Stroke

SPECIAL REPORT

Standardized Nomenclature for Modified Rankin Scale Global Disability Outcomes

Consensus Recommendations From Stroke Therapy Academic Industry Roundtable XI

Jeffrey L. Saver, MD*; Napasri Chaisinanunkul, MD*; Bruce C.V. Campbell, MBBS, BMedSc, PhD; James C. Grotta, MD; Michael D. Hill, MD, MSc; Pooja Khatri, MD, MS; Jaren Landen, PhD; Maarten G. Lansberg, MD; Chitra Venkatasubramanian, MD; Gregory W. Albers, MD; on behalf of the XIth Stroke Treatment Academic Industry Roundtable

ABSTRACT: The modified Rankin Scale (mRS), a 7-level, clinician-reported, measure of global disability, is the most widely employed outcome scale in acute stroke trials. The scale's original development preceded the advent of modern clinimetrics, but substantial subsequent work has been performed to enable the mRS to meet robust contemporary scale standards. Prior research and consensus recommendations have focused on modernizing 2 aspects of the mRS: operationalized assignment of scale scores and statistical analysis of scale distributions. Another important characteristic of the mRS still requiring elaboration and specification to contemporary clinimetric standards is the Naming of scale outcomes. Recent clinical trials have used a bewildering variety, often mutually contradictory, of rubrics to describe scale states. Understanding of the meaning of mRS outcomes by clinicians, patients, and other clinical trial stakeholders would be greatly enhanced by use of a harmonized, uniform set of labels for the distinctive mRS outcomes that would be used consistently across trials. This statement advances such recommended rubrics, developed by the Stroke Therapy Academic Industry Roundtable collaboration using an iterative, mixed-methods process. Specific guidance is provided for health state terms (eg, Symptomatic but Nondisabled for mRS score 1; requires constant care for mRS score 5) and valence terms (eg, excellent for mRS score 1; very poor for mRS score 5) to employ for 23 distinct numeric mRS outcomes, including: all individual 7 mRS levels; all 12 positive and negative dichotomized mRS ranges, positive and negative sliding dichotomies; and utility-weighted analysis of the mRS.

Key Words: certification ■ consensus ■ fatal outcome ■ ischemic attack, transient ■ quality improvement

The modified Rankin Scale (mRS) is a clinician-reported measure of global disability. The mRS serves a uniquely important role in stroke trial investigation and stroke clinical care. It is the most common primary outcome measure in acute stroke clinical trials and in large-scale stroke care quality improvement programs.[1–4] Further, it is formally recommended by regulatory agencies and clinical trial methodology consensus groups worldwide for use in acute stroke clinical trials.[5–8] Accordingly, it is important that approaches to mRS implementation, scoring, and reporting be widely agreed upon.

HISTORY AND CHARACTERISTICS OF THE mRS

Because the Rankin Scale's development preceded the advent of modern clinimetrics, it was not the product of the sophisticated design, derivation, and validation process currently used to create assessment scales.[9] Rather, it was created by a clinician, John Rankin, using his own holistic judgement, for a specific use-case in 1957.[10] But it satisfied a need in the field for a broad rating of disability outcomes and so was taken up and employed

Correspondence to: Jeffrey L. Saver, MD, UCLA Comprehensive Stroke Center, 710 Westwood Plaza, Los Angeles, CA 90095. Email jsaver@mednet.ucla.edu
*J.L. Saver and N. Chaisinanunkul are co-first authors.

This manuscript was sent to Theresa A. Jones, Guest Editor, for review by expert referees, editorial decision, and final disposition.
The Data Supplement is available with this article at https://www.ahajournals.org/doi/suppl/10.1161/STROKEAHA.121.034480.
For Sources of Funding and Disclosures, see page xxx.

Stroke is available at www.ahajournals.org/journal/str

Nonstandard Abbreviations and Acronyms

mRS	modified Rankin Scale
STAIR	Stroke Therapy Academic Industry Roundtable

in increasing numbers of studies. In the 1980s, it was usefully modified by the addition of categories of asymptomatic and fatal outcome levels by the UK-TIA (United Kingdom Transient Ischaemic Attack) trialists,[11] expanding from the original 5-level to the current 7-level structure of the mRS.

Although many later scales were developed to assess similar functional outcomes as the mRS, often using more sophisticated derivation methodologies, the mRS retained its preeminent position for several reasons. Two sources are historically contingent, related to the timing of its initial appearance. First, the mRS had first-mover advantage. When the mRS was one of the few available broad disability scales, many raters trained and became certified in administering it. It was difficult for new scales that would require additional training to dislodge the established mRS. Second, the mRS benefitted from a network effect, under which the value of a product or service increases as usage increases. New studies desiring to compare their results to prior work had to use the mRS, as it had been the metric used in previous studies.

But several reasons for the wide adoption of the mRS are intrinsic to the scale, reflecting genuinely advantageous features. The mRS can be performed rapidly. The mRS can be administered by individuals from broad training backgrounds, not just physicians.[12–14] The mRS captures outcomes over the entire range of disability states, ranging from normal through several levels of disability to death; some other scales capture only subsegments of this range.[7,15,16] As a measure of global disability, the mRS directly provides assessment of morbidity required by the European Medicines Agency.[6] The mRS has desirable population distributional properties, with substantial proportions of patients being assigned to each of its 7 component levels, avoiding the floor and ceiling effects that affect some other scales.[7,16,17] Another strength is that the increments on the scale are relatively evenly, although not perfectly, spaced in terms of quality of life values assigned to them by patients and practitioners.[18]

An additional advantage of the mRS is that, via different historical trajectories, its definition of disability and that of organized medicine, as reflected in the recommendations of the World Health Organization, have become coterminous. The World Health Organization in 2001 established a new definition of disability, incorporating both medical and societal factors, characterizing the negative aspects of the interaction between an individual with a health condition and that individual's environmental and social context. Disability is defined as an umbrella term that reflects difficulties encountered in any or all of 3 dimensions of functioning:

1. Impairments: problems in body function or structure
2. Activity limitations: difficulties encountered by an individual in executing a task or action
3. Participation restrictions: problems experienced by an individual's involvement in life situations.

