

**Constructing an Adaptive Care Model  
for the Management of Disease-  
Related Symptoms Throughout the  
Course of Multiple Sclerosis**

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**Clinical Discussion**

# Performance Measures for MS

- Determining whether persons with MS receive appropriate, comprehensive healthcare requires tools for measuring quality
- The National Quality Measures Clearinghouse (NQMC) currently lists 1 measure for MS:
  - Palliative care: percentage of adult patients with a progressive, debilitating disease who have a palliative care plan documented in the medical record. 2009 Nov. NQMC:005642
- Traditional MS measures (eg, Expanded Disability Status Scale) are appropriate for assessing outcomes in clinical trials but not always practical for the real-world setting
- No other measures established for MS
  - The NMSS and AAN are currently in the process of developing performance measures for MS

# Quality Indicators for MS

- 25 MS symptom domains and 14 general health domains of MS care have been identified
  - Based on literature review and patient/provider interviews and discussions
  - Rated by a multidisciplinary panel (N=15), including 4 patients with MS
- 86 preliminary indicators were drafted, 76 of which were validated
- This comprehensive set of quality indicators for MS care can be used to assess quality of care and guide the design of interventions to improve care among MS patients

# Quality Indicators for MS Symptoms

Domains of MS Symptoms	Measure
Anxiety	<ul style="list-style-type: none"><li>• Management of anxiety</li></ul>
Bladder /Urinary Dysfunction	<ul style="list-style-type: none"><li>• Assessment of urinary symptoms</li><li>• Assessment for UTI upon hospital admission</li><li>• Management of post-void residual urine</li><li>• Avoid treatment of asymptomatic bacteriuria</li><li>• Test for antibiotic susceptibility with recurrent UTI</li><li>• Work-up of chronic subjective bladder symptoms</li></ul>
Bowel Dysfunction	<ul style="list-style-type: none"><li>• Assessment for bowel function</li><li>• Management of constipation</li><li>• Work-up of fecal incontinence</li></ul>
Cognitive Dysfunction	<ul style="list-style-type: none"><li>• Assessment for cognitive deficits</li><li>• Management of cognitive deficits</li></ul>
Depression	<ul style="list-style-type: none"><li>• Assessment for depression</li><li>• Treatment of depression</li></ul>

# Quality Indicators for MS Symptoms (cont)

Domains of MS Symptoms	Measure
Fatigue	<ul style="list-style-type: none"><li>• Assessment of fatigue</li><li>• Work-up for fatigue</li><li>• Review of medications causing fatigue</li><li>• Management of primary fatigue</li></ul>
Mobility/Falls	<ul style="list-style-type: none"><li>• Assessment for mobility impairments</li><li>• Work-up of mobility impairments or falls</li></ul>
Pressure Ulcers	<ul style="list-style-type: none"><li>• Assessment for risk of pressure ulcers</li><li>• Assessment for pressure ulcers in long-term facility</li><li>• Use of specialty mattresses</li><li>• Prevention of pressure ulcer</li></ul>
Relapses	<ul style="list-style-type: none"><li>• Documentation of occurrence of relapses</li><li>• Differentiate relapse from pseudo-relapse</li></ul>

# Quality Indicators for MS Symptoms (cont)

Domains of MS Symptoms	Measure
Sexual Dysfunction	<ul style="list-style-type: none"><li>• Assessment of erectile dysfunction</li><li>• Management of erectile dysfunction</li><li>• Assessment of female sexual dysfunction</li><li>• Work-up of sexual dysfunction</li><li>• Referral to specialist with expertise</li></ul>
Spasticity	<ul style="list-style-type: none"><li>• Assessment of spasticity</li><li>• Work-up of spasticity</li><li>• Management of persistent spasticity</li></ul>
Speech	<ul style="list-style-type: none"><li>• Management of dysarthria</li></ul>
Swallowing	<ul style="list-style-type: none"><li>• Assessment of dysphagia</li><li>• Formal tests of swallowing function</li><li>• Referral for swallowing dysfunction</li><li>• Offer of feeding tube</li></ul>

# Quality Indicators for General MS Care

General Health Domains of MS Care	Measure
At Time of Diagnosis: Medical Evaluation—Appropriateness and Timeliness	<ul style="list-style-type: none"><li>• Documentation of diagnostic criteria</li><li>• Timely initial diagnosis</li></ul>
At Time of Diagnosis: Patient Education	<ul style="list-style-type: none"><li>• Explanation of diagnostic work-up</li><li>• Offer of information to newly diagnosed patient</li></ul>
Management of Exacerbations and Activities of Daily Living (ADL) Difficulties	<ul style="list-style-type: none"><li>• Rehabilitation evaluation following an exacerbation</li><li>• Assessment of ADL difficulties</li><li>• Rehabilitation evaluation for ADL difficulties</li><li>• Treatment with steroids</li><li>• Communication of risks and benefits of steroids</li><li>• Comprehension of risks and benefits of steroids</li></ul>

# Quality Indicators for General MS Care (cont)

General Health Domains of MS Care	Measure
After Diagnosis: Patient Education	<ul style="list-style-type: none"><li>• Assessment for informational needs</li></ul>
Disease-Modifying Agents	<ul style="list-style-type: none"><li>• Treatment of clinically isolated syndrome</li><li>• Disease-modifying agents for relapsing forms of MS</li></ul>
	<ul style="list-style-type: none"><li>• Lab tests for persons on interferon beta therapy</li><li>• Lab tests for persons on high-dose interferon beta therapy</li><li>• Documentation when starting mitoxantrone or natalizumab</li><li>• Cardiac monitoring with mitoxantrone</li><li>• Communication of risks and benefits of disease-modifying treatments</li><li>• Comprehension of risks and benefits of disease-modifying</li></ul>



# Quality Indicators for General MS Care (cont)

General Health Domains of MS Care	Measure
Provision of Community and Social Resources/Patient Self-Management	<ul style="list-style-type: none"><li>• Assessment of problems with work or education</li><li>• Management of temperature</li><li>• Complementary and alternative medications</li></ul>
Establishment, Integration, and Coordination of Care	<ul style="list-style-type: none"><li>• Visit to neurologist or physiatrist</li><li>• Access to primary care provider</li><li>• Follow-up of new medication</li><li>• Contact for usual source of care</li><li>• Documentation of consultation by referring physician</li></ul>
Health Promotion	<ul style="list-style-type: none"><li>• Assessment of exercise habits</li><li>• Recommendation of exercise</li><li>• Assessment of general symptoms</li></ul>

# Quality Indicators for General MS Care (cont)

General Health Domains of MS Care	Measure
General Preventive Care	<ul style="list-style-type: none"><li>• Mammogram</li><li>• Pap smear</li><li>• Colon cancer screening</li><li>• Influenza immunization</li><li>• Pneumococcal polysaccharide vaccine</li><li>• Osteoporosis screening</li></ul>
Health Insurance and Disability Programs	<ul style="list-style-type: none"><li>• Awareness of health insurance and disability programs</li></ul>

# Quality Indicators for MS

- Most highly rated MS care domains were:
  - Appropriateness and timeliness of the diagnostic work-up
  - Bladder dysfunction
  - Cognition dysfunction
  - Depression\*
  - Disease-modifying agent usage
  - Fatigue\*
  - Integration of care
  - Mobility/falls\*
  - Spasticity\*

\*Measure selected for PI CME activity.

