

# Long-Term Treatment Optimization in Individuals with Multiple Sclerosis Using Disease-Modifying Therapies: A Nursing Approach



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**A**bstract: The introduction of disease-modifying therapies (DMTs) for multiple sclerosis (MS) over the last 7 years has had a significant effect on the management of those living with this disease. Initially, the focus of improving treatment outcomes was on ensuring adherence to therapy by managing drug-related adverse events. However, treatment adherence is only one facet of ensuring optimal health outcomes for patients using DMTs. Therefore, a group of 80 nurses from Canada and the United States (The North American MS Nurses' Treatment Optimization Group) developed an evidence-based nursing approach to address the various factors involved in obtaining optimal patient outcomes. The goal of this nursing approach is to ensure the best possible clinical, subclinical, psychosocial, and quality-of-life outcomes for patients with MS using DMTs.

The newer disease-modifying therapies (DMTs) for multiple sclerosis (MS)—interferon beta-1a (Rebif, Avonex), interferon beta-1b (Betaseron®) and glatiramer acetate (Copaxone®)—are the first agents shown to have a direct influence on altering the course of relapsing MS and, as such, have heralded a new era in the pharmacological treatment of the disease.

However, despite the availability and use of these agents, some patients with MS may continue to experience relapses, disease progression, and a poor quality of life. Traditionally, improving these outcomes has focused on ensuring adherence to therapy by managing treatment-

related adverse events. Adherence to therapy, however, is only one factor that is important in ensuring optimal medical and health outcomes for patients using DMTs. Other important factors that have an impact on the overall clinical and health status of patients include patient appropriateness for therapy and readiness to initiate treatment; treatment efficacy; adequate education about MS, available therapies, and self-injection training; monitoring and management of possible treatment-related adverse events; and the patient's physical, cognitive, and psychosocial status.

Achieving optimal patient outcomes is greatly influenced by the healthcare team's collaboration and assistance in identifying and overcoming problems in each of these areas. Therefore, in late 2002, MS nurses from Canada and the United States convened in Montreal, Quebec, Canada, to develop an evidence-based resource outlining nursing strategies to address potential problems that may affect the patient's overall health status and thereby achieve optimal treatment outcomes for MS patients. The result of their extensive work and collaboration is the Nursing Approach (Fig 1) presented in this paper.

*Optimization* is formally defined as the "act, process, or methodology of making something as fully perfect, functional, or effective as possible" (Merriam-Webster On-Line, 2002). Therefore, for this nursing approach, treatment optimization refers to the process used to

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ensure the best possible clinical, subclinical (e.g., magnetic resonance imaging [MRI]), psychosocial, and quality-of-life outcomes for patients with MS using DMTs.

The purpose of this paper is to guide and assist nurses through this challenging, long-term process of treatment optimization. In the first three steps of the Nursing Approach—initial assessment and patient selection, treatment selection, and patient education and self-injection training—strategies are provided to ensure that the patient is both suitable for and ready to initiate DMT, that the patient receives the most appropriate therapy possible, and that the patient receives adequate education about MS and the available therapies as well as self-injection training. For the latter steps—long-term clinical, MRI, laboratory, and psychosocial assessments and the monitoring of treatment adherence—strategies are provided for suboptimal responses on any one of these parameters. The ultimate goal in each step of this Nursing Approach is to optimize the treatment of patients with MS using DMTs.

### Initial Assessment and Patient Selection

The process of long-term treatment optimization begins with a thorough clinical and psychosocial assessment of the patient to ensure that he or she is an appropriate candidate for DMT and is ready to select and initiate treatment. To set the stage for long-term treatment optimization, the nurse should establish a trusting and supportive nurse-patient relationship at the time of initial assessment and onward.

### Initial Assessment

Many patients undergoing the initial assessment to determine treatment readiness and appropriateness for therapy have been recently diagnosed with MS. Therefore,

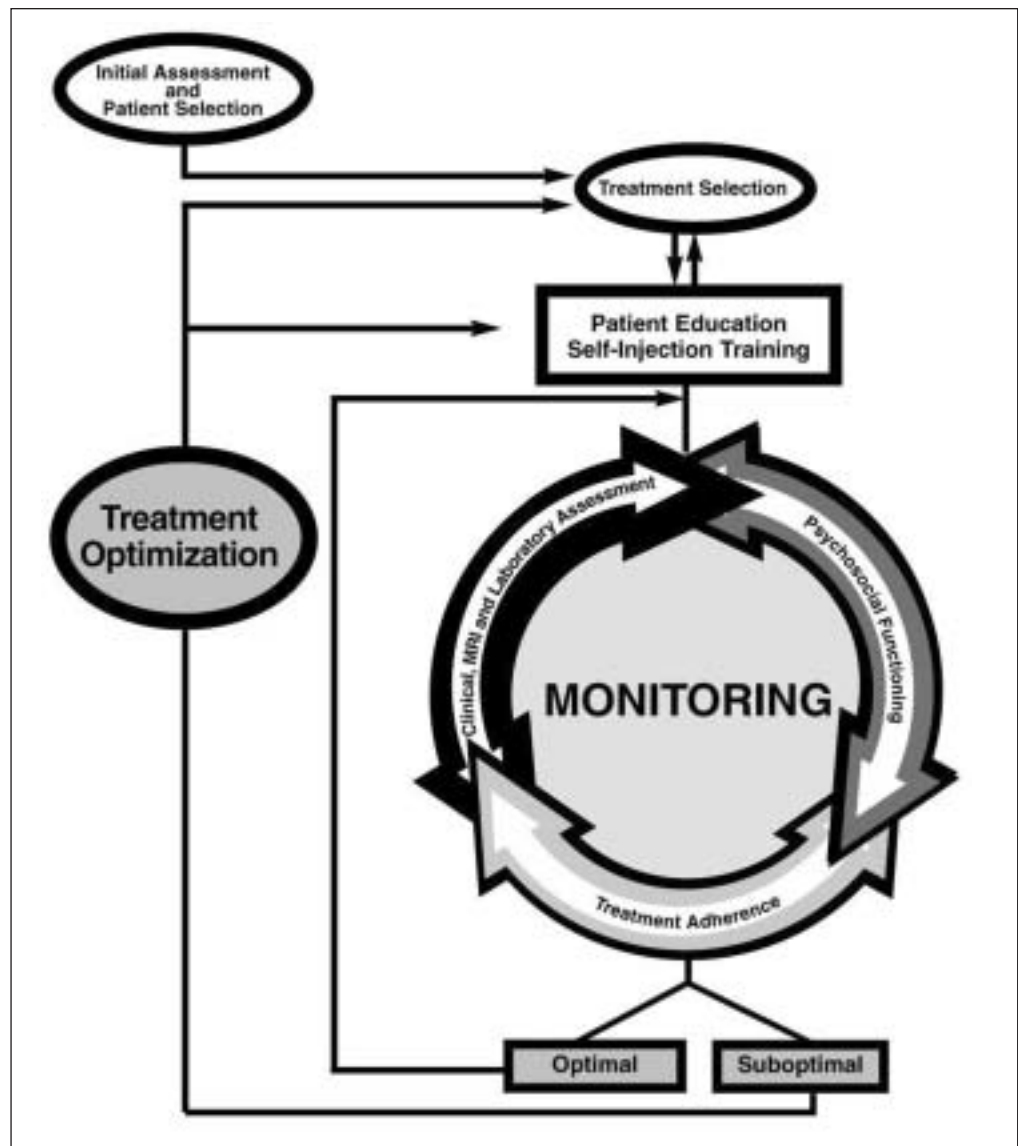


Figure 1. Nursing approach to long-term treatment optimization in individuals with MS using DMTs

before discussing issues surrounding therapy, the nurse should conduct an initial assessment that includes the following (Larivaara, Kiuttu, & Taanila, 2001):

- Establishing the patient's perceptions of the illness
- Providing a basic diagnosis
- Responding to the patient's feelings about the diagnosis
- Assessing the patient's knowledge of the illness
- Providing details of the diagnosis
- Assessing the patient's understanding of the disease.

