

Disability and treatment patterns of multiple sclerosis patients in United States: A comparison of veterans and nonveterans

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Abstract—The Veterans Health Administration (VHA) is the largest integrated healthcare system in the world and provides care to approximately 20,000 multiple sclerosis (MS) patients. Here, we report that these MS patients are disproportionately more likely to be older, male, unemployed, and disabled with lower levels of education and financial resources when compared to veterans not receiving care within the VHA or to nonveteran MS patients. When comparing the VHA MS patients to a cohort of nonveteran MS patients matched for age, sex, and disability, we found that veterans receiving care within the VHA were equally likely to have received care from a neurologist and more likely to have received care from rehabilitation specialists and primary care physicians than nonveterans. Similarly, veterans in the VHA were more likely to receive therapy with certain symptomatic medications but were less likely to be treated with disease-modifying agents for MS (DMAMS) than nonveterans. When treated with DMAMS, they are more likely to be treated with Avonex and significantly less likely to receive treatment with Copaxone or Novantrone.

Key words: *databases, disability, disease-modifying agents for multiple sclerosis, multiple sclerosis, symptomatic therapy, treatment patterns, Veterans Health Administration.*

INTRODUCTION

Multiple sclerosis (MS), one of the most common disabling diseases of young adults, is an inflammatory demyelinating disorder of the central nervous system with an estimated prevalence of about 250,000 to 350,000 patients in the United States (U.S.) (1,2). First symptoms of the disease usually appear at the young adult age, but the disease may also become evident later in life. The course of MS is highly variable and makes studies of etiology and possible mechanisms of treatment challenging. For most patients, MS starts with a relapsing-remitting pattern with episodic exacerbations of neurological dysfunction, which remit completely or partially. Over the years, for most patients, the disease develops into the secondary progressive form with accumulated disability (1,3,4).

The cause of MS is unclear, but it is currently believed that an environmental trigger initiates the disease in genetically susceptible hosts (5). Although the etiology of MS is unclear, epidemiological studies have identified the demographic characteristics that increase the risk for developing MS to be female gender, Caucasian race, relatively high socioeconomic status, and geographic location (1,5).

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There are Food and Drug Administration (FDA)-approved disease-modifying agents for MS (DMAMS), which the National Multiple Sclerosis Society recommends that patients start as early in the disease course as possible (6,7). However, at best, these are partially effective therapies and very expensive. Therefore, the type of healthcare insurance carried by patients may impact their treatment patterns (8). MS remains progressive in the majority of patients, generally resulting in chronic symptoms and disability, which also require medical intervention (3,4). Recent estimates of disease-associated costs place the average direct and indirect health-related costs per MS patient per year at \$35,000 (9–11). For a large healthcare system, such as the VHA, that may provide care for up to 20,000 MS patients, the direct healthcare costs for MS patients can be quite significant.

In this paper, using data from the NARCOMS (North American Research Committee on MS) Patient Registry, we compare the demographic characteristics and treatment of those veteran MS patients who receive their healthcare from the VHA to that of veterans not in the VHA and nonveterans.

NARCOMS PATIENT REGISTRY

The NARCOMS Patient Registry, a project of the Consortium of MS Centers in collaboration with Yale University, is a long-term study initiated at the end of 1996 to promote and facilitate clinical and epidemiological research in MS (12). The Registry, with more than 20,000 participants, provides us with a unique opportunity to study MS patient characteristics and treatment patterns in a large sample. We have used this database to investigate the demographics and current treatment patterns among U.S. patients in contrast to U.S. veterans diagnosed with MS receiving care in the VHA (13).

Participation in the Registry is patient-driven. Patients are recruited through various sources, including an “800” phone number, the Registry web site, MS centers, various publications, lectures, support groups, and direct mailings. Registry participants receive a quarterly publication with research articles on current issues in MS and information on recruiting for clinical trials (14).

A group of Registry patients is veterans from the U.S. Armed Forces who receive their care from the U.S. VHA (4). This is a unique healthcare delivery system in the United States, and it resembles nationalized health-

care systems such as that of Canada. The VHA offers comprehensive healthcare to eligible veterans for their medical needs and prescriptions, as well as preventive care (15).

With the help of the Eastern Paralyzed Veterans Association (EPVA) and Paralyzed Veterans of America (PVA), the NARCOMS Patient Registry conducted a concentrated recruitment of veterans with MS in 1998. As a result, over 4,000 veterans registered. Thus, this database is in a unique position to do a comparison study between veterans and nonveterans in terms of demographic characteristics, MS characteristics, and treatment patterns.

DATA COLLECTION

As patients enrolled in the Registry, we collected data with the use of mailed questionnaires and a secure web site on the Internet. The prerequisite for participation is diagnosis with MS. We collected data on demographic information, healthcare insurance, MS-related medical history, DMAMS, symptomatic therapies, and healthcare services used. We also collected disability and handicap data using validated patient-driven instruments. Two disability and handicap scales were used. The PDDS (Patient-Determined Disease Steps) is an eight-level scale (0 = normal to 8 = bedridden) that measures disability and correlates highly with EDSS (Expanded Disability Status Scale) (Spearman correlation = 0.93) (16). Like the EDSS, the PDDS is heavily influenced by gait (17). The Performance Scales reflect disability in eight domains of functions: mobility, hand function, fatigue, vision, cognitive, sensory, bladder function, and spasticity (16). Patients rate their disability in each of these functions on a scale of 0 (normal) to 5 (total disability). Time sensitive data are updated every 6 months for the majority of the registrants, and new questions are added specific to a hypothesis being tested.

Patients were assigned a disease type according to their responses to a set of questions regarding the presence of relapses at any time in the course of their disease and their disability over the previous year. Patients with relapsing-stable MS are those who report a relapse at some time in the course of their disease, but who also report that their disability is the same as or better than 1 year before the time of completing the questionnaire. The relapsing-worsening category includes patients who

have experienced a relapse and indicate that their symptoms have worsened within the last year. This category may include patients with secondary progressive MS as well as relapsing patients who are accumulating disability because of the relapses. The category of primary progressive MS includes patients who have never experienced a relapse at any time in their disease course.

MS PATIENT CHARACTERISTICS

There were 4,257 Registry participants with MS who were honorably discharged from the U.S. military and qualified as veterans. The VHA group consists of 2,150 veterans who receive healthcare from the VHA. The non-VHA group includes 2,107 veterans who do not receive their healthcare from the VHA. The nonveteran group ($n = 16,119$) contains all other registrants. The data reported here were collected and updated as of September 2001.

