MULTIPLE SCLEROSIS: TAKING A FRESH LOOK AT A CHALLENGING DISEASE

Quick Reference Guide

This guide provides information at-a-glance for reference in the diagnosis, treatment and counsel of people who are living with Multiple Sclerosis.

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Multiple Sclerosis: Taking a Fresh Look at a Challenging Disease

This toolkit provides current information about the standards for diagnosing MS, formularies for standard or novel pharmacologic therapy, non-pharmaceutical options, studies on MS drugs and their levels of evidence, and algorithm for the management of clinically isolated syndrome, at risk, and active relapsing-remitting multiple sclerosis.

Common Standards for Diagnosing Multiple Sclerosis

Diagnosis criteria for MS include clinical and paraclinical laboratory assessments. A diagnosis is supported by a single MRI scan showing:

- Concomitant presence of T2 or 'fluid attenuated inversion recovery' (FLAIR)
- Contrast-enhanced lesions

Relapsing-Remitting Multiple Sclerosis presents as:

- Relapsing symptoms or one clinical episode of symptoms typical for MS
- A confirmatory brain MRI and, where appropriate, spinal cord MRI and/or oligoclonal bands in the CSF.

If a diagnosis is in question and there is no evidence suggesting an ischemic or neoplastic etiology, additional studies may assist in diagnosis:

- Anti-nuclear antibody
- Anti-DNA antibody
- Anti-Smith antibodies
- Anti-SSA and anti-SSB antibodies
- Serum and CSF angiotensin-converting enzyme levels
- CSF cytology
- Serum VDRL, and FTA if indicated
- CSF VDRL if indicated by serum results
- HIV
- MRI of the cervical and thoracic spine
- Fluorescein angiography of retina/audiometry, anti-thyroid peroxidase antibody and if optic nerve and or spinal cord disease are present
- Serum/CSF anti-aquaporin IgG

If the above workup does not confirm a diagnosis, consider repeating MRI of the brain every six months to evaluate for any new or gladolinium-enhancing lesions.

Standardized MRI protocols are available on the Consortium of Multiple Sclerosis Center's website (http://www.mscare.org/?page=MRI_protocol)

Table 1: The 2010 McDonald Criteria for Diagnosis of Multiple Sclerosis Clinical Presentation and Additional Data Needed for Diagnosis[113]

Clinical Presentation	Additional Data Needed for MS Diagnosis
≥2 attacks[a]; objective clinical evidence of ≥2 lesions or objective clinical evidence of 1 lesion with reasonable historical evidence of a prior attack[b]	None[c]
≥2 attacks[a]; objective clinical evidence of 1 lesion	Dissemination in space, shown by ≥1 T2 lesion in at least 2 of 4 MS-typical regions of the CNS (periventricular, juxtacortical, infratentorial, or spinal cord)[d]; or Await a further clinical attacka implicating a different CNS site
1 attack[a]; objective clinical evidence of ≥2 lesions	Dissemination in time, shown by simultaneous presence of asymptomatic gadolinium-enhancing and nonenhancing lesions at any time; or A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, irrespective of its timing relative to a baseline scan; or Await a second clinical attack[a]
1 attack[a]; objective clinical evidence of 1 lesion (clinically isolated syndrome)	≥1 T2 lesion in at least 2 of 4 MS-typical regions of the CNS (periventricular, juxtacortical, infratentorial, or spinal cord)[d]; or Await a second clinical attacka implicating a different CNS site; and, for DIT: Simultaneous presence of asymptomatic gadolinium-enhancing and nonenhancing lesions at any time; or A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, irrespective of its timing relative to a baseline scan; or Await a second clinical attack
Insidious neurologic progression suggesting MS (PPMS)	1 year of disease progression (retrospectively or prospectively determined) plus 2 of 3 of the following criteria[d]: 1. Evidence for DIS in the brain based on ≥1 T2 lesions in the MS-characteristic (periventricular, juxtacortical, or infratentorial) regions 2. Evidence for DIS in the spinal cord based on ≥2 T2 lesions in the cord 3. Positive CSF (isoelectric focusing evidence of oligoclonal bands and/or increased IgG index)

Dissemination in time (DIT); Dissemination in space (DIS); Immunoglobulin G (IgG).

