

# Multiple Sclerosis:

## Best Practices in Nursing Care

*Disease Management, Comprehensive Care,  
Pharmacologic Management, Nursing Research*

5th Edition

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Ms. Halper has no relationships to disclose.



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### Foreword

Multiple sclerosis (MS) has a major impact on the lives of patients and their families. Its unpredictable course leaves those affected with an uncertain future. Recent advances in understanding about the disease and its treatment have dramatically improved the way that healthcare professionals can help patients and their families. Healthcare professionals, in addition to determining an MS diagnosis and providing supportive care, can now direct treatment toward changing the disease course. As a result, MS nurses worldwide are faced with many challenges as they meet the needs of patients in the rapidly changing field of MS. The MS Nurse Specialists Consensus Committee has drawn on research, educational, and practical experiences to develop a new and cohesive model of nursing care in MS—one that will sustain and educate nurses in their clinical practice, promote nursing research, and inspire a new generation of MS nurses as they enter the field. This model is a recurrent theme of the International Organization of Multiple Sclerosis Nurses (IOMSN).

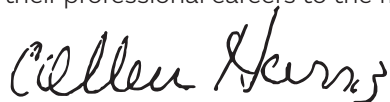
The definition of MS nursing is as follows: The MS nurse is a competent expert who collaborates with those affected by MS and shares knowledge, strength, and hope. As the role of nurses continues to evolve, there is a need to establish a cohesive model of MS nursing practice along with specific standards for best practice in MS nursing care. Nursing practice aims to manage and influence the patient's illness by supporting the use of disease-modifying treatments (DMTs); facilitating symptom management; promoting safe, maximal function; and supporting a wellness-oriented quality of life. Activities that are essential to patient care can be grouped into three categories: establishing care, continuing care, and sustaining care.

Together, these interwoven areas provide a framework for a comprehensive, cohesive model for MS nursing practice that can be applied to the care of all patients with MS, regardless of disease classification or level of disability.

This monograph, now in its 5th edition, was created by the aforementioned MS Nurse Specialists Consensus Committee, made up of nurses who specialize in MS care (see page 39 for a complete listing of the committee's original members), and includes valuable new information. Like the previous editions, this monograph is designed to enhance MS nursing care with regard to disease management, pharmacologic treatment, and nursing research. The information herein was drawn from MS and nursing literature, research in MS and other chronic illnesses, and the years of experience of the distinguished participants on this project. This monograph will assist nurses in fulfilling their universal purpose of providing high-quality, compassionate care to patients and families affected by MS. Specifically, this publication is designed to help nurses to:

1. Describe the epidemiology and pathology of MS
2. Explain how MS nursing has evolved with new technology and treatment approaches
3. Identify domains in MS nursing
4. Define evidence-based practice in MS nursing
5. Explain key competencies within each domain
6. Identify various nursing roles in caring for patients and families affected by MS
7. Describe the role of MS nursing practice in optimizing MS treatments
8. Describe pharmacologic treatment of the disease course and symptoms
9. Describe limitations and gaps in MS research

We hope the information provides a framework to support the sustained value of the work of nurses who are dedicating their professional careers to the field of MS.



