Neuropalliative care in the ALS Clinic: Prognosis, Therapies, and Models of Care

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Objectives

- Understand clinical disease trajectory and prognostication in ALS
- Identify the impact of disease-modifying and supportive care interventions on prognosis and quality of life
- Compare and contrast models of care in the ALS ambulatory clinic setting

Outline

- Brief Overview of ALS
- Clinical Trajectory and Prognostication
- Effect of Therapeutic and supportive interventions on prognosis and quality of life
- Models of Care in the ALS ambulatory setting

Amyotrophic Lateral Sclerosis (ALS) Epidemiology

- Most common of the motor neuron diseases
- Annual incidence is estimated to be about 2.1 to 3.8 per 100,000 person years globally
- currently estimated prevalence of about 17 million people living with ALS in the USA, or 5 per 100,00 persons annually
- Male sex is a risk factor – 2:1 male to female predominance
- Average age of onset is 51 to 66 for sporadic cases, 45 for familial

Tiryaki E, Horak HA. ALS and other motor neuron diseases. *Continuum (Minneap Minn)*. Oct 2014;20(5 Peripheral Nervous System Disorders):1185-207. doi:10.1212/01.CON.0000455886.14298.a4

Longinetti E, Fang F. Epidemiology of amyotrophic lateral sclerosis: an update of recent literature. *Curr Opin Neurol*. 10 2019;32(5):771-776. doi:10.1097/WCO.0000000000000730

A brief note about genetics:

- 90-95% are sporadic, 5-10% are familial
- Most common genes are SOD1 (20% of familial ALS typically strong AD penetrance but with exceptions) and C9orf72
- Everyone is truly unique – there is huge variability within families and between for age of onset and gene expression due to gene-environment interaction
- * due to the low yield it is not advised for an asymptomatic person to seek out genetic testing unless more than one family member has ALS or family member has a known pathogenic mutation

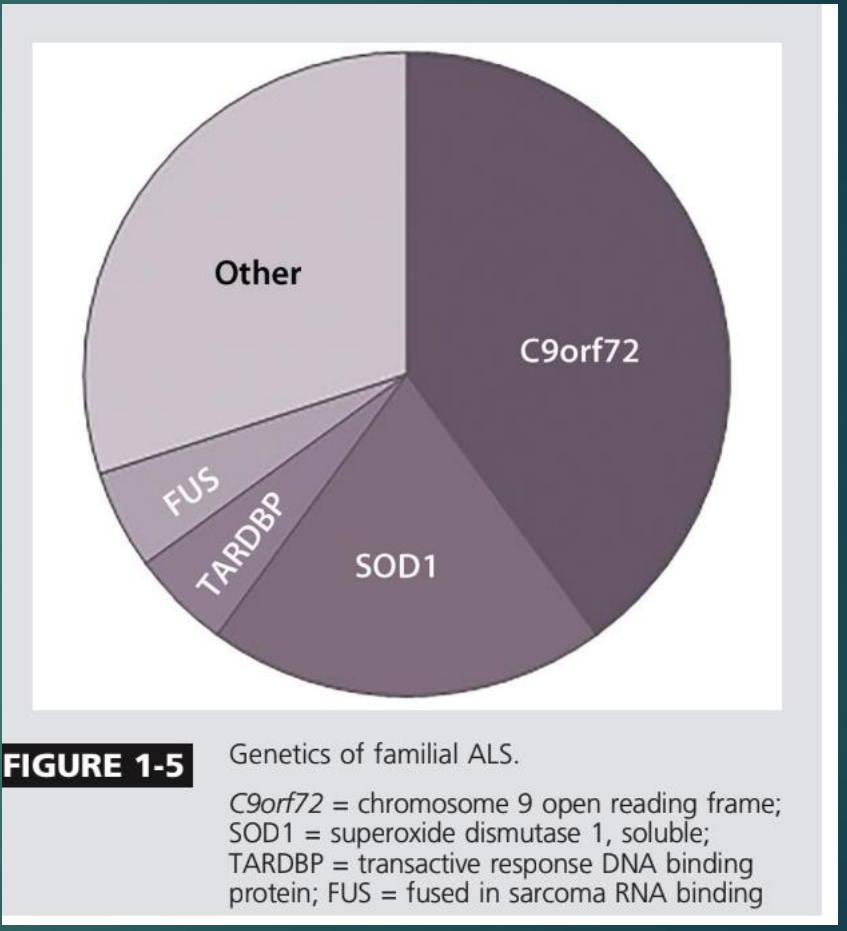


FIGURE 1-5 Genetics of familial ALS.

C9orf72 = chromosome 9 open reading frame; SOD1 = superoxide dismutase 1, soluble; TARDBP = transactive response DNA binding protein; FUS = fused in sarcoma RNA binding

Tiryaki E, Horak HA. ALS and other motor neuron diseases. *Continuum (Minneap Minn)*. Oct 2014;20(5 Peripheral Nervous System Disorders):1185-207. doi:10.1212/01.CON.0000455886.14298.a4

Pathophysiology

- Neurodegenerative disorder of the upper and lower motor neurons
- Classically localizes to the Anterior Horn, but in reality includes the corticobulbar and corticospinal tracts
- Clinically this results in **spastic weakness** or atrophic **flaccid weakness** of the tongue, pharynx, larynx, face, arms, legs, and respiratory muscles
- Other symptoms include cognitive deficits, pseudobulbar affect, bladder hyperactivity/urinary retention, constipation due to abdominal muscle weakness
- Cardiac failure/arrhythmia are not a typical feature of disease