The mRS aligns well with this definition, as each of these 3 dimensions of functioning have leading roles in determining 2 of the 6 scale transitions. The presence of impairments determines the transitions from mRS score 0 to mRS score 1 (symptoms) and mRS score 5 to mRS score 6 (death). The presence of activity limitations determines the transitions from mRS score 3 to mRS score 4 (ambulation and bodily self-care) and mRS score 4 to mRS score 5 (constant nursing care). Participation restrictions determine the transitions from mRS score 1 to mRS score 2 (able to work) and mRS score 2 to mRS score 3 (able to live independently).

After the mRS proved highly useful, becoming increasingly used as the primary end point in acute stroke trials despite its original pragmatic derivation, substantial work was performed to provide it with important additional clinimetric features, strengthening it to become a robust measure that would meet contemporary standards for assessment tools. Hitherto, these modernizing activities for the mRS have focused on 3 key aspects: (1) Formalized Scoring; (2) Rater Training, and (3) Statistical Analysis. With regard to Scoring, the mRS as originally promulgated included only 2 or 3 short phrases characterizing each mRS level to guide clinician-raters in assigning an mRS score to a patient. There was no guidance on what steps the rater was to take to determine which of the phrases applied to a particular patient, so that score assignment was holistic and intuitive, rather than operationalized and objective. As a result, inter-reliability was only fair in assigning mRS scores. To address this weakness, multiple groups developed approaches to make mRS scoring more uniform, including rater certification, centralized core laboratory scoring, and structured assessment systems.[14,19–22] These succeeded in converting the mRS to a measure with well-operationalized scoring and were the subject of prior consensus recommendation statements from both Stroke Therapy Academic Industry Roundtable (STAIR) and additional trial methodology consensus groups.[7,23]

With regard to Statistical Analysis, as a 7-level ordinal scale, the mRS may be statistically interrogated in a variety of ways, including dichotomized at various cut points; trichotomized at various cut points; with use of prognosis-adjusted sliding dichotomies; as a full, ordinal 7-level scale; and with levels weighted by their health utility value.[17,18,24] Each of these modes of statistical analysis has advantages and disadvantages. Initial trials often used dichotomized approaches, in part because they

 Stroke. 2021;52:00–00. DOI: 10.1161/STROKEAHA.121.034480

were easier to perform and interpret in the era before widespread availabilities of computing resources and statistical software. But with the availability of programs to perform more sophisticated analyses, investigations demonstrated that the most powerful mode of analysis of the mRS for any particular study was determined by the individual study's expected mRS outcome distribution in the control group and the expected change in this distribution in the treatment group.[24] Following these investigations, recommendations regarding when to employ each of the available statistical analytic modes of the mRS were issued by both STAIR and additional trial methodology consensus groups.[17,25–27]

Another important characteristic of the mRS still requiring elaboration and specification to contemporary clinimetric standards is the *Naming* of scale outcomes. For a study's findings to be useful to clinicians, patients, families, policy-makers, and payors, it is critical that the meaning of a difference in score outcomes between groups be able to be stated in a clear, accessible, and uniform manner. As is well known, it is important to characterize not only the statistical significance of a trial finding but also the clinical significance.[28,29] Statistical significance is a statement about the likelihood of findings being due to chance. Clinical significance is a statement about the magnitude of the treatment effect and its practical value for clinical practice. A necessary condition for clinicians and patients to assess the clinical significance of trial findings is that they unambiguously understand the nature of the health state(s) being increased or decreased by study treatment. As a result, several consensus and governmental groups, including the International Patient Decision Aids Standards Collaboration, the Plain Language Association International Health Literacy group (PLAIN), the National Institutes of Health, and the US Health Resources and Services Administration, have formally recommended that health states and disease states be conveyed not in purely numeric or technical terms, but in plain language accessible and understandable by all.[30–34] As per the PLAIN collaboration, a communication is in plain language if its wording, structure, and design are so clear that the intended audience can easily find what they need, understand what they find, and use that information.[31]

Broadly, outcomes on ordinal scales can be assigned 4 types of short labels: (1) numeric values, (2) scalar/