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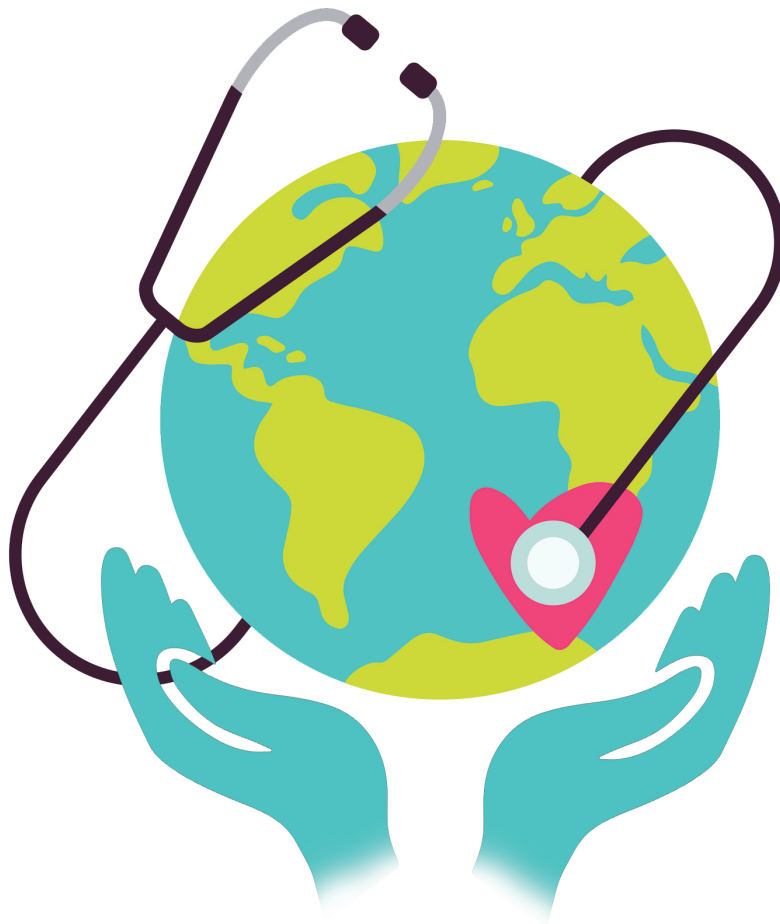
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## Introduction

MS is a chronic, inflammatory, frequently debilitating neurological disease that most often affects young adults in the prime of their lives. While nurses contribute significantly to the care of these patients, basic and advanced nursing education has not typically stressed care of patients with chronic and disabling disease. Thus, nurses in MS clinical settings may not always feel prepared to handle the diverse and variable needs of these patients. In addition, rapid advances in technology and medications used for MS, escalating healthcare costs, shorter hospital stays, and an increased emphasis on home care and patient self-care challenge nurses to face increasingly diverse responsibilities in caring for patients with MS. Nurses not only must help meet the healthcare requirements of these patients but often must also serve as the hub of communication, education, advocacy, and counseling for patients, their families or care partners, and other healthcare professionals.

The growing number of MS nurses worldwide requires networking and involvement with one another. The IOMSN was founded for this purpose and now has numerous international affiliates. It is incumbent upon MS nurses to share knowledge and experience with one another.

This monograph is intended to be a tool for MS nurses who are seeking clarification of their roles and responsibilities as well as for nurses interested in pursuing MS care as a specialty. It provides an overview of the MS disease process, proposes a definition and model for MS nursing, identifies medications used to manage MS and control symptoms, and explores the potential for MS nursing research to improve patient care.



### Overview of Multiple Sclerosis

MS is characterized by patchy loss of the myelin sheath that surrounds nerve fibers, which can be visualized on imaging scans as plaques or lesions in the brain and spinal cord. Demyelination disrupts electrical conduction of the nerves in the central nervous system (CNS), producing variable changes in sensory, motor, and cognitive function. Early on in the disease process, however, patients may not experience any symptoms despite continued disease activity. In addition, there may be permanent and irreversible axonal loss, accounting for ongoing disability in the spectrum of manifestations of the disease.