a. An attack (relapse; exacerbation) is defined as patient-reported or objectively observed events typical of an acute inflammatory demyelinating event in the CNS, current or historical, with duration of at least 24 hours, in the absence of fever or infection. It should be documented by contemporaneous neurologic examination, but some historical events with symptoms and evolution characteristic for MS, but for which no objective neurologic findings are documented, can provide reasonable evidence of a prior demyelinating event. However, reports of paroxysmal symptoms (historical or current) should consist of multiple episodes occurring over not less than 24 hours. Before a definite diagnosis of MS can be made, at least 1 attack must be corroborated by findings on neurologic examination, visual evoked potential response in patients reporting prior visual disturbance, or MRI consistent with demyelination in the area of the CNS implicated in the historical report of neurologic symptoms.

b. Clinical diagnosis based on objective clinical findings for 2 attacks is most secure. Reasonable historical evidence for 1 past attack, in the absence of documented objective neurologic findings, can include historical events with symptoms and evolution characteristics for a prior inflammatory demyelinating event. However, at least 1 attack must be supported by objective findings.

c. No additional tests are required. However, it is desirable that any diagnosis of MS be made with access to imaging based on these criteria. If imaging or other tests (for instance, CSF) are undertaken and are negative, extreme caution needs to be taken before making a diagnosis of MS, and alternative diagnoses must be considered. There must be no better explanation for the clinical presentation, and objective evidence must be present to support a diagnosis of MS.

d. Gadolinium-enhancing lesions are not required; symptomatic lesions are excluded from consideration in patients with brainstem or spinal cord syndromes.

Table 2: Major Red Flags that Point Definitively to a Non-MS Alternative Diagnosis[117]	
Red Flag	**Examples of Alternate Diagnosis**
Clinical features	
Bone lesions	Histiocytosis; Erdheim Chester disease
Lung involvement	Sarcoidosis; Lymphomatoid granulomatosis
Multiple cranial neuropathies or polyradiculopathy	Chronic meningitis, including sarcoidosis and tuberculosis; Lyme disease
Peripheral neuropathy	B12 deficiency; adrenoleukodystrophy; metachromatic leukodystrophy; Lyme disease
Tendon xanthomas	Cerebrotendinous xanthomatosis
Cardiac disease	Multiple cerebral infarcts; brain abscesses with endocarditis; right to left cardiac shunting
Myopathy	Mitochondrial encephalomyopathy (e.g., MELAS); Sjögren's syndrome
Renal involvement	Vasculitis; Fabry disease; systemic lupus erythematosus
Extrapyramidal features	Whipple's disease; multisystem atrophy; Wilson's disease
Livedo reticularis	Antiphospholipid antibody syndrome; systemic lupus erythematosus; Sneddon's syndrome
Retinopathy	Mitochondrial encephalomyopathy; Susac, and other vasculitides (retinal infarction); neuronal ceroid lipofuscinosis
Diabetes insipidis	Sarcoidosis; histiocytosis; neuromyelitis optica
Increase serum lactate level	Mitochondrial disease
Hematological manifestations	Thrombotic thrombocytopenic purpura; vitamin B12 deficiency; Wilson's disease (hemolytic anemia); copper deficiency
Mucosal ulcers	Behçet's disease
Myorhythmia	Whipple's disease
Hypothalamic disturbance	Sarcoidosis; neuromyelitis optica; histiocytosis
Recurrent spontaneous abortion or thrombotic events	Antiphospholipid antibody syndrome; thrombotic thrombocytopenic purpura; metastatic cancer with hypercoagulable state
Rash	Systemic lupus erythematosus; T-cell lymphoma; Lyme disease; Fabry disease
Arthritis, polyarthalgias, myalgias	Systemic lupus erythematosus; Lyme disease; fibromyalgia
Amyotrophy	Amyotrophic lateral sclerosis; syringomyelia; polyradiculpathy
Headache or meningismus	Venous sinus thrombosis; chronic meningitis; lymphoma or glioma; vasculitis; systemic lupus erythematosus
Persistently monofocal manifestations	Structural lesion (e.g., Chiari malformation); cerebal neoplasm
Cerebral venous sinus thrombosis	Behçet's disease; vasculitis; chronic meningitis; antiphospholipid or anti-cardiolipin antibody syndromes
Cortical infarcts	Embolic disease; thrombotic thrombocytopenic purpura; vasculitis
Hemorrhages/microhemorrhages	Amyloid angiopathy; Moya Moya disease; CADASIL; vasculitis
Meningeal enhancement	Chronic meningitis; sarcoidosis; lymphomatosis; CNS vasculitis
Calcifications on CT	Cysticercosis; toxoplasmosis; mitochondrial disorders

