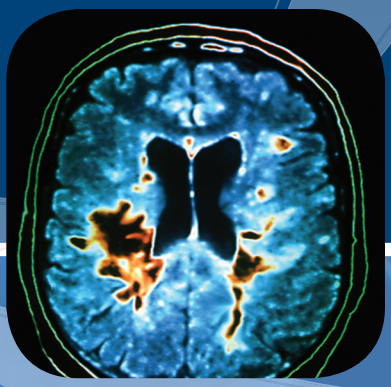
dialogues IN CLINICAL PRACTICE



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Practical Strategies for Managing Multiple Sclerosis in the Federal Healthcare System

COMPLIMENTARY CME/CE

This CME/CE-certified publication, distributed as a supplement to *U.S. Medicine*, describes the assessment and treatment of multiple sclerosis (MS), with a special emphasis on the needs of patients treated within the federal healthcare system. It discusses the role of disease-modifying treatments, current methods for monitoring treatment response, approaches to wellness and symptomatic management, and the unique characteristics of and resources available for patients with MS who are treated within the Veterans Health Administration system.

NOTE: In Spring 2012, the FDA required labeling changes for fingolimod regarding cardiovascular safety. Fingolimod is now contraindicated in patients who have certain preexisting or recent (within last 6 months) heart conditions or stroke or who are taking certain antiarrhythmic medications. All patients receiving fingolimod for the first time should be monitored for bradycardia for at least 6 hours after the first dose. Obtain an ECG before the first dose and at the end of the observation period, with hourly monitoring of heart rate and blood pressure. Use continuous ECG monitoring until symptom resolution in patients with symptomatic bradycardia. Extend continuous ECG monitoring overnight in patients requiring pharmacologic intervention for symptomatic bradycardia and in those who have a higher risk of bradycardia or heart block or who may not tolerate bradycardia. Please refer to the current prescribing information for complete safety information. (Reference: http://www.fda.gov/Drugs/DrugSafety/ucm303192.htm)

Med-IQ® Inspiring Medical Education

A supplement to *U.S. Medicine*

U.S. MEDICINE THE VOICE OF FEDERAL MEDICINE

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CME/CE Information

Target Audience

This activity is intended for physicians, neurologists, clinical pharmacists, nurse practitioners, physician assistants, and psychologists who manage the health of beneficiaries in the federal healthcare system, including the Veterans Administration and the military through all branches of service in the Department of Defense.

Series Overview/Statement of Need

Multiple sclerosis (MS), a chronic, disabling neurologic disease, requires specialty care and coordination. Despite many advances in the understanding and treatment of this complex disease, several challenges remain. It is important for clinicians to understand the role of disease-modifying treatments and symptomatic management approaches, the full range of treatment options available, and strategies for monitoring treatment response and disease progression.

Each year, the United States Veterans Health Administration (VHA) treats an estimated 20,000 veterans with MS. This number, as well as the burden imposed on the VHA system by this disabling disease, is expected to increase substantially in the coming years. Clinicians in the federal healthcare system require focused education to help them better recognize and manage this complex, progressive neurologic disorder and become aware of the resources available within the VHA system.

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Mitchell T. Wallin, MD, MPH, has indicated no real or apparent conflict.

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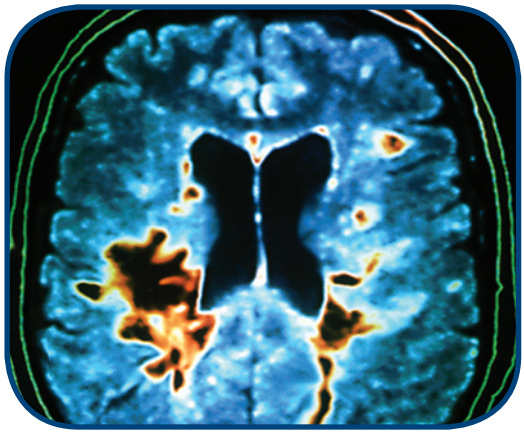

Learning Objectives

Upon completion, participants should be able to:
- Explain the importance of early and ongoing treatment in MS
- Outline the differences in disease presentation and treatment between veteran and non-veteran MS population, and describe resources available through the VHA to optimize the care of veterans with MS
- Identify appropriate patient candidates for DMTs, select appropriate treatment options, and describe methods for monitoring disease status
- Describe key components of symptomatic management and wellness approaches to MS

TABLE OF CONTENTS

MULTIPLE SCLEROSIS IN THE FEDERAL HEALTHCARE SYSTEM

Introduction

Multiple sclerosis (MS) is the most common progressive neurologic disorder of young adults and contributes to considerable physical, psychologic, and economic burden.[1,2] This disease is of particular concern for clinicians in the federal healthcare system, where it is associated with high rates of healthcare use, disability benefits, and rising costs associated with increasing disability over time.[3,4] More than 6,000 veterans are considered to have a service-connected disability for MS because they developed it or presented with related symptoms during or within 7 years of their military service.[5] These patients are often followed by the United States (US) Veterans Health Administration (VHA) from the time of diagnosis through the end of life.[6] Despite considerable advances in the treatment of MS, the disease progresses in most patients, posing management challenges for patients and healthcare professionals alike. This publication summarizes current therapeutic options available for treating patients with MS and reviews practical considerations for managing patients with MS within the federal healthcare system.

Epidemiology

Both genetic and environmental factors have been shown to contribute to the risk of developing MS.[7] Although the cause of MS remains unknown, recent epidemiologic studies have shown that geography, vitamin D levels, smoking, and viral infections can significantly influence one's risk.[8] Currently, this condition is estimated to affect 350,000 to 400,000 people in the US; it has a median onset of 30 years of age, has a median duration of 30 to 40 years, and affects twice as many women as men.[9-11] Between 1998 and 2002, more than 20,000 veterans were identified as having received a diagnosis code for MS.[5]

Clinical Course

MS is an inflammatory demyelinating and neurodegenerative disease of the human central nervous system (CNS), characterized by episodes of neurologic dysfunction that recover in variable degrees but lead to considerable disability.[12] Much of the underlying disease process is clinically silent, continuing to develop even when patients do not experience symptoms.[13] Although inflammatory changes and episodic CNS demyelination characterize the early relapsing stage of MS, inflammatory events become less frequent and a neurodegenerative phase emerges over time.[14]

Variations in the distribution and extent of demyelination and axonal and neuronal loss throughout the white and gray matter of the CNS contribute to a range of symptoms.[15] Spinal cord damage can result in motor symptoms, including weakness and spasticity, imbalance (particularly in lower limbs), sensory

symptoms (eg, tingling, numbness, and pain), and bladder, bowel, and sexual dysfunction. Brainstem and cerebellar involvement is signaled by eye movement, swallowing dysfunction, and ataxia. Involvement of the optic nerves can result in impaired vision.[16] Cognitive impairment is commonly associated with MS (such as attention, information processing efficiency, and short-term memory) and may limit daily activities and reduce health-related quality of life.[17]

Unique Qualities of Patients in the Federal Healthcare System

As a group, patients with MS who are being managed within the VHA system are thought to differ in some ways from patients with MS in the general population.

Presentation. Among military personnel, MS most commonly presents before the age of 40 years and is often diagnosed during military service or soon after.[18] Veterans, in fact, may be diagnosed at a younger age than non-veterans.[19] According to current Department of Defense statistics, unadjusted incidence rates are highest in the Air Force and Coast Guard, lower in the Army and Navy, and lowest in the Marine Corps.[18]

Characteristics. There are some unique features of the Veteran population with MS. In 2006, Guarnaccia et al found that, compared with the cohort of patients from a pivotal phase 3 trial for interferon beta-1b, their veteran cohort was more likely to be male, older, and more disabled.[20] In addition, this study reported a higher percentage of non-Caucasian patients than is typically found in civilian populations.[20] Similarly, when comparing a veteran population who received their care through the VHA to both the general population with MS and to veterans who received their care elsewhere, Lo and colleagues found that veterans with MS who were treated through the VHA were more likely to be male, have the lowest proportion of primary progressive disease, have the highest proportion of relapsing-worsening disease, and live with the disease longer.[21] Of note, however, the study conducted by Lo et al may have had a higher prevalence of disabled veterans, and a more recent study by Culpepper et al in 2008 found that the subtypes of MS and general disability assessments in veterans with MS are fairly similar to those of other large population registries.[22]

Challenges Faced by Patients and Clinicians

Veterans with MS and those who provide care for them within the VHA face unique challenges concerning access to care and treatment options.

Access to Care. The coordination and continuity of care is challenging in both civilian and veteran settings, and access to services and care is a general issue for patients with MS.[23,24] Although patients who are serviced by the VHA may theoretically have better access to integrated, multidisciplinary care such as rehabilitation, social workers, psychologists, and urologists, they may still face geographic difficulties in obtaining care for MS-related impairments, especially specialist care.[19,21,25] Furthermore, veterans are more likely than non-veterans to be treated by a primary healthcare professional, but only 51.5% of veterans treated within the VA see an MS specialist once a year.[21,26]

Treatment Options. Although disease-modifying treatments (DMTs) have emerged as the current standard of care for treating patients with MS, disability may progress slowly over time; therefore, patients with MS may also require nonpharmacologic interventions (eg, rehabilitation) to manage disease exacerbations and improve disability and function.[21,27,28] Because some studies suggest that veterans with MS are more likely than non-veterans with MS to have progressive forms of the disease and carry a significant disability burden (eg, fatigue, cognitive deficits), nonpharmacologic strategies may be particularly useful for a subset of the veteran population.[21]

CLINICAL CONSIDERATIONS

Our faculty advisors pointed out that most veterans (60% to 70% by their estimates) do not receive care within the VHA system. They noted that this is, in large part, due to the prioritization of care by the VHA. In the current framework, service-connected veterans have the highest priority, followed by non-service-connected veterans with lower incomes. Faculty added that many veterans who are not service connected are ineligible for VA care because their incomes are above the annual income threshold.