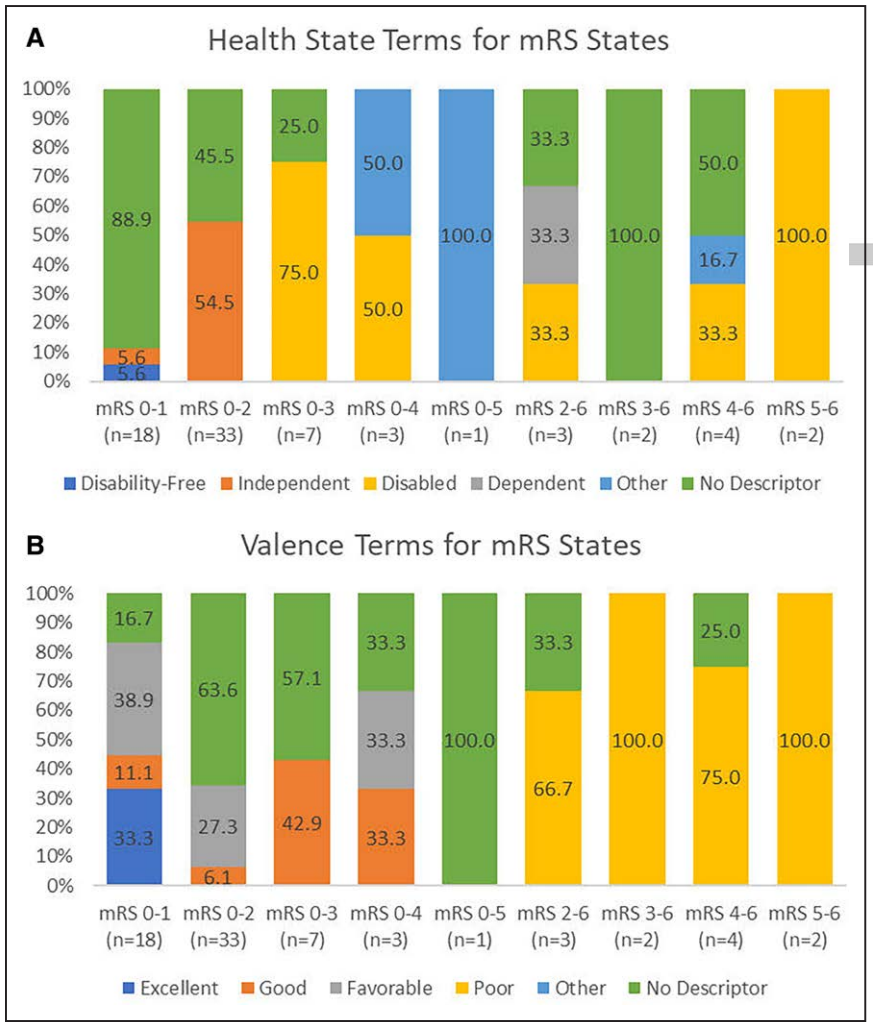

Figure 1. Stacked bar chart showing distributions of rubrics used to describe modified Rankin Scale (mRS) outcomes states in acute stroke clinical trials from 2000–2020. **A**, Health State terms; (**B**) valence terms. Extreme variability is demonstrated. For example, for health state terms, the label independent and its cognates were applied to both mRS score 0 to 1 and mRS score 0 to 2; the term disabled and its cognates were applied to mRS score 2 to 6, mRS score 4 to 6, and mRS score 5 to 6. Also many trials (54%) provided no meaningful health state descriptor. For valence terms, the label good was applied to mRS score 0 to 1, mRS score 0 to 2, mRS score 0 to 3, and mRS score 0 to 4; the term favorable was applied to mRS score 0 to 1, mRS score 0 to 2, and mRS score 0 to 4; and the term poor was applied to mRS score 2 to 6, mRS score 3 to 6, mRS score 4 to 6, and mRS score 5 to 6. Also, many trials (44%) provided no meaningful valence descriptor.

intensifier terms, (3) health state terms, and (4) valence terms. All have been employed for the mRS, but in an unsystematic and often contradictory manner. As a result, the meaning of the results of clinical trials using the mRS as the primary end point is often obscure and opaque to readers.

Two of these label types were included in Rankin's original description of the scale: numeric values and scalar/intensifier terms. However, both of these rubric categories are intrinsically unable to usefully convey the meaning of mRS outcomes. The mRS has 7 distinctly enumerated levels: mRS score 0, 1, 2, 3, 4, 5, and 6. But these numeric values alone provide no information about the qualitative contours of their outcome levels. A phrase like Treatment B yielded a 5% absolute increase in patients with a score of mRS 0 to 2 has no clinical import for readers not already intimately familiar with the mRS. Scalar and intensifier terms identify different degrees of the nouns or adjectives they modify. The original mRS denoted its categories with 5 scalar/intensifier terms modifying the noun disability: no significant disability/slight disability/moderate disability/moderately severe disability/severe disability. Unfortunately, scalar/intensifier terms tend to lose interpretability when applied to 4 or more levels of outcome. Such is the case with the mRS. The distinctions between slight versus moderate, moderately severe versus severe, and other transitions is not conveyed with any clarity by the scalar labels.

In contrast, the other 2 brief rubric types—health state terms and valence terms—do have the potentialvto provide meaningful descriptor terms for each of the mRS levels. But as they were not employed in the original delineation of the scale, the appropriate labels within these categories to affix to the mRS levels was unspecified. Driven by the ineluctable need to use such terms to convey study results, many clinical trialists have deployed them, but in a bewildering variety of ways, often in mutually contradictory fashion. Health state terms indicate the presence or absence of particular states of being. Health state appellations applied to different mRS levels have included: Disability-free, Disabled, Independent, Dependent, Ambulatory, Non-Ambulatory, and Capable of Bodily Self-Care.

CONSENSUS PROCESS

The Consensus recommendations were developed using a mixed-methods process. The STAIR X1 group meeting was attended by 142 participants, including 40 academic physician and scientists who design and conduct acute stroke clinical trials, 14 NIH Program Officers, 15 FDA officials, and 73 industry representatives including industry scientists, physicians, and executives. The academic participants included noninterventional vascular neurologists (28), neuroendovascular interventionalists (5), neurocritical care neurologists (3), neurosurgeons (2), statisticians (1), and preclinical neuroscientists (1). Geographically, attendees were from the United States (120), Canada (2), Europe (11), Asia (8), and Australia (1). There were 76 men and 66 women.