Table 2: Major Red Flags that Point Definitively to a Non-MS Alternative Diagnosis[117] *(continued)*	
Red Flag	**Examples of Alternate Diagnosis**
MRI Features	
Selective involvement of the anterior temporal and inferior frontal lobe	CADASIL
Lacunar infarcts	Hypertensive ischemic disease; CADASIL; Susac syndrome
Persistent gadoliunium-enhancement and continued enlargement of lesions	Lymphoma; glioma; vasculitis; sarcoidosis
T2-hyperintensity in the dentate nuclei	Cerebrotendinous xanthomatosis
Simultaneous enhancement of all lesions	Vasculitis; lymphoma; sarcoidosis
T1-hyperintensity of the pulvinar	Fabry disease; hepatic encephalopathy; manganese toxicity
Large and infiltrating brainstem lesions	Behçet's disease; pontine glioma
Predominance of lesions at the cortical/subcortical junction	Sarcoidosis or other chronic meningitis; lymphoma or other CNS neoplasm

Table 3: Differential Diagnosis of Neuromyelitis Optica or Multiple Sclerosis[128]			
Features		**Multiple Sclerosis**	**Neuromyelitis Optica**
Attacks are bilateral		Rarely	Usually
Visual loss severity		Less, with more improvement	More, with less improvement
White matter lesions on brain MRI		Usually	Rarely and usually resolving
Transverse myelitis		Rarely	TM in spinal MRI often spanning ≥3 spinal cord
Clinical involvement beyond spinal cord and optic nerve		Usually	Rarely
Tissue destruction and cavitations		Less than NMO	More than MS
CSF Analysis	Oligoclonal bands	Frequently	Rarely
	Protein contents	Lower than NMO	Higher than MS
Treatment	DMTs	Effective	Ineffective even worsening
	Corticosteroids	First line of treatment	First line of treatment

Table 4. Overview of Currently Available and Emerging Disease-Modifying Therapies

Therapy	Administration Mode	Description/Mechanism of Action	Indication/Status
IIFNβ-1a/b	• FNβ-1a: bcutaneous (high-dose) or intramuscular (low-dose) injections • IFNβ-1b:bcutaneous	• Immunomodulatory agents • Prevents trafficking of inflammatory cells into the CNS by inhibiting matrix metalloproteinase enzymes on BBB	• First-line therapy • Relapsing forms • Clinically isolated syndrome
Glatiramer acetate	Subcutaneous injection	• Promotes proliferation of cytokines and inhibits antigen-specific T-cell activation by competing with MBP antigenic sites • Suppresses autoreactive Tcells that have migrated into the CNS	• First-line therapy • Relapsing forms • Clinically isolated syndrome
Natalizumab	Intravenous infusion	• Monoclonal antibody • Selective inhibition of VLA-4[α4β1] integrins BBB preventing lymphocyte migration into the brain parenchyma	• Relapsing forms • Second-line therapy
Fingolimod	Oral	• Small molecule • S1P receptor inhibitor • Prevents migration of lymphocytes from the lymphoid organs into the blood circulation	• Relapsing forms
Teriflunomide	Oral	• Leflunomide metabolite • Immunomodulatory agen • Selective reversible inhibition of dihydroorotate dehydrogenase that blocks de novo pyrimidine synthesis in rapidly proliferating cells, including autoreactive T and B lymphocytes	• Relapsing forms
Alemtuzumab	Intravenous infusion	• Monoclonal antibody • CD52 inhibitor • Depletes inflammatory lymphocytes and leads to distinctive pattern of lymphocyte repopulation	• NDA submitted 2012
Dimethyl fumarate (BG-12)	Oral	• Citric acid cycle product • Exerts neuroprotective action in addition to anti-inflammatory effects, via the activation of the Nfr- 2 pathway	• Relapsing forms
Laquinimod	Oral	• CNS-active immunomodulator • Crosses BBB to regulate CNS inflammation and neurodegeneration • Enhances secretion of anti- inflammatory cytokines • Upregulates brain-derived neurotrophic factor	• Phase 3

Blood brain barrier (BBB); Central nervous system (CNS); Myelin basic protein (MBP); New drug application (NDA); Sphingosine 1-phosphate (S1P).