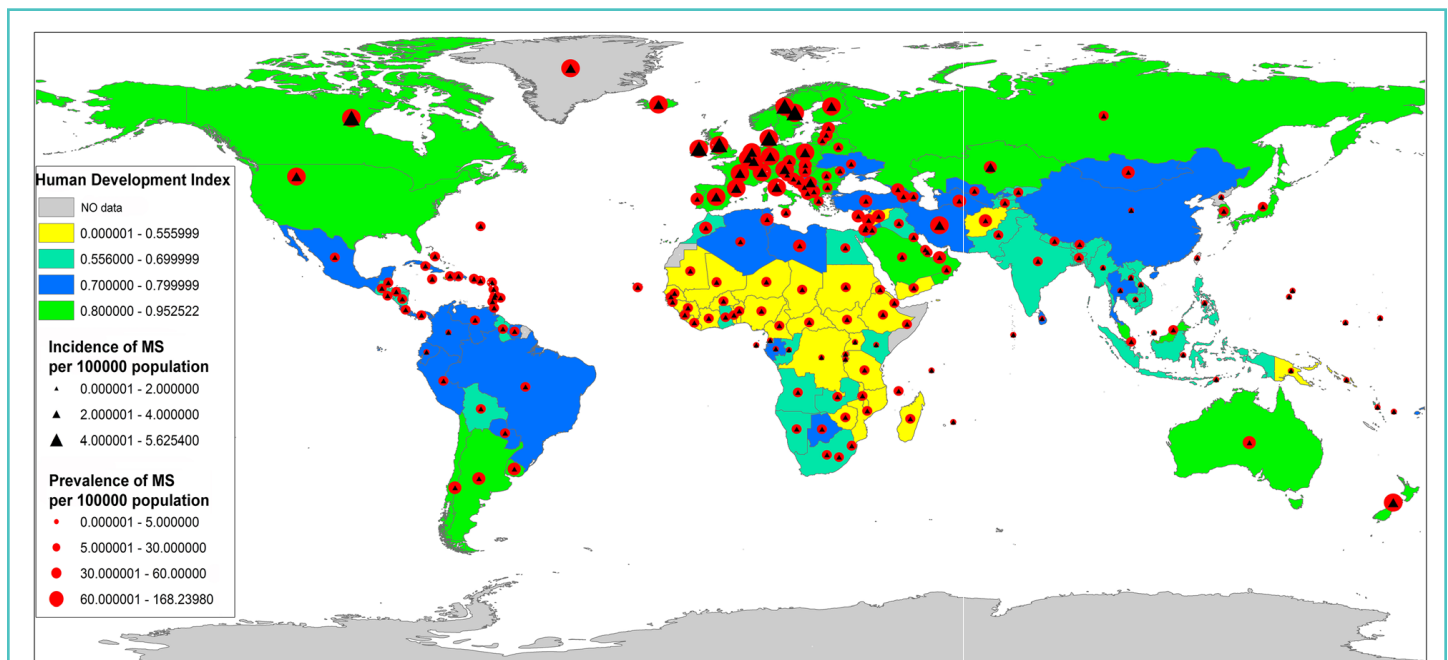
The cause of MS is not known. Research suggests that MS is a consequence of an abnormal autoimmune response to myelin, one that develops after exposure to some environmental agent—possibly a virus such as the Epstein-Barr virus<sup>1</sup>—in genetically predisposed individuals. When the immune response is triggered, activated lymphocytes migrate across the blood-brain barrier (BBB) into the CNS. Once inside, these cells interact with macrophages and other cells, stimulating production of inflammatory cytokines that break down the BBB. The combined effects of this autoimmune response cause the demyelination, axonal damage, and scarring seen on cranial and spinal magnetic

resonance images (MRIs) in patients with MS.<sup>2</sup> Axonal degeneration and axonal transection may lead to permanent neurological dysfunction and may begin early in the disease course.<sup>2</sup> In addition, brain atrophy may occur early and is thought to reflect irreversible tissue damage.<sup>3</sup>

MS prevalence worldwide varies, is increasing, and is highest in Europe, Canada, the United States, Australia, and New Zealand (**Figure 1**).<sup>4</sup> An estimated 2.8 million people worldwide,<sup>4</sup> 1 million people in the United States,<sup>5</sup> and 90,000 people in Canada<sup>6</sup> have MS. People diagnosed with the disease are typically young, and onset usually begins in early adulthood.<sup>5</sup> Women are more than 2-4 times as likely as men to be diagnosed with MS.<sup>4</sup> In the past, it was believed that MS was primarily a disease of White people of European ancestry, but today it is increasingly affecting Black individuals as well.<sup>7</sup>

MS is unpredictable in its overall course, in the type and severity of symptoms experienced by each patient, and in its long-term outcome. Although the disease is seldom fatal, it can be severely disabling. Before the advent of disease-modifying therapies (DMTs), approximately one-third of patients required ambulatory assistance within 10 years of their diagnosis.<sup>8</sup> Today, earlier diagnosis and treatment with DMTs appear to slow the progression of MS and have brought hope to those affected by the disease.<sup>9</sup>

**Figure 1. Worldwide Prevalence of MS**



Source: Reprinted from Moghaddam VK, Dickerson AS, Bazrafshan E, et al. Socioeconomic determinants of global distribution of multiple sclerosis: an ecological investigation based on Global Burden of Disease data. *BMC Neurol.* 2021;21:145.