MATCHED GROUPS COMPARISON

As demonstrated in the next section, veterans with MS differ substantially from the normal demographics of large groups of MS patients. Since duration of disease, age, gender, and relapse rate correlate significantly with outcome from the standpoint of disability, direct comparison of treatment patterns in these disparate groups would be relatively uninformative (18). Therefore, to compare the treatment patterns between VHA veteran and nonveteran MS patients, we matched each VHA veteran with a nonveteran according to age, gender, and disability using the PDDS scale. This yielded comparable groups of significant size for studying treatment patterns ($n = 1,704$ per group).

STATISTICAL ANALYSIS

Analyses were done with the use of the SAS statistical package version 8 (SAS Institute, Inc., Cary, NC). We present descriptive analyses and evaluate group differences by using the chi-square test or the Fisher exact test for the unmatched group. For the matched group, we used McNamer's test. For contrasts of dimensional variables, the Student t-test and the Wilcoxon rank-sum test were used for the unmatched groups. For the

matched groups, paired t-tests were used. Bonferroni method was used to adjust the p values when doing multiple comparison tests.

RESULTS

Demographic Comparisons

The demographic characteristics of participants in the NARCOMS Patient Registry are very similar to those identified in the "Portrait of Multiple Sclerosis," published by the National Multiple Sclerosis Society in 1989 (19). Overall, the Registry data agree with the generally accepted MS patient characteristics: 77 percent are female, 94 percent are Caucasian, and 37 percent are classified as disabled. Average age at time of first symptom onset is 29, and average disease duration from symptom onset is 18 years. Forty-nine percent are categorized as relapsing-stable MS, 36 percent relapsing-worsening MS, and 10 percent primary progressive MS. Twenty percent of patients report having blood relatives with MS (1,5).

Veteran MS patients in the VHA were compared to veterans not in the VHA and to the rest of the patients in the NARCOMS Registry (**Table 1**). The 3:1 female-to-male ratio normally seen in MS is reversed in the veteran population, particularly among veterans in the VHA (1). The mean age of VHA veterans and non-VHA services (53 and 52 years, respectively) is significantly higher than the rest of the MS population (46 years, $p < 0.0001$). There is a significant difference in duration of the disease among veterans in VHA, non-VHA veterans, and the rest of MS patients (18, 14, and 11 years, respectively; $p < 0.0001$). Of veterans using the VHA, 14 percent are employed as compared to 32 percent of veterans in the non-VHA group and 38 percent of the rest of the MS population ($p < 0.0001$). A higher proportion of VHA patients report a yearly income below \$30,000 (43 percent) than in the non-VHA veteran (35 percent) and nonveteran patients (34 percent) ($p < 0.0001$).

As expected, a higher proportion of VHA patients reports relapsing-worsening disease (42 percent) as compared to all other patients (36 percent). The percent of patients reporting primary progressive MS is higher in both veteran cohorts, which is not unexpected in that this form of MS is more common in men (18,20,21). Similarly, a lower number of patients in the VHA group reported having a relapse in the past year (65 percent)

Table 1.

Characteristics of veterans in and out of VA system and nonveteran MS patients in the NARCOMS Registry. (Less than 2% of patients have missing information in most categories, unless noted otherwise.)

Characteristics	VHA Veterans (n = 2,150)	Non-VHA Veterans* (n = 2,107)	Nonveterans† (n = 16,119)
Mean age (±SD), y	53 (±11)	52 (±11) ^{††}	46 (±10) [¶]
% Male	85	66 [¶]	17 [¶]
Mean duration of disease (±SD), y	18 (±12)	14 (±11) [¶]	11 (±9) [¶]
% Education: associate's degree & lower	67	61 [¶]	61 [¶]
% Income ≤ \$30,000	43	35 [¶]	34 [¶]
% Employed outside home	14	32 [¶]	38 [¶]
Disease Course[‡]			
% Relapsing-stable	39	43 ^{‡‡}	49 [¶]
% Relapsing-worsening	42	36 [¶]	36 [¶]
% Primary progressive	12	15 ^{††}	10 ^{††}
% Ever had a relapse	80	78 ^{††}	85 ^{**}
% Relapse in past year [§]	65	63 ^{‡‡}	69 ^{††}

* Comparison between veterans in VHA and veterans not in VHA.
† Comparison between veterans in VHA and nonveterans.
‡ Approximately 6% in each cohort are unsure.
§ Denominator is the number of patients whoever had relapse.

¶ Significant at $p < 0.0001$ (Bonferroni adjusted).
** Significant at $p < 0.01$ (Bonferroni adjusted).
†† Significant at $p < 0.05$ (Bonferroni adjusted).
‡‡ Not significant at $p < 0.05$ (Bonferroni adjusted).

as compared to the rest of MS population (69 percent) ($p < 0.05$), which is consistent with the older mean age of the veterans group (18).

As seen in **Table 2**, disability, in general, is significantly higher in veterans than in the nonveterans. The mean PDDS in the VHA veterans is 5.0, whereas it is

Table 2.

Mean handicap and disability scores of veterans in and out of VHA and nonveteran MS patients (±SD).

Disability and Handicap Scales	VHA Veterans (n = 2,150)	Non-VHA Veterans* (n = 2,107)	Nonveterans† (n = 16,119)
PDDS	5.0 (±2.1)	4.0 (±2.3) [§]	3.6 (±2.3) [§]
Performance Scales score [‡]	2.4 (±1.0)	1.9 (±0.9) [§]	1.8 (±0.9) [§]
Performance Scale Subscores			
Cognition	2.0 (±1.4)	1.6 (±1.3) [§]	1.6 (±1.3) [§]
Hand function	2.5 (±1.6)	1.9 (±1.5) [§]	1.7 (±1.4) [§]
Vision	1.9 (±1.4)	1.4 (±1.3) [§]	1.4 (±1.2) [§]
Spasticity	2.5 (±1.5)	2.0 (±1.4) [§]	1.9 (±1.4) [§]
Fatigue	3.2 (±1.3)	2.8 (±1.4) [§]	2.7 (±1.4) [§]
Pain (not tremor)	2.1 (±1.5)	1.6 (±1.4) [§]	1.7 (±1.4) [§]
Depression	1.5 (±1.3)	1.2 (±1.1) [§]	1.3 (±1.2) [§]
Bladder	2.6 (±1.5)	2.0 (±1.4) [§]	1.9 (±1.4) [§]

* Comparison between veterans in VHA system and veterans not in VHA system.