# MS Symptomatology

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# MS-Related Symptoms

- Prevalence of MS ~400,000 in the U.S. and >2.5 million worldwide
  - 85% **relapsing-remitting** → >50% will develop **secondary-progressive** within 10 years
  - 10% **primary-progressive**
  - 5% **progressive-relapsing**
- MS therapies can decrease/control
  - Frequency of relapses
  - New radiological lesion formation
- *Lack of guidance/consensus on managing chronic MS-related symptoms*

# What Drives QOL in MS?

Symptom	Respondents experiencing the problem (n=2265)	Respondents reporting problem as 'moderate' or 'high' (n=2265)	Respondents reporting symptom improvement on DMT (n=266)
Fatigue	96%	88%	41%
Balance and dizziness	92%	74%	27%
Loss of mobility	91%	79%	52%
Sensory problems	88%	54%	28%
Bladder problems	87%	70%	39%
Loss of memory and concentration	87%	52%	17%
Spasticity	82%	54%	34%
Vision problems	82%	41%	21%
Pain	81%	50%	50%
Bowel problems	74%	45%	36%
Sexual problems	70%	42%	33%
Tremor	68%	30%	35%
Speech and swallowing problems	68%	26%	42%

# Medical and Pharmacy Cost Trends for Commercially Insured Patients With MS

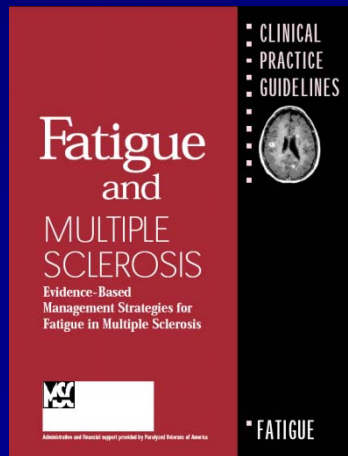
Year	Total Medical Expenditures		Total Pharmacy Expenditures		Medical + Pharmacy Expenditure Trend	
	N	Total Paid	N	Total Paid	PPPY	Compared with Previous Year
2006	361	\$4.5 million	354	\$6.2 million	\$29,652	NA
2007	360	\$4.5 million	350	\$6.2 million	\$29,584	-0.2%
2008	361	\$5.3 million	351	\$7 million	\$34,044	15.1%
2009	360	\$5.6 million	349	\$7.9 million	\$37,592	10.4%

Data are from a commercial Midwestern health plan of approximately 1.4 million members. N = number of members with 1 or more medical or pharmacy claim(s) in the given analysis year. PPPY= per patient per year. All PPPY calculations use 361 members, although not every member may have had medical or pharmacy expenditures in a given year.

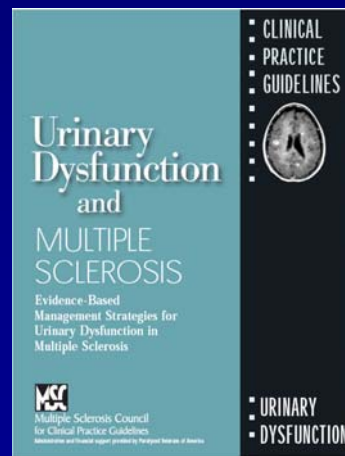
# Clinical Practice Guidelines on MS-Related Symptoms

- The Consortium of MS Centers (CMSC) has developed clinical practice guidelines for fatigue, urinary dysfunction, and spasticity

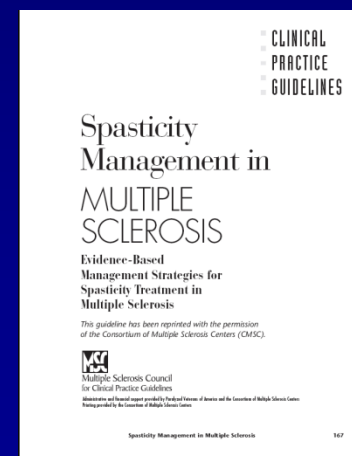
## *Evidence-Based Management Strategies for Fatigue and MS*



## *Evidence-Based Management Strategies for Urinary Dysfunction in MS*



## *Evidence-Based Management Strategies for Spasticity in MS (2005)*



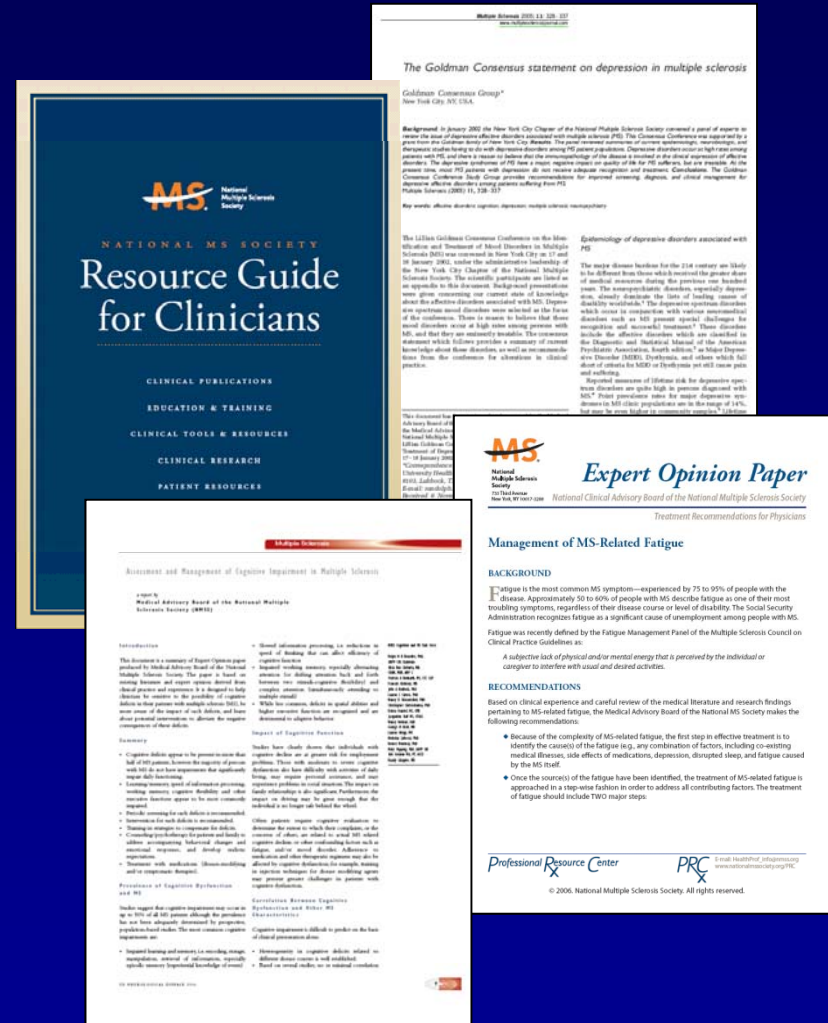
<http://www.ms-care.org/cmsc/News/CMSC-Information-Publications.html>.

Haselkorn JK, et al. *J Spinal Cord Med*.2005;28:167-199.



# Clinical Practice Guidelines on MS-Related Symptoms (cont)

- The National MS Society (NMSS) has adopted consensus statements/expert opinion papers on the following MS-related symptoms:
  - Depressive mood disorders
  - Cognitive impairment
  - Fatigue



Goldman Consensus Group. *Mult Scler.* 2005;11:328-337.  
 NMSS. *US Neurological Disease.*2004.