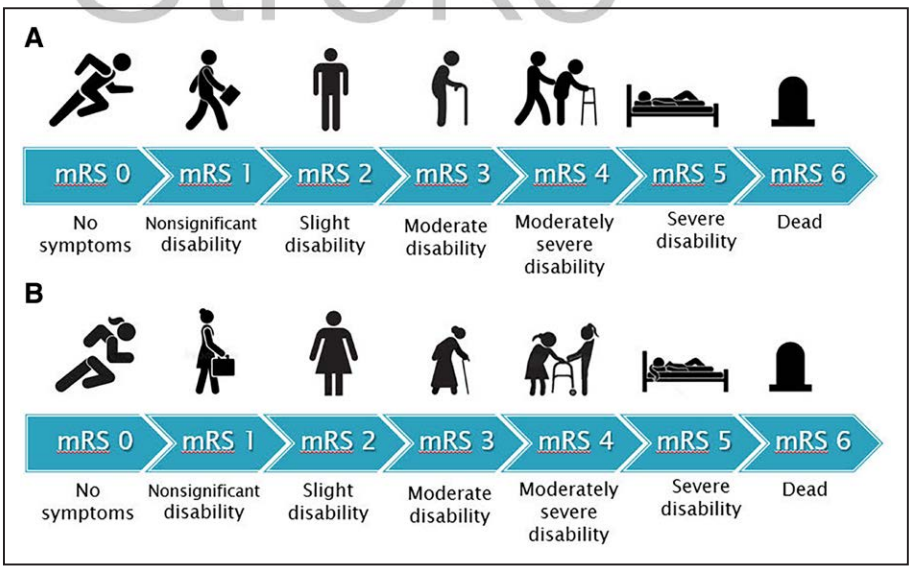

Figure 2. Examples of use of person-icons to illustrate the 7 modified Rankin Scale (mRS) health states.
Panel (**A**) provides a set of male person icons. Panel (**B**) provides a set of female person-icons. A running figure represents the highest, symptom-free functional level (mRS score 0); a walking figure carrying a briefcase represents having symptoms but able to work (mRS score 1); a figure standing still represents being able to live independently (mRS score 2); a bent figure with a cane represents more severe impairment causing dependency but not loss of ambulation without assistance on another person (mRS score 3); a figure using a walker being helped by a caregiver represents loss of ambulation without assistance of another person and/or loss of ability to perform bodily self-care (mRS score 4); a bedridden figure represents needing continuous care (mRS score 5); and gravestones represent fatal outcome (mRS score 6). These figures are labeled with health-state terms. In the Appendix are figures labeled with scalar/intensity terms (Figure IIA and IIB in the Data Supplement) and valence terms (Figure IIIA and IIIB in the Data Supplement).

 Stroke. 2021;52:00–00. DOI: 10.1161/STROKEAHA.121.034480

Table 1. Recommended Health State Terms for mRS Levels

Level	Can	…But	Health state terms
mRS 0	No symptoms	…	Normal
mRS 1	Do work/leisure/school activities fulltime	…has symptoms	Symptomatic but nondisabled
mRS 2	Live alone for >1 wk	…can't do work/leisure/school activities fulltime	Disabled but independent
mRS 3	Walk*	…can't live alone for >1 wk	Dependent but ambulatory
mRS 4	Not require constant nursing care	…can't walk* nor do body self-care	Not ambulatory nor capable of body self-care
mRS 5	Alive	…requires constant care	Requires constant care
mRS 6	…	Not alive	Dead

mRS indicates modified Rankin Scale.
*Some modern versions of mRS evaluate independent mobility (eg, independent with wheelchair) rather than independent ambulation

Before the meeting, to provide an evidential foundation for the consensus statement, 2 of the co-authors (J.L.S. and N.C.) performed an evidence synthesiss analyzing mRS terminology in major acute stroke trials between 2000 and 2020. Based on this data, they drafted a first version of this statement which was circulated to attendees before the event. At the meeting, the recommendations were discussed in plenary and breakout sessions. A larger writing group (all the co-authors) then revised the draft based on meeting discussions. The revised draft was circulated to all STAIR attendees soliciting additional comments and suggestions. Once received, these were incorporated into the final version of the statement.

The background evidence synthesis identified 90 major acute stroke trials between 2000 and 2020 that reported the mRS as a primary, secondary, or additional outcome (see Evidence Synthesis Methods and Results in the Data Supplement). Overall, 46% used health state terms to describe mRS outcomes, but the labels were highly inconsistent across studies (Figure 1). For example, the term Disabled has been applied to 5 different outcome ranges: mRS score 2 to 5; mRS score 3 to 5; mRS score 4 to 5; mRS score 5; and ordinal mRS shift. Valence terms are words that describe the degree of attractiveness or desirability of an individual or a condition. Valence appellations applied to different mRS levels have included: Excellent, Good, Favorable, Fair, and Poor. In the evidence synthesis analysis of acute stroke trials reported between 2000 and 2020, 56% used valence terms to describe mRS outcomes (Figure 1). But again, the labels were applied highly inconsistently across different trials. For example, the term Good outcome has been applied to 5 different outcome ranges: mRS score 0 to 1, mRS score 0 to 2, mRS score 0 to 3, mRS score 0 to 4, and ordinal mRS shift. While this terminological disarray persists, neither health state terms nor valence terms convey any stable meaning to clinicians, patients, policy-makers, and payors. They are at best ambiguous. Worse, they can actively mislead the reader to a perception of outcome character very different from that which actually transpired.

Table 2. Recommended Valence Terms for mRS Levels

Level	Can	…But	Valence
mRS 0	No symptoms	…	Ideal
mRS 1	Do work/leisure/school activities fulltime	…has symptoms	Excellent
mRS 2	Live alone for >1 wk	…can't do work/leisure/school activities fulltime	Good
mRS 3	Walk*	…can't live alone for >1 wk	Fair
mRS 4	Not require constant nursing care	…can't walk* nor do body self-care	Poor
mRS 5	Alive	…requires constant care	Very poor
mRS 6	…	Not alive	…

mRS indicates modified Rankin Scale.
*Some modern versions of mRS evaluate independent mobility (eg, independent with wheelchair) rather than independent ambulation.