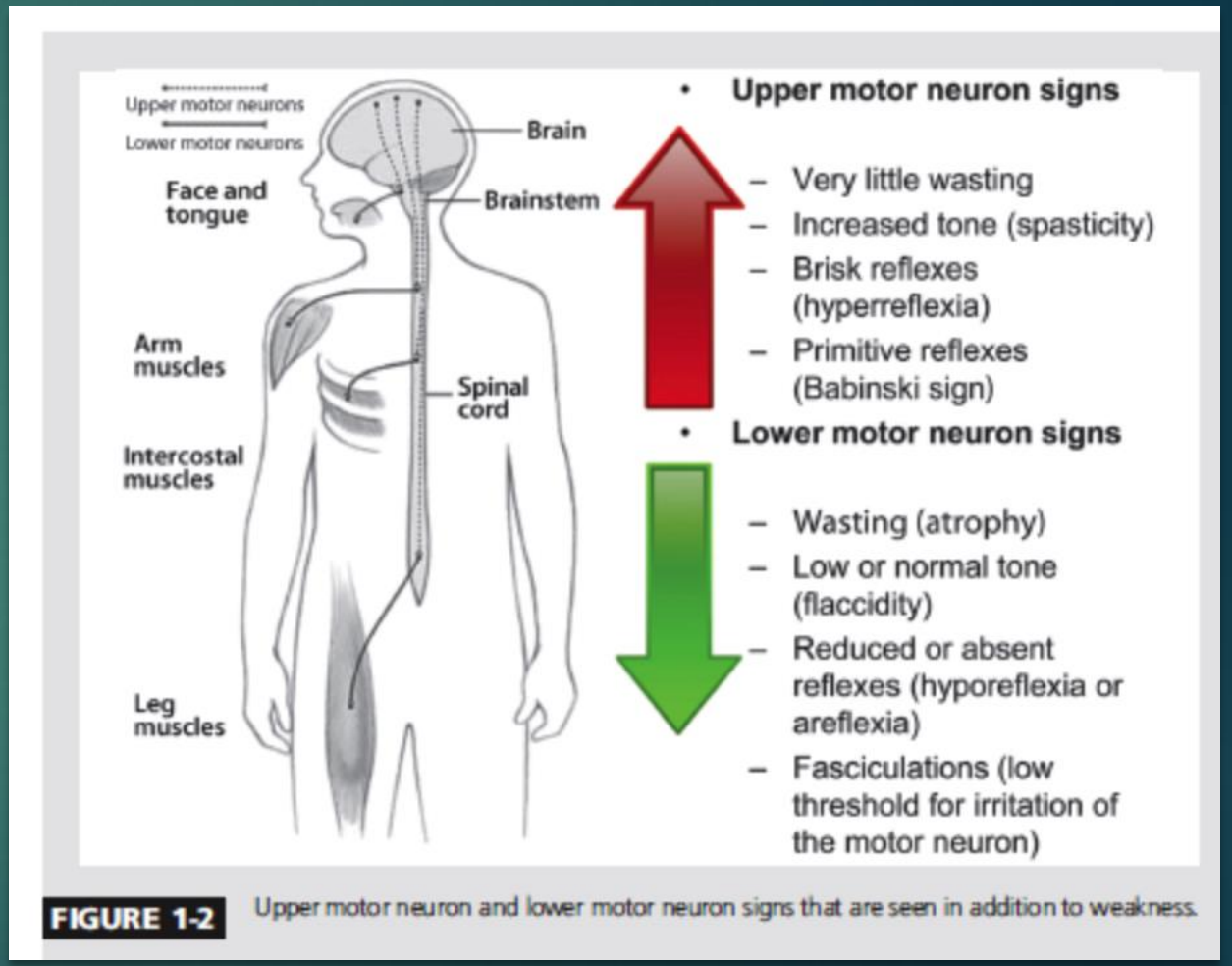


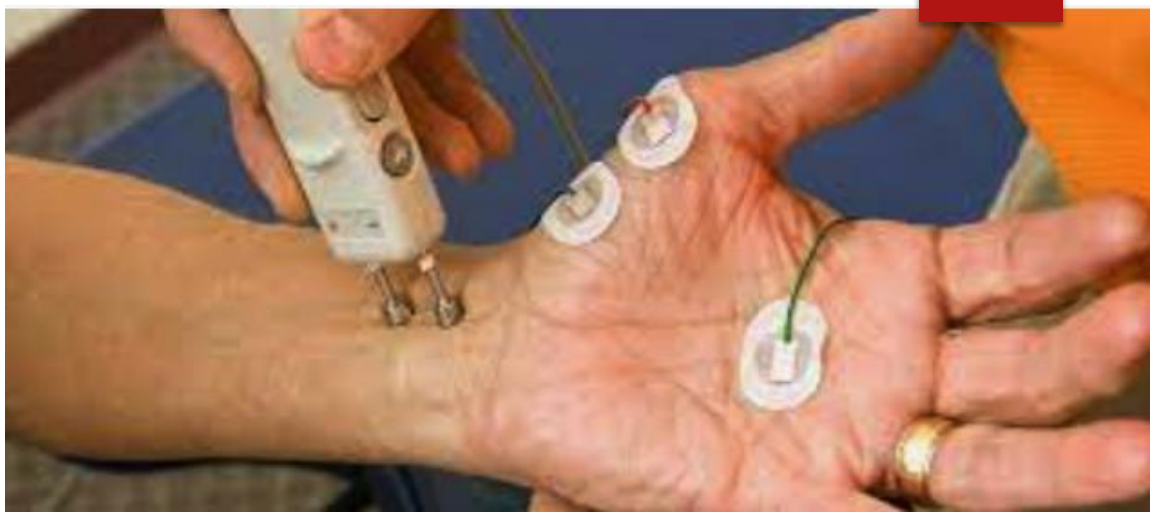
FIGURE 1-2 Upper motor neuron and lower motor neuron signs that are seen in addition to weakness.

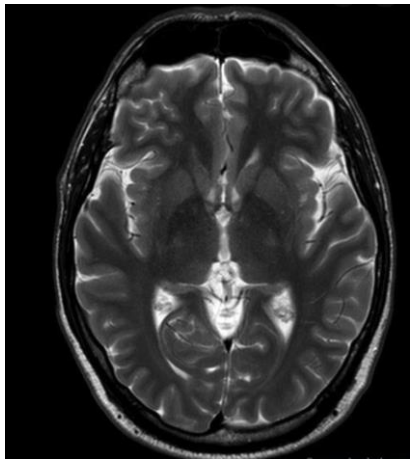
Talbott EO, Malek AM, Lacomis D. The epidemiology of amyotrophic lateral sclerosis. *Handb Clin Neurol*. 2016;138:225-38. doi:10.1016/B978-0-12-802973-2.00013-6

The Journey to a Diagnosis – Living with Uncertainty

- There is no one confirmatory test for ALS
- Median time to diagnosis is about 12 months, range 9 to 24 months
- Patients will often have experienced minimizing of symptoms, multiple MRI scans of the brain, C spine, L spine, T spine, increasingly complex laboratory workup, and often multiple NCS/EMG studies
- General Neurologists are at times hesitant to diagnose
- Results in New diagnosis disclosure encounters with patients who have weeks to months left, no diagnosis, no medical equipment at home

Longinetti E, Fang F. Epidemiology of amyotrophic lateral sclerosis: an update of recent literature. *Curr Opin Neurol*. 10 2019;32(5):771-776. doi:10.1097/WCO.0000000000000730





Clinical Trajectory

Early Course –

Painless weakness in one clinical region with some degree of functional compromise
- e.g. Bulbar (dysarthria or dysphagia) vs Limb onset

Disease Progression –

-Spread of weakness to other body regions, progression of severity of bulbar +/- limb +/- respiratory +/- impairment.
-Loss of independence in various domains.

End-stage -

- Near complete loss of independent function, respiratory failure (total dependence on NIV/TIV), nutritional failure (PEG dependence),

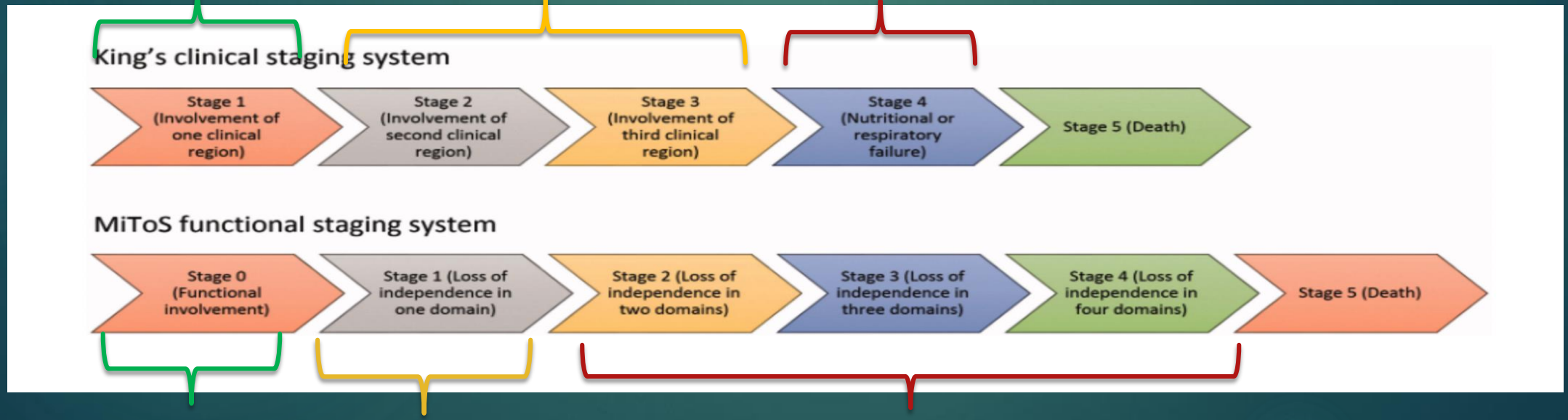
Staging

- Milano-Torino functional staging system vs King's
- *Clinical regions: Bulbar, Upper Limb, Lower Limb
- *Respiratory failure – requirement for NIV
- *Nutritional failure – requirement for PEG
- *Domains –defined by loss of autonomy in domains on the ALSFRS