## Diagnosis and Presenting Symptoms

The symptoms of MS are unpredictable and may be mild, moderate, or severe. Symptoms may appear as an acute attack, also known as an exacerbation or a relapse, or they may become chronic, with clinical and functional deterioration defining disease progression. Each patient differs in the types and intensity of symptoms, depending on the areas of the CNS that are affected.

Patients with MS may experience fatigue, visual disturbances, weakness, poor ambulation, elimination (bowel and bladder) problems, pain and other abnormal sensations, and sexual dysfunction.<sup>10</sup> Other symptoms include vertigo, tremor, speech difficulties, depression, cognitive changes, and Lhermitte's sign (a sudden transient sensation of electric shock that occurs with forward flexion of the neck).<sup>10</sup>

Because neurological impairments are often transient and symptoms manifest themselves in different ways, MS can be challenging to discern. A patient's history, including gender, birthplace, family history, and age when symptoms first began, is critical in the diagnostic process.<sup>11</sup>

## McDonald Diagnostic Criteria

Ultimately, diagnosis is made according to the McDonald Criteria, incorporating both clinical and imaging findings.<sup>11</sup> To be diagnosed with clinically definite MS, a patient is required to have experienced two or more attacks (known as dissemination in time or DIT) with neurological symptoms referable to two or more lesions in the CNS (known as dissemination in space or DIS).<sup>11</sup> Attacks must be separated by at least 1 month, last 24 hours or more, and occur independently of any other disease or condition, including increased body temperature from fever or increased ambient temperature.<sup>11</sup> Fewer than two attacks and/or clinical evidence of only one lesion requires DIT or DIS as shown by magnetic resonance imaging (MRI), positive cerebrospinal fluid (CSF) findings, and/or abnormal evoked potential testing.<sup>11</sup> Insidious neurological progression suggestive of MS requires evidence (retrospective or prospective) of disease progression lasting for at least 1 year as well as two out of three additional findings (ie, positive brain MRI, positive spinal MRI, positive CSF).<sup>11</sup> Central vein sign has also emerged as a marker for MS and is the imaging manifestation of the periventricular nature of demyelinating plaques.<sup>12</sup> It can be helpful in differentiating MS from mimics.

MRI scans of the brain and spinal cord have become essential to diagnosis, detecting lesions (or plaques) as discrete areas of brightness or high intensity, usually in the white matter of the brain and spinal cord. On MRI, MS lesions appear ovoid, and their size may range from a few millimeters to more than a centimeter in diameter.<sup>13</sup>

MRI techniques and equipment are evolving to improve understanding of MS and to help guide treatment decisions. In addition, new MRI international guidelines for MS were published in August 2021 as a collaboration among The Consortium of Multiple Sclerosis Centers (CMSC), the Magnetic Resonance Imaging in Multiple Sclerosis (MAGNIMS) study group, and the North American Imaging in Multiple Sclerosis (NAIMS) Cooperative.<sup>14</sup> These guidelines were developed in an attempt to standardize imaging protocols for MS to avoid misdiagnosis and allow comparison of sequential scans. The committee has created a two-sided card for patients to present to radiologists when going for scans to assist with standardization (**Figure 2**). This card can be downloaded by clinicians at The CMSC website ([https://mscare.org/page/MRI\\_protocol](https://mscare.org/page/MRI_protocol)) to distribute to their patients.<sup>15</sup>

