medicines that were applied in correlation to the King´s clinical stage of ALS. Four cohorts were differentiated according King’s clinical stage that was reached by any given patient. The most advanced King’s clinical stage was counted per patient, irrespective of previously passed clinical stages. King’s clinical stage 1 translated to the involvement of one clinical region. Stage 2 and 3 was reached with the involvement of a second and third clinical region, respectively. Stage 4 referred to nutritional or respiratory failure, as defined by the use of percutaneous endoscopic gastrostomy (PEG) or ventilation therapy (non-invasive or invasive), respectively.
**Statistical methods**

Descriptive statistics were used for the statistical analysis (frequency in percent, mean, median, standard deviation in ±). Group comparisons employed t-test for scale variables. P values were reported at a 95% confidence interval. The data were analysed using SPSS (version 25.0).