RECOMMENDATIONS

Understanding of the meaning of mRS outcomes by clinicians, patients, and other clinical trial stakeholders would be greatly enhanced by a harmonized, uniform set of brief labels for the distinctive mRS outcomes that would be used consistently across trials. This Consensus statement advances such recommended rubrics. Specific guidance is provided for 23 distinct numeric mRS outcomes, including: all 7 individual mRS levels (0, 1, 2, 3, 4, 5, 6); all 6 potential positive dichotomized mRS ranges (mRS score 0, mRS score 0–1, mRS score 0–2, mRS score 0–3, mRS score 0–4, and mRS score 0–5); all 6 potential negative dichotomized mRS ranges (mRS score 1–6, mRS score 2–6, mRS score 3–6, mRS score 4–6, mRS score 5–6, and mRS score 6); positive sliding dichotomy; negative sliding dichotomy; ordinal shift across mRS levels; and utility-weighted analysis of the mRS (Tables 1 through 6).

The recommended brief rubrics here advanced were derived in an iterative, mixed-methods process. Sources of constraint and guidance for label selection were 5-fold. First, all selections were informed by and required to adhere to the brief, 9 to 16 word, state descriptions provided by Rankin in the original formulation of the Scale. Second the findings of the systematic evidence synthesis of trials reported between 2000–2020 were analyzed. For

Table 3. Recommended Health State Terms for mRS Ranges

Cut point	Key feature	Better outcome	Worse outcome
0 vs 1–6	Symptoms	Normal	Symptomatic or dead
0–1 vs 2–6	Able to do work/leisure/school activities fulltime	Nondisabled	Disabled or dead
0–2 vs 3–6	Able to live alone for >1 wk	Independent	Dependent or dead
0–3 vs 4–6	Able to walk	Ambulatory or bodily needs-capable or better	Not ambulatory nor bodily needs-capable or dead
0–4 vs 5–6	Constant care	Not requiring constant care or better	Requires constant care or dead
0–5 vs 6	Survival	Alive	Dead

mRS indicates modified Rankin Scale.

a minority of mRS outcome states, the systematic review indicated consensus regarding terminology had spontaneously occurred, as reflected in uniform actual usage across trial reports. The unambiguous rubrics already established for these mRS states were maintained. Third, relevant guidance from United States and international governmental agencies was identified and incorporated. For example, the US Social Security Administration legally establishes the definition of what constitutes the Disabled health state in the United States. The law defines disability on the basis of participation limitation, as the inability to do any substantial gainful activity by reason of any medically determinable physical or mental impairment.[35] Fourth, 9 formal systems for assigning mRS scores used in various trials were reviewed and labeling approaches used widely across the systems or advanced with compelling reasoning were incorporated. Finally, the appellation choices synthesized from these first 4 sources were compiled in a draft recommendation document circulated premeeting to clinical trialists, statisticians, regulators, and study sponsors attending the XIth meeting of the STAIR in October 2020. The proposal was revised iteratively in response to 2 rounds of verbal and written feedback from attendees, leading to a final article approved for promulgation by the STAIR consensus group. Formal recommendations are advanced for both health state terms and valence terms for mRS outcomes.

In addition, the consensus group noted that person-icon figures have been found helpful in conveying to the lay public the meaning of score levels on the Expanded Kurtzke Disability Scale in multiple sclerosis.[36,37] A similar figural approach could aid understanding of the mRS, especially by lay individuals. While no single figure can convey the full range of function that occurs at each mRS level, symbolic figure-icons can provide useful visual indices of gradations of disability. Example potential sets of male and female person-icons to visually depict each mRS level are shown in Figure 2, and we encourage the development of additional representations.

SITUATING THESE RECOMMENDATIONS IN THE EXISTING FRAMEWORK OF mRS CONDUCT AND INTERPRETATION

It is important to clarify aspects regarding how the current terminology recommendations fit within the established framework of mRS conduct and interpretation.

First, this document is intended to suggest rubrics that can be applied to communicate mRS scores; it is not intended to alter in any way the methodology for obtaining those scores. mRS scores should continue to be rated using one of the standard rating techniques (eg, Rankin Structured Interview, video-certified raters, Rankin Focused Assessment, Simplified mRS Questionnaire [SmRSQ], mRS-9Q, etc).[14,19,21,22,38] These standard assessments will yield mRS scores of 0, 1, 2, 3, 4, 5, 6. The current document provides recommendations on health state and valence terms to be applied to briefly convey the meaning of those scores after they have been derived.

Second, the terms we advance for individual mRS states reflect that the mRS is a rater-determined scale,

Table 4. Recommended Valence Terms for mRS Ranges

Cut point	Key feature	Better outcome	Worse outcome
0 vs 1–6	Symptoms	Ideal	Less than ideal
0–1 vs 2–6	Able to do work/leisure/ school activities fulltime	Excellent	Less than excellent
0–2 vs 3–6	Able to live alone for >1 wk	Good or better	Less than good
0–3 vs 4–6	Able to walk	Fair or better	Less than fair
0–4 vs 5–6	Constant care	Poor or better	Very Poor
0–5 vs 6	Survival	Alive	Dead

mRS indicates modified Rankin Scale.

Table 5. Recommended Health State Terms and Valence Terms for mRS Sliding Dichotomy Outcomes

Outcome	Health state term	Valence term
When slide analysis counts only better than expected outcome as positive outcome		
Better	Better than expected	Favorable
Worse	As expected or worse	Unfavorable
When slide analysis counts both expected or better than expected outcome as positive outcome		
Better	As expected or better	Favorable
Worse	Worse than expected	Unfavorable

mRS indicates modified Rankin Scale.