The initial assessment also should include a thorough evaluation of clinical and psychosocial factors that may be barriers to appropriate treatment selection and initiation at a later stage. The level of the patient's disability, concomitant illnesses, and cognitive and physical functioning may all have a significant impact on both treatment decisions and outcomes. For example, cognitive impairments such as difficulty in learning and recalling

new information can interfere with a patient's ability to understand the rationale for therapy as well as the complex treatment regimen (Holland et al., 2001a).

Psychosocial factors such as the availability of support networks, financial resources, and the patient's sense of control over MS may also affect overall patient outcomes and therefore need to be assessed during the treatment selection process. Data from the Consortium of MS Centers' (CMSC) North American Research Committee on MS (NARCOMS) Patient Registry have shown that patients with lower incomes and educational levels and those with limited private insurance coverage are less likely to adhere to therapeutic regimens (Vollmer, 2002).

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*Nurses can use this model to determine the appropriate time to encourage therapy.*

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These variables may have a negative impact on the process of treatment optimization. In addition, patients who believe that health is determined by outside forces (external locus of control) are less likely to initiate or adhere to treatment than patients who believe that health is under their control (internal locus of control; Rotter, 1966). However, nurses can help patients feel more in control of their disease by ensuring that they actively participate in the clinical decision-making process and by providing access to support networks and financial resources.

#### **Appropriateness for Therapy**

The nurse, in collaboration with the neurologist, should ensure that the patient is indeed an appropriate candidate for DMT. Currently available local and/or national selection criteria should be utilized to ensure appropriateness for therapy (e.g., Oger & Freedman, 1999).

#### **Treatment Readiness**

Education alone is often not enough to enable patients to consider the initiation of DMT. The common patient question that nurses need to address in this step of the Nursing Approach is, "I'm feeling OK, so why do I need to start on treatment?" The theory of adult learning holds that people become ready to learn when they have a need to know something in order to cope more satisfactorily with tasks or problems (Knowles, 1980).

The transtheoretical model of behavior change is useful in determining patient readiness for treatment (Holland et al., 2001b; Prochaska, Redding, Harlow, Rossi, & Velicer, 1994). This model describes the process of change as long term and dynamic. Using this model, persons with MS pass through five stages as they incorporate lifestyle changes: (a) precontemplation, (b) contemplation, (c) preparation, (d) action, and (e) maintenance. In the precontemplative stage, the patient is unaware of or

is unconcerned about the benefits of treatment with a DMT and denies the personal need for therapy. The patient actively considers therapy in the contemplative stage and expresses a determination to initiate therapy in the preparation stage. In the action stage, the patient engages in the administration of therapy and in the maintenance stage continues treatment indefinitely (Holland et al., 2001b).

Nurses can use this model to determine the appropriate time to encourage therapy. The goal is to match interventions to the individual's stage of change. For example, action-oriented techniques, such as self-injection demonstrations, should not be used if the patient is still only considering treatment options (i.e., contemplative stage). Instead, patients in this stage require information about the process of initiating treatment, anticipated benefits, and potential side effects (Holland et al., 2001b).

The nurse should also assess the patient's expectations of treatment before therapy begins, because these expectations can greatly affect overall patient outcomes at a later stage. A recent pilot study as well as clinical expertise have found that, prior to treatment initiation, most patients with relapsing-remitting MS are concerned about drug effectiveness, increased fatigue, and whether treatment will make them feel sick (Lagendyk et al., 2002). These are also commonly cited reasons for treatment discontinuation. Mohr et al. (1996) found that 34%–57% of patients who begin interferon beta (IFN $\beta$ ) therapy have unrealistically optimistic pretreatment expectations. Those patients who maintained unrealistic treatment expectations, despite therapy-related educational interventions, were significantly less likely to adhere to therapy than patients with more realistic expectations. Nonadherence to an effective therapeutic regimen will have a negative impact on the benefit achieved by treatment. Therefore, direct nursing support to setting realistic treatment expectations prior to therapy selection and initiation may help ensure treatment adherence at a later stage and thereby promote treatment optimization, particularly in situations in which treatment benefit is not immediately obvious.

Even if the patient is not yet ready to initiate treatment, an individualized care plan should be developed at this point, in collaboration with the patient as well as his or her family. This plan should be flexible, dynamic, and responsive to the changing needs and level of readiness of the patient and family.

The primary objective of the initial assessment and patient selection step in the Nursing Approach is to ensure that the patient is both appropriate for and ready to select and initiate treatment. By ensuring treatment readiness prior to therapy selection, the nurse increases the likelihood of treatment optimization at a later stage.

## Treatment Selection

Sustained treatment with interferon beta-1a (IFN $\beta$ -1a), interferon beta-1b (IFN $\beta$ -1b), and glatiramer acetate (GA) in persons with relapsing-remitting MS has been associated with several positive outcomes (Bornstein et al., 1987; Chofflon, 2000; Durelli et al., 2002; IFN $\beta$  Multiple Sclerosis Study Group, 1993; IFN $\beta$  Multiple Sclerosis Study Group & The University of British Columbia MS/MRI Analysis Group, 1995; Jacobs et al., 1996; Johnson et al., 1995; O'Connor, 2002; Panitch et al., 2002; Paty & Li, 1993; PRISMS Study Group, 1998; PRISMS Study Group & The University of British Columbia MS/MRI Analysis Group, 2001; Rudick et al., 1997; Simon et al., 1998). Thus, Canadian and international guidelines emphasize the need to start treatment with these agents early in the disease course (Freedman et al., 2002; Oger & Freedman, 1999). For best results, the patient should be continued on treatment as long as benefit is realized and therapy is tolerated.

However, the process of treatment selection is not simple, because the four DMTs differ in their mode of preparation, dosage level, side-effect profile, route of administration, and proven efficacy on key patient outcome measures (i.e., relapses, progression, and MRI). Furthermore, cultural, lifestyle, and financial issues will have an impact on treatment decisions and therefore should be assessed thoroughly prior to treatment selection. The objective of these assessments is to ensure that the treatment regimen corresponds with the patient's lifestyle and cultural values. The cost of the available DMTs will also affect treatment decisions. Knowledge of financial services and resources may help the patient achieve greater financial independence; hence, nurses should direct patients and their families to community-, employee-, or government-linked financial support programs that may help address issues specific to their financial situations (The Canadian MS Nurses' Network, 2000). Family and emotional support is also critical for ensuring optimal treatment outcomes. Therefore, the nurse, in collaboration with family- and community-based healthcare professionals, should ensure appropriate support networks are available to the patient.