Table 5. Summary of Efficacy Data of Disease-Modifying Therapies for Relapsing-Remitting Multiple Sclerosis[a]

	IFNβ-1a (IM)	IFNβ-1a (SC)	IFNβ-1b (SC)	Glatiramer Acetate	Natalizumab	Fingolimod	Teriflunomide 14 mg[b]
ARR reduction over 2 years, %	32 *P* = 0.02	32 *P*<0.005	34 *P* = 0.0001	29 *P* = 0.007	68 *P*<0.001	55 *P*<0.001	37 *P*<0.001
Relapse-free patients, DMT vs. placebo control, %	38 vs 26 *P* = 0.03	32 vs 16 *P*<0.005	31 vs 16 *P* = 0.007	34 vs 27 *P* = 0.098	72 vs 46 *P*<0.001	70 vs 46 *P*<0.001	57 vs 46 *P* = 0.003
Disability progression, % reduction	37 *P* = 0.02	31 *P*<0.05	29	12	42 *P*<0.001	30 *P* = 0.02	30 *P* = 0.03
Gd-enhancing lesions, % reduction	52 *P* = 0.05	84 *P*<0.001	NR	29 *P* = 0.003	92 *P*<0.001	82 *P*<0.001	80 *P*<0.001
New or enlarging T2 lesions, % reduction	33 *P* = 0.002	78 *P*<0.0001	83 *P* = 0.009	31 *P*<0.003	83 *P*<0.001	75 *P*<0.001	77 *P*<0.001

[a]Data based on 2-year, placebo-controlled, pivotal, phase 3 randomized controlled trials.
[b]Results of TEMSO trial evaluating teriflunomide after 1-year follow-up.
Annualized relapse rate (ARR); Disease-modifying therapies (DMT); Gadolinium (Gd); Not reported (NR).

Table 6. Adverse Effects Associated with Available Disease-Modifying Therapies for Multiple Sclerosis

Disease-Modifying Therapy	Associated Common Adverse Events	
IFN□1a IFN□1b	• Injection-site reaction • Flu-like symptoms • Lipoatrophy • Hematopoietic abnormalities	• Hepatic enzyme abnormalities • Depression* • Lipoatrophy (in IM formulation)
Glatiramer acetate	• Injection-site reactions • Lipoatrophy	• Hypersensitivity/allergic reactions • Systemic post-injection reactions
Natalizumab	• Systemic post-injection reactions • Hepatic enzyme abnormalities	• Infections • Progressive multifocal encephalopathy
Fingolimod	• Cardiac abnormalities: bradycardia, atrioventricular block • Hypertension • Hepatic enzyme abnormalities	• Infections • Respiratory changes • Macular edema
Teriflunomide	• Hepatic enzyme abnormalities • Fetal harm/birth defects • Hair loss or thinning	• Diarrhea • Nausea • Flu-like symptoms
Dimethyl fumarate	• Lymphopenia • Flushing • Gastrointestinal disorders: abdominal pain, diarrhea, nausea, vomiting, dyspepsia	• Skin disorders: pruritus, rash, erythema • Urinary albumin present • Increased: aspartate aminotransferase, alanine aminotransferase

*Relationship to treatment uncertain.

Table 7. Summary of Fingolimod Phase 3 Efficacy Results in Patients with Relapsing MS [170-172]

	FREEDOMS [Kappos 2010]			TRANSFORMS [Cohen 2010]		
	Placebo (n = 418)	Fingolimod 0.5 mg (n = 425)	Fingolimod 1.25 mg (n = 429)	IFNβ-1a* (n = 431)	Fingolimod 0.5 mg (n = 429)	Fingolimod 1.25 mg (n = 420)
Primary endpoint						
Annualized relapse rate	0.40	0.18 *P* <0.001	0.16 *P* <0.001	0.33	0.16 *P* <0.001	0.20 *P* <0.001
Secondary endpoints						
Relapse-free patients (%)	45.6	70.4 *P* <0.001	74.7 *P* <0.001	69.3	82.6 *P* <0.001	79.8 *P* <0.001
Absence of disability progression (%)	81.0	87.5 *P* = 0.01	88.5 *P* = 0.004	92.1	94.1 *P* = 0.25	93.3 *P* = 0.50
Mean change from baseline EDSS score at 24 months	0.13	0.00 *P* = 0.002	-0.03 *P* = 0.002	0.01	-0.08 *P* = 0.02	-0.11 *P* = 0.06
Selected MRI outcomes						
Mean Gd-enhancing T1 lesions (n)	1.1	0.2 *P* <0.001	0.2 *P* <0.001	0.51	0.23 *P* <0.001	0.14 *P* <0.001
Mean new/enlarged T2 lesions (n)	9.8	2.5 *P* <0.001	2.5 *P* <0.001	2.6	1.7 *P* = 0.004	1.50 *P* <0.001

* 30 micrograms intramuscularly once weekly.