Table 6. Recommended Health State Terms for mRS Multilevel Outcomes

Outcome	Health state term	Better outcome	Worse outcome
Ordinal shift	Level of disability	Reduced disability	Increased disability
Utility-weighted mRS	Health-related quality of life	Improved health-related quality of life	Reduced health-related quality of life

mRS indicates modified Rankin Scale.

not a patient reported outcome. The mRS is therefore objective rather than subjective. Young patients might find even mild symptoms to be very bothersome and would not apply the valence term excellent to their outcome. However, they are unaware of or have not experienced the full range of several worse outcome states that they are not experiencing. Individual patients have limited direct experience of different disease intensities; they experience disease in depth but not in breadth. In contrast, physicians, nurses, and allied health professionals, who have direct encounters with patients with multiple conditions and diverse severities, experience disease both in depth and in breadth, albeit externally. Terms reflecting patient perspectives are best applied to patient reported outcomes, such as the EQ-5D, rather than the mRS. In addition, this issue is also rendered somewhat moot by the fact prior studies have shown that clinicians and patient/family assign remarkably similar value ratings to the 7 mRS outcome states.[18]

Third, the terms we suggest for individual mRS states are intended to reflect their absolute value, not their relative value. Patients with malignant hemispheric infarctions who were destined to have fatal outcome without intervention and instead attain an mRS score of 4 with intervention have a good relative but poor absolute outcome state. In contrast, the terms we suggest for sliding dichotomy analysis of the mRS are intended to reflect the relative value, not the objective value of each patient's outcome. The hemicraniectomy patient who attains an mRS score 4 has a favorable result considering where they were bound.

Fourth, while most often used as an outcome measure, the mRS is also sometimes employed to characterize what the patient's global disability level was before onset of the index stroke—the prestroke mRS. The terms here recommended are applicable to the prestroke mRS as well, since they are intended to characterize the intrinsic nature of each mRS health state, whether present before or after stroke.

Fifth, a limitation of the process for developing this consensus was that, although there were meeting participants from Europe, Asia, and Australia, a majority were from North America. However, the evidence synthesis did not indicate a systematic difference in terminology in trials reported from North America, Europe, and Asia. The literature search and consideration of terminology was confined to the English language; thoughtful translation/selection of terms for mRS states in additional languages is desirable to widen the benefits of a uniform approach.

CONCLUSIONS

Our intent in developing the proposed consistent set of brief rubrics for mRS outcomes is to enhance patient, clinician, and policy-maker comprehension of mRS findings in clinical trials and quality improvement initiatives. Our hope is that the harmonized nomenclature we advance will improve the usefulness and legibility of the scale, that it will be accepted by clinical trialists, regulatory agencies, and others active in stroke research and treatment, and that it will be widely adopted to improve clarity and understanding of the functional outcomes of patients after stroke.

ARTICLE INFORMATION

Affiliations

Department of Neurology and Comprehensive Stroke Center, David Geffen School of Medicine at UCLA, Los Angeles, CA (J.L.S.). Phyathai Comprehensive Stroke Center, Phyathai 1 Hospital, Bangkok, Thailand (N.C.). Department of Neurology & Melbourne Brain Centre, Royal Melbourne Hospital, Australia (B.C.V.C.). Memorial Hermann Hospital-Texas Medical Center, Houston (J.C.G.). Department of Clinical Neuroscience and Hotchkiss Brain Institute, Cumming School of Medicine, University of Calgary and Foothills Medical Centre, AB, Canada (M.D.H.). Department of Neurology and Rehabilitation Sciences, University of Cincinnati, OH (P.K.). Biogen, Cambridge, MA (J.L.). Department of Neurology and Neurological Sciences and the Stanford Stroke Center, Stanford University (M.G.L.). Division of Stroke and Neurocritical Care, Department of Neurology and Neurological Sciences and the Stanford Stroke Center, Stanford University (C.V., G.W.A.).

Acknowledgments

Saeed Ansari (The views expressed are the authors' own and do not necessarily reflect those of the National Institutes of Health, the Department of Health and Human Services, or the United States government), Johannes Boltz, Joseph P. Broderick, Alastair M. Buchan, Christopher Chen, Thomas P. Davis, Colin P. Derdeyn, Daniela Drago, Marc Fisher, Anna Grace, Walid Haddad, Michael D. Hill, William Holt, Gary Houser, Ashutosh Jadhav, W. Taylor Kimberly, Maarten G. Lansberg, David S. Liebeskind, John Kylan Lynch (The views expressed are the authors' own and do not necessarily reflect those of the National Institutes of Health, the Department of Health and Human Services, or the United States government), Eva A. Mistry, J. Mocco, Kent E. Pryor, Ralph L. Sacco, Amrou Sarraj, Sean I. Savitz, Lee H. Schwamm, Kevin Sheth, Yoram Solberg, Michael Tymianski, Achala Vagal, Steven J. Warach, Lawrence R. Wechsler, Nikolaos K. Ziogas.

Sources of Funding

None.

Disclosures

Dr Saver is an employee of the University of California. Dr Saver and Dr Sidney Starkman created the Rankin Focused Assessment while University of California employee, and Dr Saver, Dr Starkman, and University of California, Regents have made the RFA freely and permanently available as a no-fee public resource under a Creative Commons, use-freely-with-attribution license. Dr Saver and Dr Sidney Starkman also created a written vignette rater certification program for the Rankin Focused Assessment while University of California employee. The written vignettes are an optional system for training and certifying raters in the use of the free RFA resource. The University of California, Regents, along with Dr Saver and Dr Starkman, hold a copyright for the written vignette rater certification system. Any revenues received under that copyright are used to support the training of Vascular Neurology Fellows at UCLA. Dr Landen is an employee of Biogen. Dr Hill reports grants from NoNO, Inc, grants from Medtronic, grants from Boehringer

Ingelheim, and grants from Biogen outside the submitted work; in addition, Dr Hill has a patent to US Patent office Number: 62/086,077 issued and licensed; and owns stock in Pure Web Incorporated, a company that makes, among other products, medical imaging software, is a director of the Canadian Federation of Neurological Sciences, a not-for-profit group, is a director of the Canadian Stroke Consortium, a not-for-profit group, is a director of Circle NeuroVascular, Inc, and has received grant support from Alberta Innovates Health Solutions, CIHR, Heart & Stroke Foundation of Canada, National Institutes of Neurological Disorders and Stroke. Dr Khatri reports grants from Cerenovus, and consulting fees from Lumosa and Diamedica to her department, and she has received personal fees from Bayer for trial effort and from Basking Biosciences for consulting outside the submitted work. Dr Lansberg reports grants from NIH during the conduct of the study. Dr Albers reports personal fees and other from iSchemaView and personal fees from Genentech outside the submitted work. The other authors report no conflicts.