DIAGNOSIS AND COURSE OF MULTIPLE SCLEROSIS

MS is diagnosed after demonstrating neurologic episodes separated in space and time and excluding other disease states that may explain the patient's symptoms (eg, inflammatory conditions or infectious, metabolic, or neurologic disorders).[29]

Revised Diagnostic Criteria

The revised McDonald Criteria for the diagnosis of MS were published in 2011.[29] Current criteria for diagnosing patients who present with a clinically isolated syndrome (CIS) suggestive of MS or with symptoms consistent with a CNS inflammatory demyelinating disease emphasize the importance of clinical presentation, cerebrospinal fluid (oligoclonal bands and IgG Index), and magnetic resonance imaging (MRI) using standardized imaging protocols.[29,30] Noteworthy revisions in the 2011 update include the following[29]:

- The recognition of the utility of T2 lesions as reliable indicators of dissemination in time
- Clarification about the use of spinal-cord lesions as a substitute for brain lesions to confirm dissemination in space
- Guidance on the diagnosis of primary-progressive MS (PPMS) that places more emphasis on clinical and MRI (brain or spinal cord) evidence and less emphasis on cerebrospinal-fluid findings

Classification of Multiple Sclerosis

There are four main subtypes of MS, classified according to clinical course[27]:

- Relapsing-remitting (RRMS)
- Primary-progressive (PPMS)
- Secondary-progressive (SPMS)
- Progressive-relapsing (PRMS)

RRMS is characterized by acute attacks with full or partial recovery. Studies undertaken prior to the emergence of DMTs have indicated that in 50% of patients, RRMS typically pro-

gresses into SPMS, which is characterized by disease progression with or without occasional relapses, minor remissions, and plateaus.[31] PPMS progresses from the onset of disease without acute relapses, and PRMS, though relatively rare, is progressive from onset and accompanied by acute relapses with or without recovery.[31]

Benign MS (BMS) is an additional form of relapsing-remitting MS in which patients are typically free of permanent disability and experience few relapses.[32,33] This condition is estimated to affect approximately 10% to 20% of patients, although prevalence estimates vary considerably because there is little agreement on the criteria for defining the condition.[32,33]

Symptoms of MS develop when nerve signal conduction slows as a result of axonal demyelination.[1] Pathologic and MRI studies have shown that inflammation is highest in early relapsing disease and that axonal damage begins before symptoms are evident, contributing to CNS atrophy.[34] Most patients who have MS exhibit progressive neurologic deterioration without treatment; even those in remission display evidence of ongoing development of brain lesions and atrophy.[9,35]

DISEASE-MODIFYING TREATMENTS

DMTs are the cornerstone of MS therapy for RRMS.[36] These treatments target the underlying disease processes of inflammation and demyelination, inhibiting lesion formation in the brain as clinically reflected by reductions in relapse frequency and severity and as detected by MRI reductions in gadolinium-enhanced lesions and T2-lesion burden.[27,37,38]

Treatment goals for MS include the following[34,39]:

- Preventing long-term disability
- Reducing rates of relapse
- Preventing/slowing disease progression

Both the American Academy of Neurology (AAN) and the National Multiple Sclerosis Society (NMSS) recommend early and uninterrupted therapy with DMTs for patients diagnosed with relapsing forms of MS, including those with SPMS who continue to have relapses.[27,40,41] Evidence suggests that early, first-line treatment of MS with interferon-β agents may prevent the conversion of a first isolated demyelinating episode into clinically definite MS, limit the accrual of dysfunction, and slow atrophy.[34,42,43] In addition, studies have shown that early first-line use of glatiramer acetate reduces the rate of relapse and the development of new gadolinium-enhancing and T2-weighted lesions, compared with placebo.[44]

Several clinical trials and follow-up studies have underscored the clinical benefit of not only early and continuous treatment with DMTs, but also the benefits of their long-term use.[34] Broadly, these trials showed that patients with relapsing MS who were treated with interferon-β agents, glatiramer acetate, mitoxantrone, natalizumab, or fingolimod experienced a reduction in relapse rates and disease progression.[34,45-47] Furthermore, follow-up studies have shown that patients who continued to take interferon-β agents and glatiramer acetate at the time of a later follow-up visit had reduced relapse rates, decreased disability progression, and longer transition time to SPMS than did those who reported more limited exposure to MS treatment.[47,48]

Pharmacologic Options

A number of DMTs with different mechanisms of action are currently approved by the US Food and Drug Administration (FDA) for the treatment of relapsing forms of MS. These include intramuscular and subcutaneous formulations of interferon β (β-1a and β-1b), glatiramer acetate, fingolimod, natalizumab, and mitoxantrone (Table 1).

Interferon, an immunomodulatory agent, was the first agent approved for the treatment of MS and is thought to suppress T-helper cell response and reduce T-cell migration across the blood-brain barrier.[49] Although treatment with interferon β reduces conversion to clinically definite MS and lessens the rate of brain parenchymal loss in patients who present with CIS suggestive of MS, the presence of neutralizing antibodies can result in a substantial decrease in efficacy, especially when administered subcutaneously.[50]

Glatiramer acetate, another immunomodulatory agent, is thought to alter T-cell activation and differentiation.[49] Phase 3 clinical trials of therapy with glatiramer acetate have demonstrated an approximately 30% reduction in relapses as well as significant reductions in disability progression and new brain lesions as measured by MRI.[51] Current data support the use of glatiramer acetate for treating RRMS, but not progressive MS without relapses.[27,52]

Fingolimod, the first available oral agent, is approved for use in relapsing forms of MS. This sphingosine 1-phosphate (S1P) receptor modulator binds to S1P receptors on lymphocytes and prevents T cells from crossing the blood-brain barrier and invading the CNS.[53] In a clinical trial, fingolimod demonstrated significant improvements in relapse rates and MRI parameters, reduced the risk of disability progression, and reduced brain atrophy.[53]

Natalizumab, a monoclonal antibody, antagonizes very late activating antigen (VLA)-4 on leukocytes and, in doing so, blocks T-cell migration across the blood-brain barrier.[49] Natalizumab has demonstrated efficacy for RRMS following the failure of first-line therapies.[46,54] Indeed, because some studies have shown it to be superior to first-line agents in relapsing forms of MS, some neurologists are increasingly considering the use of this agent in patients with worsening MS.[55]

Mitoxantrone is an antineoplastic agent that inhibits cell replication, specifically DNA and RNA synthesis of B and T cells.[14,49] Although approved for the treatment of RRMS, SPMS, and PRMS, mitoxantrone has shown benefit only for patients who continue to experience relapses and develop new MRI lesions.[14]

In addition to the approved agents discussed above, a number of additional agents are currently being investigated or in development. These include (but are not limited to) cladribine, dimethyl fumarate, laquinimod, and teriflunomide, as well as the monoclonal antibodies alemtuzumab, daclizumab, and rituximab.[31] Studies are ongoing to determine the safety and efficacy of these agents.

Choice of Agent

The increasing complexity of therapies available for treating patients with MS underscores the need for shared decision making between patient and clinician when selecting a DMT. Factors that should be considered include the following[56]:

- Type of MS
- Proven efficacy
- Patient preference
- Ability to administer/receive injections
- Side effects
- Comorbidities (eg, depression, epilepsy)
- Ease of blood-test monitoring

AAN and NMSS guidelines recommend initiating treatment with interferon β-1 agents and glatiramer acetate as soon as pos-

TABLE 1. Disease-Modifying Treatments for Multiple Sclerosis[a]