The patient should also be encouraged to collaborate fully with the neurologist and nurse in the treatment decision-making process. In fact, the patient is the ultimate decision maker in all aspects of his or her care and treatment (Lannon, 1997). However, for some patients, the treatment decision-making process can be very difficult, and they may rely on their nurse and/or neurologist for the appropriate decision. Therefore, it is important for the nurse to verify the degree of decision-making control that is comfortable for the patient and his or her family throughout the treatment selection process.

As the primary patient educator, the nurse plays a paramount role in providing complete and objective

information on each of the DMTs and ensuring the patient receives the most effective treatment possible based on his or her individual needs. Prior to treatment selection, the effect of each of the available DMTs on relapse frequency and severity, disease progression, and MRI findings should be discussed, and reference should be made to the approved labeling and indications of each agent, as well as to the key findings of major clinical trials on DMTs.

## Efficacy of DMTs

A report by the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology assessed the clinical utility of DMTs and included recommendations for their use based on an analysis of the supporting evidence for each therapy (Goodin et al., 2002). Table 1 summarizes the rating of evidence classification scheme used for this analysis.

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**IFN $\beta$ .** On the basis of several consistent Class I studies, IFN $\beta$  has been demonstrated to reduce the relapse rate (whether measured clinically or by MRI) in patients with relapsing-remitting MS (Type A recommendation). Treatment of MS with IFN $\beta$  produces a beneficial effect on MRI measures of disease severity, such as T2 disease burden, and probably also slows sustained disability progression (Type B recommendation; Goodin et al., 2002).

On the basis of Class I and II studies and several pieces of consistent Class III evidence, it is considered probable that there is a dose-response curve associated with the use of IFN $\beta$  for the treatment of MS (Type B recommendation). It is possible, however, that a portion of this apparent dose effect may be due to differences in the frequency of IFN $\beta$  administration (rather than dose) between studies. On the basis of Class II evidence, the route of administration of IFN $\beta$  is probably not of clinical importance, at least with regards to efficacy. The side effect profile, however, does differ between routes of administration (Goodin et al., 2002).

**Glatiramer Acetate.** On the basis of Class I evidence, GA has been demonstrated to reduce the relapse rate (whether measured clinically or by MRI) in patients with relapsing-remitting MS (Type A recommendation). Treatment with GA produces a beneficial effect on MRI measures of disease severity, such as T2 disease burden, and possibly slows sustained disability progression (Type C recommendation; Goodin et al., 2002).

If a patient asks for more detailed information on the efficacy of DMTs, the nurse may review the supporting literature with the patient and or refer the patient to the

**Table 1. Rating of Evidence Classification Scheme**

Recommendation Rating	Rating of Therapeutic Article
<p><b>A</b> = established as effective, ineffective, or harmful for the given condition in the specified population</p>	<p><b>Class I.</b> Prospective, randomized, controlled clinical trial with masked outcome assessment in a representative condition in the specified population. The following are required:</p> <ul style="list-style-type: none"> <li>a. Primary outcome(s) is/are clearly defined.</li> <li>b. Exclusion/inclusion criteria are clearly defined.</li> <li>c. Adequate accounting for dropouts and crossovers with numbers sufficiently low to have minimal potential for bias.</li> <li>d. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.</li> </ul>
<p><b>B</b> = probably effective, ineffective, or harmful for the given condition in the specified population</p>	<p><b>Class II.</b> Prospective matched group cohort study in a representative population with masked outcome assessment that meets a–d above, or a randomized controlled trial in a representative population that lacks one of the criteria from a–d (above).</p>
<p><b>C</b> = possibly effective, ineffective, or harmful for the given condition in the specified population</p>	<p><b>Class III.</b> All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome assessment is independent of patient treatment.</p>

*Note: From "Disease modifying therapies in multiple sclerosis: Report of the Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines," by D.S. Goodin, E.M. Frohman, G.P. Garmany Jr., J. Halper, W.H. Likosky, R.D. Lublis, et al., 2002, Neurology, 58, p. 171. Copyright 2002 by the American Academy of Neurology Enterprises, Inc. Adapted with permission.*

neurologist. The patient's existing knowledge of DMTs obtained through external sources (e.g., the Internet, publications, and/or other patients or healthcare professionals) will also affect treatment decisions. Therefore, it is important for the nurse to assess the patient's existing knowledge base and the reliability of the information provided to him or her. In cases where the information provided or source of information is questionable, the nurse should reeducate the patient on treatment efficacy, approved product indications, and side effect profiles.

Another important factor to consider is the treatment philosophy of the healthcare team responsible for the care and management of the patient. Despite evidence that early and sustained treatment with the DMTs has a significant positive effect on the disease process, some physicians continue to believe that the majority of patients have a "benign" course and therefore delay prescribing therapy until the disease progresses (Holland et al., 2001a). One study found that more than 60% of patients who discontinued therapy were told to do so by their physician (Hadjimichael & Vollmer, 1999). However, to ensure treatment optimization, the healthcare team, as well as the patient, must be committed to the selection and initiation of the most appropriate treatment for the patient, and the long-term treatment protocol. A treatment contract between the nurse and patient may be one

way to help ensure commitment. In addition to discussing the importance of adhering to therapy, the contract should also include criteria for when to consider discontinuing the current treatment (e.g., lack of treatment efficacy) and/or switching to another DMT.

The primary goal in this step of the Nursing Approach is to ensure that, from the very beginning, the patient receives the most effective therapy possible based on his or her individual needs. Choosing the most appropriate treatment from the onset may help ensure optimal patient outcomes in the long term.

### Patient Education and Self-Injection Training

The primary goal of patient education is to empower patients (through

knowledge) to take responsibility for managing their disease. In this way, the patient takes an active role in planning and implementing self-care and self-healing activities (The Canadian MS Nurses' Network, 2000). This sense of empowerment and self-efficacy has been shown to be a significant predictor of adherence to immunomodulating therapy (Fraser, Hadjimichael, & Vollmer, 2001) and therefore may promote long-term treatment optimization. However, although education helps promote optimal patient outcomes, it will only be successful if the learner is motivated to learn. Thus, it is important for the nurse to time education to patient readiness to learn (The Canadian MS Nurses' Network, 2000).

Also, education does not end once the patient has learned to self-administer therapy. Rather, education in MS is an ongoing process that responds to the changing needs of patients throughout the course of their disease. Again, it is the MS nurse who plays a central role in this long-term educational process.

### Psychoeducational Approach to Patient Education

MS centers throughout North America often use a psychoeducational approach to patient education. Psychoeducation is a multifaceted educational process that has been found to be effective in promoting optimal patient outcomes (Marciniak, Johnson, & Foley, 1991).