# MS Functional Composite (MSFC)

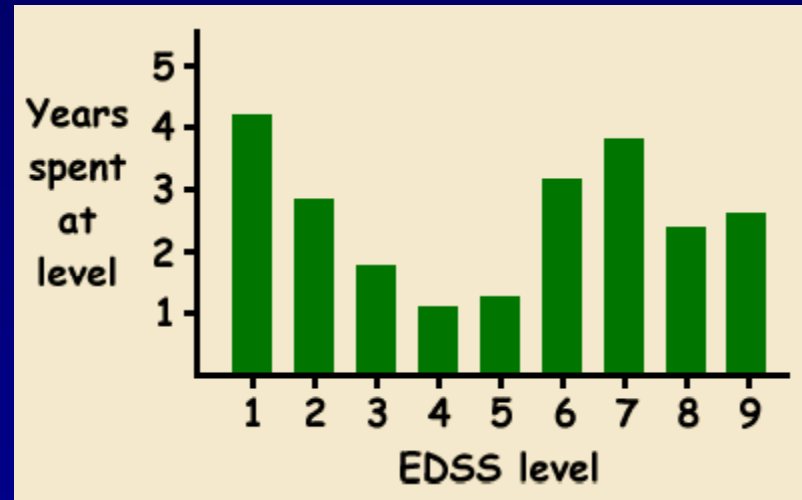
- 3-part, standardized, quantitative, assessment instrument for use in clinical studies of MS
  - Timed 25-foot walk
  - 9-Hole Peg Test (9-HPT)
  - Paced Auditory Serial Addition Test (PASAT-3)
- Developed by a special NMSS Task Force on Clinical Outcomes Assessment
- Designed as a multidimensional scale to reflect the varied clinical expression of MS across patients and over time
- The three components of the MSFC measure leg function/ambulation, arm/hand function, and cognitive function



# Expanded Disability Status Scale (EDSS)

- Quantifies disability in 8 functional systems and allows neurologists to assign a Functional System Score (FSS) in each of these:

- Pyramidal
- Cerebellar
- Brainstem
- Sensory
- Bowel and bladder
- Visual
- Cerebral
- Other



- EDSS levels 1.0 to 4.5 refer to people with MS who are fully ambulatory; levels 5.0 to 7.5 are defined by the impairment to ambulation; levels  $\geq 8.0$  are non-ambulatory

# Expanded Disability Status Scale (EDSS)

0.0	Normal neurological examination
1.0	No disability, minimal signs in one functional system (FS)
1.5	No disability, minimal signs in more than one FS
2.0	Minimal disability in one FS
2.5	Mild disability in one FS or minimal disability in two FS
3.0	Moderate disability in one FS, or mild disability in three or four FS. Fully ambulatory
3.5	Fully ambulatory but with moderate disability in one FS and more than minimal disability in several others
4.0	Fully ambulatory without aid, self-sufficient, up and about some 12 hours a day despite relatively severe disability; able to walk without aid or rest some 500 meters
4.5	Fully ambulatory without aid, up and about much of the day, able to work a full day, may otherwise have some limitation of full activity or require minimal assistance; characterized by relatively severe disability; able to walk without aid or rest some 300 meters.
5.0	Ambulatory without aid or rest for ~200 meters; disability severe enough to impair full daily activities (work a full day without special provisions)
5.5	Ambulatory without aid or rest for ~100 meters; disability severe enough to preclude full daily activities
6.0	Intermittent or unilateral constant assistance (cane, crutch, brace) required to walk ~100 meters with or without resting
6.5	Constant bilateral assistance (canes, crutches, braces) required to walk ~20 meters without resting
7.0	Unable to walk beyond approximately five meters even with aid, essentially restricted to wheelchair; wheels self in standard wheelchair and transfers alone; up and about in wheelchair some 12 hours a day
7.5	Unable to take more than a few steps; restricted to wheelchair; may need aid in transfer; wheels self but cannot carry on in standard wheelchair a full day; May require motorized wheelchair
8.0	Essentially restricted to bed or chair or perambulated in wheelchair, but may be out of bed itself much of the day; retains many self-care functions; generally has effective use of arms
8.5	Essentially restricted to bed much of day; has some effective use of arms retains some self care functions
9.0	Confined to bed; can still communicate and eat.
9.5	Totally helpless bed patient; unable to communicate effectively or eat/swallow
10.0	Death due to MS

# MS Symptomatology

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Assessment and Treatment of  
Depression

# Depression and MS

- Psychiatric disorders such as major depression are known to have a higher prevalence in patients with MS compared with the normal population
  - Lifetime risk for depression in patients with MS ranges from 40%-60%
  - Age and sex-adjusted prevalence rates are twice as high in MS patients compared with patients with other chronic diseases
- Depression can exacerbate cognitive dysfunction in MS
  - Suicidal ideation
- Due to a lack of well designed trials of pharmacotherapy or psychotherapy in MS, management of depression follows recommendations of general psychiatry
- *Unlike some aspects of MS, depression is treatable!*

# Depression: Causes Linked to MS

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- Psychosocial effects of MS disability
- Direct effect of lesions on brain structures involved in regulating and maintaining mood state
- Untoward effects of interferon (IFN)- $\beta$  for treating MS, which may be associated with mood changes
- Immune dysfunction

# Depression: Goldman Consensus Recommendations (2002)

Specific recommendations from the Goldman Consensus Conference of 2002 include the following:

- 1) Clinical groups which routinely care for MS patients should institute regular screening measures for the identification of depression, such as the Beck Depression Inventory, using a threshold of 13 for positive screens.
- 2) Patients who meet screening thresholds for depression, or who endorse any positive responses to suicide inquiries, should be actively assessed for severity and quality of depression, and considered for follow-on treatment recommendations.
- 3) Treatment plans for depression among MS patients should be individualized, using psychotherapeutic, psychopharmacologic, or integrated approaches, depending upon individual circumstances, and preferences. Available evidence suggests that pharmacotherapy and certain psychotherapies are equally effective for depressive disorders in MS populations, yet the Consensus Group strongly recommends that these treatment modalities be combined in an integrated biopsychosocial treatment plan whenever possible. Treatment plans should be followed through to eradication of depressive symptomatology.
- 4) Greater standardization of the therapeutic approach to depression in MS should be sought, through the development and testing of an algorithm which is uniquely crafted to this clinical domain.
- 5) Continuing clinical research should be encouraged into the neurobiologic and psychologic bases of depressive disorders in MS patients, and into therapeutic responses to currently available and newly developing treatment modalities.

**1) Institute regular screening measures for depression (eg, Beck Depression Inventory)**

**2) Patients who meet screening thresholds for depression or have suicidal tendencies, should be actively assessed and treated**

**3) Treatment plans for depression should be individualized using integrated approaches**

**4) Standardize therapeutic approach to depression through use of an algorithm**

**5) Continue clinical research on neurologic and psychologic mechanisms of depression as well as therapeutic responses**



# Depression: Assessment

During initial or follow-up visit, consider options for depression assessment

No time for assessment with objective measures

- Rapid screening (U.S. Preventative Services Task Force 2-question test)
- If ambiguous results, reschedule for objective assessment or refer to mental health professional

Limited time for formal assessment with objective measures

- Unidimensional depression measure, eg:
  - Beck Depression Inventory-Fast Screen
  - Chicago Multiscale Depression Inventory