AGENT (TRADE NAME)	MECHANISM OF ACTION	DOSE (ROUTE)	ADVERSE EVENTS[b]	COMMENTS
Fingolimod (Gilenya)	Modulator of the sphingosine-1-phosphate receptor, which leads to internalization of the receptor	0.5 mg daily (oral)	• Bradycardia (primarily a first-dose effect) • Infection • Macular edema • Respiratory effects • Elevated liver enzymes • Hypertension	• May be a potential first-line therapeutic option, but most clinicians are not currently using it as such because of uncertainty about long-term safety • CBC testing prior to initiating treatment • Pregnancy category C
Glatiramer acetate (Copaxone)	Amino acid polymer with immune-modifying properties, such as induction of suppressor T-cell activity	20 mg/day (SC)	• Injection-site reactions and necrosis • Postinjection systemic reactions (flushing, chest pain, palpitations, anxiety, dyspnea, throat constriction, urticaria) • Lipoatrophy • Lymphadenopathy	• A first-line therapeutic option • No laboratory testing required • Pregnancy category B
Interferon β-1a (SC: Rebif, IM: Avonex)	Anti-inflammatory cytokines with multiple immunomodulatory effects, including enhancement of suppressor T-cell activity, reduction of cytokine production, down regulation of antigen presentation, and inhibition of lymphocyte trafficking	SC: Titrate to 22 mcg or 44 mcg 3 times weekly (SC) IM: 30 mcg once weekly	• Flu-like symptoms (muscle aches, fever chills, headaches, fatigue) • Injection-site reactions and necrosis • Depression • Hematologic and liver-function abnormalities • Hypersensitivity • Seizures • Cardiovascular disorders • Autoimmune disorders	• A first-line therapeutic option • Requires regular laboratory testing • Can generate NAbs • Pregnancy category C
Interferon β-1b (Betaseron, Extavia)		Titrate to 0.25 mg every other day (SC)		
Mitoxantrone (Novantrone[c])	Anthracenedione that intercalates into DNA inhibiting B-cell, T-cell, and macrophage proliferation and impairing antigen presentation	12 mg/m^2 every 3 months; cumulative lifetime maximum of 140 mg/m^2 (IV)	• Cardiotoxicity • Cardiac arrhythmias • Secondary amenorrhea • Alopecia • UTIs • Nausea • Secondary acute myelogenous leukemia	• A second-line therapeutic option, but toxicity limits its clinical applications • Serious risks involve cardiomyopathy, treatment-related leukemia, and infertility • Pregnancy category D
Natalizumab (Tysabri)	Anti-adhesion monoclonal antibody that blocks leukocyte migration into inflamed tissue	300 mg monthly (IV)	• PML • Infection • Hypersensitivity reactions • Depression • Cholelithiasis	• A second-line therapeutic option; the advent of the JC antibody test, however, may increase this agent's use in early therapy • Serious risk of PML • Can generate NAbs • Pregnancy category C

CBC = complete blood count; DNA = deoxyribonucleic acid; FDA = US Food and Drug Administration; IM = intramuscular; IV = intravenous; NAbs = neutralizing antibodies; PML = progressive multifocal leukoencephalopathy; SC = subcutaneous; UTI = urinary tract infection.
[a] Agents are listed alphabetically, not in order of preference.
[b] This list of events is not all inclusive.
[c] This brand-name product is no longer available.
Derived from prescribing information for individual agents and Brandes DW, et al. A review of disease-modifying therapies for MS: maximizing adherence and minimizing adverse events. *Curr Med Res Opin*. 2009;25:77-92.

sible following a diagnosis of RRMS.[27,40] Because interferon β-1 agents and glatiramer acetate have similar efficacy, selection is primarily based on the presence and severity of comorbidities, adverse effects, and patient preference.[44,56]

CLINICAL CONSIDERATIONS

Although fingolimod was approved by the FDA in 2010, guidelines have not yet offered recommendations for this agent's place in therapy, and the short- and longer-term risks are still being evaluated. Because of the potential for infection and possible effects on vision and cardiovascular status, our faculty experts suggest that it would be prudent to consider more established first-line agents such as interferon β and glatiramer acetate before considering fingolimod.

NMSS guidelines recommend natalizumab for patients who have had an inadequate response to, or who are unable to tolerate, other MS therapies and mitoxantrone for select patients with worsening relapsing disease or worsening SPMS.[40]

Of note, natalizumab is associated with a risk of progressive multifocal leukoencephalopathy (PML)—a serious and potentially fatal opportunistic infection caused by the JC virus (JCV)—and, as a result, this agent is administered under a strict protocol.[55,57] An expert consensus panel recommended that natalizumab be considered in patients who: (1) have had a suboptimal response to interferon β or glatiramer acetate, (2) cannot tolerate interferon β or glatiramer acetate, or (3) fall into a poor prognosis category (eg, devastating relapse at onset, early high rate of relapse, rapid onset of disability).[55] Natalizumab may be considered as a first-line treatment for this latter category of patients.[55]

Risk factors for the development of PML include prior, long-term, and concurrent treatment with immunosuppressive agents, duration of treatment with natalizumab, and the presence of JCV antibodies.[55,58] Until recently, validated methods for determining JCV status have been unavailable. However, assays that have been evaluated in clinical studies to assess blood for the presence of JCV antibodies are currently in development. These assays will help stratify patient risk of PML prior to treatment initiation.[55,59]

Mitoxantrone is the only FDA-approved agent for worsening RRMS, SPMS, and PRMS and can be used in different regimens for patients who are accumulating residual disability from repeated attacks and for those with rapid disability and evidence of continued inflammatory lesions.[40,60,61]

> **CLINICAL CONSIDERATIONS**
>
> Our faculty advisors noted that the safety of mitoxantrone has been called into question. It is associated with significant cardiotoxicity at low and cumulative doses, which limits patient lifetime exposure.[62,63] In addition, the risk of developing treatment-related acute leukemia is approximately 0.8/100, and our faculty expert estimated that at least 25% of those who develop this condition die.[62,63] Because of these serious concerns, the faculty commented that many neurologists no longer use this medication to treat MS.

Special Considerations in Veterans That Affect Choice of Agent. The unique characteristics of patients with MS being treated by the VHA—such as the type of MS, age, and symptom burden—may influence treatment decisions. The following considerations should be taken into account when selecting a DMT:

- Treatment pattern data within the VHA suggest that veterans with MS who are treated with DMTs are more likely to be treated with interferon β and glatiramer acetate; mitoxantrone use within the VHA has almost been completely eliminated because of concerns related to serious side effects[64]
- Although inflammatory disease activity is prominent in RRMS, it is less so in progressive MS, which is characterized by destructive and degenerative processes, and agents such as interferon β have less of an effect once MS has entered a secondary progressive phase[34]
- Data suggest that younger patients (aged 20-29 years) tend to respond more favorably to DMTs; because studies suggest that veterans with MS tend to be older than their non-veteran counterparts, veterans, as a group, may have a reduced response to DMTs[9,20,21]
- Symptomatic medication use is higher among veterans who receive care in the VHA system than it is among veterans who receive care outside of the VHA system and among non-veterans with MS because of more severe disability[21]
- A cohort study found that 74% of patients with MS were taking at least one CNS medication that interfered with cognition and worsened processing speed, sustained attention, and fatigue; clinicians must carefully consider the potential CNS side effects of MS medication when choosing an agent for patients in the VHA population[4,65]

Challenges Associated With Disease-Modifying Treatments

Although DMTs have shifted the therapeutic paradigm in the treatment of relapsing MS, efficacy is partial and limited, due, in part, to variations in the pathology of MS and patient response to therapy.[61,66] For example, the course of MS disease in African American patients may be more disabling than the course in Caucasian patients, and men with MS may be less responsive to interferon-β treatment and experience greater progression of disability than women.[67,68]

Monitoring Disease Status. Because DMTs are only partially effective, clinicians should anticipate breakthrough disease or suboptimal response.[61] Continued disease activity while on therapy is characterized by multiple relapses, increased disability, and radiologic activity.[61,69] Natural-history studies have shown that most patients with early MS have one to two relapses every 2 years; therefore, relapse counting is an important outcome measure for assessing response to DMTs, and higher rates may indicate a suboptimal response.[61] Similarly, in studies of patients who were treated with interferon β, those with more than two active lesions on MRI 1 year after initiating treatment had a greater risk of experiencing an early increase in disability after 2 years of treatment than were those with two or fewer lesions.[70] Disability progression (as measured by the expanded disability status scale [EDSS]—the most commonly used standardized and validated measure of functional abilities and disease progression) can also help predict the failure of interferon-β treatment.[71] In addition, the presence of neutralizing antibodies is associated with incomplete response to therapy in patients being treated with interferon β.[61]

On the basis of these factors, patients monitoring strategies should include the following[61,66,69,72]:

- Planning follow-up visits in advance—clinical check-ups 3 months after beginning therapy and twice annually thereafter
- Educating patients about the side effects, risks, and rationale for DMTs
- Educating patients to recognize symptom changes that could indicate suboptimal response, especially when subtle changes are anticipated
- Counting the number of relapses
- Measuring changes in EDSS scores
- Identifying the presence of gadolinium-enhancing or T2 lesions on MRI
- Identifying the presence of biologic markers such as interferon-β neutralizing antibodies (NAbs) and anti-natalizumab antibodies
- Assessing and optimizing patient adherence
- Excluding other potential causes before attributing changes to suboptimal response

Other measures that can be used to specifically identify patients with breakthrough disease include patient reporting of MS-related symptoms, adverse effects, and health-related quality of life.[61,66,73]

Adherence Issues. Patient adherence to therapy is essential to optimize therapeutic outcomes associated with DMTs because gaps in treatment are associated with a greater probability of severe relapse.[74] Unfortunately, several factors can limit adherence (Table 2). MS can progress silently, and patients who are not experiencing relapses or symptoms of progression may not

TABLE 2. Adherence Barriers and Improvement Strategies

ADHERENCE BARRIERS	ADHERENCE IMPROVEMENT STRATEGIES
• Side effects or risk of adverse effects • Perceived lack of therapeutic efficacy • How patient feels as result of treatment • Degree of self-control that patients feel they have over the disease • Previous history of nonadherence • Fear, disgust, anxiety, and autonomic response to injection • Treatment fatigue • Psychiatric comorbidities • Cost of medication • Stress and coping style • Deterioration of injecting (fine-motor) skills as disease progresses • Cognitive function	• Assess adherence at each visit or via Internet-based tools • Reinforce the benefits and rationale for treatment • Remind patients that available agents reduce the incidence, frequency, and severity of relapses • Remind patients who are in remission that although they may not be experiencing relapses or signs of progression, the disease may be active at a subclinical level, and continuation of therapy is necessary to help reduce disease burden • Educate patients and caregivers about adverse effects • Avoid side effects by gradually escalating the dose when starting treatment, providing premedication pain relievers, and recommending evening administration • Recognize missed appointments, missed refills, and patient evasiveness • Help patients cope with adverse events such as flu-like symptoms or injection-site reactions • Provide technique reminders and recommend dose schedulers and medication diaries

