

# MEDCAC Meeting

## September 22, 2021

American Association of Neurological Surgeons  
American College of Radiology  
American Society of Neuroradiology  
Congress of Neurological Surgeons  
Society of NeuroInterventional Surgery

# Disclosures

- Michael Chen, MD, SNIS--Consultant: Genentech, Medtronic, Penumbra, Microvention, Stryker, Imperative Care, GE, Siemens
- Joshua Hirsch, MD, ACR--Medtronic consultant and investor InNeuroCo and DSMB Balt
- Mahesh Jayaraman, MD, SNIS—One time compensation from Medtronic for speaking at 2018 International Stroke Conference in 2018
- James Milburn, MD, ASNR—Imperative Care, Consultant Penumbra, Inc., Speaker
- Clemens Schirmer, MD, AANS/CNS—No Conflicts

# QUESTION 1: Primary health outcomes

- **More confident:**
  - **mRS $\geq$ 3**
  - **mRS <3 or equal to pre-stroke mRS**
- **Less confident:**
  - Other kinds of stroke
  - Decrease in mRS of  $\geq$ 2 points

*Modified Rankin score is weighted, and numerical change in score highly dependent on where along spectrum the patient is*



## COMMENTS, OPINIONS, AND REVIEWS

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# Outcomes Validity and Reliability of the Modified Rankin Scale: Implications for Stroke Clinical Trials

## A Literature Review and Synthesis

Jamie L. Banks, MSc, PhD and Charles A. Marotta, MD, PhD

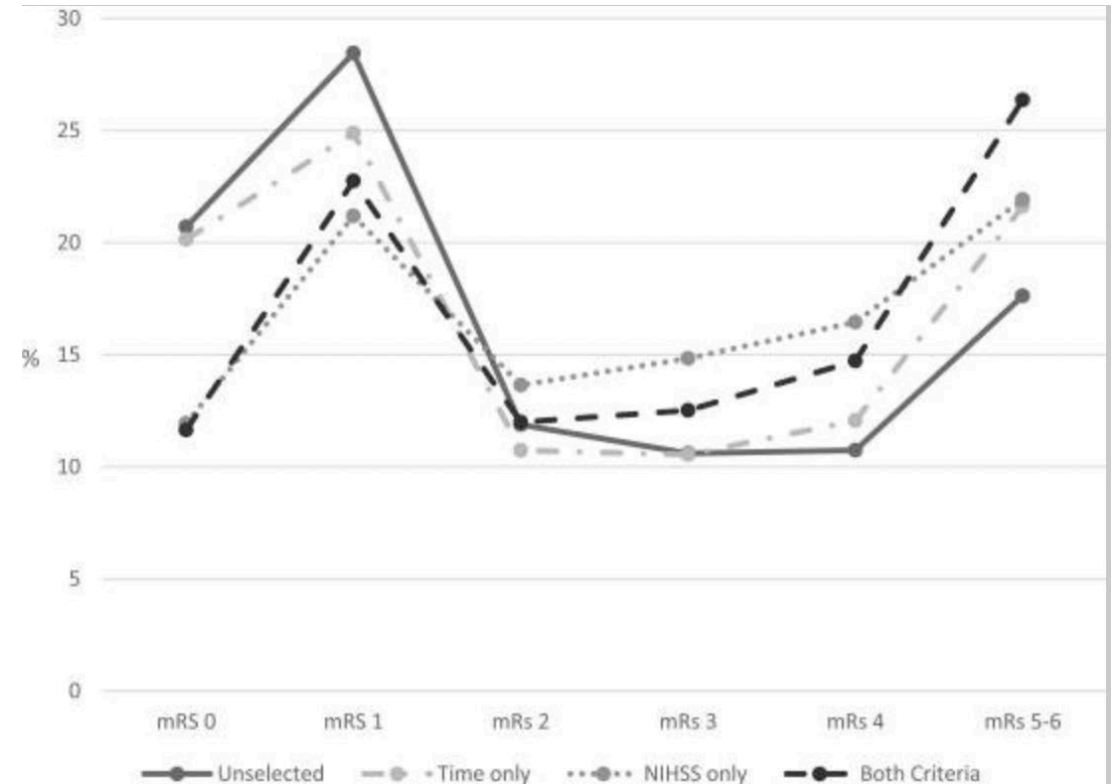
1. High inter-rater reliability, improves with structured interviews
2. Construct validity well documented
3. Convergent validity well documented
4. *Need to consider comorbidities and socioeconomic factors when applying/interpreting mRS*

# Discussion

- 90 day length for followup seems most appropriate
- mRS cutoffs depend on the question being studied and should be calibrated based on subgroup from mRS<3 which would indicate functional independence
- Composite endpoints that include mortality may not necessarily reflect the primary concern regarding stroke which is disability.
- Better choices of end point substantially strengthen trial power for a given trial size or allow reduced sample sizes without loss of statistical power

# Notes about mRS outcomes

- The distribution of mRS scores at discharge according to usual acute ischemic stroke trials selection criteria is
  - Not normally distributed
  - Sample size calculations are sensitive to this (t-test vs OLR calculation)



# QUESTION 2: Primary health outcomes

- **More confident:**
  - **Discharge disposition to rehabilitation (home vs. inpatient facility)**
- **Less confident:**
  - Hospitalization length of stay for index procedure
    - Length of stay highly variable depending on comorbidities, hospital services, weekend effect, physician preferences
  - Number of unscheduled re-admissions related to cerebrovascular disease
    - Likely not very often