† Comparison between veterans in VHA system and nonveterans.

‡ Mean and standard deviation of performance scale score taken from the average performance score (i.e., cognition → bladder) of each subject within a cohort.

§ Significant at $p < 0.0001$.

only 4.0 in non-VHA veterans and 3.6 in nonveteran MS patients ($p < 0.0001$). Comparison of the PDDS, even when correcting for age, indicates a significantly higher level of disability in veterans in general and in veterans receiving healthcare within the VHA in particular (data not shown). Similarly, VHA veterans report higher levels of handicap on all performance scale subscores as compared to non-VHA veterans and nonveterans ($p < 0.0001$). There is a trend for slightly higher handicap and disability scores in non-VHA veterans as compared to nonveterans,

which is consistent with the slightly older age and male gender of this group (18).

Patterns of Symptomatic Medication Use

Table 3 demonstrates patterns of use of selected classes of symptomatic therapies for MS patients in each group that are reporting moderate to total handicap on the performance scale subscores for fatigue, spasticity, bladder dysfunction, or depression. The overall use of medications for fatigue is slightly lower in VHA veterans (23.8 percent) than in non-VHA veterans (25 percent)

Table 3.
Current use of symptomatic drugs by MS patients in Registry (%).

Selected Symptomatic Drugs	VHA Veterans (<i>n</i> = 2,150)	Non-VHA Veterans* (<i>n</i> = 2,107)	Nonveterans† (<i>n</i> = 16,119)
Total number of patients with fatigue‡	<i>n</i> = 1572	<i>n</i> = 1285	<i>n</i> = 9300
Medications used for fatigue	23.8	25.0	26.7††
Symmetrel	18.6	12.9§	14.8¶
Cylert	2.5	5.3¶	4.7¶
Ritalin	3.0	2.6	3.0
Provigil	2.7	7.2§	7.8§
Dexedrine	0.4	0.2	0.5
Total number of patients with spasticity‡	<i>n</i> = 1075	<i>n</i> = 771	<i>n</i> = 5203
Medications used for spasticity	69.5	64.7	66.3
Lioresal	50.7	42.0¶	41.3§
Valium	18.3	11.4§	12.5§
Neurontin	12.6	14.5	15.1
Elavil	12.0	8.3††	10.2
Zanaflex	12.3	19.3¶	19.4§
Klonopin	9.9	8.8	9.4
Botox	0.5	0.5	0.5
Total number of patients reporting bladder problems‡	<i>n</i> = 1053	<i>n</i> = 745	<i>n</i> = 5008
Medications used for bladder dysfunction	32.3	25.5**	34.1
Ditropan	26.0	17.3§	23.1
Ditropan XR	1.7	3.6††	5.8§
DDAVP (Desmopressin)	0.9	0.8	1.4
Detrol	5.0	6.7	9.3§
Macrochantin	3.6	2.0	3.1
Levsinex	1.1	1.5	1.4
Total number of depressed patients‡	<i>n</i> = 322	<i>n</i> = 227	<i>n</i> = 1766
Drugs used for depression	38.8	37.4	42.6
Prozac	15.2	14.5	17.8
Paxil	6.5	7.5	6.5
Zoloft	18.9	15.0	16.9
Effexor	1.6	3.5	4.6††
Total number of patients with pain‡	<i>n</i> = 588	<i>n</i> = 414	<i>n</i> = 3199
Drugs used for pain	14.1	8.5††	8.5§
Tegretol	11.6	7.5	6.9§
Dilantin	—	—	—

* Comparison between veterans in VHA system and veterans not in VHA system.

† Comparison between veterans in VHA system and nonveterans.

‡ Includes only patients who report moderate to total disability in fatigue, spasticity, depression, bladder/bowel, or pain.

§ Significant at $p < 0.0001$ (Bonferroni adjusted).

¶ Significant at $p < 0.001$ (Bonferroni adjusted).

** Significant at $p < 0.01$ (Bonferroni adjusted).

†† Significant at $p < 0.05$ (Bonferroni adjusted).

and nonveterans (26.7 percent) ($p < 0.05$), even though veterans overall report significantly higher levels of fatigue (as seen in **Table 2**). The use of specific antifatigue agents varies substantially between the VHA population and the non-VHA population of MS patients. In particular, modafinil (Provigil) is used at a low rate within the VHA population (2.7 percent), as compared to non-VHA MS patients (>7 percent) despite a recent approval for this agent by the FDA for an MS indication ($p < 0.0001$). The percent of VHA veterans and nonveterans on medication for spasticity, bladder dysfunction, and depression are similar. Curiously, non-VHA veterans (25.5 percent) report a substantially lower use of bladder medications when controlled for symptom severity than VHA veterans (32.3 percent) ($p < 0.01$).

Despite similar overall use of symptomatic medications in the symptom categories of spasticity, bladder dysfunction, and depression, there are differences in the patterns of use of specific agents. For example, newer medications such as Zanaflex, Ditropan XR, Detrol, and Effexor are significantly less likely to be used by VHA veterans with MS than non-VHA MS patients ($p < 0.05$ to 0.0001).

Comparison of Matched Veterans and Nonveterans

To allow us more accurately to explore issues related to treatment patterns between nonveterans and veterans receiving care within the VHA, we did an analysis matching for age, gender, and disability. The results of this match are demonstrated in **Table 4**. Although some statistically significant differences remain between the

two groups, the magnitude of these differences is small. Since currently available DMAMS (disease-modifying agents for MS) are approved, in general, only for patients with relapsing forms of MS, our matched cohorts should be biased toward the VHA veteran population. This is because our matched group exhibits a slightly higher percentage of VHA veterans reporting a relapse in the past year (55 percent) as compared to nonveterans (51 percent) ($p < 0.046$). The magnitude of this difference is also small. Therefore, we believe the two groups provide a reasonable basis for investigating treatment patterns in veterans receiving care from the VHA as compared to nonveterans receiving care outside of the system.