Supplemental Materials

Expanded Materials and Methods
Online Figure I
Online Tables I and II

REFERENCES

1. Duncan PW, Jorgensen HS, Wade DT. Outcome measures in acute stroke trials: a systematic review and some recommendations to improve practice. *Stroke.* 2000;31:1429–1438. doi: 10.1161/01.str.31.6.1429
2. Banks JL, Marotta CA. Outcomes validity and reliability of the modified Rankin Scale: implications for stroke clinical trials: a literature review and synthesis. *Stroke.* 2007;38:1091–1096. doi: 10.1161/01.STR.0000258355.23810.c6
3. Jahan R, Saver JL, Schwamm LH, Fonarow GC, Liang L, Matsouaka RA, Xian Y, Holmes DN, Peterson ED, Yavagal D, et al. Association between time to treatment with endovascular reperfusion therapy and outcomes in patients with acute ischemic stroke treated in clinical practice. *JAMA.* 2019;322:252–263. doi: 10.1001/jama.2019.8286
4. Keselman B, Gdovinová Z, Jatuzis D, Melo TPE, Vilionskis A, Cavallo R, Frol S, Jurak L, Koyuncu B, Nunes AP, et al. Safety and outcomes of intravenous thrombolysis in posterior versus anterior circulation stroke: results from the safe implementation of treatments in stroke registry and meta-analysis. *Stroke.* 2020;51:876–882. doi: 10.1161/STROKEAHA.119.027071
5. Hicks KA, Mahaffey KW, Mehran R, Nissen SE, Wiviott SD, Dunn B, Solomon SD, Marler JR, Teerlink JR, Farb A, et al; Standardized Data Collection for Cardiovascular Trials Initiative (SCTI). 2017 Cardiovascular and stroke endpoint definitions for clinical trials. *Circulation.* 2018;137:961–972. doi: 10.1161/CIRCULATIONAHA.117.033502
6. European Medicines Agency. Guideline on clinical investigation of medicinal products for prevention of stroke and systemic embolic events in patients with non-valvular atrial fibrillation. 2014;2020. https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-clinical-investigation-medicinal-products-prevention-stroke-systemic-embolic-events_en.pdf Accessed October 2020.
7. Lees KR, Bath PM, Schellinger PD, Kerr DM, Fulton R, Hacke W, Matchar D, Sehra R, Toni D; European Stroke Organization Outcomes Working Group. Contemporary outcome measures in acute stroke research: choice of primary outcome measure. *Stroke.* 2012;43:1163–1170. doi: 10.1161/STROKEAHA.111.641423
8. Higashida RT, Furlan AJ, Roberts H, Tomsick T, Connors B, Barr J, Dillon W, Warach S, Broderick J, Tilley B, et al; Technology Assessment Committee of the American Society of Interventional and Therapeutic Neuroradiology; Technology Assessment Committee of the Society of Interventional Radiology. Trial design and reporting standards for intra-arterial cerebral thrombolysis for acute ischemic stroke. *Stroke.* 2003;34:e109–e137. doi: 10.1161/01.STR.0000082721.62796.09
9. Broderick JP, Adeoye O, Elm J. Evolution of the modified Rankin Scale and its use in future stroke trials. *Stroke.* 2017;48:2007–2012. doi: 10.1161/STROKEAHA.117.017866
10. Rankin J. Cerebral vascular accidents in patients over the age of 60. II. Prognosis. *Scott Med J.* 1957;2:200–215. doi: 10.1177/003693305700200504
11. Farrell B, Godwin J, Richards S, Warlow C. The United Kingdom transient ischaemic attack (UK-TIA) aspirin trial: final results. *J Neurol Neurosurg Psychiatry.* 1991;54:1044–1054. doi: 10.1136/jnnp.54.12.1044
12. Bruno A, Akinwuntan AE, Lin C, Close B, Davis K, Baute V, Aryal T, Brooks D, Hess DC, Switzer JA, et al. Simplified modified Rankin Scale questionnaire: reproducibility over the telephone and validation with quality of life. *Stroke.* 2011;42:2276–2279. doi: 10.1161/STROKEAHA.111.613273
13. Quinn TJ, Dawson J, Walters MR, Lees KR. Variability in modified Rankin scoring across a large cohort of international observers. *Stroke.* 2008;39:2975–2979. doi: 10.1161/STROKEAHA.108.515262
14. Saver JL, Filip B, Hamilton S, Yanes A, Craig S, Cho M, Conwit R, Starkman S; FAST-MAG Investigators and Coordinators. Improving the reliability of stroke disability grading in clinical trials and clinical practice: the Rankin Focused Assessment (RFA). *Stroke.* 2010;41:992–995. doi: 10.1161/STROKEAHA.109.571364
15. Lee SY, Kim DY, Sohn MK, Lee J, Lee SG, Shin YI, Kim SY, Oh GJ, Lee YH, Lee YS, et al. Determining the cut-off score for the Modified Barthel Index and the modified Rankin Scale for assessment of functional independence and residual disability after stroke. *PLoS One.* 2020;15:e0226324. doi: 10.1371/journal.pone.0226324
16. Saver JL. Optimal end points for acute stroke therapy trials: best ways to measure treatment effects of drugs and devices. *Stroke.* 2011;42:2356–2362. doi: 10.1161/STROKEAHA.111.619122
17. Bath PM, Lees KR, Schellinger PD, Altman H, Bland M, Hogg C, Howard G, Saver JL; European Stroke Organisation Outcomes Working Group. Statistical analysis of the primary outcome in acute stroke trials. *Stroke.* 2012;43:1171–1178. doi: 10.1161/STROKEAHA.111.641456
18. Chaisinanunkul N, Adeoye O, Lewis RJ, Grotta JC, Broderick J, Jovin TG, Nogueira RG, Elm JJ, Graves T, Berry S, et al; DAWN Trial and MOST Trial Steering Committees; Additional contributors from DAWN Trial Steering Committee. Adopting a patient-centered approach to primary outcome analysis of acute stroke trials using a utility-weighted modified Rankin Scale. *Stroke.* 2015;46:2238–2243. doi: 10.1161/STROKEAHA.114.008547
19. Quinn TJ, Lees KR, Hardemark HG, Dawson J, Walters MR. Initial experience of a digital training resource for modified Rankin Scale assessment in clinical trials. *Stroke.* 2007;38:2257–2261. doi: 10.1161/STROKEAHA.106.480723
20. López-Cancio E, Salvat M, Cerdà N, Jiménez M, Codas J, Llull L, Boned S, Cano LM, Lara B, Molina C, et al; REVASCAT investigators. Phone and video-based modalities of central blinded adjudication of Modified Rankin Scores in an endovascular stroke trial. *Stroke.* 2015;46:3405–3410. doi: 10.1161/STROKEAHA.115.010909
21. Wilson JT, Hareendran A, Grant M, Baird T, Schulz UG, Muir KW, Bone I. Improving the assessment of outcomes in stroke: use of a structured interview to assign grades on the modified Rankin Scale. *Stroke.* 2002;33:2243–2246. doi: 10.1161/01.str.0000027437.22450.bd
22. Bruno A, Shah N, Lin C, Close B, Hess DC, Davis K, Baute V, Switzer JA, Waller JL, Nichols FT. Improving modified Rankin Scale assessment with a simplified questionnaire. *Stroke.* 2010;41:1048–1050. doi: 10.1161/STROKEAHA.109.571562
23. Fisher M, Albers GW, Donnan GA, Furlan AJ, Grotta JC, Kidwell CS, Sacco RL, Wechsler LR; Stroke Therapy Academic Industry Roundtable IV. Enhancing the development and approval of acute stroke therapies: Stroke Therapy Academic Industry roundtable. *Stroke.* 2005;36:1808–1813. doi: 10.1161/01.STR.0000173403.60553.27
24. Saver JL, Gornbein J. Treatment effects for which shift or binary analyses are advantageous in acute stroke trials. *Neurology.* 2009;72:1310–1315. doi: 10.1212/01.wnl.0000341308.73506.b7
25. Fisher M, Hanley DF, Howard G, Jauch EC, Warach S; STAIR Group. Recommendations from the STAIR V meeting on acute stroke trials, technology and outcomes. *Stroke.* 2007;38:245–248. doi: 10.1161/01.STR.0000255951.37434.aa
26. Saver JL, Jovin TG, Smith WS, Albers GW, Baron JC, Boltze J, Broderick JP, Davis LA, Demchuk AM, DeSena S, et al; STAIR VIII Consortium. Stroke treatment academic industry roundtable: research priorities in the assessment of neurothrombectomy devices. *Stroke.* 2013;44:3596–3601. doi: 10.1161/STROKEAHA.113.002769
27. Sajobi TT, Zhang Y, Menon BK, Goyal M, Demchuk AM, Broderick JP, Hill MD. Effect size estimates for the ESCAPE trial: proportional odds regression versus other statistical methods. *Stroke.* 2015;46:1800–1805. doi: 10.1161/STROKEAHA.115.009328
28. Leung WC. Balancing statistical and clinical significance in evaluating treatment effects. *Postgrad Med J.* 2001;77:201–204. doi: 10.1136/pmj.77.905.201
29. Ranganathan P, Pramesh CS, Buyse M. Common pitfalls in statistical analysis: Clinical versus statistical significance. *Perspect Clin Res.* 2015;6:169–170. doi: 10.4103/2229-3485.159943
30. Elwyn G, O'Connor A, Stacey D, Volk R, Edwards A, Coulter A, Thomson R, Barratt A, Barry M, Bernstein S, et al; International Patient Decision Aids Standards (IPDAS) Collaboration. Developing a quality criteria framework for patient decision aids: online international Delphi consensus process. *BMJ.* 2006;333:417. doi: 10.1136/bmj.38926.629329.AE