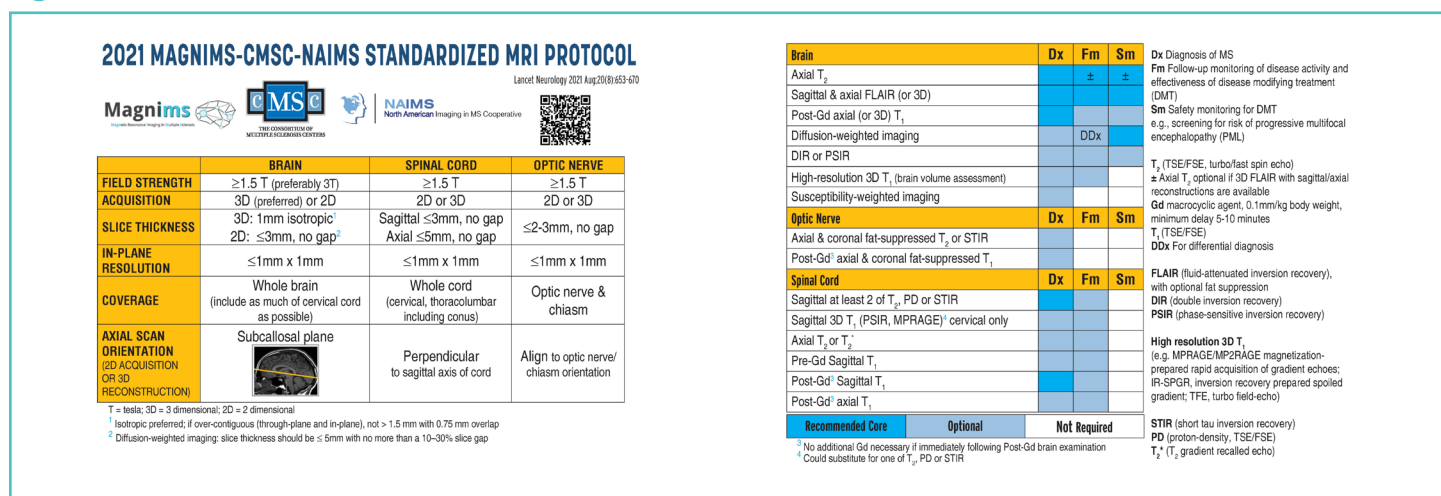
Additional diagnostic procedures may include evoked potential testing (ie, visual evoked potentials [VEPs], brainstem auditory-evoked potentials [BAEPs], or somatosensory-evoked potentials [SSEPs]), which may show slowed nerve conduction even when positive neurological findings are not elicited on examination. Optical coherence tomography (OCT), which measures the thickness of the retinal nerve fiber, may be done to add to the evidence of MS. Blood tests can help rule out the presence of other chronic or infectious illnesses as potential causes of MS-like symptoms, and analysis of CSF may reveal an unusually high number of cells (mostly monocytes), along with qualitative changes in immunoglobulin detected as oligoclonal bands.<sup>16</sup>

## Disease Classification

In 2013, the International Advisory Committee on Clinical Trials of MS refined MS phenotypes for the first time since they were established in 1996.<sup>17</sup> According to internationally accepted terminology, the clinical courses (or phenotypes) of MS are categorized as:

- Clinically isolated syndrome (CIS)

Figure 2. Standardized MRI Protocol Card



Used with permission from The Consortium of Multiple Sclerosis Centers. Available to download at: [https://www.msccare.org/page/MRI\\_protocol](https://www.msccare.org/page/MRI_protocol).

- Relapsing-remitting MS (RRMS) and other relapsing forms of MS
- Secondary-progressive (SPMS)
- Primary-progressive MS (PPMS)

Figure 3 describes the typical clinical course of the three forms of definite MS, although each patient will likely have a unique pattern of disease.

CIS is defined as a first inflammatory episode of the CNS and may present as optic neuritis, transverse myelitis, or a brainstem episode. CIS may represent an isolated event, or it may be a harbinger of MS. When clinical symptoms are accompanied by a positive MRI scan, research shows that 60%-80% of people with CIS will go on to develop MS within a few years.<sup>18</sup>

Another category, known as radiologically isolated syndrome or RIS, is not categorized as a separate phenotype, but may be recognized as an incidental finding on MRI.<sup>18,19</sup>

In about 85% of all MS patients, MS follows a relapsing-remitting pattern at onset, with relapses occurring randomly over many years and with minimal accumulation of disability or change in disease progression. For most patients diagnosed with relapsing MS, the disease course becomes steadily more progressive over time (unless interrupted with DMT). SPMS, as this pattern is called, may or may not involve occasional relapses, plateaus, and remissions, and is typically diagnosed retrospectively.<sup>17,19</sup> Approximately 10%-20% of patients have PPMS, characterized by a disease course that worsens continuously from onset, with occasional plateaus or temporary improvements.<sup>19</sup>