Derived from Brandes DW, et al. A review of disease-modifying therapies for MS: maximizing adherence and minimizing adverse events. *Curr Med Res Opin*. 2009;25:77-92; Cox D. Managing self-injection difficulties in patients with relapsing-remitting multiple sclerosis. *J Neurosci Nurs*. 2006;38:167-171; Costello K, et al. Recognizing nonadherence in patients with multiple sclerosis and maintaining treatment adherence in the long term. *Medscape J Med*. 2008;10(9):225; Clerico M. Adherence to interferon-beta treatment and results of therapy switching. *J Neurol Sci*. 2007;259:104-108; and Río J, et al. Factors related with treatment adherence to interferon beta and glatiramer acetate therapy in multiple sclerosis. *Mult Scler*. 2005;11:306-309.

fully appreciate the importance of remaining on medication.[75] Even when patients are committed to adherence, medication side effects, such as injection-site reactions, post-injection systemic reactions, flu-like symptoms, depression, and allergic reactions, can present challenges.[36] The type of MS can also influence adherence (eg, studies have identified poorer adherence among patients with SPMS), as can the presence of symptoms such as cognitive impairment or depression, the cost and complexity of treatment regimens, the perceived lack of therapeutic efficacy, and treatment fatigue.[76-78]

Despite these challenges, short-term studies suggest that when patients adhere to recommended DMT regimens, relapse risk is reduced, functional and cognitive abilities are optimized, and quality of life is preserved.[36] Approximately 60% to 76% of patients with MS adhere to interferon β and glatiramer acetate for 2 to 5 years; the majority of those who discontinue therapy do so within the first 6 months to 2 years.[75,77] This fact highlights the importance of establishing a therapeutic partnership built on trust and respect early in the course of therapy and reinforcing the importance of adherence with patients (Table 2).[75]

Modifying Treatment Regimens. Decisions to switch or modify therapy are typically made by a neurologist. In cases in which disease is progressing, current guidelines and expert opinion recommend that[60,69,79-81]:

- Clinicians consider modifying therapy in patients with worsening RRMS, SPMS, and PRMS
- Interferon β be discontinued in patients with high-titer, persistent interferon-β NAbs and continued disease activity while on interferon β
- Patients with acute relapse be referred for appropriate specialist treatment, which may include therapy modification or switching

When patients are exhibiting a suboptimal response to therapy, the following therapeutic options are recommended[55,60,82]:

- Continue with the current DMT in patients with minimal breakthrough disease
- Increase medication dose—head-to-head studies have suggested that higher doses of interferon administered more frequently may provide better short-term results
- Switch therapies from interferon β to glatiramer acetate (or vice versa)
- Switch to second-line therapy (natalizumab) when patients continue to have frequent relapses or excessive MRI activity
- Consider patients for clinical trials when they fail approved therapies

GENERAL WELLNESS IN MULTIPLE SCLEROSIS

The optimal management of patients with MS includes not only appropriate treatment, but also attention to general health and wellness. Health and wellness are important for recovery from exacerbations as well as for helping patients manage new and ongoing symptoms.

Optimizing Wellness

Lifestyle and health factors such as obesity, smoking, and lack of exercise can exacerbate symptoms of MS.[21,83,84] A significant percentage of veterans with MS are overweight or obese, and nutritional imbalances, which can negatively affect disease course and patient quality of life, are common.[83,85] In addition, more than one in four patients with MS smoke—a behavior that correlates with pain, poorer mental health, social isolation, and possibly disease progression.[84,86] Exercise is also integral to disease management for patients who are not experiencing an exacerbation, and a growing body of evidence links exercise to improving and maintaining functional capacity, suggesting that it confers benefits for muscle-power function, exercise-tolerance function, and mobility-related activities.[15,87] Strategies to optimize these and other wellness factors are summarized in Table 3.

Symptom Management

As MS progresses, the nature and severity of symptoms can diversify and intensify, diminishing health-related quality of life and increasing the risk of depression, fatigue, and anxiety.[88]

TABLE 3. Strategies to Optimize Wellness

WELLNESS FACTOR	EVIDENCE	STRATEGY
Obesity	• Reduced animal fat intake and increased intake of vegetable oils and seafood may reduce exacerbations and disability	• Discuss dietary patterns with patients and reinforce good nutrition • Screen and track patients' weight, and develop interventions to prevent and manage excessive weight gain • Consider bariatric surgery for morbidly obese patients who fail traditional weight loss programs
Vitamin D	• Vitamin D supplementation may benefit relapse rates, EDSS scores, and suppress T-cell proliferation	• Consider vitamin D supplementation when patient levels are deficient (≤ 20 ng/mL) or insufficient (21 to 29 ng/mL)
Smoking	• Smoking correlates with pain, poorer mental health, and social isolation and may be linked to disease progression	• Ask patients about their tobacco use • Counsel patients about quitting • Provide information about quit lines and community-support services
Rehabilitation/ exercise	• Progressive resistance training can improve muscle strength, functional capacity, and balance and can reduce fatigue and depression • Physical activity and exercise training may benefit walking impairment • Robotic technology used in rehabilitation includes gait training devices, motor performance devices, and computer-aided, non-robotic therapy orthotics	• Consider cardiopulmonary exercise training • Alternate exercise with rest to mitigate build-up of fatigue and heat stress • Suggest aquatic therapy—cool water helps to dissipate body heat, and buoyancy in water helps patients attain a greater range of motion • Individualize strength-training programs to improve muscle tone, strength, endurance, and balance between agonist/antagonist and bilateral muscle groups • Encourage patients to increase their flexibility—stretching at several points throughout the day, stretching particular muscle groups to increase muscle length resulting from loss of connective tissue elasticity and counteract the effects of spasticity • Develop an exercise prescription for the patient; when developing the prescription, consider enlisting the help of a physical therapist or clinical exercise physiologist with MS-related experience

EDSS = expanded disability status scale.

Derived from Goodman S, et al. Dietary practices of people with multiple sclerosis. *Int J MS Care*. 2008;10:47-57; Khurana SR, et al. The prevalence of overweight and obesity in veterans with multiple sclerosis. *Am J Phys Med Rehabil*. 2009;88(2):83-91; Mechanik JI, et al. AACE, TOS, and ASMBS medical guidelines for clinical practice for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient. *Obesity*. 2009;17(Suppl 1):S1-S70; Solomon AJ, et al. Multiple sclerosis and vitamin D: a review and recommendations. *Curr Neur Neurosci Rep*. 2010;10(5):389-396; Turner A, et al. Smoking among veterans with multiple sclerosis: prevalence correlates, quit attempts and unmet need for services. *Arch Phys Med Rehabil*. 2007;88(11)1394-1399; Healy BC, et al. Smoking and disease progression in multiple sclerosis. *Arch Neurol*. 2009;66(7):858-864; Cakt BD, et al. Cycling progressive resistance training for people with multiple sclerosis: a randomized controlled study. *Am J Phys Med Rehabil*. 2010;89(6):446-457; Dalgas U, et al. Resistance training improves muscle strength and functional capacity in multiple sclerosis. *Neurology*. 2009;73(18):1478-1484; Motl RW, et al. Symptom cluster and quality of life in multiple sclerosis. *J Pain Symptom Manage*. 2010;42(4):212-216; Lo A. Neurorehabilitation research laboratory at the Providence VAMC. *Med Health*. 2010;93(1):22-24; White LJ, et al. Exercise and multiple sclerosis. *Sports Med*. 2004;34(15):1077-1100.

When assessing patients with MS, it is important to remember that[34,89,90]:

- DMTs do not alleviate symptoms and deficits from existing losses of neuronal conduction
- New symptoms can occur at all phases of the disease in the form of relapse or disease progression
- MS symptoms can be subtle and are not always easily recognized as manifestations of disease
- Patients may be reluctant to draw attention to or discuss certain symptoms
- Multiple symptoms can coexist and exacerbate one another

The most common symptoms associated with MS include spasticity, fatigue, sexual dysfunction, bladder dysfunction, pain, and cognitive dysfunction; other common symptoms include mood disorders, bowel dysfunction, paroxysmal symptoms, and weakness (Table 4).[90] These symptoms can be socially distressing and disabling and may affect relationships; therefore, early and accurate recognition and treatment are critical to maximize function, improve quality of life, increase independence, and reduce morbidity.[90]

Physical Symptoms. Approximately 90% of patients with MS experience spasticity, caused by axonal degeneration or malfunction.[91] Spasticity commonly affects lower extremities and can disrupt sleep and activities of daily living.[90] Spasticity can also impair gait and mobility, and it is estimated that approximately one-half of patients with MS will reach two major clinical benchmarks of impaired mobility (EDSS scores of 4.0 and 6.0) within 10 to 20 years of disease onset.[90,92]

Bladder dysfunction (eg, incontinence, frequency, and urinary retention) can also be a source of morbidity for patients with MS.[19] These symptoms affect quality of life and can contribute to urinary-tract and associated skin infections, bladder-stone formation, and renal disease.[37,89] As many as 70% of patients also experience bowel dysfunction, potentially caused by fibrosis or low anal sphincter pressure, poor rectal sensation, and fecal incontinence.[90,91]