**Table 2. Strategies for Effective Patient Education**

Strategy	Rationale
Provide information in a clear and concise manner.	Increased understanding of information by patient helps reduce patient anxiety regarding therapy.
Provide a nondistracting, relaxing, and comfortable learning environment.	Minimizes distractions during learning process.  Increased understanding of information by patient helps reduce patient anxiety regarding therapy.  Minimizes fears associated with the disease and self-injection of therapy.  Helps identify barriers to adherence and thereby facilitates the learning process.
Use a variety of educational tools (e.g., oral and written information, videocassettes, practice vials and syringes, and one-on-one demonstrations).	Patients with MS often have some degree of cognitive impairment; therefore, instruction often needs to be repeated.  Patients experiencing stress or fear regarding MS or injection therapy may forget even the simplest verbal instructions (Kolton & Piccolo, 1988); therefore, provide learning material in a variety of media to complement verbal instructions.
Provide patients with reinforcement and acknowledge success.	Reinforcement of efforts made will increase patients' sense of control over their disease and promote adherence to the treatment plan.  Ongoing communication and reinforcement of treatment outcomes reduces unrealistic expectations of being completely exacerbation-free during treatment (Lesaux, Jadback, & Harraghy, 1999).
Involve family members in the teaching process.	Involvement of family members in patient education has been shown to minimize patients' fears regarding therapy, reinforce learning, and promote adherence to therapy (Kolton & Piccolo, 1988).

*Note: From The Canadian MS Nursing Care Plan, by The Canadian MS Nurses' Network, 2000, Mississauga, ON: IntraMedical Health Services. Copyright 2002 by IntraMedical Health Services. Reprinted with permission.*

Unlike the traditional learning model that sets educational objectives according to predetermined learning material, the psychoeducational model requires that patients and their families become actively involved in setting the goals and objectives of education as well as the educational process itself. In this model, the learner's perspective is determined before teaching is initiated, and, as such, instructional methods are tailored to the individual needs of each patient (Halper & Holland, 1997; Marciniak, Johnson, & Foley, 1991). Furthermore, the model allows for continual assessment of the patient's understanding of anticipated side effects and his or her skill development in the injection process (Halper & Holland). Strategies for effective patient education using the psychoeducation model are shown in Table 2.

MS nurses should evaluate their own effectiveness as educators and instruct patients to self-evaluate learning on a regular basis. Self-evaluation of learning empowers patients to take control of their disease.

### **Self-Injection Training**

Because DMTs are currently available only in injectable form, the introduction of these therapies requires extensive patient and family education on the following:

- Appropriate self-injection technique, including proper drug handling and reconstitution
- Site selection, rotation, and injection-site management
- Management of treatment-related systemic side effects.

The primary goal of this step in the Nursing Approach is to ensure optimal treatment outcomes by ensuring the patient self-injects appropriately and successfully manages adverse events and injection-site reactions. An important first step in this educational process is to establish whether the patient, the nurse, or the patient's caregiver will give the first injection. Ideally, patients should perform the first injection themselves with the assistance of the nurse. It is also important that patients understand the need to administer the drug as directed,

**Table 3. Model for Assessing Treatment Response Based on Patient Outcomes (i.e., Relapses, Disease Progression, and MRI Findings)**

	Notable	Worrisome	Actionable
<b>Relapses</b>			
Frequency/severity	Single mild attack	Single, moderate attack in year, beginning 6 months after initiation of therapy	More than 1 moderate or severe attack in year, beginning 6 months after initiation of therapy
Recovery	Rapid following prompt steroid treatment	Slow following prompt steroid treatment	Incomplete
<b>Progression</b>			
EDSS $\leq$ 3.5	<2 point change	2 point change	>2 point change
EDSS $\geq$ 4.0	<1 point change	1 point change	>1 point change
Clinically documented progression	No motor, minor sensory	Some motor, cognitive, or more pronounced sensory	Pronounced motor, cognitive, etc.
<b>Change from Previous MRI</b>			
New Gd-enhancing lesions	Changes in two categories	Changes in three categories	Changes in more than three categories
New T2 lesions			
Enlarging T2 (burden of disease)			
New T1 hypointense lesions			
Enlarging T1 hypointense lesions			
Increased atrophy			

*Note: From "MS patient management: Optimizing the benefits of immunomodulatory therapy," by K. Bashir, L. Buchwald, P.K. Coyle, M. Freedman, D. Jeffery, C. Markowitz, et al., June 2002, International Journal of MS Care, (suppl), 1-7. Copyright 2002 by Consortium of Multiple Sclerosis Centers and Rehabilitation in Multiple Sclerosis. Reprinted with permission.*

especially during the titration period, and that any changes from this dosing can result in either an overdose or treatment inefficacy. Once full dose is achieved, the nurse should ensure the full dose is taken as prescribed (The Canadian MS Nurses' Network, 2000).

Furthermore, all patients must be taught a safe, clean self-injection technique. Appropriate site selection and rotation help to prevent erythema and possible necrosis at the injection site (The Canadian MS Nurses' Network, 2000). Demonstration kits are provided by manufacturers of DMTs to facilitate injection technique instruction. The nurse should regularly review injection techniques and site selection/rotation throughout therapy initiation. The desired outcome of self-injection training is that the patient will inject successfully on an ongoing basis. Self-injection education, like all adult education, should be based on teaching according to the patient's needs. Therefore, assessment of the patient's knowledge base, learning style, and readiness to learn are important.

Subcutaneous injection-site reactions with IFN $\beta$  and GA therapy include pain (9%–66%) and cutaneous

reactions (46%–92%; Berlex Laboratories, 2002; Serono Inc., 2002; Teva Neuroscience, 2002). Intramuscular injection-site reactions were reported in 4% of patients (Biogen, Inc., 2003). The reported incidence of injection-site necrosis ranges from 0–5% (Berlex Laboratories; Biogen, Inc.; Serono, Inc.; Teva Neuroscience). The nurse should instruct patients to report skin reactions at every visit. Ideally, the patient should be seen in person, because it is difficult to assess skin integrity over the phone. The patient should also be instructed on nonpharmacological and pharmacological interventions for minimizing injection-site reactions.

Systemic side effects associated with IFN $\beta$  therapy include flu-like symptoms such as myalgia, headaches, chills, and fever. Approximately 50%–75% of patients experience flu-like symptoms after the first dose of IFN $\beta$  (Berlex Laboratories, 2002; Biogen,

Inc., 2003; Serono, Inc., 2002). These symptoms usually resolve within 24 hours of injection, but may persist for 3 months or more following the initiation of therapy (Munschauer & Kinkel, 1997; Walther & Hohlfeld, 1999). Nurses can help patients manage these systemic side effects in a variety of ways. For example, patients may be encouraged to administer injections in the evening to minimize the impact of side effects on daily activities. Acetaminophen or ibuprofen taken before injection and every 4 hours thereafter (for 24 hours after injection) may also provide appropriate relief of flu-like symptoms in some patients (The Canadian MS Nurses' Network, 2000; Halper, 2001). Patients should not be taken off IFN $\beta$  therapy until all options to manage flu-like symptoms have been explored.