# Notes about Disposition, LOS, readmissions as outcome measures

- Early determination of hospital discharge disposition status at an acute admission is extremely important for stroke management and the eventual outcomes of patients with stroke
- Discharge disposition pattern of patients with stroke in Tennessee was associated with the key patient characteristics of selected demographics (including race), clinical indicators, and insurance status
- These metrics measure the local stroke system of care more than the individual outcomes



# QUESTION 3: Health Outcomes

## Modified Rankin Score

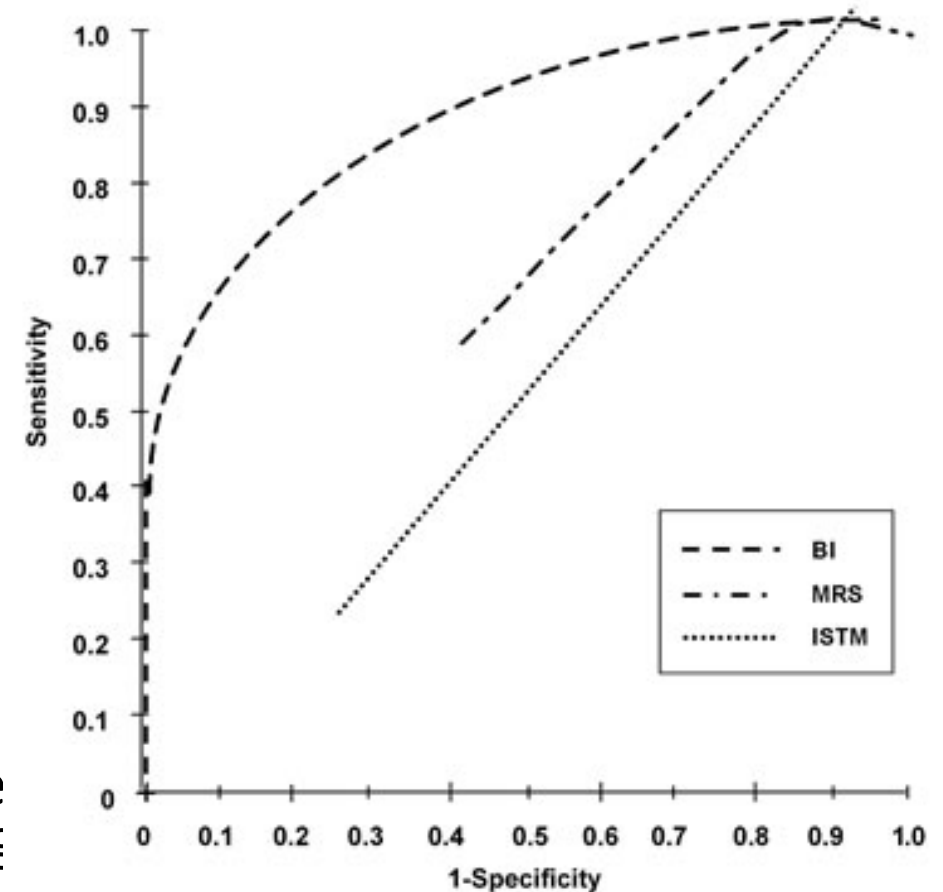
*Important measure of disability but each numeric change is not equal in value so consider weighted scoring*

## NIHSS

*Readily available, quantifiable but does not reflect disability and underrepresents right hemisphere deficits and brainstem deficits*

# Notes about mRS outcomes changes

- For a moderately disabled stroke population there are wide variations in the sensitivity to change in disability measures
- Compare to (Modified Rankin Scale (MRS) and the International Stroke Trial Measure (ISTM), Barthel Index (BI) and Functional Independence Measure (FIM))
- mRS categories are quite large; any change detected by these measures must be large and presumably clinically significant
- Though ADL scales may take longer to administer, their increased sensitivity may make them more useful in treatment trials by allowing fewer subjects to be enrolled



# Notes about NIHSS as outcome measure

- mRS lacks specificity and requires long-term follow-up interviews, which consume time and resources
- NIHSS, early after stroke may be an alternative
- Chalos et al.:
- The NIHSS within 1 week satisfies the requirements for a surrogate end point and may be used as a primary outcome measure in trials of acute treatment for ischemic stroke, particularly in phase II(b) trials

# QUESTION 4: Health Outcomes

- EQ-5D
  - Not stroke specific but most widely used generic health questionnaire in stroke
- No questions about speech or cognition—stroke specific
- Literature established:
  - Psychometric properties
  - Reasonable construct
  - Concurrent and discriminant validity
  - Accuracy for predicting outcomes
  - Responsiveness in longitudinal studies

# Notes about EQ-5D

- When using EQ-5D population norms have to be established and used to inform the future valuation of health in economic evaluations
  - Norms are not necessarily available for the stroke population
  - Validity for stroke population has been established with relatively small populations
  - It does not assess the cognitive problems many patients with stroke experience
    - Extensions e.g. EQ-5D-5L+C can be considered
  - It also does not include questions around speech. Two studies excluded patients with aphasia.
  - EQ-5D is designed for self or proxy completion, introducing bias