Pain is another common physical symptom of MS.[37] Although it results from multiple pathways and is poorly defined, an estimated 55% to 65% of patients report experiencing this symptom. Chronic pain is more common than acute pain, which presents as intense paroxysmal attacks that can worsen with age and disease progression, or subacute pain, which is frequently associated with optic neuritis.[37]

Cognitive and Emotional Complications. CNS symptoms, such as fatigue and cognitive dysfunction, can often be more severe than physical disability.[89] Fatigue is the symptom most mentioned by patients with MS, is predictive of disability independent of other neurologic impairments, and presents considerable management challenges.[93] The characteristics of MS-related fatigue are quite distinct from general fatigue in that it is usually unexpected, occurs suddenly, is most prominent in the afternoon, and is worsened by heat.[90] MS-related fatigue can exacerbate other symptoms by reducing cognition, increasing

TABLE 4. Common Symptoms of Multiple Sclerosis and Potential Interventions

SYMPTOM	ASSESSMENT	NONPHARMACOLOGIC OPTIONS	PHARMACOLOGIC OPTIONS[a]
Fatigue	• Review medications and comorbid conditions • Use Fatigue Severity Scale (FSS) to quantify symptoms • Ask patients open-ended questions to identify fatigue inducers (depression, physical exhaustion, metabolic conditions, medications)	• Sleep specialty clinic referral: sleep disorder evaluations, sleep hygiene education • Temperature control (cool-beverage consumption, cooling vest) • Treatment of underlying conditions such as spasticity or depression • Aerobic exercise, yoga, progressive passive resistance training, and cognitive behavioral therapy can decrease fatigue and improve quality of life	• CNS stimulants (eg methylphenidate) • Amantadine and modafinil
Spasticity	• Use Modified Ashworth Scale to assess severity • Identify spasticity inducers	• Rehabilitation (physical therapy, conditioning programs, adaptive exercises) • Assistive devices (orthotics, stabilizers, scooters)	• Central acting agents (eg, baclofen, tizanidine) • Benzodiazepines • Anticonvulsants • Botulinum toxin • Intrathecal baclofen pumps
Mobility and gait problems	• Assess mobility and gait and screen for fall risk (timed 25-foot walk test)	• Rehabilitation (transfer training, body weight–supported treadmill, robotics locomotor training to improve delivery of body-weight support in clinical setting) • Assistive devices (orthotics, stabilizers, scooters) • Functional electrical stimulation	• Fampridine
Bladder dysfunction	• Monitor for bladder dysfunction • Obtain postvoid residual	• Intermittent catheterization of bladder • Adequate fluid intake • Acidification of the urine (cranberry juice, vitamin C) • Catheterization technique • Pelvic floor exercises • Manual pressure	• Anticholinergics (oxybutynin for hyperreflexive bladder), tolterodine, trospium, darifenacin), desmopressin • Alpha blockers • Antibiotics for UTIs
Cognitive dysfunction/ depression	• Regular screening (Minimal Assessment of Cognitive Function in MS, Beck Depression Inventory to assess changes in mood and anxiety, Multiple Sclerosis Quality of Life Instrument, patient self-report) • Annual neurologic evaluation • Functional assessment (verbal fluency, visuospatial skills, verbal memory, working memory) • Processing speed executive function	• Lifestyle modifications to conserve energy (scheduling naps, mobility aids, orthotics) • Adjust performance expectations • Retrain patients in previously learned skills • Refer to neurologist if a new impairment develops • For depression: cognitive behavioral therapy, mindfulness training	• CNS stimulants • Antidepressants • Antipsychotics • Anxiolytic agents • For cognitive dysfunction: limit sedative drugs

CNS = central nervous system; MS = multiple sclerosis; UTI = urinary tract infection.
[a] The majority of these options reflect off-label uses of medication; please refer to the full prescribing information for safety information.
Derived from VHA. *Multiple sclerosis system of care procedures, VHA Handbook*; Braley TJ, et al. Fatigue in multiple sclerosis: mechanisms, evaluation, and treatment. *Sleep*. 2010;33:1061-1067; Tullman M. Symptomatic therapy in multiple sclerosis. *Continuum*. 2004;10(6):142-172; Oken BS, et al. Randomized controlled trial of yoga and exercise in multiple sclerosis. *Neurology*. 2004;62(11):2058-2064; Oken BS, et al. Cognition and fatigue in multiple sclerosis: potential effects of medications with central nervous system activity. *J Rehabil Res Dev*. 2006;43(1):83-90; NMSS. Management of MS-related fatigue. National Multiple Sclerosis Society 2006; Cohen BA. Identification, causation, alleviation, and prevention of complications (ICAP). *Neurology*. 2008;71(24 Suppl 3):S14-S20; Dalgas U, et al. Resistance training improves muscle strength and functional capacity in multiple sclerosis. *Neurology*. 2009;73(18):1478-1484; van Kessel K, et al. A randomized controlled trial of cognitive behavior therapy for multiple sclerosis fatigue. *Psychosom Med*. 2008;70:205-213; Van den Berg M, et al. Treadmill training for individuals with multiple sclerosis: a pilot randomized trial. *J Neurol Neurosurg Psychiatry*. 2006;77(4):531-533; Souza A, et al. Multiple sclerosis and mobility-related assistive technology: systematic review of literature. *J Rehabil Res Dev*. 2010;47(3):213-223; Thomas P, et al. Psychological interventions for multiple sclerosis. *Cochrane Database Syst Rev*. 2006;1:CD004431; Grossman P, et al. MS quality of life, depression and fatigue improve after mindfulness training: a randomized trial. *Neurology*. 2010;75(13):1141-1149; de Sa JC, et al. Symptomatic therapy in multiple sclerosis: a review for a multimodal approach in clinical practice. *Ther Adv Neurol Disord*. 2011;4(3):139-168.

depression, and limiting physical ability.[37] Of note, a diagnosis of fatigue can be complicated by the heterogeneity of its symptoms.[91]

Cognitive impairment is highly prevalent among patients with MS and can lead to potentially devastating consequences, such as unemployment, social isolation, psychiatric morbidity, and difficulty managing routine tasks.[93] Although it is not necessarily accompanied by physical disability, moderate-to-severe cognitive dysfunction can disrupt everyday activities, social situations, and family relationships.[89,93] The severity and symptoms of cognitive dysfunction vary widely and include diminutions in attention, information processing, working memory, executive functioning, and complex attention.[37,89] Impairment can be subtle, however.[89] Patients may not recognize symptoms of impairment, and they may not be picked up by the Mini-Mental State Examination (which fails to identify impairment in 75% of cognitively impaired patients).[89,90] Consequently, patients who have cognitive impairment require routine neurocognitive assessment to identify abnormalities in domains affected by MS and emerging deficits.[17]

Finally, the unpredictable and variable nature of MS can have a debilitating psychologic effect on patients. The lifetime risk of depression among those with MS is approximately 50%, and this under-recognized psychologic condition can significantly influence health-related quality of life and increase suicide risk.[90,91] In addition, depression can mimic cognitive deficits, so it is particularly important that clinicians assess and manage the mental health of patients with MS.[91]

Active Symptom Management. An active approach to symptom management can help clinicians identify symptoms that require intervention and develop an individualized care plan that includes exercise, multidisciplinary support, and pharmacologic intervention.[89] In particular, those with unstable disease or those who require complex symptom management may benefit from frequent specialty care, follow-up, or specialist referral.[11]

The *Identification, Causation, Alleviation, and Prevention of Complications* (ICAP) model offers a 4-step, cohesive approach to symptom management based on identifying specific symptomatic issues, recognizing the causes of symptoms, alleviating symptoms, and preventing long-term complications[89]:

- **Identification**—Elicit and interpret information from the patient about symptoms encountered in MS, including probing for symptoms that are not offered
- **Causation**—Determine whether the complaint is a primary or secondary symptom of MS or related to a comorbid condition
- **Alleviation**—Treat the symptom directly, address comorbidities, or minimize factors that worsen symptoms
- **Prevention**—Proactively modify factors that are causing symptoms, worsening symptoms, or leading to secondary effects

OPTIMIZING PATIENT MANAGEMENT IN THE FEDERAL HEALTHCARE SYSTEM

Veterans with MS require more healthcare visits per person than most other diagnostic groups within the VHA.[94] Accordingly, to improve care, and—in particular—access to specialty care, the VHA funded two Multiple Sclerosis Centers of Excellence (MSCoEs) in 2003, one in Baltimore (MSCoE-East) and the other in Seattle/Portland (MSCoE-West).[26] The mission of the MSCoE is to support and maintain the health, independence, quality of life, and productivity of veterans with MS through clinical care, education, and research.[11]

The MSCoEs provide resources for patients, caregivers, and clinicians.[11,80] These centers also conduct research relevant to the health needs of veterans with MS and have created a national program of education and training to ensure that healthcare professionals within the VHA are adequately educated and supported to optimally care for veterans with this condition.[4,94]

They make use of a specialized hub-and-spoke system to deliver multidisciplinary, coordinated care.[11] Each Veteran Integrated Service Network (VISN) has at least one MS Regional Program, which forms the hub that coordinates comprehensive, multidisciplinary, specialized MS care. The spokes comprise other VA Medical Centers and outpatient facilities within the local area of each hub.[11] This system integrates local and regional facilities within each VISN and is designed to ensure that patients receive timely primary and specialty care that addresses their unique healthcare needs, including, if necessary, care for spinal-cord disease.[11,26] The purpose and core resources of this model are summarized in Table 5.