Figure 1 demonstrates that veterans with MS in the VHA receive care from neurologists at levels similar to nonveteran MS patients when MS-specialized neurologists and nonspecialized neurologists are combined. Use of neurologists who are recognized as MS specialists by VHA veterans is lower (67 percent) than use of such specialists by nonveterans (76 percent) ($p < 0.0001$). The use of rehabilitation specialists (physiatrists, physical therapists, and occupational therapists) is substantially higher by veterans in the VHA (30 percent) than nonveteran MS patients (21 percent) ($p < 0.0001$). VHA veterans with MS are more likely to have received care from nurse clinicians (39 versus 20 percent) and primary care providers (57 versus 49 percent) within the last year than MS patients who received care in the private sector ($p < 0.0001$). Of interest, both groups had equal access (12 percent) to visiting nurses providing services within the home environment ($p < 0.8882$).

Table 4.

Comparison analysis between veterans in VHA and nonveteran MS patients matched by age (within 5 years), gender, and disability score (PDDS). Less than 2% of patients have missing information in all categories (except age at first onset of symptoms, which have 6% missing information).

Disease Characteristics	Veterans in VHA (<i>n</i> = 1,704)	Nonveterans (<i>n</i> = 1,704)	<i>p</i> value
% Disease course	—	—	0.005
Relapsing-stable	41	38	—
Relapsing-worsening	42	39	—
Primary progressive	9	13	—
Unsure	8	8	—
% Relapse in past year	55	51	0.046
Mean age of diagnosis (\pm SD), y	36 (\pm 9)	38 (\pm 9)	<0.0001
Mean age at first onset of symptoms (\pm SD), y	29 (\pm 9)	31 (\pm 10)	<0.0001
Mean duration of disease (\pm SD), y	16 (\pm 10)	14 (\pm 9)	<0.0001
Mean performance scale score (\pm SD)*	2.3 (\pm 1.0)	2.0 (\pm 1.0)	<0.0001

* Mean and standard deviation of performance scale score taken from average performance score (i.e., cognition \rightarrow bladder) of each subject within a group.

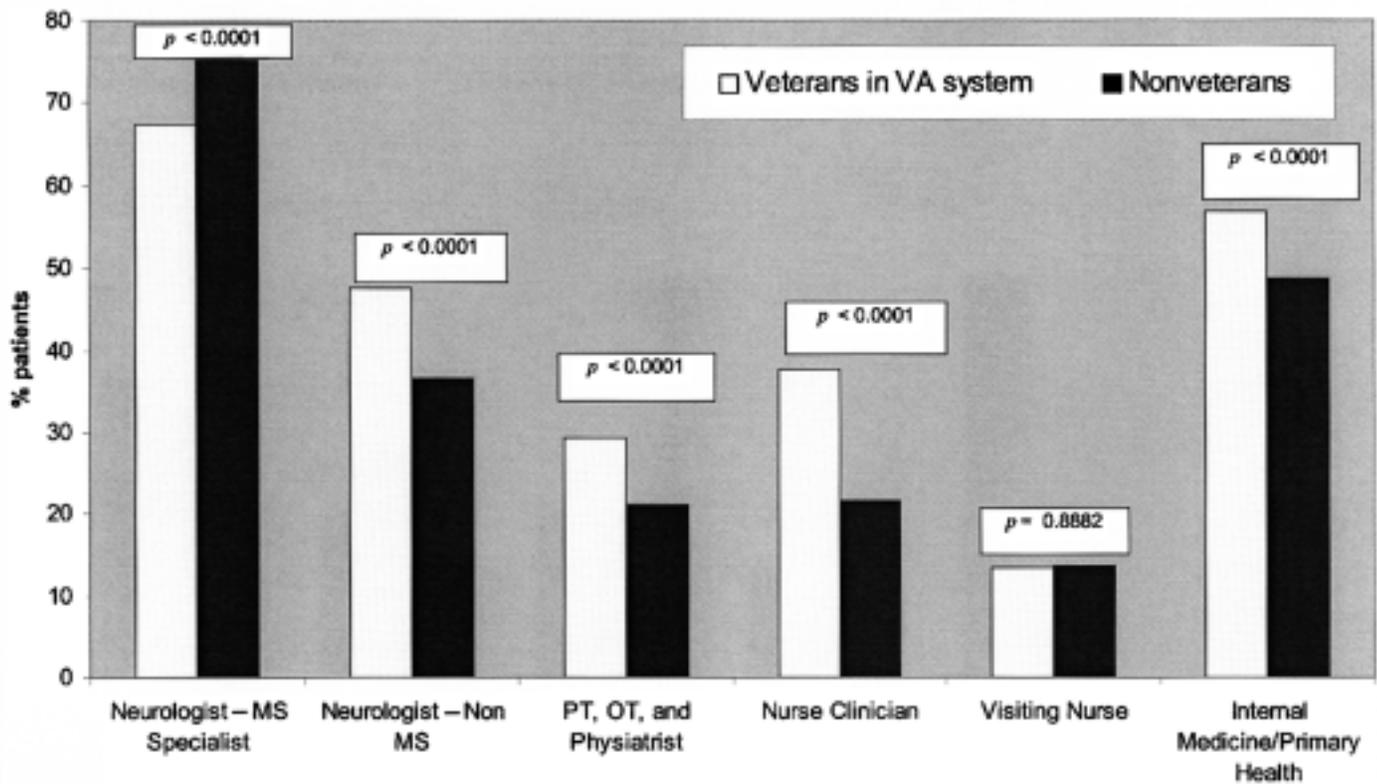


Figure 1.

Use of healthcare providers by veterans in VHA and nonveterans (matched by age, gender, and PDDS scores).

To explore patterns of medication use, we investigated the use of alternative therapies by MS patients. **Figure 2** reveals that only a minority of MS patients in either group uses over-the-counter alternative therapies regularly (<23 percent). There was no significant difference in use of alternative therapies by VHA veterans and nonveterans with relapsing forms of MS ($p > 0.15$). But VHA veterans with primary progressive MS were only half as likely (12 percent) to use alternative therapies as nonveterans MS patients with primary progressive MS (22 percent) ($p < 0.0076$).

Between 65 and 80 percent of MS patients in both groups of our study uses symptomatic medications for their MS symptoms. Relapsing-stable VHA veterans are slightly more likely to be treated with prescription medications for symptom management in MS than matched relapsing-stable MS patients receiving care in the private sector ($p = 0.0133$) (**Figure 3**). There were no differences in the overall use of symptomatic therapies between VHA veterans and nonveterans in the matched groups

with relapsing-worsening or primary progressive patterns of MS ($p = 0.0526$ and $p = 0.2354$, respectively).