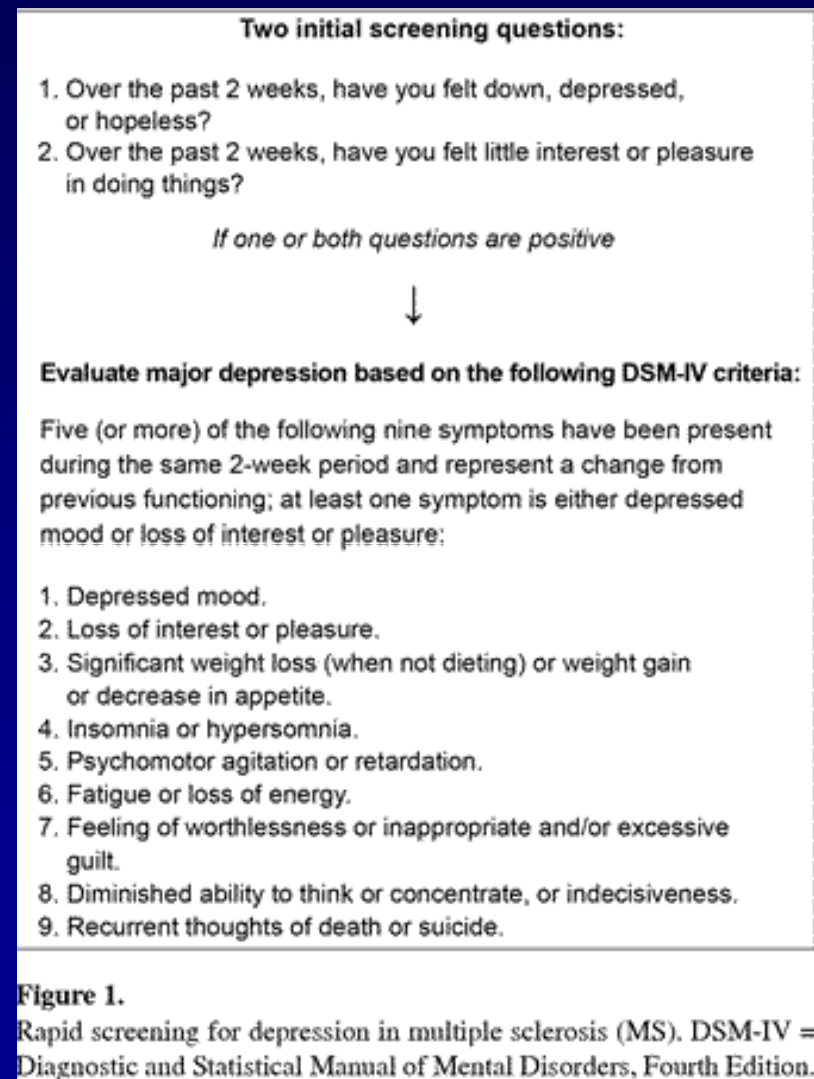
Time for multidimensional assessment

- Multidimensional quality of life measure, eg:
  - Profile of Moods States
  - Functional Assessment of MS

- If depression is determined, refer to appropriate treatment (eg, combination of counseling and medication)
- If cognitive issues and fatigue are complicating depression assessment, request neuropsychological evaluation

# Depression: Rapid Screening

- U.S. Preventive Services Task Force recommends a brief two-question screening test for assessing depression



# Depression: Rapid Screening

- Patient Health Questionnaire (PHQ-9)
  - 9-item depression scale based on DSM-IV
  - Filled out by patients and scored by the clinician
  - Two components:
    - Assess symptoms and functional impairment to make a tentative depression diagnosis
    - Derive a severity score to help select and monitor treatment

PHQ-9 Score	Provisional Diagnosis	Treatment Recommendation
5-9	Minimal Symptoms*	Support, educate to call if worse; return in 1 month
10-14	<ul style="list-style-type: none"> <li>• Minor depression<sup>†</sup></li> <li>• Dysthymia*</li> <li>• Major depression, <i>mild</i></li> </ul>	<ul style="list-style-type: none"> <li>• Support, watchful waiting</li> <li>• Antidepressant or psychotherapy</li> <li>• Antidepressant or psychotherapy</li> </ul>
15-19	Major depression, <i>moderately severe</i>	Antidepressant or psychotherapy
≥ 20	Major depression, <i>severe</i>	Antidepressant <u>and</u> psychotherapy

DSM-IV=Diagnostic and Statistical Manual of Mental Disorders Fourth Edition.

\*If symptoms present ≥2 years, then probable chronic depression warranting antidepressants or psychotherapy

<sup>†</sup>If symptoms present ≥ 1 month or severe functional impairment, consider active treatment.

NAME John Q. Sample

DATE \_\_\_\_\_

Over the last 2 weeks, how often have you been bothered by any of the following problems?

		Not at all	Several days	More than half the days	Nearly every day
1	Little interest or pleasure in doing things	0	1	2	3
2	Feeling down, depressed, or hopeless	0	1	2	3
3	Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4	Feeling tired or having little energy	0	1	2	3
5	Poor appetite or overeating	0	1	2	3
6	Feeling bad about yourself - or that you are a failure or have let yourself or your family down	0	1	2	3
7	Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8	Moving or speaking so slowly that other people could have noticed. Or the opposite - being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9	Thoughts that you would be better off dead, or of hurting yourself in some way	0	1	2	3

add columns: **2 + 10 + 3**

TOTAL: **15**

10	If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?	Not difficult at all	_____
		Somewhat difficult	_____ ✓
		Very difficult	_____
		Extremely difficult	_____

## Patient Health Questionnaire (PHQ-9)

Major depression, moderately severe

# Depression: Objective Assessment Scales

- Beck-Depression Index (BDI)<sup>1</sup>
  - Long administration time
  - High number of items assessing neurovegetative symptoms may lead to overdiagnoses of depression
- 7-item BDI-Fast Screen (BDI-FS) is the best validated BDI short form in MS—test does not confound MS-related neurological symptoms
  - Available for purchase at Psychcorp
- Chicago Multiscale Depression Inventory<sup>2</sup>
  - Alternative short instrument for assessing depression in patients with MS
  - Has good internal consistency, sensitivity, and construct validity

1. Benedict RHB, et al. *Mult Scler.*2003;9:393-396.

2. Solari A, et all. *Neurol Sci.* 2004;24:375-383.

# Depression: Multidimensional Assessment Scales

- Profile of Mood States (POMS)<sup>1</sup>
  - Measures mood and multiple dimensions of adaptation, including daily activities, fatigue, and disease status
  - The subscales appear to be intercorrelated, therefore, the effects of mood relative to other factors cannot be teased apart
- Functional Assessment of MS (FAMS)<sup>2</sup>
  - Reliability and validity in patients with MS have been confirmed
  - Divided into 6 subscales: emotional well-being (depression), mobility, symptoms, general contentment, thinking/fatigue, and family/social well-being

1. McNair DM. Manual for the Profile of Mood States. 1981.

2. Cella DF, et al. *Neurology*. 1996;47:129-133.

# Depression: Psychotherapy

- Cognitive-Behavioral Therapy (CBT)
  - Both group- and individual-based treatments reduce depressive symptoms
  - *CBT is as effective as antidepressant medication; however, the combination of CBT and pharmacotherapy is more effective than either modality alone*
  - CBT that focuses on specific coping skills and MS symptom management are generally more effective than interventions that emphasize emotional expression or knowledge
- Other Psychotherapies
  - Insight-oriented group
  - Supportive-expressive