Table 1 Functional domains and stages

ALSFRS domain	Item	Score	Functional score*
Movement (walking/self-care)†	8 Walking	4 Normal	0
		3 Early ambulation difficulties	
		2 Walks with assistance	
		1 Non-ambulatory functional movement only	1
	OR	0 No purposeful leg movement	
	6 Dressing and hygiene	4 Normal function	0
		3 Independent and complete self-care with effort or decreased efficiency	
		2 Intermittent assistance or substitute methods	
		1 Needs attendant for self-care	1
		0 Total dependence	
Swallowing	3 Swallowing	4 Normal eating habits	0
		3 Early eating problems; occasional choking	
		2 Dietary consistency changes	
		1 Needs supplemental tube feeding	1
		0 NPO (exclusively parenteral or enteral feeding)	
Communicating†	1 Speech	4 Normal speech processes	0
		3 Detectable speech with disturbances	
		2 Intelligible with repeating	
		1 Speech combined with non-vocal communication	1
	AND	0 Loss of useful speech	
	4 Handwriting	4 Normal	0
		3 Slow or sloppy; all words are legible	
		2 Not all words are legible	
		1 Able to grip pen but unable to write	1
		0 Unable to grip pen	
Breathing†	10 Dyspnea	4 None	0
		3 Occurs when walking	
		2 Occurs with one or more of: eating, bathing, dressing	
		1 Occurs at rest, difficulty breathing when either sitting or lying	1
	OR	0 Significant difficulty, considering using mechanical respiratory support	
	12 Respiratory insufficiency	4 None	0
		3 Intermittent use of NIPPV	
		2 Continuous use of NIPPV during the night	1
		1 Continuous use of NIPPV during the night and day	
		0 Invasive mechanical ventilation by intubation or tracheostomy	

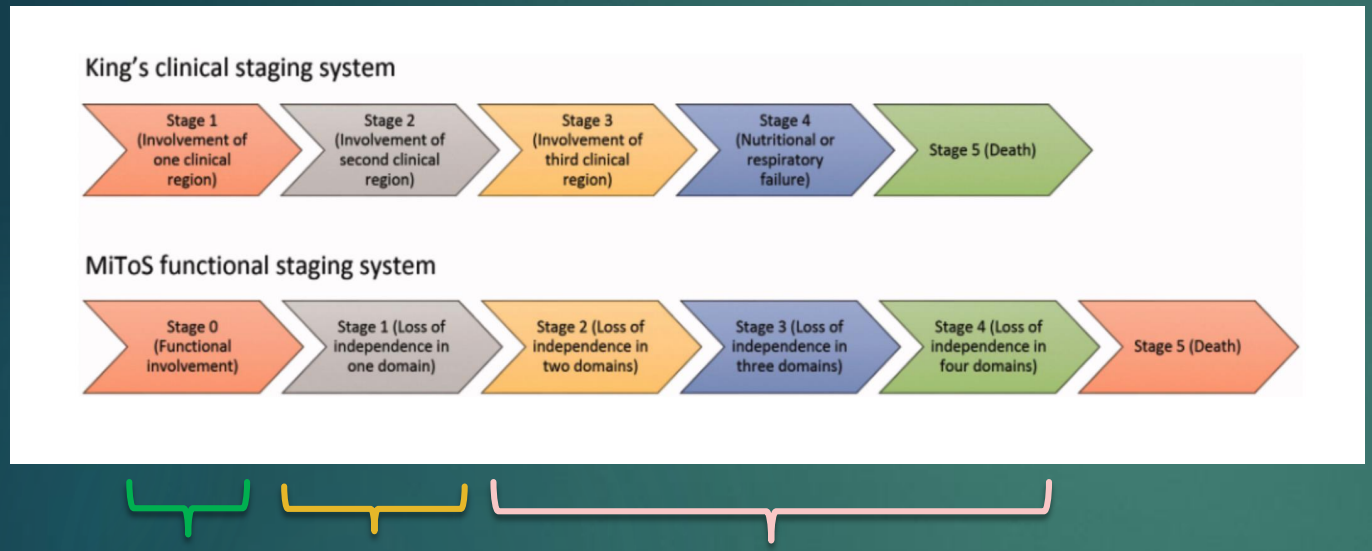
Early Disease Progression Late/End-Stage



Chiò A, Hammond ER, Mora G, Bonito V, Filippini G. Development and evaluation of a clinical staging system for amyotrophic lateral sclerosis. *J Neurol Neurosurg Psychiatry*. Jan 2015;86(1):38-44. doi:10.1136/jnnp-2013-306589

Staging and Clinical Trajectory

Early | Disease Progression | Late/End-Stage



A)

King's staging system (*n*)	Median number of months from onset (IQR)	SMT (IQR)
1 (95)	9.0 (5.4–13.0)	0.33 (0.24–0.46)
2 (49)	18.4 (12.8–22.6)	0.62 (0.51–0.73)
3 (67)	18.9 (12.6–24.6)	0.67 (0.55–0.82)
4 (32)	24.8 (17.4–30.9)	0.86 (0.79–0.95)
5 (95)	27.7 (22.0–34.0)	1.00 (1.00–1.00)

B)

Milano-Torino staging system (*n*)	Median number of months from onset (IQR)	SMT (IQR)
0 (95)	9.0 (5.4–12.9)	0.33 (0.24–0.46)
1 (94)	16.5 (11.9–22.1)	0.58 (0.49–0.71)
2 (37)	25.0 (20.0–31.7)	0.88 (0.72–0.93)
3 (12)	25.1 (21.0–30.0)	0.93 (0.86–0.97)
4 (2)	27.0 (24.1–29.8)	0.95 (0.95–0.96)
5 (95)	27.7 (22.0–34.0)	1.00 (1.00–1.00)

Chiò A, Hammond ER, Mora G, Bonito V, Filippini G. Development and evaluation of a clinical staging system for amyotrophic lateral sclerosis. *J Neurol Neurosurg Psychiatry*. Jan 2015;86(1):38-44. doi:10.1136/jnnp-2013-306589

Prognosis and Prognostic Factors

- Average prognosis is between 2 and 5 years, we commonly cite about 3 years from onset to death, which is most commonly due to respiratory failure

- Other causes of death include – cardiac arrest, coronary disease, asphyxia, and PE.

- Indicators include rapid physical decline, infection, combination of cognitive impairment, risk of aspiration.