However, the use of DMAMS by VHA veterans with relapsing-stable MS (40 percent) is significantly lower than for nonveteran MS patients with relapsing-stable MS (56 percent) ($p < 0.0001$) (**Figure 4**). This is true whether one is considering the FDA-approved therapies, such as interferon β 1a (Avonex), interferon β 1b (Betaseron), glatiramer acetate (Copaxone), and mitoxantrone (Novantrone), or non-FDA-approved immunosuppressive therapies, including azathioprine, methotrexate, corticosteroids, cyclophosphamide, and cladribine (data not shown). The one exception to this is the use of interferons and/or glatiramer acetate in primary progressive MS. Here, approximately 28 percent of both patient groups ($p = 0.8912$) are taking one of these medications despite that little to no data currently support their use in this patient population.

Table 5 presents a breakdown of use of each FDA-approved DMAMS. It indicates that of those patients treated with DMAMS, the pattern of use of individual

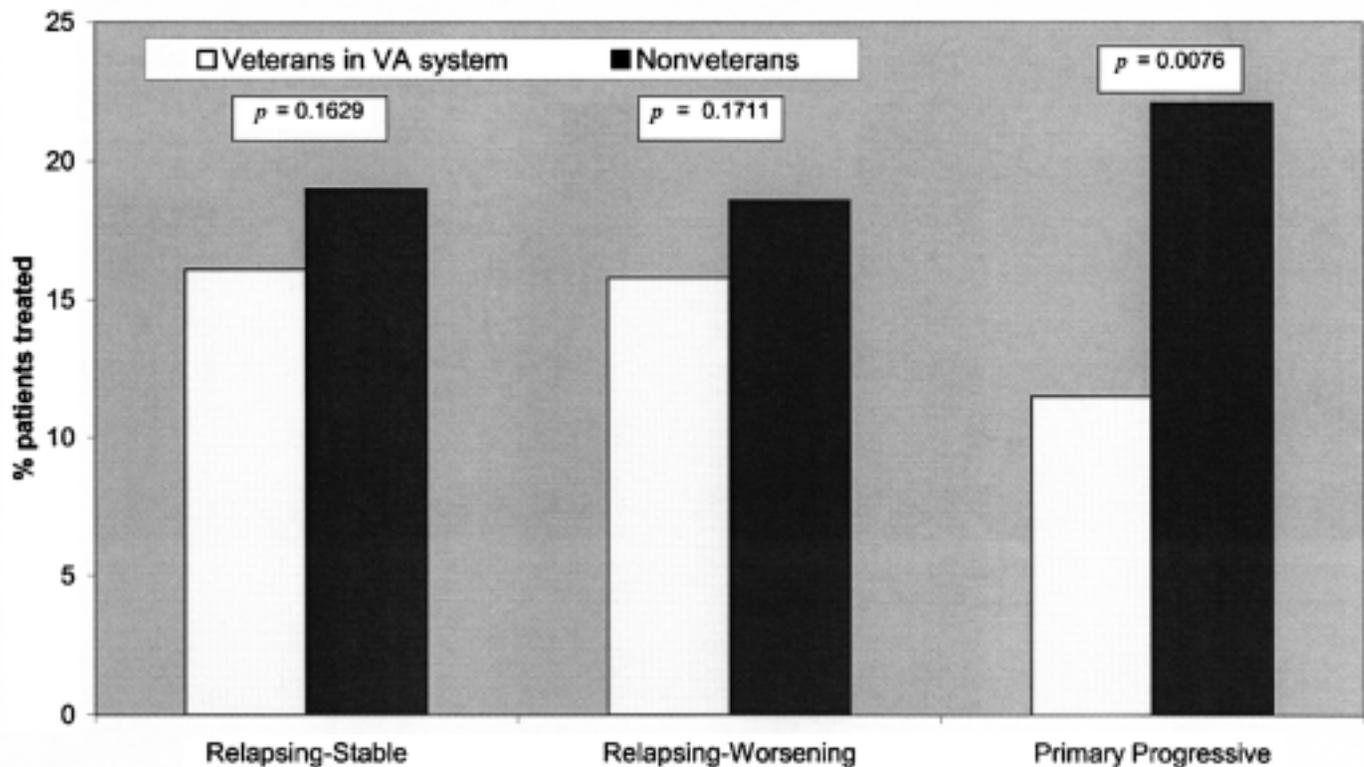


Figure 2. Current use of alternative therapies among veterans in VHA system and nonveterans (matched on age, gender, and PDSS scores) by type of MS.

agents is substantially different between veterans with MS and nonveterans. In particular, VHA veterans with MS are substantially more likely to be treated with Avonex. Among relapsing-stable VHA veterans, 54.2 percent use Avonex, whereas 48.5 percent of relapsing-worsening and 60.5 percent of primary progressive use Avonex. This compares to 41.7 percent of relapsing-stable, 38.3 percent of relapsing-worsening, and 30.8 percent of primary progressive nonveteran MS patients ($p < 0.008$, $p < 0.036$, and $p < 0.009$, respectively). VHA veterans with MS are less likely to be treated with glatiramer acetate or mitoxantrone.

DISCUSSION

Despite our database having certain selection biases, we believe it is appropriate for use in this study since both the veteran and nonveteran MS patient populations were recruited with the use of similar strategies. In addition, the demographics of the non-VHA cohort are very

similar to those described by several other authors (1,5,19). Finally, important disease characteristics, such as the percentage of patients reporting primary progressive MS, are very close to the expected percentages reported in population-based studies (20,21). These characteristics, and because the cohorts are quite large, support the use of the NARCOMS Patient Registry as a tool to explore treatment practices of different segments of the American MS patient population.