Systemic side effects noted immediately after GA injection were reported in approximately 10% of patients (Teva Neuroscience, 2002). These symptoms include chest pain, palpitations, flushing, anxiety, and dyspnea (Teva Neuroscience), but are transient and self-limited and usually do not require specific treatment. In some patients,

GA has also been associated with localized lipoatrophy at the site of injection (Drago, Brusati, Mancardi, Murialdo, & Rebora, 1999; Hwang & Orenco, 2001). The nurse must educate and prepare the patient for the possible advent of immediate post-injection reactions when using GA.

### Long-Term Assessment and Monitoring

Central to the Nursing Approach is the regular and long-term clinical, MRI, and laboratory assessment of the patient (including the assessment of physical and cognitive functioning), the evaluation of psychosocial functioning, and the monitoring of adherence to therapy. Clinical, MRI, laboratory and psychosocial outcomes, and treatment adherence are interrelated (Fig 1) such that suboptimal outcomes on one of these parameters may have an effect on the other parameters.

### Clinical, MRI, and Laboratory Assessment

A thorough clinical, MRI, and laboratory assessment should include the evaluation of immunomodulatory outcomes (i.e., relapses, progression, and MRI), laboratory values, adverse events, and physical and cognitive functioning. In addition, the nurse needs to ascertain that the patient is adhering to the treatment and to monitor injection sites and technique.

Experts have recommended that patients be seen frequently during the first 2 years after MS is diagnosed and treatment is initiated (e.g., every 3–6 months). A quantitative neurological examination should be performed at each visit, and relapses, progression, and MRI findings should be documented (Bashir et al., 2002). A model for determining treatment response based on these outcomes (Table 3) has recently been developed (Bashir et al.). The model ranks outcomes as “notable” (low level of concern), “worrisome” (moderate level of concern), or “actionable” (high level of concern). If all three outcomes (i.e., relapses, progression, and MRI findings) are “notable,” any two are “worrisome,” or any one is “actionable,” then it is likely that treatment response is suboptimal and that strategies to optimize treatment response need to be implemented (Bashir et al.).

Relapse frequency and severity, as well as speed and extent of recovery after relapse, are all judged to be important factors in determining an acceptable versus a less-than-optimal response to therapy. Relapse recovery that takes more than a few months or that is incomplete may suggest that the patient is not responding optimally to therapy. In addition, relapses affecting several systems (i.e., motor, sphincter, cerebellar, sensory) are associated with a poor prognosis (Bergamaschi, Berzuini, Romani, & Cosi, 2001) and are likely indicative of a suboptimal treatment response. In such situations, treatment choice will likely need to be reconsidered (Bashir et al., 2002).

Progression can be measured using the Kurtzke Expanded Disability Status Scale (EDSS), the MS Functional Composite (MSFC), and a well-documented clinical

examination. MRI measures of disease activity include a new gadolinium (Gd)-enhancing lesion, new or enlarging T2 hyperintense lesions, new or enlarging T1 hypointense lesions, and atrophy. Progression in disability and evidence of new or enlarging lesions are indicative of suboptimal treatment responses (Bashir et al., 2002).

As the primary patient contact, the MS nurse is usually the first healthcare professional to notice signs of exacerbations, disease progression, and other suboptimal clinical outcomes. In such cases, the patient is scheduled or referred for the appropriate examinations and assessments. If the results of these assessments show that treatment response is indeed suboptimal, the nurse should collaborate with the patient and neurologist in identifying alternative management strategies or selecting a more appropriate therapy.

The most commonly observed laboratory abnormalities in patients receiving IFN $\beta$  therapy are leukopenia, lymphopenia, neutropenia, and raised liver aminotransferase values (e.g., alanine aminotransferase [ALT] and aspartate aminotransferase [AST]). These abnormalities, however, seldom result in serious complications (Lublin et al., 1996; Munschauer & Kinkel, 1997). Nonetheless, the nurse should educate patients on the importance of regular laboratory assessments and ensure patients complete laboratory evaluations at appropriate intervals. If the patient exhibits abnormal or acute/subacute toxicities, dosage adjustments may be required.

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*At present, clinical decisions regarding therapy should be based on medical and health outcomes, not the presence of NABs.*

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Treatment with IFN $\beta$  is also associated with the production of neutralizing antibodies (NABs). However, the rate of NAB production with IFN $\beta$ -1a treatment is probably less than with IFN $\beta$ -1b treatment (Goodin et al., 2002; Multiple Sclerosis Council for Clinical Practice Guidelines, 2001). Although the presence of NABs may be associated with a reduction in clinical effectiveness of IFN $\beta$  therapy, The Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology (Goodin et al.) and the MS Council for Clinical Practice Guidelines (2001) state that the clinical utility of measuring NABs in patients on IFN $\beta$  therapy is uncertain. At present, clinical decisions regarding therapy should be based on medical and health outcomes, not the presence of NABs. Nonetheless, nurses should stay abreast of current trends in NAB measurement.

As mentioned earlier, treatment-related adverse events such as injection-site reactions and systemic side effects can also have a negative impact on patient outcomes, and therefore monitoring of these events and the implementation of strategies to minimize and/or eliminate these events by the MS nurse are critical.

Physical impairments such as motor and sensory symptoms, visual deficits, and fatigue may be barriers to optimal self-management, particularly to self-injection of a DMT (van den Noort & Holland, 1999). According to Miller (2000), individuals who are disabled and have difficulty performing self-care activities will have difficulty adhering to a prescribed medication regimen. Therefore, patients who are physically compromised may require additional assistance in dealing with treatment logistics and other aspects of their disease. The MS nurse should provide ongoing education and support to improve the patient's physical functioning, quality of life, and independence.

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*Suboptimal psychosocial functioning  
requires reeducation and interventions  
designed to optimize functioning.*

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Cognitive changes occur in 40%–70% of persons with MS (Halper, 2001). The most frequently reported cognitive problems are memory loss, difficulty in learning and recalling new information, slowed information processing speed, and problem-solving deficits (Holland et al., 2001a). Cognitive changes range from mild to severe in nature and may occur early in the course of the disease and in the absence of physical (e.g., motor, sensory) changes. Even relatively mild deficits can have an impact on patients' day-to-day lives. In many instances, cognitive difficulties are incorrectly attributed to depression or other emotional disturbances. However, proper identification and management of cognitive problems are necessary to ensure optimal patient outcomes.

Any suboptimal response in patient outcomes, laboratory evaluations, or adverse event management requires reeducation, additional assessment, and monitoring, and, in some cases, that treatment choice be reconsidered. Suboptimal cognitive or physical functioning will require reeducation and interventions designed to optimize functioning; improvements in functioning will help ensure optimal patient outcomes in the long-term.

### **Psychosocial Assessment**

Long-term assessment should include a comprehensive evaluation of the patient's psychosocial functioning. Note that psychosocial as well as physical/cognitive functioning also need to be assessed in the Initial Assessment and Patient Selection step of the Nursing Approach. However, because of the unpredictable nature of MS and the changing needs of patients throughout their lifetimes, psychosocial and cognitive/physical functioning need to be monitored on a regular basis after treatment initiation.