Expanded Disability Status Scale (EDSS); FTY720 Research Evaluating Effects of Daily Oral therapy in Multiple Sclerosis (FREEDOMS); Gadolinium (Gd); TRial Assessing injectable iNterferon vS FTY720 Oral in RrMS (TRANSFORMS).

Table 8. Summary of Efficacy Results from Teriflunomide Phase 3 TEMSO Study[179]

	Placebo (n = 63)	Teriflunomide 7 mg (n = 365)	Teriflunomide 14 mg (n = 358)
Primary endpoint			
Annualized relapse rate (%)	0.54	0.37 *P*<0.001	0.37 *P*<0.001
Secondary endpoints			
Absence of relapse during week 108 (%)	45.6	53.7 *P* = 0.01	56.5 *P* = 0.003
Patients with sustained disability progression (%)	27.3	21.7 *P* = 0.08	20.2 *P* = 0.03
Total lesion volume (mL; change from baseline)	2.21	1.31 *P* = 0.03	0.72 *P*<0.001
Gd-enhancing T1lesions per scan (n)	1.33	0.57 *P*<0.001	0.26 *P*<0.001
Patients free from Gd-enhancing T1lesions (%; n)	39.0 (135)	51.4 (180) *P*<0.001	64.1 (218) *P*<0.001
Unique active lesions per scan (n)	2.46	1.29 *P*<0.001	0.75 *P*<0.001
T1 hypointense lesion volume (mL; change from baseline)	0.53	0.50 *P* = 0.19	0.33 *P* = 0.02
Brain atrophy (mL; change from baseline)	-0.004	-0.003 *P* = 0.19	-0.003 *P* = 0.35

Gadolinium (Gd); TEriflunomide Multiple Sclerosis Oral (TEMSO)

Table 9: Summary of CARE-MS I and II Phase 3 Studies of Alemtuzumab Compared with Interferon-β1a[183-185]

	CARE-MS I			CARE-MS II		
	IFN-β1a	Alemtuzumab	*P* Value	IFN-β1a	Alemtuzumab	*P* Value
Relapse rate (%)	40	22	—	51	35	—
Relapse rate ratio (95% CI)	0.45 (0.32–0.63)	0.0001	0.51 (0.39–0.65)	0.0001		
Relapse-free at 2 yrs (%)	59	78	0.0001	47	65	0.0001
Safety						
Infusion reactions	—	90	—	—	90	—
Infections (%)	45	67	—	66	77	—
Thyroid disorders (%)	6	18	—	—	16	—
Immune thrombocytopenia (%)	0	1	—	0	1	—

Summary of complementary and alternative medicine (caM) – Vitamins, Minerals and Herbs			
Supplement/ RDA	**Role in body**	**Sources**	***Potential* MS-specific relevancy**
VITAMINS			
Vitamin D **(Vitamin D3 at 600-800 iU, women and men)**	Hormone, chemical messenger	Sunlight; fish and fortified dairy products and breakfast cereals	Protection from/reduction in risk of developing MS; helps maintain bone density Low Vitamin D levels have been associated with increased attacks, relapses, exacerbations and increased levels of disability
Vitamin A **(Women: 2300 iU; Men: 3000 iU)**	Necessary for vision; promotes normal cell growth and differentiation	Liver, eggs, cod liver oil	No definitive conclusions as to benefit or risk for people living with MS
Vitamin C **(Women: 75 mg; Men: 90 mg.)**	Builds and maintains body tissues	Citrus fruits and tomatoes	*Possible* reduced risk of urinary tract infections
Vitamin E **(22 iU, women and men)**	Prevents oxidative damage to cell membranes or linings	Vegetable oils, fruits, vegetables, nuts, meat	MS patients who increase intake of Polyunsaturated Fatty Acids (PuFAs) need to increase intake of Vitamin E accordingly. See *Complementary and Alternative Medicine and Multiple Sclerosis, 2ndedition*, by Allen Bowling, M.D., Ph.D. *(Page 25)*
Vitamin B6 **(1.3 mg ages 19-50)**	Necessary for amino acid conversions.	Fish (especially salmon and tuna), pork, chicken, beans, bananas and many vegetables	May help increase energy level of patients Symptoms associated with Vitamin B6 *overdose* may mimic MS symptoms.
Vitamin B12 **(2.4 mcg, women and men)**	Required for the production of red blood cells and proper function of the nervous system	Eggs, meat, poultry, shellfish, dairy products	Symptoms associated with Vitamin B12 *deficiencies* may mimic MS symptoms