The observation that veterans receiving care within the VHA, on average, are more disabled in all measured areas than either veterans receiving care in the private sector or nonveterans is not surprising given the criteria used for services within the VHA. VHA veterans with MS are older and more likely to be male than nonveteran MS patients or even non-VHA veterans with MS, both of which are major risk factors for disability (1,18). What is surprising is that even when comparing groups matched for age, gender, and disease duration, the VHA veterans with MS appear to have a more aggressive form of MS on average than nonveteran MS patients (data not

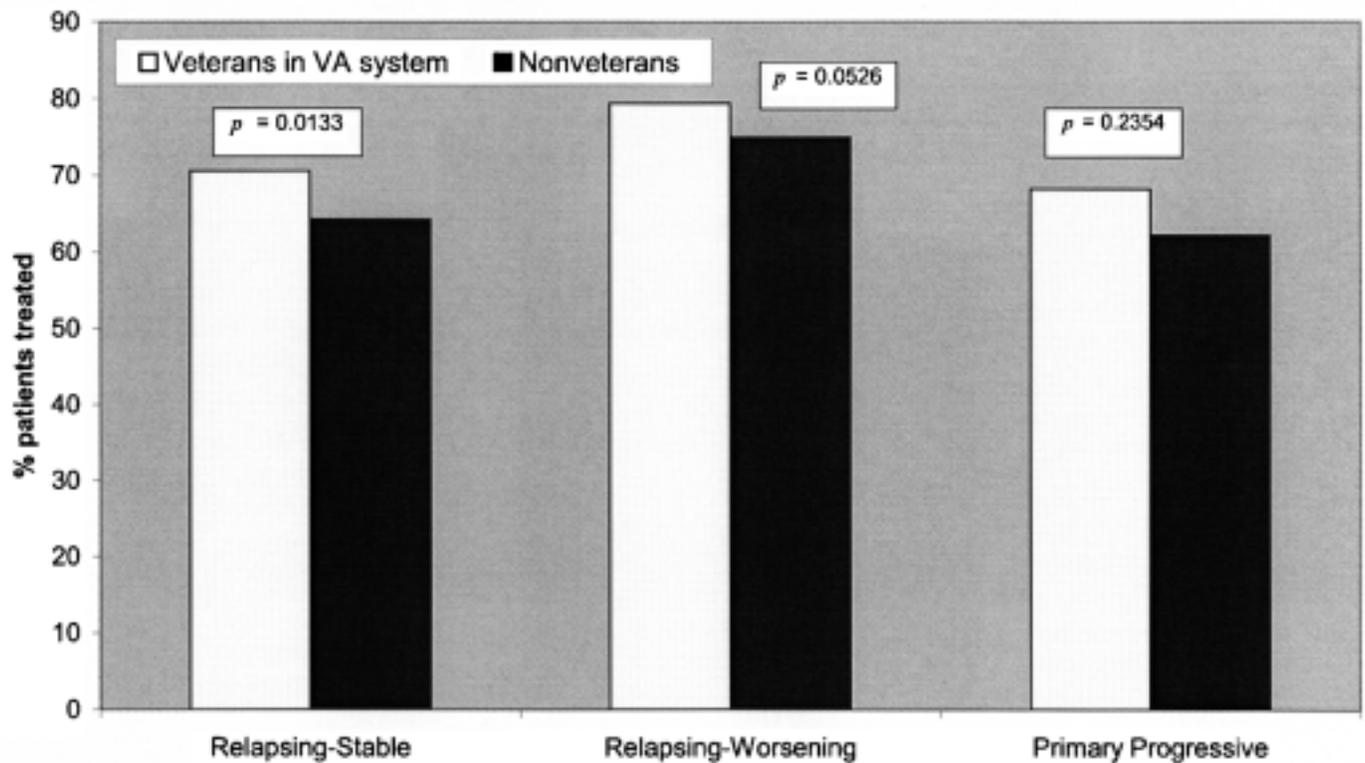


Figure 3.

Current use of symptomatic treatment among veterans in VHA and nonveterans (matched on age, gender, and PDDS score) by types of MS.

shown). The fact that the VHA MS patient population is characterized by older males who exhibit below-average levels of income and education, but have high levels of disability, has serious implications for their health-related costs.

The perception that the majority of VHA veterans with MS are in the nonrelapsing secondary progressive-phase of MS is not supported by our data. Indeed, from the standpoint of relapses, VHA veterans with MS are just as active as the non-VHA veteran and nonveteran MS patient populations. However, the percentage of patients who are in the relapsing-stable MS category is lower in the VHA population. This may be because the VHA MS patient population exhibits two risk factors for secondary progressive MS, namely male sex and older mean age (1,5,18).

Using matched groups to explore patterns of care of VHA MS patients versus nonveteran MS patients does demonstrate several significant differences. Although their access to neurologists appears to be comparable to the private sector, they are somewhat less likely to be seen in specialty clinics where they would have access to

experimental therapies and subspecialty neurology services. VHA veterans are significantly more likely to receive care from primary care providers and rehabilitation specialists. Overall, their access to healthcare providers appears to be at least comparable to and possibly superior to that of the average MS patient receiving care in the private sector.

However, the data also suggest significant differences exist in treatment patterns between the groups. Although veterans are more likely to receive symptomatic and rehabilitation therapies, they are less likely to receive DMAMS, even when matched for age, gender, and disability. However, the trend in our data suggests this gap may be narrowing (data not shown).

The pattern of use of DMAMS is more heavily biased toward Avonex than is seen in the private sector. The reason for this is unclear, but this may be a significant issue as recent studies have demonstrated superior efficacy of the higher dose formulations of interferons (22–24). The substantially lower use of Copaxone and Novantrone by VHA neurologists may reflect the slower penetration of these newer agents into the practice