# Depression: Commonly Used Pharmacologic Treatments

Drug Class	Representative Drugs and Daily Doses (min-max)	Common Side Effects
Norepinephrine Reuptake Inhibitor (tricyclic antidepressants)	<ul style="list-style-type: none"> <li>• Desipramine (100-300 mg)</li> <li>• Nortriptyline (50-200 mg)</li> <li>• Protriptyline (15-60 mg)</li> </ul>	<ul style="list-style-type: none"> <li>• Lethargy</li> <li>• Anticholinergic symptoms</li> <li>• Cardiovascular effects</li> </ul>
Selective Serotonin Reuptake Inhibitor	<ul style="list-style-type: none"> <li>• Citalopram (20-40 mg)</li> <li>• Escitalopram (10-20 mg)</li> <li>• Fluoxetine (20-80 mg)</li> <li>• Sertraline (50-200 mg)</li> </ul>	<ul style="list-style-type: none"> <li>• Insomnia</li> <li>• Insomnia</li> <li>• Sexual dysfunction</li> </ul>
Selective Norepinephrine Reuptake Inhibitor	<ul style="list-style-type: none"> <li>• Desvenlafaxine (50-100 mg)</li> <li>• Duloxetine (40-60 mg)</li> <li>• Mirtazapine (15-45 mg)</li> <li>• Nefazodone (300-600 mg)</li> </ul>	<ul style="list-style-type: none"> <li>• Nausea</li> <li>• Nausea</li> <li>• Somnolence</li> <li>• Weight gain</li> </ul>
Norepinephrine Dopamine Reuptake Inhibitor	Bupropion (150-450 mg)	Seizures, psychosis
Serotonin Norepinephrine Reuptake Inhibitor	Venlafaxine (75-225 mg)	Sustained hypertension, Withdrawal syndrome



# MS Symptomatology

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Assessment and Treatment of  
Fatigue

# Fatigue

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- Among the most common symptoms in MS—reported by at least 75% of patients
- Most debilitating symptom for many patients
  - Surpassing pain and physical disability
- Main cause of impaired QOL among MS patients
  - Independent of depression or disability
- Significant socioeconomic consequences
  - Loss of work hours or even employment
- May be multifactorial—increased prevalence of depression and sleep disorders

# Fatigue:

## Krupp's Fatigue Severity Scale (FSS)

- Used in many MS-related fatigue studies showing acceptable internal consistency, stability over time, and sensitivity to change
- Scoring is done by calculating the average response to the questions (adding up all the answers and dividing by 9)
  - People with depression alone score about 4.5
  - People with fatigue related to MS, SLE or CFIDS average about 6.5

During the past week, I have found that:	Score						
1. My motivation is lower when I am fatigued.	1	2	3	4	5	6	7
2. Exercise brings on my fatigue.	1	2	3	4	5	6	7
3. I am easily fatigued.	1	2	3	4	5	6	7
4. Fatigue interferes with my physical functioning.	1	2	3	4	5	6	7
5. Fatigue causes frequent problems for me.	1	2	3	4	5	6	7
6. My fatigue prevents sustained physical functioning.	1	2	3	4	5	6	7
7. Fatigue interferes with carrying out certain duties and responsibilities.	1	2	3	4	5	6	7
8. Fatigue is among my three most disabling symptoms.	1	2	3	4	5	6	7
9. Fatigue interferes with my work, family, or social life.	1	2	3	4	5	6	7

# Fatigue:

## Modified Fatigue Impact Scale (MFIS)

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- Proposed by the MS Council for Clinical Practice Guidelines
- Contains 21 items with multidimensional assessment: physical, cognitive, and psychosocial functioning
- Easy to use, good reproducibility, and strong correlation with FSS; administered in 5-10 min

# Modified Fatigue Impact Scale (MFIS)

Because of my fatigue during the past 4 weeks....	Never	Rarely	Some- times	Often	Almost Always
1. I have been less alert.	0	1	2	3	4
2. I have had difficulty paying attention for long periods of time.	0	1	2	3	4
3. I have been unable to think clearly.	0	1	2	3	4
4. I have been clumsy and uncoordinated.	0	1	2	3	4
5. I have been forgetful.	0	1	2	3	4
6. I have had to pace myself in my physical activities.	0	1	2	3	4
7. I have been less motivated to do anything that requires physical effort.	0	1	2	3	4
8. I have been less motivated to participate in social activities.	0	1	2	3	4
9. I have been limited in my ability to do things away from home.	0	1	2	3	4
10. I have had trouble maintaining physical effort for long periods.	0	1	2	3	4
11. I have had difficulty making decisions.	0	1	2	3	4
12. I have been less motivated to do anything that requires thinking.	0	1	2	3	4
13. My muscles have felt weak.	0	1	2	3	4
14. I have been physically uncomfortable.	0	1	2	3	4
15. I have had trouble finishing tasks that require thinking.	0	1	2	3	4
16. I have had difficulty organizing my thoughts at home or at work.	0	1	2	3	4
17. I have been less able to complete tasks that require physical effort.	0	1	2	3	4
18. My thinking has been slowed down.	0	1	2	3	4
19. I have had trouble concentrating.	0	1	2	3	4
20. I have limited my physical activities.	0	1	2	3	4
21. I have needed to rest more often or for longer periods.	0	1	2	3	4

# Fatigue:

## Neurological Fatigue Index (NFI-MS)

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- Recently validated, 23-item, patient-reported summary scale
- Scoring
  - **Physical**: add values for items 1-8
  - **Cognitive**: add values for items 9-12
  - **Relief by diurnal sleep or rest**: add values for items 13-18
  - **Abnormal nocturnal sleep and sleepiness**: add values for items 19-23
  - **Summary**: add the values for items 1-7, 9, 11, and 12

# NFI-MS Neurological Fatigue Index

Date:

Name: \_\_\_\_\_ Age: \_\_\_\_\_ Sex: \_\_\_\_\_

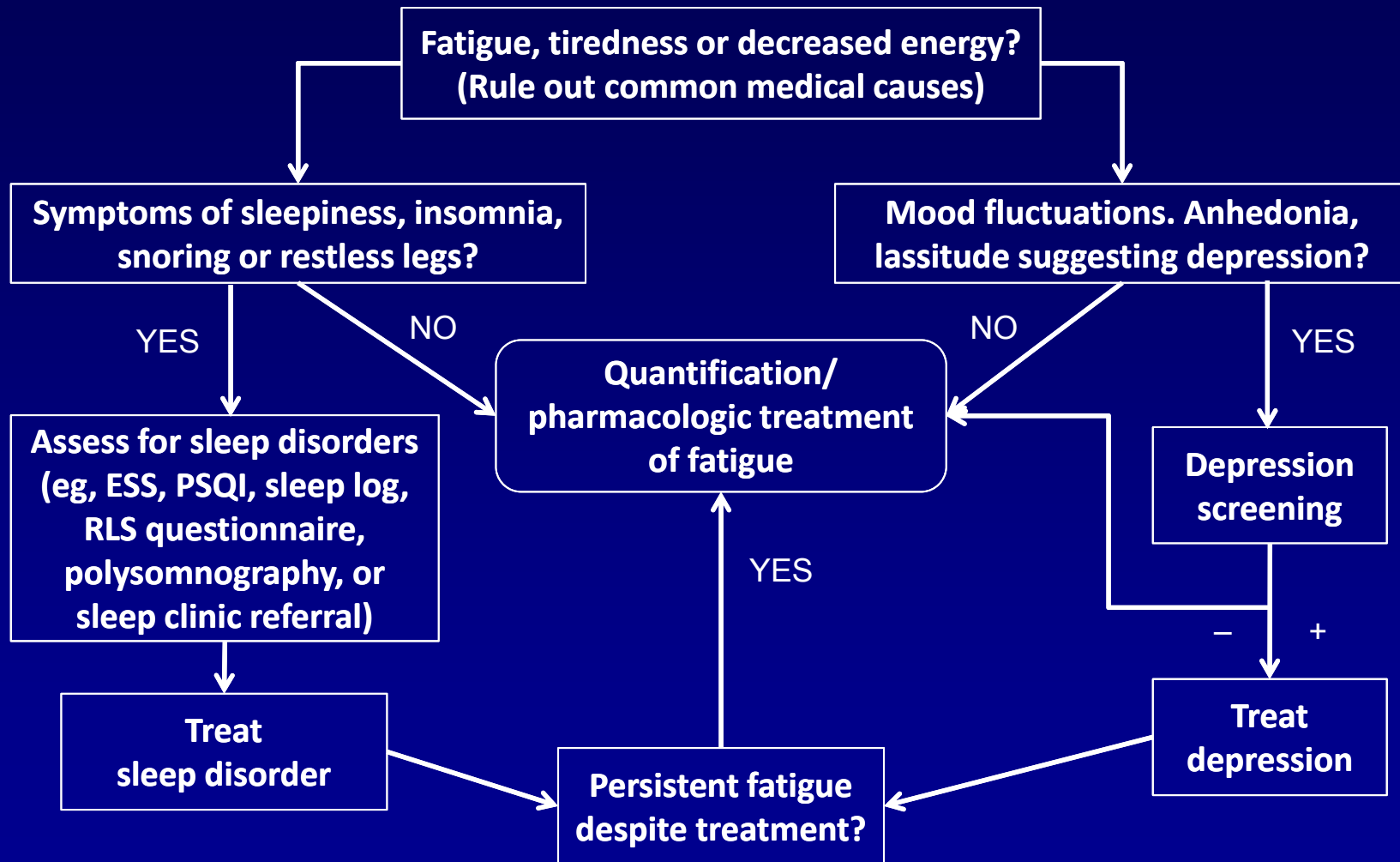
Instructions: For each statement, tick ✓ the box which best sums up your response as to how you have been feeling in the past two weeks.