Connolly S, Galvin M, Hardiman O. End-of-life management in patients with amyotrophic lateral sclerosis. *Lancet Neurol*. Apr 2015;14(4):435-42. doi:10.1016/S1474-4422(14)70221-2

Trajectory of ALS Progression classified by ALSFRS

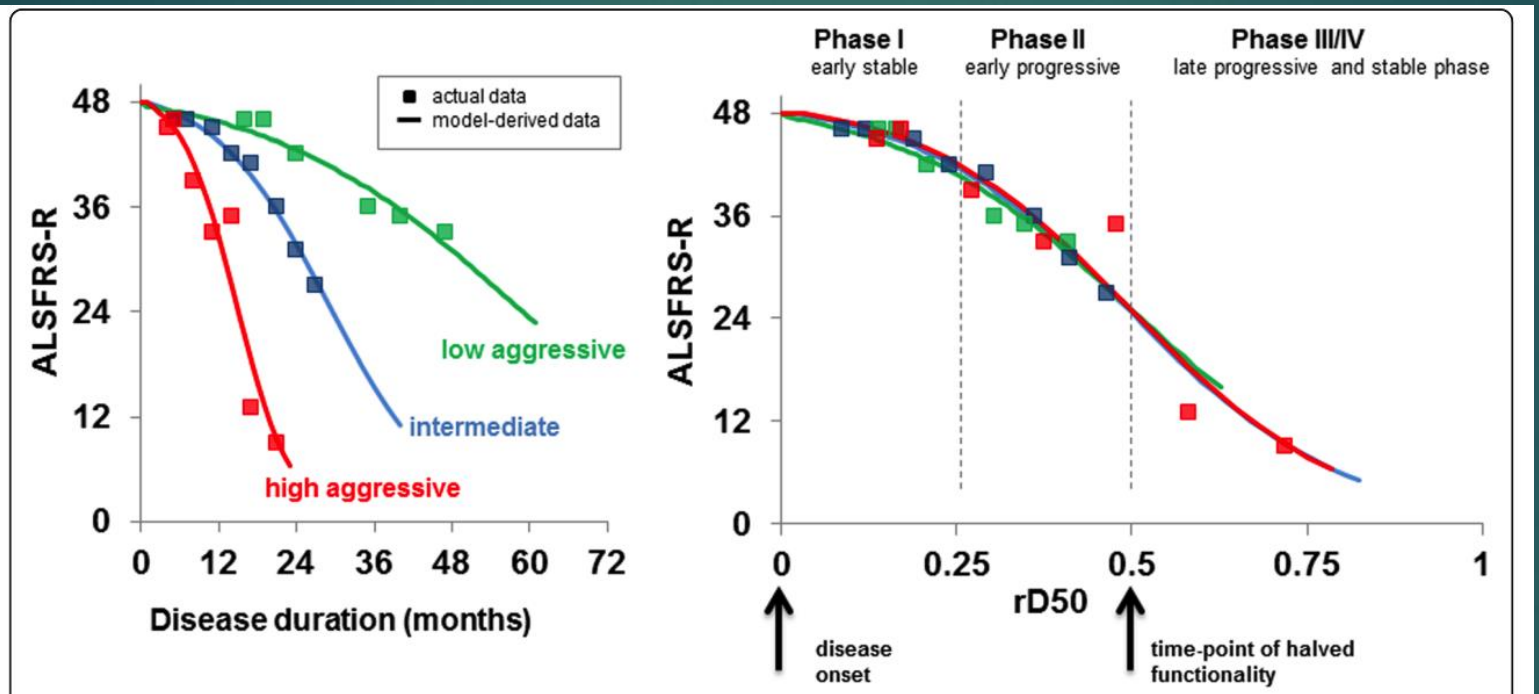
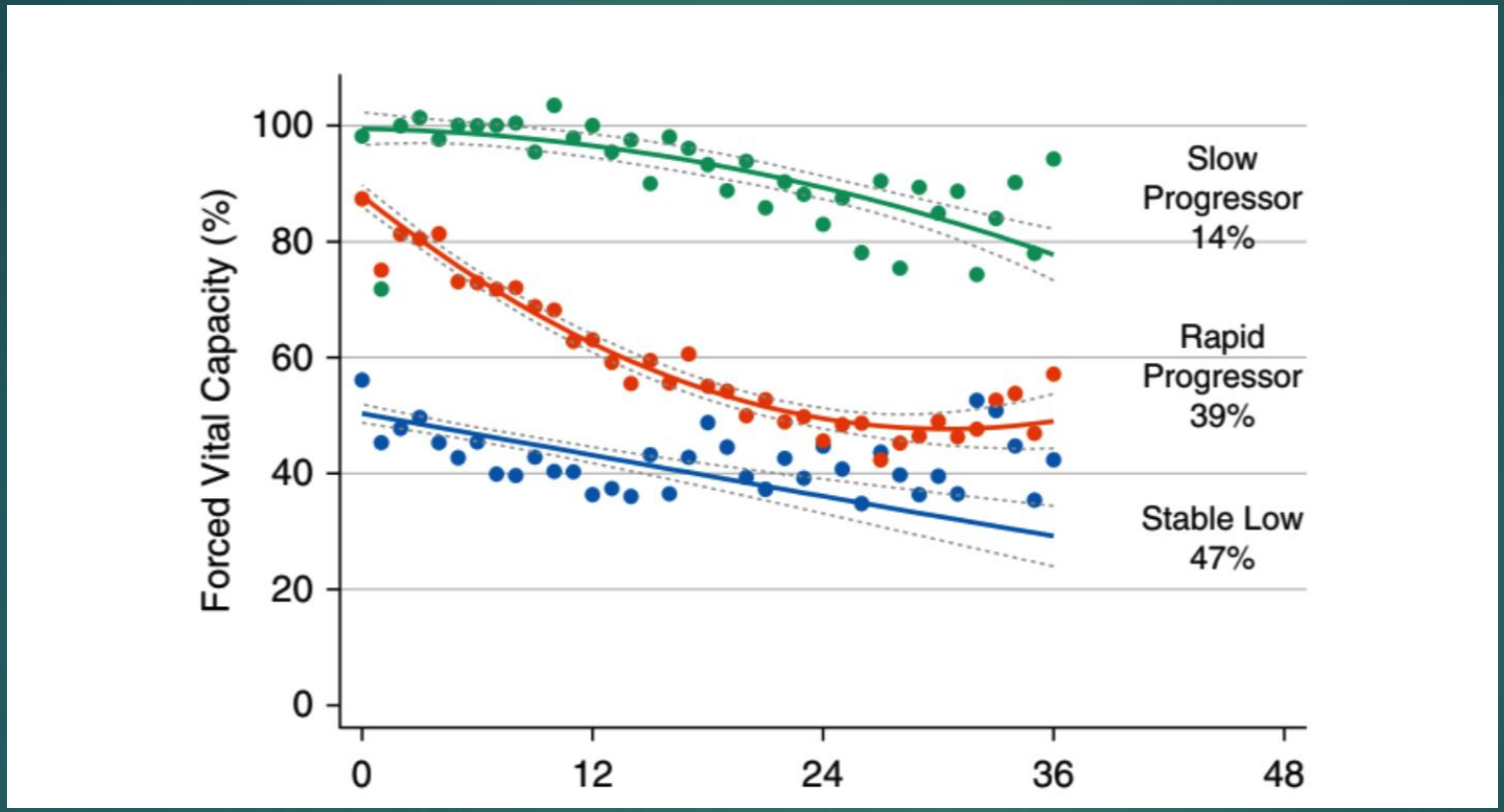


Fig. 1 The D50 model and rD50-derived disease phases. The model yields three key descriptive parameters: D50 as the time taken in months for ALSFRS-score to drop to 24 points, dx as the time constant of ALSFRS-R decay, and the rD50, which describes individual disease course covered in reference to D50. **a** D50 and dx are calculated from actual ALSFRS-R scores for 3 representative patients with distinct disease profiles; high, moderate, and low disease aggressiveness. **b** Normalization with rD50 allows for comparability between patients with vastly different disease time scales and shows that patients proceed through similar phases of functional decline independent of individual disease aggressiveness

Prell T, Gaur N, Steinbach R, Witte OW, Grosskreutz J. Modelling disease course in amyotrophic lateral Sclerosis: pseudo-longitudinal insights from cross-sectional health-related quality of life data. Health Qual Life Outcomes. 2020 May 1;18(1):117. doi: 10.1186/s12955-020-01372-6. PMID: 32357946; PMCID: PMC7195704.