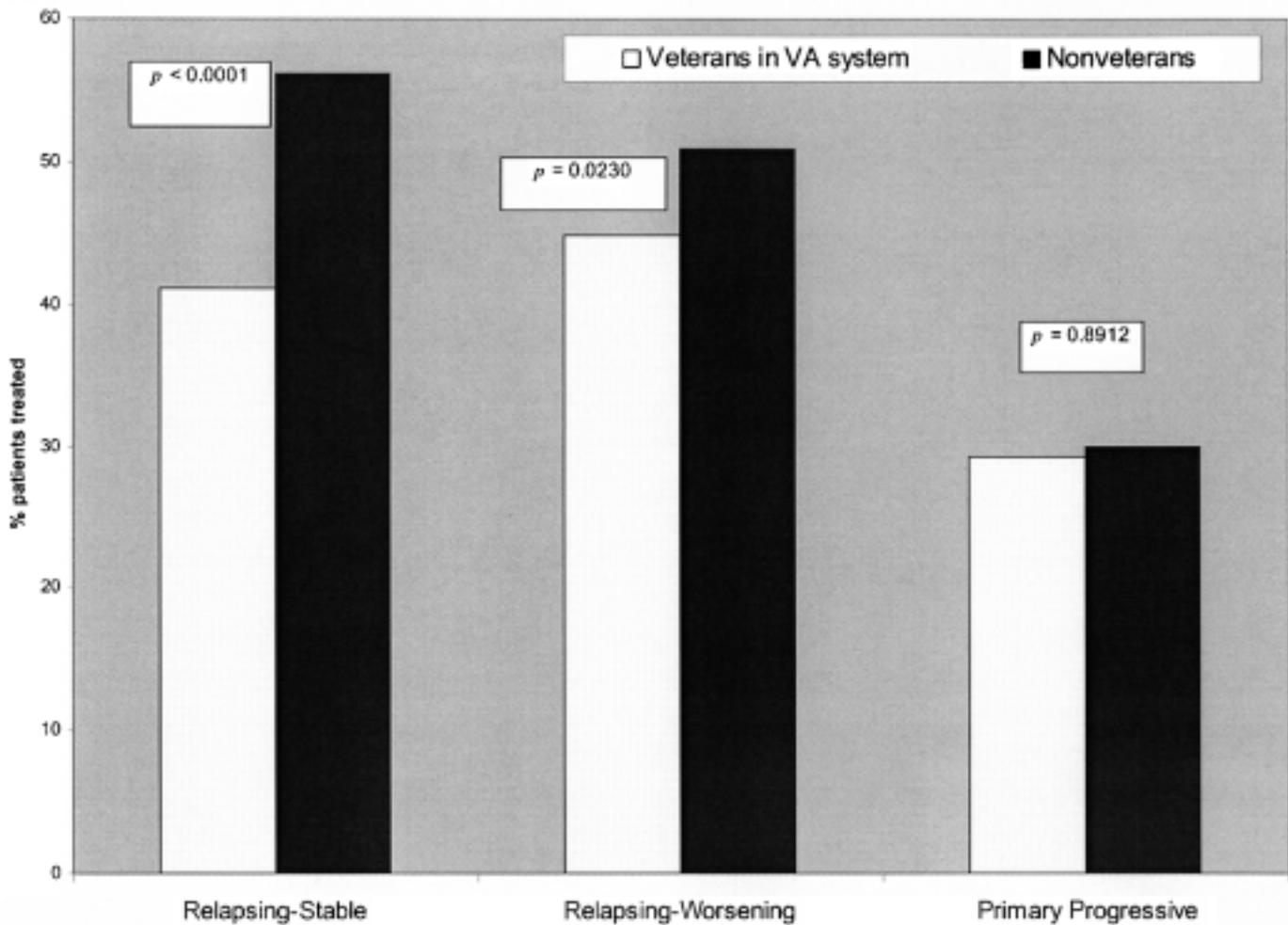


Figure 4.
Current use of Avonex, Betaseron, Copaxone, and/or Novantrone (DMAMS) therapy.

patterns of the VHA physicians (25–27). Since our data demonstrate the vast majority of prescriptions for DMAMS are written by neurologists (data not shown), one can speculate that the differences in the patterns of prescription are due to differences in educational opportunities between VHA and non-VHA neurologists. This deserves further investigation.

CONCLUSIONS

Veterans receiving care within the VHA appear to have superior access to primary care physicians and rehabilitation specialists. As expected in large centralized healthcare service organizations, the penetration of new therapies is somewhat slower than seen in the private sec-

tor. Although there is a gap in DMAMS treatment for veterans in the VHA, our data suggest this gap is narrowing. Nevertheless, there are significant variations in practice in the use of DMAMS between the VHA neurologists and non-VHA neurologists. We did not investigate the reasons for these differences in treatment practice, but suggest they deserve further investigation. In addition, some treatment patterns both in the VHA and in the private sector do not appear to be rational given studies and consensus guidelines for use of DMAMS (7). With its centralized information, the VHA management systems appear to have a significant opportunity to improve quality and cost efficiency of care provided to MS patients that could be used as a model by other healthcare systems providing care to MS patients.

Table 5.

Current use of Avonex, Betaseron, Copaxone, and Novantrone (DMAMS) therapy among veterans in VHA and nonveterans (matched on age, gender, and PDDS scores) by types of MS.

Immunologic Therapies	Veterans in VHA (n = 1,704)	Nonveterans (n = 1,704)	p value
Relapsing-stable	(n = 275)	(n = 348)	—
Avonex	54.2	41.7	0.008
Betaseron	30.2	28.7	>0.2
Copaxone	14.9	27.0	0.001
Novantrone	0.7	2.6	>0.2
Relapsing-worsening	(n = 309)	(n = 334)	—
Avonex	48.5	38.3	0.036
Betaseron	27.5	28.4	>0.2
Copaxone	22.3	28.1	>0.2
Novantrone	1.6	5.1	0.062
Primary progressive	(n = 43)	(n = 65)	—
Avonex	60.5	30.8	0.009
Betaseron	20.9	33.9	0.15
Copaxone	16.3	33.9	0.18
Novantrone	2.3	1.5	>0.2

In conclusion, the VHA provides care to a cohort of MS patients who exhibit higher levels of disability and handicap than non-VHA veterans and nonveterans receiving care in the private sector. Since healthcare costs are directly related to levels of disability and handicap in MS patients, the VHA bears a disproportionately large share of the cost of this patient population as compared to the private sector.

