A primary set of outcome measures for amyotrophic lateral sclerosis (ALS) has been identified to include manual muscle testing (MMT), the Modified Ashworth Scale (MAS), Berg Balance Scale (BBS), Six-Minute Walk Test (6MWT), Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R), and Amyotrophic Lateral Sclerosis Assessment Questionnaire (ALSAQ-40). These tools have been grouped by categories of the International Classification of Functioning, Disability, and Health framework.1 Concentration was placed on body functions and structures, activities, and participation as the main domains that are affected in this patient population.

If 6 outcome measures exceeds what is typical for a “core set,” this list could be trimmed to MMT, the 6MWT, and ALSFRS-R. These measures are routine in clinical care since they indicate changes in strength and physical function, which are known biomarkers of ALS disease progression.2 They quantify the most common ALS-related impairments of muscle weakness, fatigue, and decreased functional mobility.3,4 The remaining outcome measures add to the context of a patient case by pinpointing the effects of ALS on their quality of life and bodily systems, but knowing their strength, endurance, and participation restrictions are most valuable for future planning.

Body Functions and Structures

***Manual Muscle Testing (MMT):***MMT is a standardized measure of muscle strength and function that is pertinent in determining the loss of voluntary motor activity that is characteristic of ALS. The MMT scale ranges from 0 to 5, with 0 representing no muscle function and 5 representing normal strength.5,6 Grade 3 strikes a middle ground in which a limb can sustain movement against gravity, while upper grades indicate sufficient muscle power to combat resistance.5 Pluses and minuses have been incorporated to create a more step-wise scale with clearer classification of muscle strength. In knowing a patient’s current strength levels and any noticeable trends over time, a physical therapist (PT) can cater their treatment plan to submaximal exercise with caution to overexertion and further muscle breakdown. Depending on the patient’s actual strength and its distribution proximally or distally, prescription of the proper adaptive equipment can provide physical support for mobility and endurance during physically demanding tasks and even less demanding tasks in their daily routine.

For ALS patients, a decline is strength often translates to respiratory dysfunction, the inability to ambulate, and difficulty performing activities of daily living (ADLs).5 Tracking this decline and its effects through strength testing is central to understanding the impact of PT on vital function, as well as the progression of disease despite treatment. However, it has been established that MMT has its limitations as a subjective tool that does not meet the requirements of an interval scale.5 Research has shown that MMT can be performed reliability, but some argue that quantitative muscle testing is a more sensitive indicator of meaningful change.5,7 Protocols suggest using a strain gauge force transducer7; but due to the simplicity and efficiency in obtaining a whole-body picture of strength in MMT, it continues to be the preferred method of testing.

*Age Group:* MMT is appropriate for patients of all ages.6 It is regularly used in both pediatric- and adult-based care.

*Treatment Setting:* MMT is not limited to a particular treatment setting. It can be implemented in acute, inpatient, outpatient, home, and skilled settings with modifications as necessary. Its process will mostly remain the same, but positional adjustments may be needed to accommodate the mobility of the patient.

*Level of Chronicity:* As an outcome measure that is intended to monitor declines in muscle strength, MMT is expected to be performed at any point after ALS diagnosis.5,6 It is considered a core measure to document the strength of patients in both the acute and chronic stages of disease.

*Functional Level:* A patient’s functional level does not necessarily dictate the use of MMT; however, a measurement of strength may be more crucial in the early and middle stages of ALS when a patient progresses from independent ambulation to assisted ambulation as a result of widespread muscle weakness. In the late stages of ALS, it is known that most voluntary muscles have become paralyzed, and quantifying this lack of strength is not as important as assisting the patient in navigating their daily functions.8

***Modified Ashworth Scale (MAS):*** The denervation of upper motor neurons in ALS patients often manifests as spasticity. Spasticity is considered to be a velocity-dependent muscle tightness associated with abnormal increases in muscle tone.9 Its presence can add to a patient’s functional decline and further reduce their quality of life, so its management tends to be a priority. It is tackled with both pharmaceutical and rehabilitation therapy, calling for a clinical tool that measures changes in tone with any sort of intervention.10

The MAS is a 6-point numerical scale from 0 to 4, “with 0 being no resistance and 4 being a limb rigid in flexion or extension.”9 Besides whole numbers within this range, the MAS features a sixth point, 1+, that was added to the original scale to increase its sensitivity.9 The MAS has been critiqued for its poor inter- and intra-rater reliability, even with this adaptation, but it remains the gold standard for muscle tone assessment.9 Without the need for equipment or extensive training, it is quick to perform, depending on the number of muscles and joints tested.9,11 These factors, along with its easily understood instructions and current standard in neurological patient care, support its inclusion in this assessment toolbox.