Supplement/ RDA	Role in body	Sources	*Potential* MS-specific relevancy
MINERALS			
Selenium **(55 mcg after age 14)**	Antioxidant	Seafood, legumes, whole grains, low-fat meats, dairy products	*Possibly* increases the immune response, which may not be desirable for people with MS
Calcium **(1000-1200 mg)**	Important in the formation of teeth and bone and in the regulation of many body processes	Dairy products, eggs, green leafy vegetables	Decreases risk factor for thinning of bones or developing osteoporosis
Zinc **(Women: 8 mg; Men: 11 mg)**			High-dose supplementation can cause a copper deficiency that can lead to copper-defi myelopathy, a condition that causes neurological symptoms that may mimic MS symptoms
HERBS			
Ginkgo Biloba	Antioxidant		May improve cognitive ability, memory, concentration; may improve fatigue; inhibits platelet activating factor (paF), which can cause a decrease in the activity of certain immune cells
Echinacea (Echinacea purpurea)	Decreases duration of common cold symptoms		May stimulate the immune system, which is a theoretical risk to people with MS
St. John's Wort	Antidepressant		May pose risk of interaction with some medications commonly used by people with MS; caution is suggested
Valerian	Sleep aid		No definitive conclusions as to benefit or risk for people living with MS
Asian Ginseng	Enhances physical performance , resistance to stress and aging		No definitive conclusions as to benefit or risk for people living with MS
Cranberry	Used to prevent or treat urinary tract infections		People living with MS should never self-treat a UTI only with cranberry juice because of the serious consequences of UTIs for MS patients
Oral Cannabis Extract (OCE) and Synthetic Tetrahydrocannabinol (THC)	Used to reduce patient-reported symptoms of spasticity and pain		Probably ineffective for improving objective measures of spasticity or improvements in tremor Note: Oromucosal Cannabinoid Spray is sometimes used to improve urinary incontinence but has not been proven for significant benefit

Summary of complementary and alternative medicine (caM) – Diet and Exercise		
MS-relevant Symptom	**Potential contributors/indicators**	**Diet and exercise strategies**
Fatigue **(Neuromuscular, depression-related, MS lassitude)**	Decreased appetite and activity, loss of interest in food preparation, poor eating habits	• Moderate exercise can stimulate energy, reduce fatigue • Make every meal count nutritionally • Keep meals quick and easy • Follow a menu plan • Stock up on healthy, basic staples
Emotional changes **(Mood swings, depression)**	Decreased appetite and activity	• Moderate exercise can stimulate mood, decrease depression • Tune into how mood affects food choices • Eat meals with other people to help stay connected
Mobility issues **(Weight management)**	Being overweight or underweight	• Exercise can help manage weight and maximize range of motion and flexibility • Balance food intake and activity level • Eliminate foods with low nutritional value • Control portions • Consume “light” versions of foods when possible
Bone Health	Lack of adequate physical activity sedentary lifestyle	• Exercise helps protect weight-bearing bone mass • Eat a calcium-rich diet: fish, low-fat or nonfat dairy, low-oxate dark green veggies, calcium-fortified prepared foods • Use calcium supplements: Calcium Carbonate offers best value but must be taken with food; Calcium Citrate absorbs more easily and can be taken on empty stomach • Get enough Vitamin D, which helps with the absorption of calcium
Bladder concerns	Frequency, urgency, self-imposed fluid restrictions for “managing” bladder problems, concentrated urine and associated irritation	• Take daily oral medications with a full glass of water • Build in water breaks throughout the day • Eat foods with a high water content (lettuce, squash, watermelon, tomatoes, broccoli, strawberries, etc.) • Limit fluids containing caffeine, aspartame, alcohol • Include cranberry juice or tablets in daily intake
Constipation	Bowel incontinence	• Exercise helps maintain regular bowel and bladder function • Consume 25-30 grams of fiber daily through cereal grains, nuts, seeds, vegetables, fruits • Consider a fiber supplement if adequate intake is not achieved through diet