Trajectory of ALS Progression classified by FVC



Ackrivo J, Hansen-Flaschen J, Jones BL, Wileyto EP, Schwab RJ, Elman L, Kawut SM. Classifying Patients with Amyotrophic Lateral Sclerosis by Changes in FVC. A Group-based Trajectory Analysis. Am J Respir Crit Care Med. 2019 Dec 15;200(12):1513-1521. doi: 10.1164/rccm.201902-0344OC. PMID: 31322417; PMCID: PMC6909832.

Characteristics of Trajectory Groups

Table 3. Baseline Penn Comprehensive ALS Center Cohort Characteristics by Most Likely Trajectory Group

Variable	Stable Low (*n* = 397)	Rapid Progressor (*n* = 329)	Slow Progressor (*n* = 111)
Age at diagnosis, yr	65 ± 12*†	62 ± 12*	60 ± 13†
Sex, M, *n* (%)	199 (50)*	199 (61)*	67 (60)
Race, *n* (%)			
White	312 (79)*†	283 (86)*	105 (94)†
African American	54 (13)	19 (6)	3 (3)
Other	31 (8)	27 (8)	3 (3)
BMI class, *n* (%)			
<18.5 kg/m^2	30 (7)*†	7 (2)*	0 (0)†
18.5–24.9 kg/m^2	173 (44)	131 (40)	44 (40)
25–29.9 kg/m^2	123 (31)	122 (37)	40 (36)
>30 kg/m^2	71 (18)	69 (21)	27 (24)
Diagnosis delay, yr	1.0 (0.6–1.4)	1.0 (0.5–1.5)‡	1.4 (0.6–2.7)‡
Symptom onset to first visit, yr	1.1 (0.7–2.0)†	1.2 (0.8–2.0)‡	2.0 (1.0–3.3)†‡
El Escorial criteria, *n* (%)			
Definite ALS	117 (29)*†	54 (16)*‡	5 (5)†‡
Possible ALS	103 (26)	84 (26)	29 (26)
Probable ALS	106 (27)	117 (36)	30 (27)
Suspected ALS	71 (18)	74 (22)	47 (42)
Symptom onset site, *n* (%)			
Limb	271 (68)*†	255 (78)*	98 (88)†
Bulbar	126 (32)	74 (22)	13 (12)
FVC seated, % predicted	56 ± 18*†	88 ± 14*‡	99 ± 13†‡

Ackrivo J, Hansen-Flaschen J, Jones BL, Wileyto EP, Schwab RJ, Elman L, Kawut SM. Classifying Patients with Amyotrophic Lateral Sclerosis by Changes in FVC. A Group-based Trajectory Analysis. Am J Respir Crit Care Med. 2019 Dec 15;200(12):1513-1521. doi: 10.1164/rccm.201902-0344OC. PMID: 31322417; PMCID: PMC6909832.

Associated Prognosis of Trajectory Group

Table 3. Baseline Penn Comprehensive ALS Center Cohort Characteristics by Most Likely Trajectory Group

Variable	Stable Low (*n* = 397)	Rapid Progressor (*n* = 329)	Slow Progressor (*n* = 111)	
0	8 (<1)	5 (<1)	2 (<1)	
Time to respiratory insufficiency, mo	11.4 (7.5–16.4)*†	19.2 (13.1–27.4)*‡	34.0 (24.3–40.2)†‡	<0.001
Survival, mo	18.8 (13.0–26.6)*†	21.7 (14.8–29.0)*‡	25.6 (17.1–33.4)†‡	<0.001
Survival from symptom onset, mo	29.0 (21.1–38.1)*†	31.5 (24.0–41.8)*‡	35.1 (27.2–45.3)†‡	<0.001

Prell T, Gaur N, Steinbach R, Witte OW, Grosskreutz J. Modelling disease course in amyotrophic lateral Sclerosis: pseudo-longitudinal insights from cross-sectional health-related quality of life data. Health Qual Life Outcomes. 2020 May 1;18(1):117. doi: 10.1186/s12955-020-01372-6. PMID: 32357946; PMCID: PMC7195704.

- Unfavorable prognostic factors
  - Genetics (For example some AD SOD1 with high penetrance)
  - Lower BMI at onset (<25)
  - ALSFRS score <40 at diagnosis
  - Rapid diagnosis (<10 months)
  - Bulbar-onset
  - Age over 65

Rosenbohm A, Peter R, Dorst J, et al. Life Course of Physical Activity and Risk and Prognosis of Amyotrophic Lateral Sclerosis in a German ALS Registry. *Neurology*. 11 09 2021;97(19):e1955-e1963. doi:10.1212/WNL.0000000000012829

Table 3 Median (First and Third Quartile) Survival Time From Interview in Months by Prognostic Covariates in 376 ALS Cases

	No.	Median survival time(Q1, Q3), mo
Age, y		
<65	161	24.6 (13.9, 49.3)
≥65	215	15.8 (7.4, 27.7)
Sex		
Male	212	19.1 (10.4, 44.9)
Female	164	16.1 (9.7, 29.2)
BMI, kg/m^2		
≤25	221	16.6 (8.5, 38.7)
>25	155	22.5 (11.0, 37.0)
ALS-FRS-R score		
<40	205	13.6 (6.6, 24.9)
≥40	171	27.5 (16.1, 54.7)
Bulbar onset		
No	249	19.9 (11.2, 42.2)
Yes	122	16.6 (8.3, 27.3)
PEG		
No	349	18.7 (11.1, 38.7)
Yes	25	6.9 (4.0, 19.7)
Diagnostic certainty, El Escorial criteria		
Possible	110	23.5 (11.2, 56.6)
Probable	234	17.5 (10.7, 34.4)
Definite	32	11.2 (6.1, 20.2)
Time from disease onset to interview, mo		
≤10	190	16.6 (9.9, 29.3)
>10	186	20.3 (10.8, 50.3)

A Practical Approach to prognosticating – (NO TRACH)

- Short years
  - ALS patient with no respiratory or swallowing impairment (FVC above 80% and normal diet, normal MIP (Above -60), no supine drop, ALSFRS >40, some independent function despite clinical symptoms, weight stable
- Months to a short year
  - Loss of function in at least one domain, no respiratory or nutritional failure
- Months (less than 6)
  - FVC <50% OR requiring continuous NIV OR short of breath even at rest
  - Loss of functional independence in at least two domains
  - PEG required for nutritional maintenance even if still able to take some PO
- Weeks to short months
  - Using AVAPS majority of waking and sleeping hours with few breaks, multiple ER visits, +/-dependent in all ADL's, severe fatigue, total loss of function in all domains

Disease Modifying Therapies: Burdens and Benefits

- US – FDA has approved two therapies for the treatment of ALS

- Riluzole
  - PO (film and tablet)