1. I can become tired easily	Strongly Disagree <input type="checkbox"/>	Disagree <input type="checkbox"/>	Agree <input type="checkbox"/>	Strongly Agree <input type="checkbox"/>
2. Sometimes I lose my body strength	Strongly Disagree <input type="checkbox"/>	Disagree <input type="checkbox"/>	Agree <input type="checkbox"/>	Strongly Agree <input type="checkbox"/>
3. My limbs can become very heavy	Strongly Disagree <input type="checkbox"/>	Disagree <input type="checkbox"/>	Agree <input type="checkbox"/>	Strongly Agree <input type="checkbox"/>
4. My body can't keep up with what I want to do	Strongly Disagree <input type="checkbox"/>	Disagree <input type="checkbox"/>	Agree <input type="checkbox"/>	Strongly Agree <input type="checkbox"/>
5. The longer I do something the more difficult it becomes	Strongly Disagree <input type="checkbox"/>	Disagree <input type="checkbox"/>	Agree <input type="checkbox"/>	Strongly Agree <input type="checkbox"/>
6. Sometimes I have no option but to simply stop what I've been doing	Strongly Disagree <input type="checkbox"/>	Disagree <input type="checkbox"/>	Agree <input type="checkbox"/>	Strongly Agree <input type="checkbox"/>
7. I usually get tired on most days	Strongly Disagree <input type="checkbox"/>	Disagree <input type="checkbox"/>	Agree <input type="checkbox"/>	Strongly Agree <input type="checkbox"/>
8. I can become weak even if I've not been doing anything	Strongly Disagree <input type="checkbox"/>	Disagree <input type="checkbox"/>	Agree <input type="checkbox"/>	Strongly Agree <input type="checkbox"/>
9. Sometimes I really have to concentrate on what are usually simple things	Strongly Disagree <input type="checkbox"/>	Disagree <input type="checkbox"/>	Agree <input type="checkbox"/>	Strongly Agree <input type="checkbox"/>
10. I have problems with my speech when I'm tired	Strongly Disagree <input type="checkbox"/>	Disagree <input type="checkbox"/>	Agree <input type="checkbox"/>	Strongly Agree <input type="checkbox"/>
11. My coordination gets worse as the day goes on	Strongly Disagree <input type="checkbox"/>	Disagree <input type="checkbox"/>	Agree <input type="checkbox"/>	Strongly Agree <input type="checkbox"/>

Instructions: For each statement, tick ✓ the box which best sums up your response as to how you have been feeling in the past two weeks.

12. Mental effort really takes it out of me	Strongly Disagree <input type="checkbox"/>	Disagree <input type="checkbox"/>	Agree <input type="checkbox"/>	Strongly Agree <input type="checkbox"/>
13. I need to rest in the day	Strongly Disagree <input type="checkbox"/>	Disagree <input type="checkbox"/>	Agree <input type="checkbox"/>	Strongly Agree <input type="checkbox"/>
14. I need to sleep in the day	Strongly Disagree <input type="checkbox"/>	Disagree <input type="checkbox"/>	Agree <input type="checkbox"/>	Strongly Agree <input type="checkbox"/>
15. Sleep in the day can really help me	Strongly Disagree <input type="checkbox"/>	Disagree <input type="checkbox"/>	Agree <input type="checkbox"/>	Strongly Agree <input type="checkbox"/>
16. Resting allows me to carry on	Strongly Disagree <input type="checkbox"/>	Disagree <input type="checkbox"/>	Agree <input type="checkbox"/>	Strongly Agree <input type="checkbox"/>
17. I try to get everything done in the morning	Strongly Disagree <input type="checkbox"/>	Disagree <input type="checkbox"/>	Agree <input type="checkbox"/>	Strongly Agree <input type="checkbox"/>
18. I try to rest or sleep beforehand, if I know I've got to do something that requires a lot of effort	Strongly Disagree <input type="checkbox"/>	Disagree <input type="checkbox"/>	Agree <input type="checkbox"/>	Strongly Agree <input type="checkbox"/>
19. I get a feeling as if I have not slept for a couple of nights	Strongly Disagree <input type="checkbox"/>	Disagree <input type="checkbox"/>	Agree <input type="checkbox"/>	Strongly Agree <input type="checkbox"/>
20. I yawn a lot	Strongly Disagree <input type="checkbox"/>	Disagree <input type="checkbox"/>	Agree <input type="checkbox"/>	Strongly Agree <input type="checkbox"/>
21. I sometimes wake in the night for no reason	Strongly Disagree <input type="checkbox"/>	Disagree <input type="checkbox"/>	Agree <input type="checkbox"/>	Strongly Agree <input type="checkbox"/>
22. When I awake in the morning I feel unrefreshed	Strongly Disagree <input type="checkbox"/>	Disagree <input type="checkbox"/>	Agree <input type="checkbox"/>	Strongly Agree <input type="checkbox"/>
23. Often in the morning, I don't feel like getting out of bed	Strongly Disagree <input type="checkbox"/>	Disagree <input type="checkbox"/>	Agree <input type="checkbox"/>	Strongly Agree <input type="checkbox"/>

# Fatigue: A Systematic Approach to Treatment



ESS=Epworth Sleepiness Scale; PSQI=Pittsburgh Sleep Quality Index; RLS=restless legs syndrome



# Fatigue: Commonly Used Pharmacologic Treatments

Drug	Daily Dose (min-max)	Common Side Effects
Amantadine	200–600 mg	Anorexia, nausea, insomnia, visual hallucinations, blurred vision, gastrointestinal symptoms, livedo reticularis, peripheral edema, dry mouth, urinary retention
Aminopyridine	5–60 mg	Dizziness, insomnia, parasthesias, asthenia, nausea, headache, tremor, light-headedness, epileptic seizures , anxiety
Carnitine	1–6 g	Insomnia, nervousness, gastrointestinal symptoms
Disease-modifying treatments (DMTs)	Standard DMT doses	Vary depending on specific DMT
Modafinil	100–400 mg	Restlessness, loss of appetite, insomnia, nervousness, dizziness, headache, nausea, asthenia