CLINICAL CONSIDERATIONS

Although the VHA provides healthcare (including medication) for eligible patients who have MS, additional benefits are available for veterans who developed symptoms of MS during active military service or within 7 years after honorable discharge.[6] These benefits may include[6]:

- Home-modification benefits to assist with residential adaptations
- Assistance in purchasing mobility devices
- In-home assistance for activities of daily living
- Supportive services such as respite or skilled nursing care
- Monthly disability pension

TABLE 5. Multiple Sclerosis Center of Excellence Resources

LOCATION	DESCRIPTION	TOOLS	KEY RESOURCE
Regional center (hub)	• **Purpose:** At least one MS regional program per VISN • **Personnel:** Physician, nurse, social worker, and administrative assistant • **Practice:** The hub coordinates care for patients at a local medical center and at outlying facilities in the VISN via: - Outpatient clinic treatment - Annual evaluation and care-plan review - Annual completion of electronic clinical data surveillance tool	**Provider-support tools:** • Electronic medical records • Informatics tools (eg, morbidity measures to track outcomes and decision-support tools) • Telehealth: home telehealth, intrafacility telehealth, and store-and-forward telehealth • Internet-based portals–MyHealtheVet • Open-access scheduling • Remote visits • Clinical practice guidelines on diagnosis, therapy, symptom management, and benefits available through the VHA	***VHA handbook*** provides information on: • Diagnostic and therapeutic healthcare services required by patients with MS, including primary care • Disease-modifying treatments • Symptomatic pharmacologic therapies
Spoke site	• **Purpose:** Works with the regional hub to deliver care to the local MS population • **Personnel:** A care coordinator is assigned to help with care at each spoke facility • **Practice:** Spokes coordinate with the hub and provide care locally via consultations and referrals using telehealth and informatics	**Patient-support tools/resources:** • Targeted education via home Internet system • Telehealth support • Compliance tools	***MSCoE Informational Web site*** for providers and veterans with MS that supports: • Information sharing • Content adapted for patients • Question-and-answer feature

MSCoE = Multiple Sclerosis Centers of Excellence; MS = multiple sclerosis; VHA = Veterans Health Administration; VISN = Veteran Integrated Service Network.
Wallin MT. Integrated multiple sclerosis care: new approaches and paradigm shifts. *J Rehabil Res Dev*. 2010;47(6):ix-xiv.

CONCLUSION

Therapeutic advances are shifting the treatment of MS toward early and continuous intervention with a range of DMTs. In addition, new agents have recently been approved or are under investigation for the treatment of MS-related symptoms, including gait impairment and spasticity. Newer DMTs, although potentially more efficacious, also have more untoward effects and, therefore, require monitoring by MS specialty providers. To optimize patient outcomes, those with MS generally require the involvement of a number of specialists. Ideally, this care should be coordinated through a specialized network, such as that provided within the framework of the MSCoEs. When applied appropriately, these programs can help maintain patient function and quality of life and prevent complications.

REFERENCES

1. Noseworthy JH, Lucchinetti C, Rodriguez M, Weinshenker BG. Multiple sclerosis. *N Engl J Med*. 2000;343:938-952.
2. Kobelt G, Berg J, Atherly D, Hadjimichael O. Costs and quality of life in multiple sclerosis: a cross-sectional study in the United States. *Neurology*. 2006;66(11):1696-1702.
3. Culpepper WJ, Ehermantraut M, Wallin MT, Flannery K, Bradham DD. Veterans Health Administration multiple sclerosis surveillance registry: the problem of case-finding from administrative databases. *J Rehabil Res Dev*. 2006;43(1):17-24.
4. Haselkorn JK. Veterans Health Administration Multiple Sclerosis Centers of Excellence: clinical care, education, informatics, and research. *J Rehabil Res Dev*. 2006;43:vii-x.
5. Multiple Sclerosis Centers of Excellence. Description of VHA MS cohort. VHA utilization and VHA expenditures: preliminary analyses. www.va.gov/MS/library/vha_mscoe_desriptive%20report_year1_feb27_2004_1.doc. Accessed August 15, 2011.
6. US Department of Veterans Health Administration. Multiple sclerosis center of excellence. Last updated March 8, 2011. www.va.gov/MS/index.asp. Accessed August 15, 2011.
7. Hafler DA, Slavik JM, Anderson DE, O'Connor KC, De Jager P, Baecher-Allan C. Multiple sclerosis. *Immunol Rev*. 2005;204:208-231.
8. Ascherio A, Munger K. Epidemiology of multiple sclerosis: from risk factors to prevention. *Semin Neurol*. 2008;28(1):17-28.
9. Hirst C, Ingram G, Pearson O, Pickersgill T, Scolding N, Robertson N. Contribution of relapses to disability in multiple sclerosis. *J Neurol*. 2008;255:280-287.
10. Alonso A, Hernán MA. Temporal trends in the incidence of multiple sclerosis: a systematic review. *Neurology*. 2008;71(2):129-135.
11. Veterans Health Administration. *Multiple sclerosis system of care procedures, VHA Handbook*. Department of Veterans Affairs. www.va.gov/MS/documents/MSHandbook09.pdf. Accessed August 15, 2011.
12. Compston A, Coles A. Multiple sclerosis. *Lancet*. 2008;372(9648):1502-1517.
13. Trapp BD. Neurodegeneration: the pathologic evidence. *Adv Stud Med*. 2009;9(2):37-41.
14. Spain RI, Cameron MH, Bourdette D. Recent developments in multiple sclerosis. *BMC Med*. 2009;7:74.
15. Rietberg MB, Brooks D, Uitdehaag BMJ, Kwakkel G. Exercise therapy for multiple sclerosis. *Cochrane Database Syst Rev*. 2004;3:CD003980.
16. Borazanci AP, Harris MJ, Schwendimann RN, et al. Multiple sclerosis: clinical features, pathophysiology, neuroimaging and future therapies. *Future Neurol*. 2009;4(2):229-246.
17. Chiaravalloti ND, DeLuca J. Cognitive impairment in multiple sclerosis. *Lancet Neurol*. 2008;7:1139-1151.
18. Deussing E. Multiple sclerosis, active component, U.S. Armed Forces, 2000-2009. *MSMR*. 2011;18(1):12-15.
19. Marrie RA, Cutter G, Tyry T, Campagnolo D, Vollmer T. Differences in bladder care for veterans with multiple sclerosis by treatment location. *Int J MS Care*. 2009;11:91-97.
20. Guarnaccia JB, Aslan M, O'Connor TZ, et al. Quality of life for veterans with multiple sclerosis on disease-modifying agents: relationship to disability. *J Rehabil Res Dev*. 2006;43:35-44.
21. Lo AC, Hadjimichael O, Vollmer TL. Treatment patterns of multiple sclerosis patients: a comparison of veterans and non-veterans using the NARCOMS registry. *Mult Scler*. 2005;11(1):33-40.
22. Culpepper WJ, Bradham D, Bever C, Bourdette D. Epidemiologic description of VA multiple sclerosis surveillance registry. *Int J MS Care*. 2008;10(Supp 1):S15.
23. Forbes A, While A, Taylor M. What people with MS perceive to be important to meeting their needs. *J Adv Nurs*. 2007;58(1):11-22.
24. Cheng EM, Crandall CJ, Bever CT Jr, et al. Quality indicators for multiple sclerosis. *Mult Scler*. 2010;16(8):970-980.
25. Hatzakis M Jr, Haselkorn J, Williams R, Turner A, Nichol P. Telemedicine and the delivery of health services to veterans with MS. *J Rehabil Res Dev*. 2003;40(3):265-282.
26. Culpepper WJ, Cower-Ripley D, Litt ER, McDowell T-Y, Hoffman PM. Using geographic information system tools to improve access to MS specialty care in Veterans Health Administration. *J Rehabil Res Dev*. 2010;47(6):583-592.
27. Goodin DS, Frohman EM, Garmany JR, et al. Disease modifying therapies in multiple sclerosis: Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. *Neurology*. 2002;58: 169-178.
28. Khan F, Pallant JF, Brand C, Kilpatrick TJ. Effectiveness of rehabilitation intervention in persons with multiple sclerosis: a randomized controlled study. *J Neurol Neurosurg Psychiatry*. 2008;79(11):1230-1235.
29. Polman CH, Reingold S, Banwell B, et al. Diagnostic criteria for multiple sclerosis: 2010 revisions to the "McDonald Criteria." *Ann Neurol*. 2011;69: 292-302.
30. Simon JH, Li D, Traboulsee A, et al. Standardized MR imaging protocol for multiple sclerosis: Consortium of MS Centers consensus guidelines. *Am J Neuroradiol*. 2006;27:455-461.
31. Gawronski KM, Rainka MM, Patel MJ, Gengo FM. Treatment options for multiple sclerosis: current and emerging therapies. *Pharmacotherapy*. 2010;30(9):916-927.
32. Amato MP, Zipoli V, Goretti B, et al. Benign multiple sclerosis: cognitive, psychological and social aspects in a clinical cohort. *J Neurol*. 2006;253: 1054-1059.
33. Gold R, Wolinsky JS, Amato MP, Comi G. Evolving expectations around management of multiple sclerosis. *Ther Adv Neurol Disord*. 2010;3(6):351-367.
34. Comi G. Shifting the paradigm toward earlier treatment of multiple sclerosis with interferon beta. *Clin Ther*. 2009;31(6):1142-1157.
35. Fisniku LK, Brex PA, Altmann DR, et al. Disability and T2 MRI lesions: a 20-year follow-up of patients with relapse onset of multiple sclerosis. *Brain*. 2008;131:808-817.
36. Caon C, Saunders C, Smrtka J, et al. Injectable disease-modifying therapy for relapsing-remitting multiple sclerosis: a review of adherence data. *J Neurosci Nurs*. 2010;42(5 Suppl):S5-S9.
37. Crayton H, Heymann RA, Rossman HS. A multimodal approach to managing the symptoms of multiple sclerosis. *Neurology*. 2004;63(Suppl 5):S12-S18.
38. IFNB Multiple Sclerosis Study Group. Interferon beta-1b is effective in relapsing-remitting multiple sclerosis. Clinical results of a multicenter, randomized, double-blind, placebo controlled trial. *Neurology*. 1993;43(4): 655-661.
39. Trojano M, Pellegrini F, Fuiani A, et al. New natural history of interferon β-treated relapsing multiple sclerosis. *Ann Neurol*. 2007;61:300-306.
40. National Multiple Sclerosis Society. Disease Management Consensus Statement 2008. www.nationalmssociety.org/for-professionals/healthcare-professionals/publications/expert-opinion-papers/index.aspx. Accessed August 15, 2011.
41. Goodin DS. Disease-modifying therapy in multiple sclerosis: update and clinical implications. *Neurology*. 2008;71(24 Suppl 3):S8-S13.
42. Clerico M, Contessa G, Durelli L. Interferon-beta1a for the treatment of multiple sclerosis. *Expert Opin Biol Ther*. 2007;7(4):535-542.
43. Halper J. The psychosocial effect of multiple sclerosis: the impact of relapses. *J Neurol Sci*. 2007;256 (Suppl 1):S34-8.
44. O'Connor P, Filippi M, Arnason B, et al. 250 microg or 500 microg interferon beta-1b versus 20mg glatiramer acetate in relapsing–remitting multiple sclerosis: a prospective, randomised, multicentre study. *Lancet Neurol*. 2009;8:889-897.
45. Edan G, Morrisey S, Le Page E. Rationale for the use of mitoxantrone in multiple sclerosis. *J Neurol Sci*. 2004;223:35-39.
46. Polman CH, O'Connor PW, Havrdova E, et al. A randomized, placebo-controlled trial of natalizumab for relapsing multiple sclerosis. *N Engl J Med*. 2006;354:899-910.
47. Ford C, Goodman AD, Johnson K, et al. Continuous long-term immunomodulatory therapy in relapsing multiple sclerosis: results from the 15-year analysis of the US prospective open-label study of glatiramer acetate. *Mult Scler*. 2010;16(3):342-350.
48. Ebers GC, Reder AT, Traboulsee A, et al. Long-term follow-up of the original interferon-β1b trial in multiple sclerosis: design and lessons from a 16-year observational study. *Clin Ther*. 2009;31(8):1724-1736.