## Active versus inactive, progressive versus not progressive

**disease.** An assessment of whether the disease is active or inactive is also used in classifying MS. Active disease signifies a patient has had recent clinical relapses or has new or evolving MRI evidence. Inactive disease is defined as the absence of recent clinical relapses or changes on MRI.<sup>17</sup> For example, a patient who is classified as having SPMS or PPMS may experience a relapse or new MRI activity and be described as having active MS.

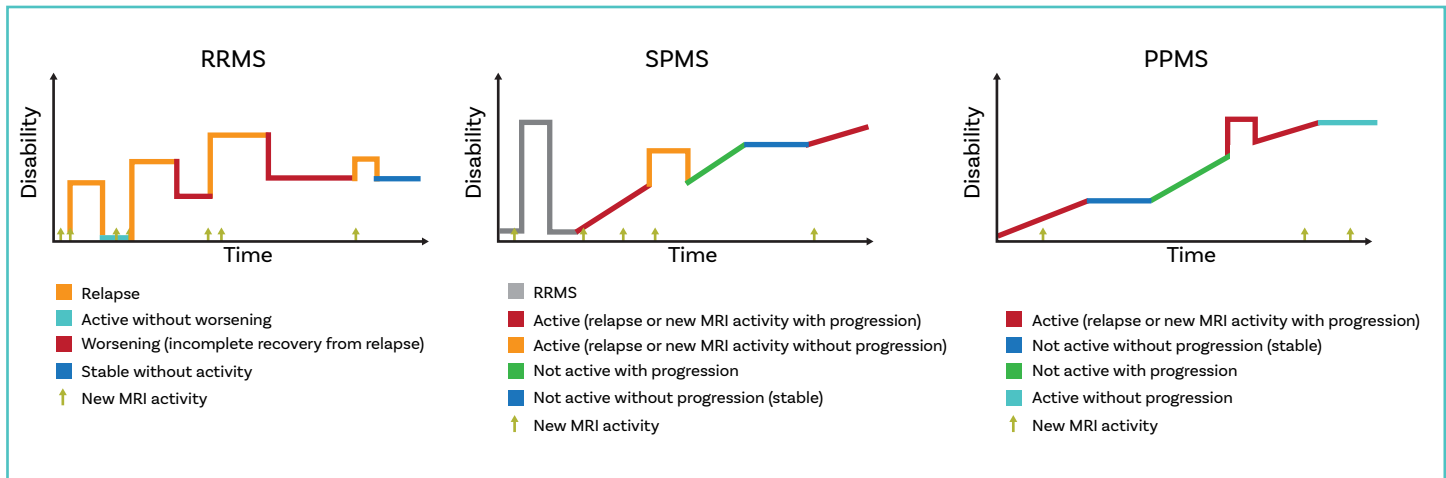
MS is also categorized as “progressive”—meaning there is evidence of accumulation of disability over time with or without clinical relapses or MRI changes—or “not progressive” disease, with no changes clinically or on imaging.<sup>17</sup>

## Evolution of Multiple Sclerosis Treatment and Nursing Practice

Since the second half of the 20th century, the understanding of MS and its diagnosis and treatment have evolved from a hopeless prognosis, characterized in 1948 by the National Multiple Sclerosis Society (NMSS) as the “crippler of young adults,” to a manageable, treatable, chronic condition, a new vision of MS. This evolution drew a wide range of healthcare professionals to the field of MS, including specialist nurses, rehabilitation professionals, and counselors.

