

Outcome Measures in Multiple Sclerosis Research

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Outcome Measures in MS

- Clinical measures:
 - Relapses
 - Global measures
 - Expanded Disability Status Scale (EDSS)
 - Multiple Sclerosis Functional Composite (MSFC)
 - Specific function testing
 - Modified Ashworth
 - Low Contrast Visual Acuity
 - Symbol Digit Modalities Test
- Imaging Measures:
 - MRI
 - Optical Coherence Tomography (OCT)
- Patient reported outcomes

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Relapses

Relapse:

- New or worsening symptom for >24 hours without precipitating factor
- Advantage:
 - Clinically relevant
- Disadvantages:
 - Subjective
 - Hard to quantify severity

Common Relapse-Based Outcomes:

- Annualized relapse rate
- Time to first relapse

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Expanded Disability Status Scale (EDSS)

0	Normal exam
1 – 1.5	No disability apparent to patient
2 – 2.5	Minimal disability
3 – 3.5	Moderate disability
4 – 4.5	Relatively severe disability
5 – 5.5	Disability affects daily routine
6 – 6.5	Walking with assistance
7 – 7.5	In wheelchair; able to transfer
8 – 8.5	In wheelchair or bed; can aid in some ADLs
9 – 9.5	Confined to bed

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EDSS cont'd

- Grades are assigned (from 0-5 or 0-6) for each functional system:
 - Vision
 - Brainstem
 - Pyramidal
 - Cerebellar
 - Sensory
 - Bowel/bladder
 - Cerebral

- Overall EDSS score is defined by a combination of functional system scores and mobility

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EDSS cont'd

- *Advantages:*
 - Widely used
 - FDA recognized outcome measure

- *Disadvantages:*
 - Different segments of scale have different focus
 - Weighted towards walking
 - Relatively insensitive to change, particularly at higher end of scale
 - Equal scores may not have equal underlying meaning

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Multiple Sclerosis Functional Composite (MSFC)

- A 3-part assessment measuring lower extremity function, upper extremity function and cognition. Includes:
 - Timed 25-foot walk (T25FW)
 - 9-hole peg test (9HPT)
 - Paced Auditory Serial Addition Test (PASAT)

- Z-scores assigned for individual components and composite

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9 Hole Peg Test



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MSFC Considerations

Advantages:

- May be administered by non-neurologists
- More balanced across disease dimensions
- May be more sensitive to change than EDSS

Disadvantages:

- Not as widely accepted as outcome measure
- Does not account for vision changes
- PASAT disliked by patients

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Function Specific Outcome Measures:

Modified Ashworth Scale (spasticity)

Grade	Description
0	No increase in muscle tone
1	Slight increase in muscle tone, manifested by catch/release, or by minimal resistance at the end of the range of motion when the affected part(s) is moved in flexion or extension
2	Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder of the range of movement (ROM)
3	More marked increase in muscle tone through most of ROM, but affected part(s) easily moved
4	Considerable increase in muscle tone, passive movement difficult
5	Affected part(s) rigid in flexion and extension

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Modified Ashworth Testing



Spinal Cord B C Craven

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Function Specific Outcome Measures

Low Contrast Visual Acuity



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Function Specific Outcome Measures

Symbol Digit Modalities Test (cognition)

≥	±	«	π	ж	ψ	Δ	ο	↑
1	2	3	4	5	6	7	8	9

ψ	±	π	ψ	±	ο	≥	Δ	↑	ж	±	«	±	≥	Δ
6	2	4												
ж	Δ	↑	ο	π	«	Δ	↑	ж	±	«	«	«	ж	ψ
ο	±	«	π	ж	ψ	≥	ο	±	≥	±	«	«	ψ	ο
≥	π	«	ψ	ж	±	Δ	ο	↑	ο	±	«	π	ж	«
±	±	«	π	ж	ψ	ο	±	ο	≥	±	«	π	ο	ψ
«	π	«	Δ	«	π	Δ	ο	↑	Δ	«	«	Δ	ж	ψ
≥	±	«	±	ж	«	±	ο	«	≥	±	±	π	Δ	ψ

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Imaging Outcome Measures-MRI

MRI

- Common outcomes:
 - New T2 or contrast-enhancing lesions
 - T2 Lesion volume
 - Brain volume (atrophy)

- Sensitive to subclinical disease progression

- May not correlate well with degree of disability

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Imaging Outcome Measures-OCT

Optical Coherence Tomography (OCT)

- Uses near infrared light
- Measures retinal nerve fiber layer thickness
- Higher correlation with disability
- Variability in technique

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Imaging Outcome Measures

Advantages:

- Potential shorter duration of studies
- Often less subjective

Disadvantages:

- Variable clinical correlation
- Technology costs
- Potential decreased site participation

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Patient Reported Outcomes

- Increasingly popular
- Clinically relevant to patients
- Examples:
 - Modified Fatigue Impact Scale (MFIS)
 - Bladder Control Scale

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Outcome Measures in Progressive MS

- Clinical Measures Useful?
 - Rare relapses
 - EDSS less sensitive to change at higher scores
 - Disability progression difficult to quantify with current measures
- Imaging Measures Useful?
 - Minimal new or enhancing lesions
 - Atrophy on MRI or RNFL thinning on OCT may be better options
- Clear need to further develop outcome measures for progressive MS

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Summary

Types of outcome measures:

- Clinical: relapse, rating scales
- Imaging: MRI, OCT
- Patient reported outcomes

When determining whether to participate in a clinical trial, consider:

- Ease of administration
- Enough staff to conduct the necessary testing?
- Potential MRI/OCT requirements

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Questions?

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