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
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

Expanded Disability Status Scale (EDSS)

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

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
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

9 Hole Peg Test
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

Function Specific Outcome Measures:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
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<tbody>
<tr>
<td>0</td>
<td>No increase in muscle tone</td>
</tr>
<tr>
<td>1</td>
<td>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</td>
</tr>
<tr>
<td>2</td>
<td>Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder of the range of movement (ROM)</td>
</tr>
<tr>
<td>3</td>
<td>More marked increase in muscle tone through most of ROM, but affected part(s) easily moved</td>
</tr>
<tr>
<td>4</td>
<td>Considerable increase in muscle tone, passive movement difficult</td>
</tr>
<tr>
<td>5</td>
<td>Affected part(s) rigid in flexion and extension</td>
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</tbody>
</table>
Modified Ashworth Testing

Function Specific Outcome Measures

Low Contrast Visual Acuity
Function Specific Outcome Measures

Symbol Digit Modalities Test (cognition)

<table>
<thead>
<tr>
<th>2</th>
<th>3</th>
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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
### 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

### Imaging Outcome Measures

**Advantages:**
- Potential shorter duration of studies
- Often less subjective

**Disadvantages:**
- Variable clinical correlation
- Technology costs
- Potential decreased site participation
Patient Reported Outcomes

- Increasingly popular
- Clinically relevant to patients

Examples:
- Modified Fatigue Impact Scale (MFIS)
- Bladder Control Scale

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
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

Questions?