During the 1970s, 1980s, and early 1990s, MS patient care could be described as a “diagnose and adios” approach, because interventions available at the time could provide temporary relief but had no lasting impact on the disease

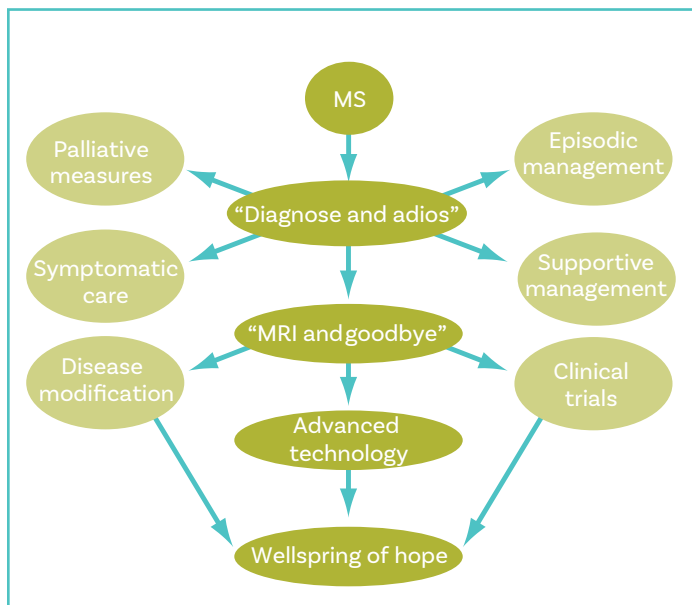


**Figure 3. Types and Courses of Clinically Definite MS**

MRI=magnetic resonance imaging; PPMS=primary-progressive multiple sclerosis; RRMS=relapsing-remitting multiple sclerosis; SPMS=secondary-progressive multiple sclerosis. Used with permission of National MS Society.

course (Figure 4). Treatment was mostly palliative and focused on alleviating symptoms and reducing inflammation. Few clinics were devoted specifically to MS, and few nurses were involved in patient care. Even with the advent of MRI technology in the latter part of the 20th century, MS care did not change substantially beyond what Dr. Labe C. Scheinberg described as “MRI and goodbye.”<sup>20,21</sup>

During the 1990s, MS care improved substantially with the introduction of the immunomodulatory agents interferon  $\beta$ -1b (IFN beta-1b; Betaseron®, Extavia®), interferon  $\beta$ -1a (IFN beta-1a; Avonex®, Rebif®), and glatiramer acetate (Copaxone®, Glatopa®, generic). As of 2022, there are over 20 injectable, infusible, and oral DMTs available to treat MS.<sup>22</sup>

**Figure 4. Evolution of Multiple Sclerosis Treatment**

Adapted with kind permission from June Halper. The phrases “diagnose and adios” and “MRI and goodbye” were coined by Labe C. Scheinberg, MD.

The availability and efficacy of immunomodulatory agents and advances in diagnostic and monitoring techniques have brought new hope to patients with MS and their families. These changes, along with cost-containment pressures within the healthcare system and expanding prescriptive authority for advanced practice nurses, have led to a dramatic and ongoing expansion in the role of nurses who treat patients with MS. Treatment has shifted from a focus on crisis intervention and maintenance to a focus on prevention, symptom management, wellness, and empowerment. The nurse has emerged as a pivotal member of a multidisciplinary team who provides education, skills development, and healthcare delivery for patients with MS and their families.

MS nurses now treat patients in primary, acute, specialized, and rehabilitative settings. MS nurses are educators and advocates. Some have prescriptive privileges, and most work closely with the patient in monitoring and assessing treatment outcomes. MS nurses often initiate, coordinate, or contribute to clinical research. Many are active participants in national and international organizations, such as the IOMSN, that have evolved to support professional education, networking, advocacy, and research on behalf of patients with this perplexing and challenging disorder.

As the role of MS nurses continues to evolve, the need has arisen to establish a cohesive model of MS nursing practice along with specific standards for best practice in MS nursing care. This monograph provides a framework for this model and proposes a philosophy of care that seeks to empower nurses worldwide. The monograph describes

many of the responsibilities of MS nursing, encapsulates best practices in patient assessment and treatment, and explores current and potential areas of nursing research in MS—all with the goal of enriching nurses and other professionals and thereby improving the health and quality of life of all those affected by MS.