49. Menge T, Weber MS, Hemmer B, et al. Disease-modifying agents for multiple sclerosis recent advances and future prospects. *Drugs*. 2008;68:2445-2468.
50. Jeffery DR, Markowitz CE, Reder AT, Weinstock-Guttman B, Tobias K. Fingolimod for the treatment of relapsing multiple sclerosis. *Expert Rev Neurother*. 2011;11(2):165-183.
51. Johnson KP, Brooks BR, Cohen JA, et al. Copolymer 1 reduces relapse rate and improves disability in relapsing-remitting multiple sclerosis: results of a phase III multicenter, double-blind, placebo-controlled trial. *Neurology*. 1995;45:1268-1276.
52. Wolinsky JS, Narayana PA, O'Connor P, et al. Glatiramer acetate in primary progressive multiple sclerosis: results of a multinational, multicenter, double-blind, placebo-controlled trial. *Ann Neurol*. 2007;61(1):14-24.
53. Kappos L, Radue E-W, O'Connor P, et al. A placebo-controlled trial of oral fingolimod in relapsing multiple sclerosis. *N Engl J Med*. 2010;362:387-401.
54. Rudick RA, Stuart WH, Calabresi PA, et al. Natalizumab plus interferon beta-1a for relapsing multiple sclerosis. *N Engl J Med*. 2006;354(9):911-923.
55. Coyle PK, Foley JF, Fox EJ, et al. Best practice recommendations for the selection and management of patients with multiple sclerosis receiving natalizumab therapy. *Mult Scler*. 2009;15:S26-S36.
56. Bowen J. Choosing a disease modifying therapy to use for multiple sclerosis. www.va.gov/MS/articles/Choosing_A_Disease_Modifying_Therapy_DMT_to_Use_for_Multiple_Sclerosis.asp Accessed August 15, 2011.
57. US Food and Drug Administration. Tysabri (natalizumab): update of health-care professional information. www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm199965.htm. Accessed August 15, 2011.
58. US Food and Drug Administration. FDA Drug Safety Communication: safety update on progressive multifocal leukoencephalopathy (PML) associated with Tysabri (natalizumab). www.fda.gov/drugs/drugsafety/ucm252045.htm. Accessed August 15, 2011.
59. Gorelik L, Lerner M, Bixler S, et al. Anti-JC virus antibodies: implications for PML risk stratification. *Ann Neurol*. 2010;68(3):295-303.
60. National Multiple Sclerosis Society. Changing therapy in relapsing multiple sclerosis: considerations and recommendations of a task force of the National Multiple Sclerosis Society. www.nationalmssociety.org/for-professionals/healthcare-professionals/publications/expert-opinion-papers/index.aspx. Accessed August 15, 2011.
61. Cohen BA, Khan O, Jeffery DR, et al. Identifying and treating patients with suboptimal responses. *Neurology*. 2004;63(Suppl 6):S33-S40.
62. Marriott JJ, Miyasaki JM, Gronseth G, O'Connor PW. Evidence report: the efficacy and safety of mitoxantrone (Novantrone) in the treatment of multiple sclerosis. *Neurology*. 2010;74(18):1463-1470.
63. Kingwell E, Koch M, Leung B, Isserow S, et al. Cardiotoxicity and other adverse events associated with mitoxantrone treatment for MS. *Neurology*. 2010;74:1822-1826.
64. Vollmer TL, Hadjimichael O, Preiningerova J, Ni W, Buenconsejo J. Disability and treatment patterns of multiple sclerosis patients in United States: a comparison of veterans and nonveterans. *J Rehabil Res Dev*. 2002;39(2):163-174.
65. Oken BS, Flegal K, Zajdel D, et al. Cognition and fatigue in multiple sclerosis: potential effects of medications with central nervous system activity. *J Rehabil Res Dev*. 2006;43(1):83-90.
66. Rudick RA, Polman CH. Current approaches to the identification and management of breakthrough disease in patients with multiple sclerosis. *Lancet Neurol*. 2009;8:545-559.
67. Marrie RA, Cutter G, Tyry T, Vollmer T, Campagnolo D. Does multiple sclerosis-associated disability differ between races? *Neurology*. 2006;66:1235-1240.
68. Tomassini V, Paolillo A, Russo P, et al. Predictors of long-term clinical response to interferon beta therapy in relapsing multiple sclerosis. *J Neurol*. 2006;253:287-293.
69. Freedman MS, Forrestal FG. Canadian treatment optimization recommendations (TOR) as a predictor of disease breakthrough in patients with multiple sclerosis treated with interferon beta-1a: analysis of the PRISMS study. *Mult Scler*. 2008;14:1234-1241.
70. Río J, Rovira A, Tintoré M, et al. Relationship between MRI lesion activity and response to IF8N-beta in relapsing-remitting multiple sclerosis patients. *Mult Scler*. 2008;14(4):479-484.
71. Portaccio E, Zipoli V, Siracusa G, Sorbi S, Amato MP. Switching to second-line therapies in interferon-beta-treated relapsing-remitting multiple sclerosis patients. *Eur Neurol*. 2009;61:177-182.
72. International Working Group for Treatment Optimization in MS. Treatment optimization in multiple sclerosis: report of an international consensus meeting. *Eur J Neurol*. 2004;11:43-47.
73. Miller A, Dishon S. Health-related quality of life in multiple sclerosis: the impact of disability, gender and employment status. *Qual Life Res*. 2006;15(2):259-271.
74. Al-Sabbagh A, Bennet R, Kozma C, et al. Medication gaps in disease modifying therapy for multiple sclerosis are associated with an increased risk of relapse: findings from a national managed care database. *J Neurol*. 2008;255(Suppl 2):S79.
75. Costello K, Kennedy P, Scanzillo J. Recognizing nonadherence in patients with multiple sclerosis and maintaining treatment adherence in the long term. *Medscape J Med*. 2008;10(9):225.
76. Cohen BA. Adherence to disease-modifying therapy for multiple sclerosis. *Int J MS Care*. 2006;(February Supplement):32-37.
77. Río J, Porcel J, Téllez N, et al. Factors related with treatment adherence to interferon beta and glatiramer acetate therapy in multiple sclerosis. *Mult Scler*. 2005;11:306-309.
78. Clerico M. Adherence to interferon-beta treatment and results of therapy switching. *J Neurol Sci*. 2007;259:104-108.
79. Goodin DS, Biermann LD, Bohlega S, et al. Integrating an evidence-based assessment of benefit and risk in disease-modifying treatment of multiple sclerosis. *Curr Med Res Opin*. 2007;23:2823-2832.
80. Consortium of Multiple Sclerosis Centers. Comprehensive Care in Multiple Sclerosis. White Paper. 2010. http://mscare.org/cmsc/. Accessed August 15, 2011.
81. Caon C. Maximizing therapeutic outcomes in patients failing on current therapy. J Neurol Sci. 2009;277(Suppl 1):S33-36.
82. Freedman MS, Cohen B, Dhib-Jalbut S, et al. Recognizing and treating suboptimally controlled multiple sclerosis: steps toward regaining control. *Curr Med Res Opin*. 2009;25:2459-2470.
83. Goodman S, Gulick EE. Dietary practices of people with multiple sclerosis. *Int J MS Care*. 2008;10:47-57.
84. Healy BC, Ali EN, Guttman CR, et al. Smoking and disease progression in multiple sclerosis. *Arch Neurol*. 2009;66(7):858-864.
85. Khurana SR, Bamer AM, Turner AP, et al. The prevalence of overweight and obesity in veterans with multiple sclerosis. *Am J Phys Med Rehabil*. 2009;88(2):83-91.
86. Turner A, Kivlahan DR, Kazis LE, Haselkorn JK. Smoking among veterans with multiple sclerosis: prevalence correlates, quit attempts and unmet need for services. *Arch Phys Med Rehabil*. 2007;88(11)1394-1399.
87. White LJ, Dressendorfer RH. Exercise and multiple sclerosis. *Sports Med*. 2004;34(15):1077-1100.
88. Grossman P, Kappos L, Gensicke H, et al. MS quality of life, depression and fatigue improve after mindfulness training: a randomized trial. *Neurology*. 2010;75(13):1141-1149.
89. Cohen BA. Identification, causation, alleviation, and prevention of complications (ICAP). *Neurology*. 2008;71(24 Suppl 3):S14-S20.
90. Tullman M. Symptomatic therapy in multiple sclerosis. *Continuum*. 2004;10(6):142-172.
91. de Sa JC, Airas L, Bartholome E, et al. Symptomatic therapy in multiple sclerosis: a review for a multimodal approach in clinical practice. *Ther Adv Neurol Disord*. 2011;4(3):139-168.
92. Motl RW, Suh Y, Weikert M. Symptom cluster and quality of life in multiple sclerosis. *J Pain Symptom Manage*. 2010;42(4):212-216.
93. Samkoff LM, Goodman AD. Symptomatic management in multiple sclerosis. *Neurol Clin*. 2011;29:449-463.
94. Wallin MT. Integrated multiple sclerosis care: new approaches and paradigm shifts. *J Rehabil Res Dev*. 2010;47(6):ix–xiv.