- Edaravone
  - IV
  - PO (liquid)

Riluzole

Saitoh
Lacomblez
Bensimon

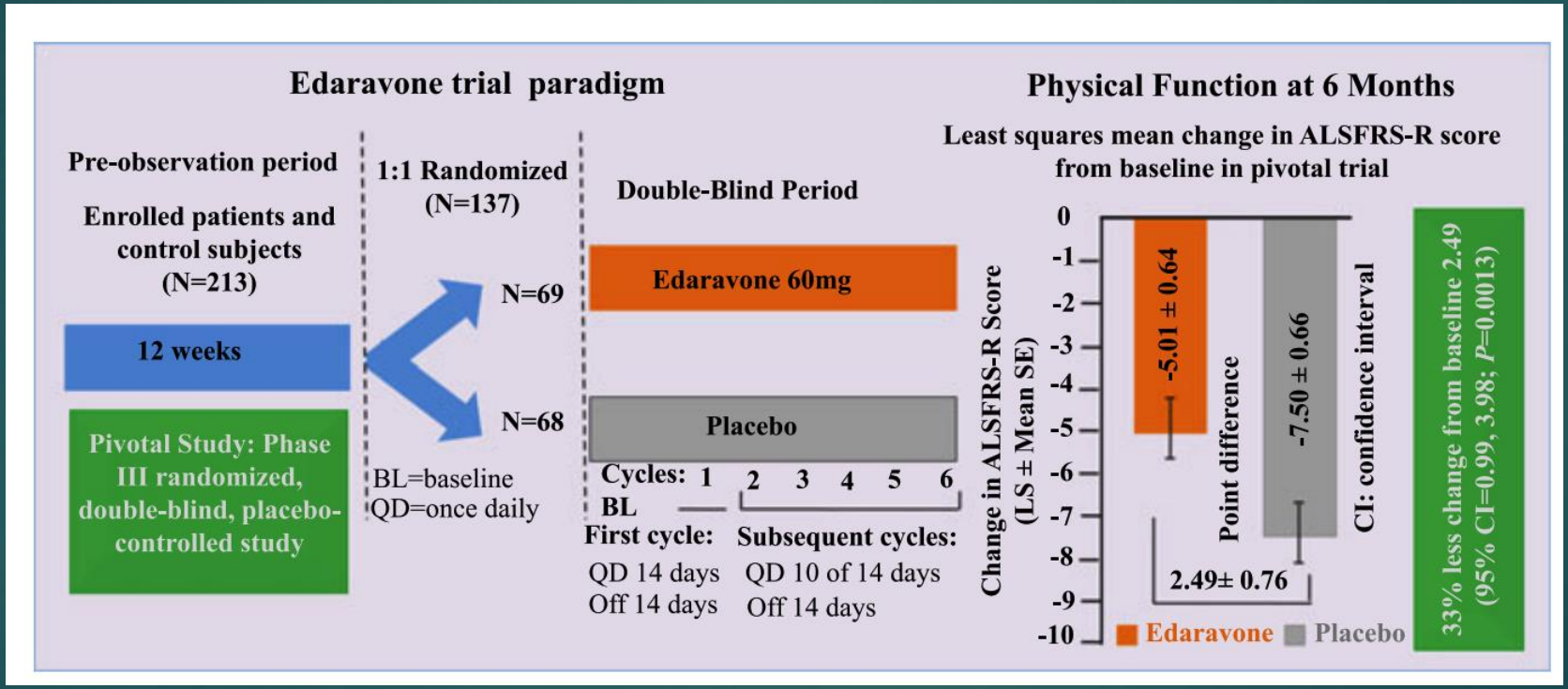
- Approved since 1995 – reduces activity at pre and post-synaptic glutamatergic nerve terminals
- Efficacy data endpoint was for survival -extends survival by 2-3 months
- Bensimon et al 1994 (n=155) – RTC. 1 year survival difference of 58% vs 74%. Median survival time 449 days vs 542 days
- and Lacomblez et all 1996 (n=959) – RTC. Primary end-point was survival without tracheostomy. At 12 months RR was significantly better for riluzole vs placebo, at 18 months no advantage.
- Overall conclusions of pooled analysis:
  - **1 year survival probability is increased by 9%, median survival is about 15 months vs 12 months**

Bensimon G, Lacomblez L, Meininger V. A controlled trial of riluzole in amyotrophic lateral sclerosis. ALS/Riluzole Study Group. N Engl J Med. 1994 Mar 3;330(9):585-91. doi: 10.1056/NEJM199403033300901. PMID: 8302340.

Lacomblez L, Bensimon G, Leigh PN, Guillet P, Meininger V. Dose-ranging study of riluzole in amyotrophic lateral sclerosis. Amyotrophic Lateral Sclerosis/Riluzole Study Group II. Lancet. 1996 May 25;347(9013):1425-31. doi: 10.1016/s0140-6736(96)91680-3. PMID: 8676624.

Edaravone

- FDA approved 2017
- Pivotal RTC 2017 – self selected those with independent ambulation, less severe disease
- Efficacy endpoint was slowed progression; observational data and small RTC demonstrates survival advantage (29.5 months vs 23.5 months)



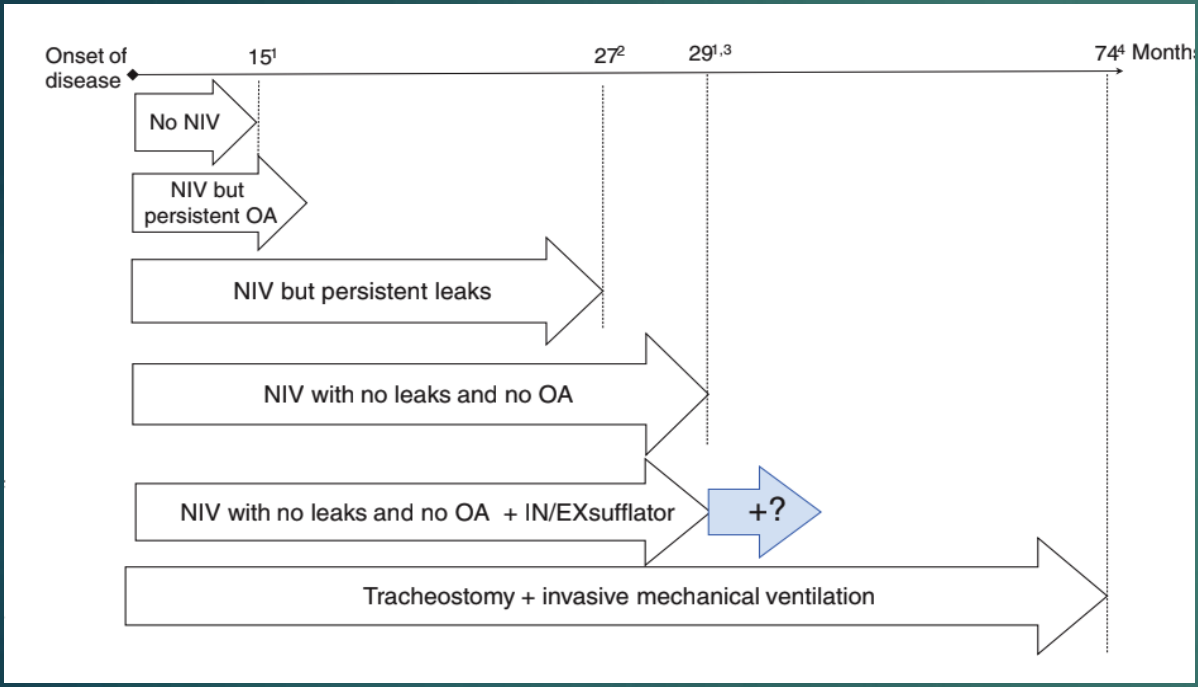
Saitoh Y, Takahashi Y. Riluzole for the treatment of amyotrophic lateral sclerosis. *Neurodegener Dis Manag*. 12 2020;10(6):343-355. doi:10.2217/nmt-2020-0033