*Age Group:* One source denotes the MAS being appropriate for patients ages 6 to 12 and 18 to 64,11 but it has been administered in patients across older age groups.12 A sharp demarcation in age is unlikely with this outcome measure, and with the onset of ALS being primarily in the fifth and sixth decades of life, evaluating geriatric patients is of smaller concern.

*Treatment Setting:* The MAS is not limited to a particular treatment setting. It can be implemented in acute, inpatient, outpatient, home, and skilled settings with modifications as necessary.

*Level of Chronicity:* The MAS can be used to monitor changes in muscle tone with or without targeted treatment,9 and therefore, it is acceptable for ALS patients in both the acute and chronic stages of disease. It is considered a supplemental outcome measure for this diagnosis, regardless of its timing.

*Functional Level:* A patient’s functional level does not necessarily dictate the use of the MAS. Functional level is expected to decline with ALS progression, while spasticity may or may not increase as a primary symptom. With this pattern in mind, spasticity may no longer need to be quantified using the MAS, depending on the patient’s clinical presentation and goals for PT. But it is important to note that it can still be applicable.

Activities

***Six-Minute Walk Test (6MWT):*** The 6MWT provides insight into a patient’s aerobic capacity and endurance, which are negatively affected by the course of ALS.13 As more upper and lower motor neurons degenerate, ALS patients demonstrate weakness of the lower extremities and respiratory musculature, fatigue, loss of balance, and spasticity that slowly inhibits their ability to walk.14 Per Russo et al,15 walking capacity has actually “been shown to be the only independent predictor of survival when compared to other functions of activity of daily living in ALS patients.” Thus, evaluation of walking capacity via the 6MWT can be prognostic and useful in determining the level of functional impairment that ambulatory patients with ALS have. Furthermore, the distance traveled in the 6MWT can guide clinical decision-making and help to evaluate the efficacy of therapeutic interventions in the early stage of ALS.15

The 6MWT is strongly correlated with the Timed Up and Go Test, 10-Minute Walk Test, and ALSFRS-R, which are outcome measures that have a long-standing history of being used in the ALS population.15 Even though the 6MWT is relatively new to ALS patients, recent studies have proven that it is a valid, responsive, and reliable measure in both short- and long-term administration.14,15 Assistive devices can be used when walking, so patients with walkers, canes, or ankle-foot orthoses are allowed to participate without changes to their typical ambulation patterns. With utilization of a stop watch, clearly outlined path, and chair, the 6MWT is a speedy and inexpensive method of gathering data about a patient’s activity.

*Age Group:* The 6MWT is appropriate for patients of ambulatory ages, typically beginning at 2 years old.13

*Treatment Setting:* The 6MWT can be performed in a variety of treatment settings, including acute, inpatient, outpatient, home, and skilled. Use of the 6MWT is not dictated by the setting per se, but rather the available space. Patients require a minimum distance of 12 meters to walk,13 and accessing a cleared pathway of this distance may be a barrier in some locations.

*Level of Chronicity:* The more “chronic” an ALS diagnosis is, the less likely a patient will be able to participate in the 6MWT. This is because their ability to walk and engage in other ADLs declines with longer periods of denervation.14 So the 6MWT is suitable for the acute, or early, stages of ALS when patients are able to ambulate independently or with an assistive device, not when they are dependent on a wheelchair for mobility.