# MS Symptomatology

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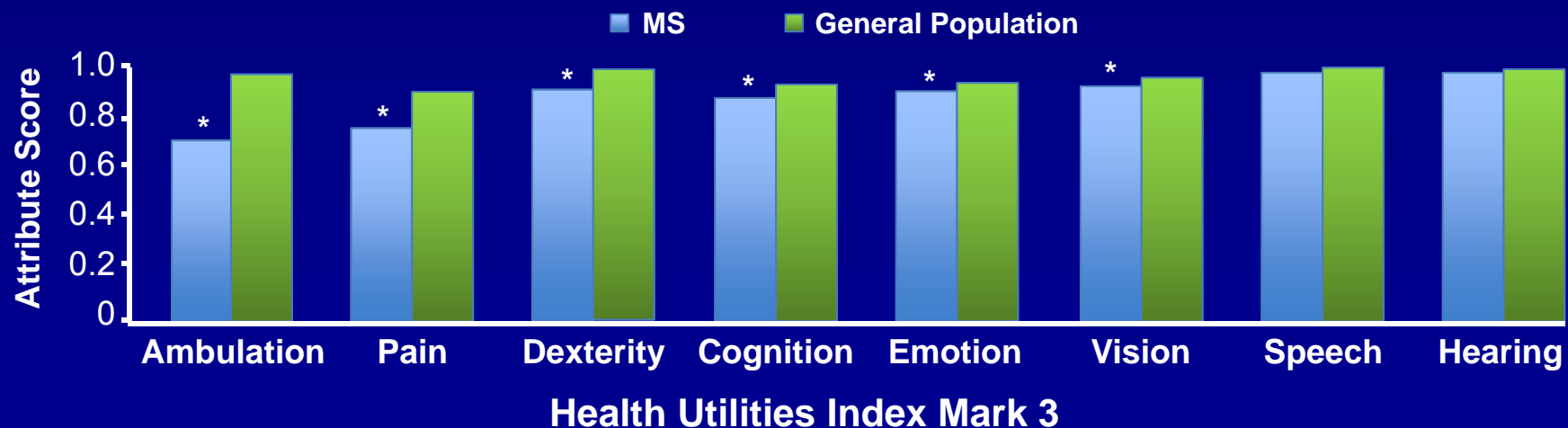
Assessment and Treatment of  
Mobility Impairment

# Mobility Impairment

- One of the most well-recognized characteristics of MS—reported in up to 90%
- Among MS patients treated with DMDs, only 52% reported some improvement in mobility
- By 15 years after MS diagnosis:
  - ~40% probability for needing some form of walking assistance
  - ~25% probability for use of a wheelchair

# Mobility Impairment (cont)

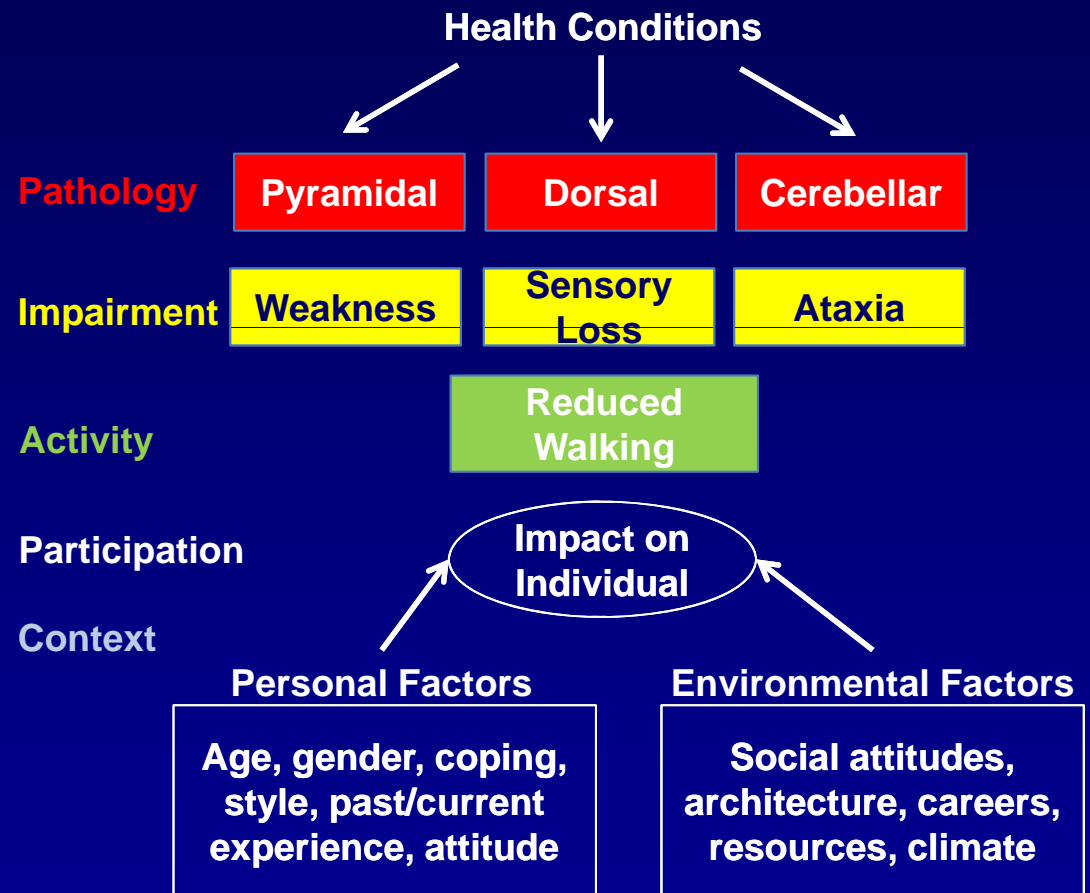
- Impaired mobility, especially related to walking ability, impacts functional activity and independence
- Gait parameters (eg, walking speed and stride length) have been reported to be significant predictors of patient dependence in activities of daily living ( $P<0.05$ )
- Mobility is often given the highest priority by patients among factors affecting QOL



\* $P<0.05$ ; lower attribute score indicates higher priority.