Psychosocial issues such as dysphoric mood, lack of support networks, and financial concerns can have a significant impact on treatment outcomes. The lifetime prevalence for major depression in MS ranges from 40%

to 60% (Sadovnick et al., 1996). The symptoms of depression include feelings of hopelessness, despair and guilt, fatigue, insomnia, and suicidal ideation (Halper & Holland, 1997). In fact, compared to the general population, individuals with MS are reported to have an increased suicide rate (Sadovnick, Eisen, Ebers, & Paty, 1991). Depression reduces the patient's willingness or desire to take medication or improve well-being. Mohr et al. (1997) found that 41% of patients reported new or increased depression within 6 months after starting therapy and that these patients were more likely to discontinue therapy than nondepressed patients. And, as mentioned earlier, discontinuation of an effective treatment regimen is one of several factors that may lead to suboptimal patient outcomes. However, when treatment for depression was administered (i.e., antidepressants or psychotherapy), patients were more likely to continue on immunomodulating therapy (Mohr et al., 1997). Therefore, the MS nurse should assess for depression and suicidal ideation and refer the patient to his/her family physician or a consulting psychiatrist/psychologist for treatment. If medication for depression is prescribed, treatment response should be monitored.

Patients may also react negatively to the multiple changes and losses imposed by the diagnosis and progressive disability, such as role changes, loss of social/financial status, employment and independence, and sexuality and family issues (The Canadian MS Nurses' Network, 2000). At this time, many patients abdicate responsibility for themselves and their own care. However, the availability and use of support networks and programs have been shown to promote self-management and adherence (Madonna & Keating, 1999) and thereby may promote treatment optimization. These programs provide comfort as well as media for exchange of information and emotions. Nurses should also assist patients in obtaining funding for therapy by directing them to financial assistance services and resources. Knowledge of these services may help patients achieve greater financial independence.

Therefore, in addition to the assessment of physical aspects of the disease, the assessment of psychosocial issues is an integral component of long-term treatment optimization. Research suggests that using an orderly and systematic approach to assessing psychosocial problems, determining appropriate interventions, initiating a collaborative plan, and evaluating the efficacy of this plan can significantly increase patient adherence to therapy, improve self-care skills, and assist patients in adapting to MS (Taylor & Cress, 1987). These positive outcomes play a significant role in ensuring treatment optimization.

Suboptimal psychosocial functioning requires reeducation and interventions designed to optimize functioning. The ultimate goal in this step of the Nursing Approach is to help ensure treatment optimization by obtaining optimal psychosocial functioning.

## Treatment Adherence

Adherence is best defined as the active, voluntary, and collaborative involvement of the patient in a mutually acceptable course of behavior that results in a desired preventive or therapeutic outcome (The Multiple Sclerosis Nurse Specialists Consensus Committee, 1998). It has recently been suggested that the term *adherence* be used to replace the term *compliance* when referring to therapy, because many patients believe *compliance* is value-laden, (i.e., that is, implies that the patient is subordinate to the healthcare professional (Halper, 2001).

Although adherence to therapy is important for ensuring optimal treatment outcomes, in some circumstances, treatment discontinuation may be warranted, particularly in situations in which treatment response is suboptimal. NARCOMS data indicate that one of the most frequently cited reasons for discontinuing a DMT is perceived lack of treatment benefit (Vollmer, 2002). In addition, one survey found that of the 350 patients who volunteered information on their past drug history, 90% had been switched to another agent. Lack of treatment efficacy was the primary reason cited for the change in therapy (Eyring, Wood, Sherman, & Simone, 2002). Therefore, when monitoring treatment adherence, the nurse and neurologist should first determine whether perceived and/or actual treatment ineffectiveness is responsible for nonadherence. In such cases, the nurse should collaborate with both the neurologist and patient to determine whether alternative strategies can be implemented or whether switching to another DMT is required.

The nurse should also identify whether any of the following possible barriers to adherence are present (The Canadian MS Nurses' Network, 2000; Holland et al., 2001a):

- perceived low value of treatment
- lack of information on therapies or misinformation
- unrealistic expectations for therapies
- number and frequency of drugs currently being taken by the patient
- patient's perception of MS (e.g., patient is in denial)
- cognitive deficits (e.g., memory and judgment problems)
- temporary worsening of MS symptoms after therapy has been initiated
- drug administration challenges and/or fears of self-injection
- difficulty coping with side effects of therapy
- social situations and/or cultural beliefs that are incongruent with therapy regimen
- financial concerns (e.g., lack of coverage for treatment expense)
- contradictory messages from healthcare providers and peers
- lack of professional support.

The CMSC's NARCOMS data reveal that patients are most likely to discontinue therapy in the first 6 months after initiation of treatment and that temporary worsening of symptoms and flu-like side effects are often cited as reasons for discontinuation (Vollmer, 2002). A study by Mohr et al. (1998), for example, found that 11% of patients discontinued therapy 4 months after initiation, largely because of treatment-related adverse events that they believed signaled a worsening of disease. Therefore, to help ensure adherence to an effective treatment regimen, the nurse should assist patients in setting realistic goals for therapy and should instruct patients on the use of strategies to manage flu-like symptoms and other treatment-related side effects.

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*Therefore, the nurse should create an environment in which dialogue is encouraged and patients feel at ease discussing problems.*

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The quality of the nurse-patient relationship and clinic setting also have a significant impact on treatment outcomes. Many patients report that the way they are treated by their healthcare team has a significant impact on whether or not they follow medical advice. Long waits, feeling rushed, not having opinions valued or time to ask questions, feeling patronized and being ignored in the decision-making process have all been reported by patients to have a negative impact on the patient-professional relationship and medication adherence (Feuerstein et al., 1998). One study found the highest rates of adherence to immunomodulating therapy at clinics where nurses and other healthcare professionals were considered more empathetic, where a sense of purpose was instilled in the patients, and where less formal relationships with patients were promoted (Mohr et al., 1999). In fact, the active involvement of nurses in the overall management of patients with MS has been shown to increase patient adherence to MS-treatment regimens (Collingworth, Gould, & Wainwright, 1997). Therefore, the nurse should create an environment in which dialogue is encouraged and patients feel at ease discussing problems.

Finally, as mentioned earlier, 34%–57% of patients who initiate a DMT have unrealistically optimistic expectations for therapy; these patients are less likely to succeed on therapy when side effects occur (Mohr et al., 1996). Throughout the course of therapy, the nurse plays a central role in realigning unrealistic therapeutic expectations.

The primary goal in this step of the Nursing Approach is to ensure that the patient follows an effective treatment regimen so that the best possible physical, psychosocial, and quality-of-life outcomes are achieved.

## Treatment Optimization

Treatment optimization is the underlying goal of every step of the Nursing Approach. Therefore, ensuring optimal patient outcomes depends on several factors as well as the complex interplay between these factors: patient appropriateness for therapy and readiness to initiate treatment; efficacy of therapy; ongoing education on the disease; self-injection training and the management of possible treatment-related adverse events; the patient's physical, cognitive, and psychosocial functioning; and adherence to an effective therapeutic regimen.