*Functional Level:* Similar to level of chronicity level, the higher functioning the patient is, the easier it will be for them to participate in the 6MWT. If they are ambulatory, such as in the early and middle stages of disease, the 6MWT may be a justifiable choice for an outcome measure. Once most of their muscles have become paralyzed, ambulation is improbable and other ways of tracking progression should be pursued.8

***Berg Balance Scale (BBS):*** In combination with gait disturbances, ALS patients tend to experience decreased balance and other neurological deficits that predispose them to falls. Sometimes, their lower extremity impairments make it harder for them to maintain their balance. In fact, lower extremity weakness is related to the need to use an assistive device for ambulation, decreased gait speed, and a lower BBS score.16 The BBS assesses patients’ functional balance abilities with 14 static and dynamic items. For each item, a patient is challenged to sustain a position or perform a postural adjustment for its completion. They are scored on a 5-point ordinal scale from 0 to 4, with 0 indicating an inability to finish the task entirely and 4 indicating successful completion of the task criterion.17,18 The BBS is recognized as having excellent internal consistency and reliability, allowing therapists to trust its results.16,19

Identifying contributing factors to impaired balance and falls are imperative for fall prevention and equipment prescription in ALS patients. With items in the BBS being varied between sitting, standing, and transfers, the therapist can pinpoint activities along the spectrum of ALS progression that disrupt a patient’s daily life. The clinical practice guideline for adults with neurologic conditions promotes the use of the BBS for static and dynamic sitting and standing balance assessment.19 This recommendation is strong for chronic progressive conditions, such as ALS, and is supported by 97% of PTs saying that a balance assessment is an essential component of a “core set” of outcome measures.19 Another feature that encourages its use is its high clinical feasibility, meaning that it requires minimal equipment, is free, and takes 20 minutes or less to administer.19

*Age Group:* The BBS has been verified for use in adults ages 18 years and older.18

*Treatment Setting:* The BBS is not limited to a particular treatment setting. It can be implemented in acute, inpatient, outpatient, home, and skilled settings with modifications as necessary.

*Level of Chronicity:* High-level evidence indicates that the BBS is applicable to both acute and chronic neurologic conditions, including those that are progressive.19

*Functional Level:* It can be assumed that a patient who functions at a lower level will be unsuccessful in completing the criterion of every BBS task, thereby resulting in a lower score. This means that ALS patients can continue to attempt the BBS as their disease progresses, but its results may be less clinically useful when they are dependent on physical assistance for item completion and receiving a score of 0. Ambulation is excluded from the list of activities, which allows the prolonged use of the BBS into the stages of ALS where walking is problematic; however, the items that require higher functioning skills, such as turning 360 degrees, may still pose a reasonable challenge, even when ambulating from one point to another is not required.

Participation

***Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R):*** The ALSFRS-R looks beyond impairments in body functions and structures and activities to determine how they affect physical function in patients with ALS.20 The ALSFRS-R questions inquire about a patient’s capability for certain ADLs, such as swallowing, writing, dressing, and breathing. Altogether, they cover the domains of gross motor activity, fine motor activity, respiratory function, and nutrition. The respiratory component of the ALSFRS-R was added to the original version to increase its applicability to the later course of disease,20 particularly since patients’ respiratory muscle function is not compromised until after months or years of bulbar weakness.

As one of the few disease-specific outcome measures that addresses participation, the ALSFRS-R is considered the gold standard of measuring disease progression. Repeated administration allows therapists to define how ALS is affecting a patient’s body by documenting changes in motor and speech impairment. This leads to better preparation for further reductions in physical function, based on which regions are primarily affected, how quickly the ALS is developing, and what interventions are best at that time.

The decision to use the ALSFRS-R is backed by strong psychometric properties in the categories of inter- and intra-rater reliability, test-retest reliability, internal consistency, and validity.20,22 Values for the standard error of measurement and minimal detectable change have also been published,21 which corresponds to a noticeable change in the patient’s ability, whether it be positive or negative in relation to their outcome.

*Age Group:* An age bracket for the ALSFRS-R has not been set, so it operates under the assumption that it is intended for any patient who has been diagnosed with ALS.

*Treatment Setting:* The ALSFRS-R is not limited to a particular treatment setting. It can be implemented in acute, inpatient, outpatient, home, and skilled settings either face-to-face or via telephone.21,23

*Level of Chronicity:* The ALSFRS-R is designed to assess one’s physical function for the duration of their condition, meaning that it is appropriate for patients in both the acute and chronic stages of ALS. Activities such as speech, salivation, swallowing, and breathing continue to be pertinent after larger forms of movement have stopped.