Rilzuole vs Riluzole + Edaravone

- International study, Multicenter cohort from 12 ALS centers 2017 to 2020
- N = 324 patients, Riluzole vs Riluzole + Edaravone IV
- No significant difference in primary vs secondary endpoints (ALSFRS point progression, survival, time to respiratory failure) in a 12 month period
- Interestingly adherence and satisfaction scores for treatment were high despite the lack of efficacy and the infusion frequency

Witzel S, Maier A, Steinbach R, et al. Safety and Effectiveness of Long-term Intravenous Administration of Edaravone for Treatment of Patients With Amyotrophic Lateral Sclerosis. *JAMA Neurol*. 02 01 2022;79(2):121-130. doi:10.1001/jamaneurol.2021.4893

Impact of NIV/TIV on survival and QOL



- Median survival improvement for NIV of 14 months in all ALS variants, and as many as 19 months for bulbar-onset
- NIV has been repeatedly demonstrated to improve QoL, but does not prevent aspiration.
- Does allow for speech and PO intake

Morelot-Panzini C, Bruneteau G, Gonzalez-Bermejo J. NIV in amyotrophic lateral sclerosis: The 'when' and 'how' of the matter. *Respirology*. 06 2019;24(6):521-530.

doi:10.1111/resp.13525

Bourke SC, Tomlinson M, Williams TL, Bullock RE, Shaw PJ, Gibson GJ. Effects of ventilation on survival and quality of life in patients with amyotrophic lateral sclerosis: a randomised controlled trial. *Lancet Neurol*. Feb 2006;5(2):140-7. doi:10.1016/Snon-invasive1474-4422(05)70326-4

Impact of Tracheostomy on survival and QoL

- TIV median survival ranges from 74 to 82 months from disease onset
- Survival: 25 months after TIV initiation (2 years), ranges from 8 months to 3+ years
- Preservation of functional speech is not guaranteed
- In general patients and caregivers report general satisfaction with the procedure, and overall good QoL for the patient (50% with good QoL and 50% with worsened QoL, 81% would choose to do it again), caregivers (75% would advise their partner to do it again)
- Caregiver burden is very high

Table 3
Caregivers' Burden of Care

	NIV ($n = 32$)	TV ($n = 20$)	
Time spent on care	12.6 hr/ day (2–24)	14.4 h/ day (2–24)	
Wakings/night	2.3 (0–8)	2.4 (0–15)	
Health problems	63%	70%	
Quit working due to ALS	19%	60%	$P = 0.006$

- Kaub-Wittemer D, Steinbüchel N, Wasner M, Laier-Groeneveld G, Borasio GD. Quality of life and psychosocial issues in ventilated patients with amyotrophic lateral sclerosis and their caregivers. *J Pain Symptom Manage*. Oct 2003;26(4):890-6. doi:10.1016/s0885-3924(03)00323-3
- Veronese S, Valle A, Chiò A, Calvo A, Oliver D. The last months of life of people with amyotrophic lateral sclerosis in mechanical invasive ventilation: a qualitative study. *Amyotroph Lateral Scler Frontotemporal Degener*. Dec 2014;15(7-8):499-504. doi:10.3109/21678421.2014.913637

Death and Dying

- Most common cause of death is respiratory failure, followed by aspiration pneumonia, and cardiac failure
- 89% die peacefully
- EOL symptoms include coughing due to airway congestion with mucus, pain, breathing difficulties, insomnia, and restlessness, anxiety, fear.
- association between money and peacefulness, better care for the rich.
- Only 64% of ALS pts in North America were dying at home, 85% of those in Italy, 55% in Germany, 52% UK, 36% in France. Other places of death included hospitals and nursing homes
- Palliative removal from the ventilator should be done with pre-medication and anticipation of dyspnea and respiratory distress under the supervision of MD/RN with the ability to give additional medications for symptom control
- It has been demonstrated that there is an association between dyspnea and pain sensitivity

Connolly S, Galvin M, Hardiman O. End-of-life management in patients with amyotrophic lateral sclerosis. *Lancet Neurol*. Apr 2015;14(4):435-42. doi:10.1016/S1474-4422(14)70221-2

Symptom Burden and Management

TABLE 1. PAIN ETIOLOGIES AND TREATMENTS

Type of Pain	*Medications*	*Nonmedication Options*
Cramps	Baclofen Mexiletine Gabapentin Benzodiazepines Magnesium Antiepileptic drugs (levetiracetam or carbamazepine) Vitamin E	Stretching Massage
Spasticity	Baclofen (oral or intrathecal) Tizanidine Benzodiazepines Antiepileptic drugs (levetiracetam or carbamazepine) Dantrolene Carbidopa/levodopa Botulinum toxin injections	Physical therapy Stretching Neutral-position splints for hands and ankles to reduce joint contractures
Neuropathic pain	Gabapentin Pregabalin Tricyclic antidepressants	
Pressure sores		Special mattresses, pillows, custom-fitted wheelchairs Frequent repositioning
Unspecified pain (joint, etc)	Acetaminophen Nonsteroidal anti-inflammatory drugs Opiates Antiepileptic drugs Tetrahydrocannabinol and cannabidiol	Physical therapy Massage Warm and cold compresses Acupuncture

- Consider interventional pain referral
- Consider Botox for pain related to spastic contractures
- Screen for non-motor sympgoms
- **do not use 02 alone
- Seek assistance from someone with NIV experience and comfort if transitioning AVAPS to BIPAP

Everett EA, Pedowitz E, Maiser S, et al. Top Ten Tips Palliative Care Clinicians Should Know About Amyotrophic Lateral Sclerosis. *J Palliat Med*. 06 2020;23(6):842-847. doi:10.1089/jpm.2020.0046

Palliative Care in ALS: Models of Care

Models of Neuropalliative Care in the ALS multidisciplinary clinic

- There is growing recognition in the neurology community that palliative care at the primary and subspecialty level is essential to high-quality care for patients with chronic neurologic illness
- Questions remain regarding how to integrate various care models
- There is increasing attention in the literature being paid to models or care, and triggers for primary and subspecialty referral triggers

Current staffing models across 6 ALS Centers

- Models of care sharing between teams varies
- Palliative visits are sometimes trigger based, sometimes team directed, and sometimes universal
- Advantages include increased attention to symptom management and ACP
- Disadvantages include higher cost and funding needs
- No centers were identified as having chaplain staffing

Table 2 Multidisciplinary team members of outpatient care programs for patients with ALS in 6 hospitals across the United States

	Clinical staffing						
	Rush	UCLA	Hauenstein	Cedars-Sinai	Hennepin	University of CO (ALS clinic)	University of CO (NPC clinic)
Neuromuscular physician	X	X	X	X	X	X	
Neuropalliative physician	X	X	X	X	X	X	X
Neuropsychologist				X			X
Advanced practice provider			X			X	X
PM&R physician					X		
Pulmonologist	X			X	X	X	
Association representatives (ALSA and MDA)	X	X	X	X	X	X	
Clinic coordinator				X			
DME representative	X	X	X	X		X	
Genetic counselor				X			
Occupational therapist	X	X	X	X	X	X	
Physical therapist	X	X	X	X	X	X	
Registered dietician	X		X	X	X	X	
Registered nurse			X	X	X	X	X
Respiratory therapist	X	X	X		X	X	
Social worker	X	X	X	X	X	X	X
Spiritual care				X			X
Speech therapist	X	X	X	X	X	X	
Volunteers (patient ambassadors)							X

Abbreviations: ALSA = ALS Association; DME = Durable medical equipment; MDA = Muscular Dystrophy Association.