## Summary

Several factors are important for achieving optimal treatment outcomes in patients using DMTs. Because nurses are the main healthcare professionals who have day-to-day contact with patients, they play a pivotal role in ensuring optimal clinical, subclinical, psychosocial, and quality-of-life outcomes for these patients. This Nursing Approach is designed to guide and assist nurses through this demanding, long-term process of treatment optimization.

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## References

- Bashir, K., Buchwald, L., Coyle, P.K., Freedman, M., Jeffery, D., Markowitz, C., et al. (2002, June). MS patient management: Optimizing the benefits of immunomodulatory therapy. *International Journal of MS Care*, (Suppl.), 1-7.
- Bergamaschi, R., Berzuini, C., Romani, A., & Cosi, V. (2001). Predicting secondary progression in relapsing-remitting multiple sclerosis: A Bayesian analysis. *Journal of Neurological Sciences*, 189, 13-21.

- Berlex Laboratories. (2002). *Betaseron® product monograph*. Biogen, Inc. (2003). *Avonex® product monograph*.
- Bornstein, M.B., Miller, A., Slagle, S., Weitzman, M., Crystal, H., Drexler, E., et al. (1987). A pilot trial of Cop 1 in exacerbating-relapsing multiple sclerosis. *New England Journal of Medicine*, 317, 408-414.
- The Canadian MS Nurses' Network. (2000). *The Canadian MS Nursing Care Plan*. Mississauga, ON: IntraMedical Health Services.
- Chofflon, M. (2000). Recombinant human interferon beta in relapsing-remitting multiple sclerosis: A review of the major clinical trials. *European Journal of Neurology*, 7, 369-380.
- Collingworth, S., Gould, D., & Wainwright, S.P. (1997). Patient self-administration of medication: A review of the literature. *International Journal of Nursing Studies*, 34, 256-269.
- Drago, F., Brusati, C., Mancardi, G., Murialdo, A., & Reborja, A. (1999). Localized lipoatrophy after glatiramer acetate injection in patients with relapsing-remitting multiple sclerosis. *Archives of Dermatology*, 135(10), 1277-1278.
- Durelli, L., Verdun, E., Barbero, P., Bergui, M., Versino, E., Ghezzi, A., et al. & The Independent Comparison of Interferon (INCOMIN) Trial Study Group. (2002). Every-other-day interferon beta-1b versus once-weekly interferon beta-1a for multiple sclerosis: Results of a 2-year prospective randomised multicenter study (INCOMIN). *Lancet*, 359, 1453-1460.
- Eyring, S., Wood, C., Sherman, S., & Simone, M. (2002, September). *Efficacy of MS therapy is the key driver in therapy choice*. Poster session presented at the Second Joint Meeting of the Americas and European Committees for Treatment and Research in Multiple Sclerosis (ACTRIMS and ECTRIMS), Baltimore, MD.
- Feuerstein, M., Lieb-Juckstock, V., Schnaus, H., Springmann, E., Weber, B., & Wunderlich M. (1998). Compliance—a joint effort of the patient and doctor. In D. Schmidt & I. E. Leppik (Eds.), *Compliance in Epilepsy* (Epilepsy Res. Suppl. 1). Elsevier Scientific.
- Fraser, C., Hadjimichael, O., & Vollmer, T. (2001). Predictors of adherence to Copaxone therapy in individuals with relapsing-remitting multiple sclerosis. *Journal of Neuroscience Nursing*, 33, 231-239.
- Freedman, M.S., Blumhardt, L.D., Brochet, B., Comi, G., Noseworthy, J.H., Sandberg-Wollheim, M., Soelberg, S.P., & the Paris Workshop Group. (2002). International consensus statement on the use of disease-modifying agents in multiple sclerosis. *Multiple Sclerosis*, 8(1), 19-23.
- Goodin, D.S., Frohman, E.M., Garmany, G.P. Jr, Halper, J., Likosky, W.H., Lublin, F.D., et al. (2002). Disease modifying therapies in multiple sclerosis: Report of the Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. *Neurology*, 58, 169-178.
- Hadjimichael, O., & Vollmer, T.L. (April 1999). Adherence to injection therapy in MS: Patient's survey. *Neurology*, 52(Suppl. 2).
- Halper, J. (2001). *Advanced concepts in multiple sclerosis nursing care*. New York: Demos Medical Publishing, Inc.
- Halper, J., & Holland, N. (1997). *Comprehensive nursing care in multiple sclerosis*. New York: Demos Vermande.
- Holland, N., Wiesel, P., Cavallo, P., Edwards, C., Halper, J., Kalb, R., et al. (2001a). Adherence to disease-modifying therapy in multiple sclerosis: Part I. *Rehabilitation Nursing*, 26(5), 172-176.
- Holland, N., Wiesel, P., Cavallo, P., Edwards, C., Halper, J., Kalb, R., et al. (2001b). Adherence to disease-modifying therapy in multiple sclerosis: Part II. *Rehabilitation Nursing*, 26(6), 221-226.
- Hwang, L., & Orengo, I. (2001). Lipoatrophy associated with glatiramer acetate injections for the treatment of multiple sclerosis. *Cutis*, 68(4), 287-288.
- IFNβ Multiple Sclerosis Study Group. (1993). Interferon beta 1b is effective in relapsing-remitting multiple sclerosis I. Clinical results of a multicenter, randomized, double-blind, placebo-controlled trial. *Neurology*, 43, 655-661.
- IFNβ Multiple Sclerosis Study Group & the University of British Columbia MS/MRI Analysis Group. (1995). Interferon beta 1b in the treatment of multiple sclerosis: Final outcome of the randomized controlled trial. *Neurology*, 45, 1277-1285.
- Jacobs, L.D., Cookfair, D.L., Rudick, R.A., Herndon, R.M., Richert, J.R., Salazar, A.M., et al. & The Multiple Sclerosis Collaborative Research Group. (1996). Intramuscular interferon beta-1a for disease progression in relapsing remitting multiple sclerosis. *Annals of Neurology*, 39, 285-294.
- Johnson, K.P., Brooks, B.R., Cohen, J.A., Ford, C.C., Goldstein, J., Lisak, R.P., et al. (1995). 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*, 45, 1268-1276.
- Kolton, K.A., & Piccolo, P. (1988). Patient compliance: A challenge in practice. *Nurse Practitioner*, 13(12), 37-44.
- Knowles, M.S. (1980). *The modern practice of adult education: From pedagogy to andragogy*. Chicago: Folien Publishing Company.
- Legendyk, L.F., McGuinness, S.D., Bouchard, J.P., Halle, D., Jacques, F., & Metz, L.M. (2002, June). *Patient concerns prior to multiple sclerosis treatment initiation mirror reasons for discontinuation*. Paper presented at the Consortium of Multiple Sclerosis Centers Annual Meeting, Baltimore, MD.
- Lannon, S.L. (1997). Using a health promotion model to enhance medication compliance. *Journal of Neuroscience Nursing*, 29, 170-178.
- Larivaara, P., Kiuttu, J., & Taanila, A. (2001). The patient centered interview: The key to biopsychosocial diagnosis and treatment. *Scandinavian Journal of Primary Health Care*, 19, 8-13.
- Lesaux, J., Jadback, G., & Harraghy, C.E. (1999). Improving the convenience of home-based interferon beta-1a therapy for multiple sclerosis. *Journal of Neuroscience Nursing*, 31, 174-179.
- Lublin, F.D., Whitaker, J.N., Eidelman, B.H., Miller, A.E., Arnason, B.G.W., & Burks, J.S. (1996). Management of patients receiving interferon beta-1b for multiple sclerosis: Report of a consensus conference. *Neurology*, 46, 12-18.
- Madonna, M.G., & Keating, M.M. (1999). Multiple sclerosis pathways: An innovative nursing role in disease management. *Journal of Neuroscience Nursing*, 31, 332-335.
- Marciniak, M., Johnson, B., & Foley, F.W. (1991, June 15-17). *The use of the Levo chair in the management of multiple sclerosis*. Paper presented at the Consortium of Multiple Sclerosis Centres Conference; Halifax, NS.
- Merriam-Webster On-line. Retrieved November 29, 2002, from <http://www.m-w.com/cgi-bin/dictionary>
- Miller, J.F. (2000). *Coping with chronic illness: Overcoming powerlessness* (3rd ed.). Philadelphia: F.A. Davis, pp. 293-326.
- Mohr, D.C., Goodkin, D.E., Likosky, W., Gatto, N., Baumann, K.A., & Rudick, R.A. (1997). Treatment of depression improves adherence to interferon beta-1b therapy for multiple sclerosis. *Archives of Neurology*, 54, 531-533.
- Mohr, D. C., Goodkin, D. E., Likosky, W., Gatto, N., Neilley, L.K., Griffin, C., et al. (1996). Therapeutic expectations of patients with multiple sclerosis upon initiating interferon beta-1b: Relationship to adherence to treatment. *Multiple Sclerosis*, 2, 222-226.
- Mohr, D.C., Goodkin, D.E., Masuoka, L., Dick, L.P., Russo, D., Eckhardt, J., et al. (1999). Treatment adherence and patient retention in the first year of a phase-III clinical trial for the treatment of multiple sclerosis. *Multiple Sclerosis*, 5, 192-197.
- Mohr, D.C., Likosky, W., Boudewyn, A.C., Marietta, P., Dwyer, P., Van Der Wende, J., et al. (1998). Multiple sclerosis: Side effect profile and adherence to the treatment of multiple sclerosis with interferon beta-1a. *Multiple Sclerosis*, 4, 487-489.
- Multiple Sclerosis Council for Clinical Practice Guidelines. (2001). *Disease Modifying Therapies in Multiple Sclerosis: Evidence-Based Management Strategies for Disease Modifying Therapies in Multiple Sclerosis*. Washington, DC: Paralyzed Veterans of America.
- Multiple Sclerosis Nurse Specialists Consensus Committee. (1998). *Multiple sclerosis: Key issues in nursing management*. Columbia, MD: Medicalliance, Inc.