*Functional Level:* The ALSFRS-R is not necessarily limited by a patient’s functional level. It is accessible to all ALS patients because it can be administered in person or over the phone.23 This removes a barrier for those who would otherwise be limited in their ability to attend in-clinic appointments due to the progressive nature of the disease.21

Personal Factors

***Amyotrophic Lateral Sclerosis Assessment Questionnaire (ALSAQ-40):*** Most outcome measures for ALS concentrate on the physical status of patients, leaving it unclear as to how their clinical presentation relates to perceptions of their well-being. Healthy individuals, caregivers, and healthcare professionals often assume that ALS patients have a low quality of life (QOL).24 They think that patients have less energy, higher rates of depression, and greater suffering than what patients report having themselves.24 These data demonstrate the need for patient-reported outcome measures, in addition to performance-based measures, in ALS care.

The ALSAQ-40 serves to fill the aforementioned gaps with a patient-determined assessment of QOL. Its questions correlates to 5 dimensions of eating and drinking, communication, ADLs and independence, physical mobility, and emotional functioning that are rated by frequency of experiences.20 There is no consensus in the scientific community regarding which factors are most important in assessing QOL, but those included in the ALSAQ-40 seem to give a broader overview than other non-disease-specific instruments like the Short Form-36.24 The response rates for this questionnaire are high, suggesting that the items are easy to interpret and quick to fill out.24,25 Internal validity and reliability are also high, further strengthening its psychometric properties.20,25

*Age Group:* An age bracket for the ALSAQ-40 has not been set, so it operates under the assumption that it is intended for any patient who has been diagnosed with ALS.

*Treatment Setting:* The ALSAQ-40 can be performed in a variety of treatment settings, including acute, inpatient, outpatient, home, and skilled. Its use is more likely to be controlled by access to a copy of the questionnaire for patient completion, rather than the chosen setting.

*Level of Chronicity:* The ALSAQ-40 is designed to assess one’s QOL for the duration of their condition, meaning that it is appropriate for patients in both the acute and chronic stages of ALS. The components of the ALSAQ-40 are pertinent at any point after diagnosis but particularly with progressive disability.

*Functional Level:* A patient’s functional level does not necessarily dictate the use of the ALSAQ-40; however, patients who function at a lower level might be forced to record their responses in a different way. Typically, patient-reported outcome measures are completed with pencil and paper. Depending on the amount of muscle weakness that a patient has, especially in their hands and fingers, an alternative method of transcription may need to be used. Options could be manipulation of an electronic questionnaire, verbally answering to a scribe, or use of augmentative and alternative communication devices.