Phillips JN, Besbris J, Foster LA, Kramer NM, Maiser S, Mehta AK. Models of outpatient neuropalliative care for patients with amyotrophic lateral sclerosis. Neurology. 2020 Oct 27;95(17):782-788. doi: 10.1212/WNL.0000000000010831. Epub 2020 Sep 15. PMID: 32934166.

Embedded or Palliative subspecialist – Internal Referral

Table 1. Triggers for palliative care specialist consultation.

Patient-specific triggers	Disease-specific triggers
Psychosocial complexity	Cognitive or behavioral changes
Premorbid depression/anxiety	High symptom burden
Early interest in advanced care planning	Rapid decline in functional status
Presence of young children	Transition points in care:
Overburdened caregiver	Feeding tube
	Ventilatory support
	Frequent hospitalizations
	Hospice

Table 2. Topics covered during palliative care specialist initial visit with patient.

Topic covered in initial visit	Number of patients (%) ($N = 74$)
Advance care planning/goals of care	62 (84%)
Symptoms	
Anxiety/depression	26 (35%)
Coping/caregiver support	17 (23%)
Sialorrhea	10 (14%)
Dyspnea	9 (12%)
Pain	8 (11%)
Constipation	2 (3%)
Coping/caregiver support	17 (23%)
Medical decision-making	
Feeding tube	20 (27%)
Tracheostomy/ventilator	23 (31%)
Hospice	13 (18%)

Palliative Care Specialist in ALS Clinics

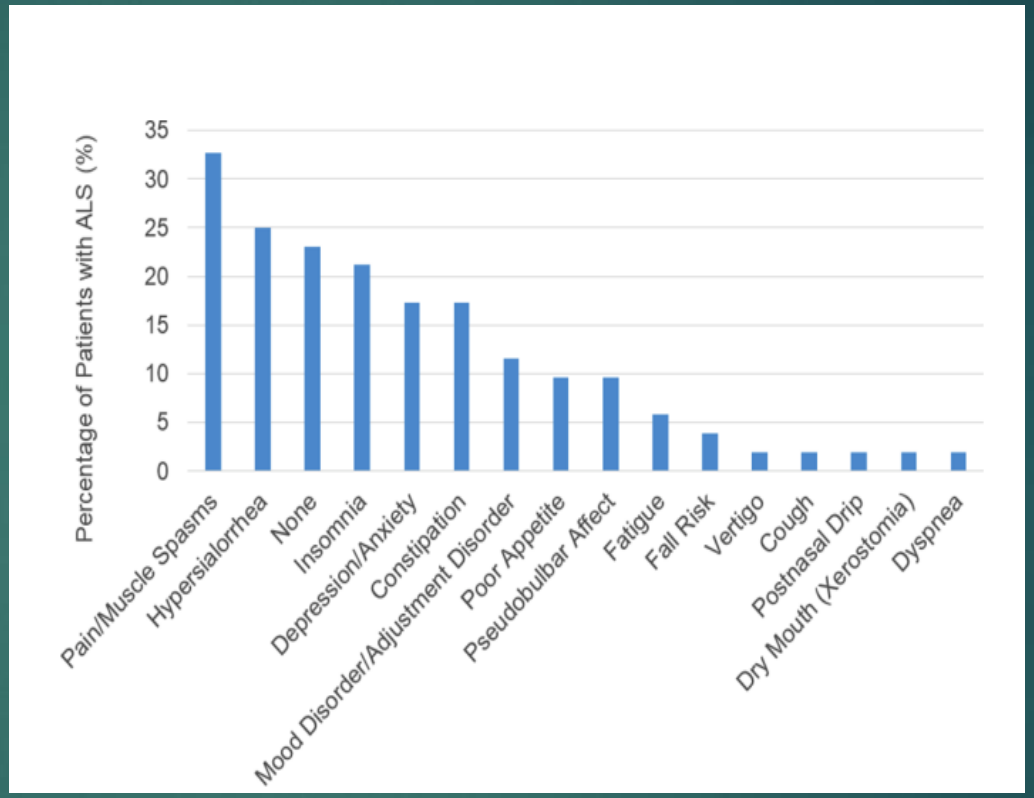
Most common referral reasons:
Advance care planning – 91%
Symptom management – 9%

Hafer J, Jensen S, Wiedau-Pazos M, Mehta AK. Assessment of feasibility and utility of universal referral to specialty palliative care in a multidisciplinary amyotrophic lateral sclerosis clinic: A cohort study. Muscle Nerve. 2021 Jun;63(6):818-823. doi: 10.1002/mus.27194. Epub 2021 Feb 18. PMID: 33533539.

Embedded or Palliative subspecialist – Universal Referral

TABLE 2 Advance care planning/goals of care topics discussed with 51 patients at their initial palliative care visit

Any advance care planning/goals of care topic	n (%)
First visit	48 (94.1%)
Advance care planning topic	
Code status	21 (40.4%)
Advance directive form (not completed, not on file)	20 (38.5%)
Tracheostomy	18 (34.6%)
Percutaneous endoscopic gastrostomy tube	18 (34.6%)
Prognosis	17 (32.7%)
Hospice	7 (13.5%)
Advance directive form (surrogate decision maker)	7 (13.5%)
Advance directive form (completed prior to visit, not on file)	6 (11.5%)
Advance directive form (completed prior to visit, on file)	6 (11.5%)
POLST form (completed prior to visit, on file)	4 (7.7%)
Physician aid in dying (End of Life Option Act)	3 (5.8%)
Hospital admissions	2 (3.8%)
POLST form (completed prior to visit, not on file)	0 (-)
POLST form (not completed, not on file)	0 (-)
Goals of care topic	
Meaning and values	30 (57.7%)
Family concerns	19 (36.5%)
Coping with diagnosis and disease	18 (34.6%)
Quality of life	10 (19.2%)
Caregiver support	7 (13.5%)
Preferences for receiving information	6 (11.5%)



75 vs 14.8% of patients were seen by a palliative care provider via universal referral. Advantages are avoiding referral trigger bias, disadvantages are resource intensive

Brizzi K, Paganoni S, Zehm A, De Marchi F, Berry JD. Integration of a palliative care specialist in an amyotrophic lateral sclerosis clinic: Observations from one center. *Muscle Nerve*. 08 2019;60(2):137-140. doi:10.1002/mus.26607

A brief plug for our QI project -

- Site: Portland VA
- Baseline assessment: Chart review and structured interviews of 20 carepartners and patients to assess for ACP, symptom management, bereavement support, spiritual care
- Intervention: Tier 1 (Internal) trigger-based referral for escalated palliative care, Tier 2 (Subspecialty clinic) trigger-based referral for escalated palliative care
- Outcome measures: Goal-concorcordant care as evidenced by chart review, evidence of high quality ACP conversation, ESAS/ALSQoL, Exit Interviews,

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