- Munschauer, F.E., & Kinkel, R.P. (1997). Managing side effects of interferon-beta in patients with relapsing-remitting multiple sclerosis. *Clinical Therapeutics*, 19, 883-893.
- O'Connor, P., on behalf of The Canadian Multiple Sclerosis Working Group. (2002). Key issues in the diagnosis and management of multiple sclerosis: An overview. *Neurology*, 59 (Suppl. 3), S1-S33.
- Oger, J., & Freedman, M. (1999). Consensus statement of the Canadian MS Clinics Network on the use of disease modifying agents in multiple sclerosis. *Canadian Journal of Neurological Sciences*, 26, 274.
- Panitch, H., Goodin, D.S., Francis, G., Chang, P., Coyle, P.K., O'Connor, P., et al. (2002). Randomized, comparative study of interferon  $\beta$ -1a treatment regimens in MS: The EVIDENCE trial. *Neurology*, 59, 1496-1506.
- Paty, D.W., & Li, D.K. (1993). Interferon beta 1b is effective in relapsing-remitting multiple sclerosis II. MRI analysis results of a multicenter, randomized, double-blind, placebo-controlled trial. *Neurology*, 43, 662-667.
- PRISMS Study Group. (1998). Randomized double-blind placebo-controlled study of interferon b-1a in relapsing-remitting multiple sclerosis. *Lancet*, 352, 1498-1504.
- PRISMS Study Group & the University of British Columbia MS/MRI Analysis Group. (2001). PRISMS-4: Long-term efficacy of interferon-beta-1a in relapsing MS. *Neurology*, 56, 1628-1636.
- Prochaska, J.O., Redding, C.A., Harlow, L.L., Rossi, J.S., & Velicer, W.F. (1994). The transtheoretical model of change and HIV prevention: A review. *Health Education Quarterly*, 21(4), 471-486.
- Rotter, J.B. (1966). Generalized expectancies for internal versus external control of reinforcement. *Psychological Monographs*, 80(1), 1-28.
- Rudick, R.A., Goodkin, D.E., Jacobs, L.D., Cookfair, D.L., Herndon, R.M., Richert, J.R., et al. & The Multiple Sclerosis Collaborative Research Group. (1997). Impact of interferon beta-1a on neurological disability in relapsing multiple sclerosis. The Multiple Sclerosis Collaborative Research Group. *Neurology*, 49, 358-363.
- Sadovnick, A.D., Eisen, K., Ebers, G.C., & Paty, D.W. (1991). Cause of death in patients attending multiple sclerosis clinics. *Neurology*, 41, 1193-1196.
- Sadovnick, A.D., Remick, R.A., Allen, J., Swartz, E., Yee, I.M., Eisen, K., et al. (1996). Depression and multiple sclerosis. *Neurology*, 46(3), 628-632.
- Serono, Inc. (2002). Rebif<sup>®</sup> product monograph.
- Simon, J.H., Jacobs, L.D., Campion, M., Wende, K., Simonian, N., Cookfair, et al. & The Multiple Sclerosis Collaborative Research Group. (1998). Magnetic resonance studies of intramuscular interferon beta-1a for relapsing multiple sclerosis. *Annals of Neurology*, 43, 79-87.
- Taylor, C.M., & Cress, S.S. (1987). *The indispensable care plan guide: Nursing '87 nursing diagnosis cards*. Springhouse, PA: Springhouse Corporation.
- Teva Neuroscience. (2002). Copaxone product monograph.
- van den Noort, S., & Holland, N.J. (1999). *Multiple sclerosis in clinical practice* (2nd ed.). New York: Demos Medical Publishing Co. Inc.
- Vollmer, T.L. (2002, June). Patient use of and compliance to disease modifying agents for MS. Paper presented at the Consortium of Multiple Sclerosis Centers Annual Meeting, Baltimore, MD.
- Walther, E.U., & Hohlfeld, R. (1999). Multiple sclerosis: Side effects of interferon beta therapy and their management. *Neurology*, 53, 1622-1627.

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