31. International Plain Language Association. What is plain language? Accessed June 2021. https://plainlanguagenetwork.org/plain-language/what-is-plain-language/.
32. National Institutes of Health. Plain language at NIH. Accessed June 2021. https://www.nih.gov/institutes-nih/nih-office-director/office-communications-public-liaison/clear-communication/plain-language.
33. Health Resources & Services Administration. Health literacy. Accessed June 2021. https://www.hrsa.gov/about/organization/bureaus/ohe/health-literacy/index.html.
34. Sue S, Wendy M. Plain language: a strategic response to the health literacy challenge. *J Public Health Policy.* 2007;28:71–93. doi: 10.1057/palgrave.jphp.3200102
35. Basic definition of disability. Code of Federal Regulations 404.1505. 2012.
36. Buzzard KA, Broadley SA, Butzkueven H. What do effective treatments for multiple sclerosis tell us about the molecular mechanisms involved in pathogenesis? *Int J Mol Sci.* 2012;13:12665–12709. doi: 10.3390/ijms131012665
37. Ben-Zacharia A. Good moves: case challenges in managing mobility in multiple sclerosis. Medscape 2012. Accessed June 2021. https://www.medscape.org/viewarticle/770601_4.
38. Patel N, Rao VA, Heilman-Espinoza ER, Lai R, Quesada RA, Flint AC. Simple and reliable determination of the modified Rankin Scale score in neurosurgical and neurological patients: the mRS-9Q. *Neurosurgery.* 2012;71:971–975. doi: 10.1227/NEU.0b013e31826a8a56