References

1. Centers for Disease Control and Prevention. The ICF: An Overview. https://www.cdc.gov/nchs/data/icd/icfoverview\_finalforwho10sept.pdf. Accessed February 23, 2021.
2. Simmons Z. Patient-perceived outcomes and quality of life in ALS. *Neurotherapeutics*. 2015;12(2):394-402. doi:10.1007/s13311-014-0322-x/.
3. Gibbons C, Pagnini F, Friede T, Young CA. Treatment of fatigue in amyotrophic lateral sclerosis/motor neuron disease. *Cochrane Database Syst Rev*. 2018;1:CD011005. doi:10.1002/14651858.CD011005.pub2.
4. Nicholson K, Murphy A, McDonnell E, et al. Improving symptom management for people with amyotrophic lateral sclerosis. *Muscle Nerve*. 2018;57(1):20-24. doi:10.1002/mus.25712.
5. Shefner JM. Strength testing in motor neuron diseases. *Neurotherapeutics*. 2017;14(1):154-160. doi:10.1007/s13311-016-0472-0.
6. Manual muscle test. Shirley Ryan Ability Lab website. https://www.sralab.org/rehabilitation-measures/manual-muscle-test. Updated May 9, 2020. Accessed February 23, 2021.
7. Colombo R, Mazzini L, Mora G, et al. Measurement of isometric muscle strength: a reproducibility study of maximal voluntary contraction in normal subjects and amyotrophic lateral sclerosis patients. *Med Eng Phys*. 2000;22(3):167-174. doi:10.1016/S1350-4533(00)00024-2.
8. Zarei S, Carr K, Reiley L, et al. A comprehensive review of amyotrophic lateral sclerosis. *Surg Neurol Int*. 2015;6:171. doi:10.4103/2152-7806.169561.
9. Harb A, Kishner S. Modified Ashworth Scale. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2020.
10. Ashworth NL, Satkunam LE, Deforge D. Treatment for spasticity in amyotrophic lateral sclerosis/motor neuron disease. *Cochrane Database Syst Rev*. 2012;(2):CD004156. doi:10.1002/14651858.CD004156.pub4.
11. Ashworth scale/modified Ashworth scale. Shirley Ryan Ability Lab website. https://www.sralab.org/rehabilitation-measures/ashworth-scale-modified-ashworth-scale. Updated May 26, 2016. Accessed February 24, 2021.
12. Blackburn M, van Vliet P, Mockett SP. Reliability of measurements obtained with the modified Ashworth scale in the lower extremities of people with stroke. *Phys Ther*. 2002;82(1):25-34. doi:10.1093/ptj/82.1.25.
13. 6 minute walk test. Shirley Ryan Ability Lab website. https://www.sralab.org/rehabilitation-measures/6-minute-walk-test. Updated April 26, 2013. Accessed February 24, 2021.
14. Sanjak M, Langford V, Holsten S, et al. Six-minute walk test as a measure of walking capacity in ambulatory individuals with amyotrophic lateral sclerosis. *Arch Phys Med Rehabil*. 2017;98(11):2301-2307. doi:10.1016/j.apmr.2017.04.004.
15. Russo M, Lunetta C, Zuccarino R, et al. The 6-min walk test as a new outcome measure in amyotrophic lateral sclerosis. *Sci Rep*. 2020;10(1):15580. doi:10.1038/s41598-020-72578-3.
16. Schell WE, Mar VS, Da Silva CP. Correlation of falls in patients with Amyotrophic Lateral Sclerosis with objective measures of balance, strength, and spasticity. *NeuroRehabilitation*. 2019;44(1):85-93. doi:10.3233/NRE-182531.
17. Core measure: Berg balance scale (BBS). Academy of Neurologic Physical Therapy website. https://neuropt.org/docs/default-source/cpgs/core-outcome-measures/core-measure-berg-balance-scale-(bbs)\_final-2019.pdf?sfvrsn=6e845043\_0. Published 2018. Accessed February 26, 2021.
18. Berg balance scale. Shirley Ryan Ability Lab website. https://www.sralab.org/rehabilitation-measures/berg-balance-scale. Updated June 30, 2020. Accessed February 26, 2021.
19. Moore JL, Potter K, Blankshain K, Kaplan SL, OʼDwyer LC, Sullivan JE. A core set of outcome measures for adults with neurologic conditions undergoing rehabilitation: A CLINICAL PRACTICE GUIDELINE. *J Neurol Phys Ther*. 2018;42(3):174-220. doi:10.1097/NPT.0000000000000229.
20. *Clinical Review Report: Edaravone (Radicava): (Mitsubishi Tanabe Pharma Corporation): Indication: For the Treatment of Amyotrophic Lateral Sclerosis*. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2019.
21. Amyotrophic lateral sclerosis functional rating scale. Shirley Ryan Ability Lab website. https://www.sralab.org/rehabilitation-measures/amyotrophic-lateral-sclerosis-functional-rating-scale. Updated January 3, 2014. Accessed February 26, 2021.
22. Lee M, McCambridge A. Clinimetrics: Amyotrophic Lateral Sclerosis Functional Rating Scale-revised (ALSFRS-R). *J Physiother*. 2018;64(4):269-270. doi:10.1016/j.jphys.2018.07.005.
23. Cedarbaum JM, Stambler N. Performance of the Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS) in multicenter clinical trials. *J Neurol Sci*. 1997;152 Suppl 1:S1-9. doi:10.1016/s0022-510x(97)00237-2.
24. Simmons Z. Patient-perceived outcomes and quality of life in ALS. *Neurotherapeutics*. 2015;12(2):394-402. doi:10.1007/s13311-014-0322-x.
25. Jenkinson C, Levvy G, Fitzpatrick R, Garratt A. The amyotrophic lateral sclerosis assessment questionnaire (ALSAQ-40): tests of data quality, score reliability and response rate in a survey of patients. *J Neurol Sci*. 2000;180(1-2):94-100. doi:10.1016/s0022-510x(00)00420-2.