# Mobility Impairment (cont)

- Different pathologies and impairments culminate in abnormal or reduced walking in MS
- Multiple factors contribute:
  - Weakness and spasticity from pyramidal tract lesions
  - Loss of proprioception and coordination from dorsal column and cerebellar lesions
  - Vestibular and visual dysfunction
  - Cognitive and mood disturbance
  - Pain



# Mobility: Commonly Used Assessment Scales

- Mobility components in
  - Expanded Disability Status Scale (EDSS)
  - Functional Assessment of MS (FAMS)
  - MS Functional Composite (MSFC)
- 12-item MS walking scale (MSWS-12)
  - Reliable and valid patient-based measure of the impact of MS on walking
  - More responsive than other walking-based scales

# 12-item MS Walking Scale (MSWS-12)

<i>In the past 2 weeks, how much has your MS ...</i>	Not At All	A Little	Moderately	Quite A Bit	Extremely
1. Limited your ability to walk?	1	2	3	4	5
2. Limited your ability to run?	1	2	3	4	5
3. Limited your ability to climb up and down stairs?	1	2	3	4	5
4. Made standing when doing things more difficult?	1	2	3	4	5
5. Limited your balance when standing or walking?	1	2	3	4	5
6. Limited how far you are able to walk?	1	2	3	4	5
7. Increased the effort needed for you to walk?	1	2	3	4	5
8. Made it necessary for you to use support when walking indoors (eg, holding on to furniture)?	1	2	3	4	5
9. Made it necessary for you to use support when walking outdoors (eg, using a stick, frame, etc)?	1	2	3	4	5
10. Slowed down your walking?	1	2	3	4	5
11. Affected how smoothly you walk?	1	2	3	4	5
12. Made you concentrate on your walking?	1	2	3	4	5

# Mobility Impairment: Nonpharmacologic Treatment

- Physical therapy or rehabilitation should always be considered when ambulation disability develops or when it is associated with rapid progression
- Maintaining adequate strength, balance, flexibility, and range of motion are complex issues
  - Stretching exercises are helpful as an initial step
  - Some patients ‘walk on their spasticity,’ with the stiff leg providing support for ambulation



# Mobility Impairment: Nonpharmacologic Treatment (cont)

- Assistive technology can increase the level of function
  - Ankle-foot orthoses can improve gait by ensuring better foot dorsiflexion
  - Canes may be useful, depending on the disability
  - Forearm crutches may help those with weakness
  - Walkers help both balance problems and weakness, while providing more safety than canes or crutches
  - Proper wheelchair/scooter seating needs an individualized approach to assure appropriate thoracolumbar, truncal, and pelvic support

# Mobility Impairment: Pharmacologic Treatment

- Dalfampridine (extended release) has received regulatory approval in the U.S. for the treatment of walking in patients with MS
- Potassium (K<sup>+</sup>) channel blocking agent thought to act by restoring conduction in focally demyelinated axons and by enhancing neurotransmission, leading to improved neurological function
  - No indication as an immunomodulator as it does not reduce relapses or slow progression

Hayes KC. *Neuropsychiatr Dis Treat.* 2011;7:229-239.

Goodman AD, et al. *Lancet.* 2009;373:732-738.

Goodman AD, et al. *Ann Neurol.* 2010;68:494-502.

# Mobility Impairment: Pharmacologic Treatment (cont)

- Two Phase II clinical trials demonstrated significant improvements walking ability of patients with four primary forms of MS
  - Consistent improvement in walking in 35-43% of patients using the Timed 25-Foot Walk Test
  - Generally well tolerated within the recommended dose of 10 mg twice daily
  - Common side effects: mild dizziness, GI discomfort, and some agitation or wakefulness
  - The risk for more serious and intolerable adverse events such as seizures increases at higher doses (20 to 30 mg twice daily)

Hayes KC. *Neuropsychiatr Dis Treat.* 2011;7:229-239.

Goodman AD, et al. *Lancet.* 2009;373:732-738.

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# MS Symptomatology

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Assessment and Treatment of  
Spasticity

# Spasticity

- Spasticity is seen in >60% of MS patients and tends to increase in severity as the disease progresses
- The mechanisms underlying spasticity in MS are still poorly understood
- If not well managed, it can lead to pain, spasms, reduced mobility, limited range of movement, and contractures
- Spasticity can also impair a range of activities including mobility, personal care and sleeping

# Spasticity: Commonly Used Assessment Scales

- Ashworth Scale and Modified Ashworth Scale
  - Easy to apply and not time-consuming
  - Poor reliability, validity, and responsiveness
- Multiple Sclerosis Spasticity Scale 88
  - 88 questions divided into 8 sections
  - Questions use interval level scores to measure subjective perception of the impact of spasticity on QOL, including both physical and psychological aspects
- Until more valid and reliable measurement tools for spasticity are developed, functional testing (eg, walking gait and speed) is recommended during assessment of spasticity

# Spasticity: Treatment Considerations

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- Is spasticity localized or generalized?
  - Localized spasticity is amenable to physiotherapy and stretching of specific muscles, splinting, and botulinum toxin
  - For generalized spasticity, oral drugs and, at a later stage, intrathecal interventions are commonly considered
- Are there features that could affect the patient's function (eg, spasms, clonus, muscle shortening, and tendon or soft tissue contractures)?

# Spasticity: Treatment Considerations (cont)

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- Is spasticity masking underlying muscle weakness and ataxia?
  - Individuals might rely on spasticity to walk or stand
  - Increased weakness and deterioration of tremor and coordination are sometimes reported side-effects of anti-spasticity medications, resulting from the reduction in muscle tone



# Spasticity: Treatment Considerations (cont)

- Are there aggravating factors?
  - Urinary and bowel dysfunction, poor posture or positioning, and pressure sores can exacerbate spasticity
  - Pain of different origins (central pain, back pain, pain originating from unrecognized fractures) also needs to be considered
- In cases of acute deterioration after a relapse or of rapid progression
  - Physical therapy is often needed to reduce spasticity and improve mobility and independence

# Spasticity: Commonly Used Pharmacologic Treatments

Drug /Drug Class	Daily Doses (min-max)	Common Side Effects
Baclofen	10-120 mg	Sedation, drowsiness, muscle weakness, paraesthesia, gastrointestinal symptoms, hallucinations, and seizures
Cannabinoids	N/A	N/A
Gabapentin	300-3600 mg	Drowsiness, somnolence, dizziness, and gastrointestinal symptoms
Tizanidine	6-36 mg	Fatigue, tiredness, somnolence, dizziness, drowsiness, dry mouth, postural hypotension, and liver function abnormalities, which improve after discontinuation; these side-effects increase with increasing drug concentrations in plasma

# Summary: Performance Improvement in MS

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- Effective MS management through comprehensive care
  - Minimize relapses and disease progression
  - Treat symptoms and address functional limitations
- Pharmacologic and nonpharmacologic interventions are necessary for multiple symptoms
- Integrated, multidisciplinary team approach can maximize outcomes and quality and life for patients with MS

# Potential Areas for Improvement

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- Follow-up appointments with specialist after diagnosis
- Regular symptom and medication review
- Patient involvement in decisions about care
- Providing/discussing care plans with patients
  - Awareness and assessment of caregivers' needs
  - Providing information for caregivers

**Constructing an Adaptive Care Model  
for the Management of Disease-  
Related Symptoms Throughout the  
Course of Multiple Sclerosis**

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**Case Encounters**

# MS Case Study

- 49-year-old female, Army veteran
  - For the past 20 years, she has worked for the postal service as a letter carrier and as a distribution clerk
- MS diagnosis made 4 years ago at VA clinic
  - At onset, her symptoms were considered mild, consisting of occasional tremors and rigidity
  - Prescribed interferon beta-1a then she continued to work as a distribution clerk



Note: Photograph does not depict actual patient; used to represent a hypothetical patient

# MS Case Study (cont)

- Patient experienced flare-up 6 months ago
  - Right-sided facial numbness and dyesthesias (numbness and tingling throughout her body)
  - Extremely painful headaches
- She has decided to seek care at your MS center
  - In addition to basic neurologic exam, what other MS-related symptoms would you assess in this patient?



Note: Photograph does not depict actual patient; used to represent a hypothetical patient

# MS Case Study (cont)

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- Neurologic exam and symptom assessment reveal the patient has been experiencing the following:
  - Hand tremors, rigidity, numbness, insomnia and headaches regularly
  - Cognitive decline and mood swings
  - Difficulty with reading comprehension and blurred vision
  - Increasing number of MS flare-ups have slowly reduced her ability to walk or maintain balance without help
  - Major depression
- What care plan would you design for this patient?