PRACTICAL STRATEGIES FOR MANAGING MULTIPLE SCLEROSIS IN THE FEDERAL HEALTHCARE SYSTEM

CME/CE EVALUATION AND POST-TEST

Expiration Date: August 28, 2012

TE025NEU11 NL1 8-29-11 1/3

To earn CME/CE credit, complete the evaluation, attestation, and post-test, answering 70 percent of the questions correctly. If completing the evaluation in print form, please use all capital letters and print your name, address, and other information requested below.

Send originals to: Med-IQ, 5523 Research Park Drive, Suite 210, Baltimore, Maryland 21228, or fax to 443 543 5210 by August 28, 2012. For mailed or faxed evaluations, allow 4 to 6 weeks from receipt of evaluation form for delivery of statement of credit.

The purpose of this evaluation is to receive your feedback so we may improve future educational activities. All responses are confidential but may be evaluated in aggregate. Thank you.

PARTICIPANT INFORMATION

Date of Participation in Activity: _____

First Name: _____ Last Name: _____

Degree/Profession: ❒ MD ❒ DO ❒ PharmD ❒ RPh ❒ PhD ❒ PA ❒ RN ❒ NP ❒ LPN ❒ Other: _____

Specialty: _____

Address 1: _____

Address 2: _____

City/State/Zip: _____

Phone: _____ Fax: _____ E-mail: _____

Type of practice: ❒ VA Medical Center ❒ Community-Based Outpatient Clinic ❒ Community Living Center ❒ VET Center

❒ Domiciliary ❒ Other _____

Approximately how many patients do you see each week? _____

Of these patients, approximately what percentage have multiple sclerosis? _____ %

ACTIVITY EVALUATION

Rate the extent to which this CME activity met the following learning objectives:	Minimally 1	2	3	4	5	6	Completely 7	N/A
1. Explain the importance of early and ongoing treatment in MS	❒	❒	❒	❒	❒	❒	❒	❒
2. Outline the differences in disease presentation and treatment between veteran and non-veteran MS populations and describe resources available through the VHA to optimize the care of veterans with MS	❒	❒	❒	❒	❒	❒	❒	❒
3. Identify appropriate patient candidates for DMTs, select appropriate treatment options, and describe methods for monitoring disease status	❒	❒	❒	❒	❒	❒	❒	❒
4. Describe key components of symptomatic management and wellness approaches to MS	❒	❒	❒	❒	❒	❒	❒	❒

Rate the extent to which this CME activity:	Minimally 1	2	3	4	5	6	Completely 7	N/A
Met your expectations	❒	❒	❒	❒	❒	❒	❒	❒
Is applicable to your practice	❒	❒	❒	❒	❒	❒	❒	❒
Used appropriate teaching methods	❒	❒	❒	❒	❒	❒	❒	❒
Provided current scientific evidence to support content	❒	❒	❒	❒	❒	❒	❒	❒
Addressed barriers to optimal patient management	❒	❒	❒	❒	❒	❒	❒	❒
Provided useful non-educational resources (eg, patient handouts, tools to assess practice, resources)	❒	❒	❒	❒	❒	❒	❒	❒
Addressed the following 6 core competencies:								
Patient care	❒	❒	❒	❒	❒	❒	❒	❒
Medical knowledge	❒	❒	❒	❒	❒	❒	❒	❒
Interpersonal and communication skills	❒	❒	❒	❒	❒	❒	❒	❒
Professionalism	❒	❒	❒	❒	❒	❒	❒	❒
Systems-based practice	❒	❒	❒	❒	❒	❒	❒	❒
Practice-based learning and improvement	❒	❒	❒	❒	❒	❒	❒	❒

	Needs Improvement 1	2	3	Average 4	5	Outstanding 6	7
Compared to all other CME activities similar to this one that I have participated in over the past year, I would rate this program as:	❒	❒	❒	❒	❒	❒	❒

Did this activity provide fair and balanced content free from commercial bias? ❒ Yes ❒ No
(Commercial bias is defined as information presented that advocates a specific proprietary business product or service of a commercial interest.)

As a result of this learning experience, what will you do differently in the care of your patients? _____

_____

How will you implement these changes? _____

Which of the following practice changes do you intend to implement as a result of participating in this learning experience?
A. I will investigate the resources available to MS patients within the VA health system
B. I will consider initiating a DMT or referring to a specialist for the initiation of a DMT in my patients with confirmed or suspected relapsing forms of MS
C. In my patients who are receiving DMTs, I will routinely monitor for medication adherence, adverse effects, and treatment response
D. I will use an active approach when evaluating patients for MS-related symptoms
E. Other (please specify): _____
F. None

Are there specific barriers to multiple-sclerosis patient management that you feel better equipped to address as a result of this activity? If so, please list them.

_____

Are there specific barriers to multiple-sclerosis patient management that this activity did not address? If so, please list them.

_____

I would like to see CME/CE activities on these topics: _____

Other comments (eg, what can we do to improve future CME/CE activities?): _____

ATTESTATION AND SIGNATURE REQUIRED TO RECEIVE CREDIT:

Physicians: I claim ❒ _____ (maximum 1.0) *AMA PRA Category 1 Credit™*

Pharmacists: I claim ❒ _____ (maximum 1.0) contact hour/0.10 CEU

Signature: _____ **Date:** _____

Post-Test

Name

(Please Print)

TE025NEU11 NL1 8-29-11 3/3

1. Which of the following factors has NOT been shown to influence the risk of developing MS?

A. Geography (latitude)
B. Smoking
C. Viral infections
D. Vitamin C levels

2. Benign MS is a form of which of the following subtypes of MS?

A. RRMS
B. PPMS
C. SPMS
D. PRMS

3. Treatment goals for MS include preventing long-term disability and reducing rates of relapse.

A. True
B. False

4. Which of the following parameters are recommended for monitoring disease status and patient response to treatment with DMTs?

A. The presence of gadolinium-enhancing or T2 lesions on MRI scans
B. Increasing EDSS scores
C. Increasing relapse rates
D. All of the above

5. When patients demonstrate suboptimal response to treatment with DMTs, which of the following is a recommended strategy for optimizing treatment:

A. Decrease dosage of interferon β
B. Switch from interferon β to glatiramer acetate (or vice versa)
C. Increase dosage of mitoxantrone
D. Increase dosage of natalizumab

6. Approximately one-half of patients with MS will reach two major clinical benchmarks of impaired mobility within 10-20 years of disease onset.

A. True
B. False

7. Veterans with MS can apply for service-connected benefits as long as the MS developed during service or within how many years after service?

A. 3 years
B. 5 years
C. 7 years
D. 10 years

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