REFERENCES

1. Paty DW, Ebers GC. Multiple Sclerosis. Philadelphia: F.A. Davis Company; 1998. p. 5–28.
2. Noseworthy JH, Lucchinetti C, Rodriguez M, Weinshenker BG. Multiple sclerosis. *New Engl J Med* 2000; 343:938–52.
3. Weinshenker BG, Bass B, Rice GP, Noseworthy J, Carriere W, Baskerville J, Ebers GC. The natural history of multiple sclerosis: a geographically based study. I. Clinical course and disability. *Brain* 1989;112:133–46.
4. Wallin MT, Page WF, Kurtzke JF. Epidemiology of multiple sclerosis in US veterans. Long-term survival after onset of multiple sclerosis. *Brain* 2000;123:1677–87.
5. Sadovnick AD, Ebers GC. Epidemiology of multiple sclerosis: A critical overview. *Can J Neurol Sci* 1993;20:17–29.
6. National Multiple Sclerosis Society Medical Advisory Board. Disease Management consensus statement. 2001. Available from URL: www.nationalmssociety.org.
7. Goodin DS, Frohman EM, Garmany GP, Halper J, Likosky WH, Lublin FD, Silberberg DH, Stuart, WH, van den Noort S. Disease-modifying therapies in multiple sclerosis: Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. *Neurology* 2002;58:169–78.
8. Vickrey BG, Shatin D, Wolf SM, Myers LW, Belin TR, Hanson RA, Shapiro MF, Beckstrand M, Edmonds ZV, Delrahim S, Ellison GW. Management of multiple sclerosis across managed-care and fee-for-service systems. *Neurology* 2000;55:1341–49.
9. Murphy N, Confavreux C, Haas J, Konig J, Rouillet E, Sailer M, Swash M, Young C, Merot J-L. Cost of Multiple Sclerosis Study Group. Economic evaluation of multiple sclerosis in the U[nited] K[ingdom], Germany, and France. *Pharmacoeconomics* 1998;13:607–22.
10. Whetten-Goldstein K, Sloan F, Goldstein LB, Kulas ED. A comprehensive assessment of the cost of multiple sclerosis in the United States. *Mult Scler* 1998;4:419–25.
11. Henriksson F, Fredrikson S, Masterman T, Jonsson B. Costs, quality of life, and disease severity in multiple sclerosis: a cross-sectional study in Sweden. *Eur J Neurol* 2001;8:27–35.
12. Vollmer T, Ni W, Stanton S, Hadjimichael O. The NARCOMS Patient Registry: A resource for investigators. *Int J Mult Scler Care* 1999;1:12–15.
13. Vollmer TL, Ni W, Hadjimichael O. Utilization patterns of immunological therapies among VA patients with multiple sclerosis. American Neurological Association 124th Annual Meeting; 1999; Seattle, WA. Abstract published in

- Annals of the 124th Annual Meeting of the American Neurological Association. Hagerstown, MD: Lippincott Williams & Wilkins, Inc. 1999 October. p. 51.
14. Vollmer TL, editor. Multiple sclerosis quarterly report. A joint publication of Eastern Paralyzed Veterans Association and the CMSC/North American Research Committee on MS. Jackson Heights, NY: Eastern Paralyzed Veterans Association.
 15. Vollmer TL, Ni W, Hadjimichael O, Auld E. A study by the North American Research Consortium on Multiple Sclerosis (NARCOMS) of patients with multiple sclerosis in the Veterans Healthcare Administration (VHA) compared to the non-VHA population. Presented at the Rehabilitation in Multiple Sclerosis/Consortium of Multiple Sclerosis Centers (RIMS/CMSC) Joint Symposium, Basel, Switzerland; 1999. [Abstract published in *Multiple Sclerosis* 1999;5 Suppl 1:S130.]
 16. Schwartz CE, Vollmer TL, Lee H. Reliability and validity of two self-report measures of impairment and disability for MS. *North American Research Consortium on Multiple Sclerosis. Neurology* 1999;52:63–70.
 17. Kurtzke J. Rating neurological impairment in multiple sclerosis and expanded disability status scale (EDSS). *Neurology* 1983;33:1444–52.
 18. Polliack ML, Barak Y, Achiron A. Late-onset multiple sclerosis. *J American Geriatric Soc* 2001;49:168–71.
 19. Minden SL, Marder WD, Harrold LN, Dor A. Multiple sclerosis: a statistical portrait. A compendium of data on demographics, disability, and health services utilization in the United States. Prepared for the National Multiple Sclerosis Society; 1993; Cambridge (MA): Abt Associates, Inc.
 20. Cottrell DA, Kremenutzky M, Rice GPA, Koopman WJ, Hader W, Baskerville J, Ebers GC. The natural history of multiple sclerosis: a geographically based study. 5. The clinical features and natural history of primary progressive multiple sclerosis. *Brain* 1999;122:625–39.
 21. McDonnell GV, Hawkins SA. Clinical study of primary progressive multiple sclerosis in Northern Ireland, UK. *J Neurol Neurosurg Psychiatry* 1998;64:451–54.
 22. IFNB Multiple Sclerosis Study Group. Interferon β 1b is effective in relapsing-remitting multiple sclerosis: clinical results of a multicenter, randomized, double blind, placebo controlled trial. *Neurology* 1993;43:655–61.
 23. PRISMS (Prevention of Relapses and Disability by Interferon β -1a Subcutaneously in Multiple Sclerosis) Study Group. Randomized double-blind placebo-controlled study of interferon β -1a in relapsing-remitting multiple sclerosis [published erratum appears in *Lancet*, 1999;353:678.]. *Lancet* 1998;352:1498–504.
 24. Jacobs LD, Cookfair DL, Rudick RA, Herndon RM, Richert JR, Salazar AM, Fischer JS, Goodkin DE, Granger CV, Simon JH, Alam JJ, Bartoszak DM, Bourdette DN, Braiman J, Brownscheidle CM, Coats ME, Cohan SL, Dougherty DS, Kinkel RP, Mass MK, Munschauer FE, Priore RL, Pullicino PM, Scherokman BJ, Weinstock-Guttman B, Whitham RH. Intramuscular interferon β 1a for disease progression in relapsing multiple sclerosis [published erratum appears in *Ann Neurol* 1996;40:480]. *Ann Neurol* 1996;39:285–94.
 25. Johnson KP, Brooks BR, Cohen JA, Ford CC, Goldstein J, Lisak RP, Myers LW, Panitch HS, Rose JW, Schiffer RB, Vollmer TL, Weiner LP, Wolinsky JS, Copolymer 1 Multiple Sclerosis Study Group. 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; 45:1268–76.
 26. Millefiorini E, Gasperini C, Pozzilli C, D'Andrea F, Bastianello S, Trojano M, Morino S, Morra VB, Bozzao A, Calo' A, Bernini MS, Gambi D, Prencipe M. Randomized placebo-controlled trial of mitoxantrone in relapsing-remitting multiple sclerosis: 24-month clinical and MRI outcome. *J Neurol* 1997;244:153–59.
 27. Edan G, Miller D, Clanet M, Confavreux C, Lyon-Caen O, Lubetzki C, Brochet B, Berry I, Rolland Y, Froment JC, Cabanis E, Iba-Zizen MT, Gandon JM, Lai HM, Mosely I, Sabouraud O. Therapeutic effect of mitoxantrone combined with methylprednisolone in multiple sclerosis: a randomized multicentre study of active disease using MRI and clinical criteria. *J Neurol Neurosurg Psychiatry* 1997; 62:112–18.