## Developing a Model of Multiple Sclerosis Nursing Practice

### Definition of a Multiple Sclerosis Nurse

The MS nurse is a competent expert who collaborates with those affected by MS and shares knowledge, strength, and hope. MS nurses can enhance adaptive and coping skills, facilitate empowerment and a sense of control, and thereby engender hope and positive attitudes among patients with MS and their family members or care partners.<sup>23</sup>

### Philosophy of Multiple Sclerosis Nursing Practice

Chronic illness has been described as having a course that can change over time but can be shaped and managed, even if the eventual outcome cannot be modified.<sup>24</sup> As applied to MS, nursing practice aims to both manage and influence the patient's illness by:

- Shaping the disease course by facilitating treatment that interrupts acute episodes and delays the progression of pathology
- Facilitating the management of symptoms and problems that occur in relation to MS
- Enhancing and promoting safe, maximal function
- Supporting wellness-focused quality of life

Because MS is unpredictable in its course and outcome, the philosophy of MS nursing must be flexible, fluid, dynamic, and responsive to changes in the patient's physical and emotional status. In addition, MS nursing care must recognize, react to, and respect demographic, socioeconomic, and cultural boundaries with care that is comprehensive, empathic, and ultimately holistic.<sup>25</sup>

In this section, to assist in understanding nursing practice issues, MS is viewed across a trajectory from prediagnosis or early diagnosis to advanced-stage disease. Practice issues are discussed for patients grouped as follows:

- Those who have just been diagnosed or have a probable diagnosis of MS or CIS, regardless of how their disease will be eventually classified
- Those with relapsing MS
- Those with progressive MS
- Those with advanced MS, including patients who have become severely disabled within a brief or substantial length of time

### Essential Care Activities

Activities that are essential to the care of patients with MS can be grouped into three main areas:

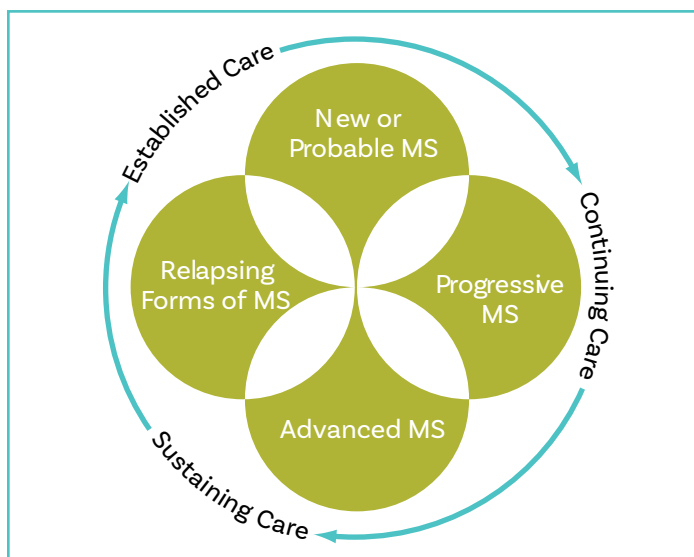
1. Establishing care
2. Continuing care
3. Sustaining care

Together, these three interwoven areas provide a framework for a comprehensive, cohesive model for MS nursing practice that can be applied to care of all patients with MS, regardless of disease classification or level of disability (**Figure 5**). Although specific activities within each area may be the same for each patient, the emphasis may shift according to the stage of disease. Establishing care is the first step toward building relationships and encouraging open communication with patients and their families or care partners. Components of establishing care include building trust, establishing partnerships, determining information needs, sharing information and decision making, and assessing each patient's support network. These activities provide a foundation that promotes empowerment, encourages positive attitudes, and fosters hope, ultimately contributing to the establishment of a strong therapeutic alliance between nurses and those receiving care.

Continuing care focuses on cultivating patient health. As part of continuing care, nurses serve as educators, counselors, and advocates. Nurses teach patients practical approaches for managing disease symptoms and medication side effects, stressing the importance of adherence to treatment. Nurses also help patients implement self-care strategies, such as self-injection; adherence tips; symptom management; and wellness strategies focused on diet, exercise, and coping with stress. Self-care strategies can enhance patients' health and give them a sense of control over their illness. As part of continuing care, nurses may also assist patients with family and vocational issues and guide patients through the many life- and health-related uncertainties associated with MS.

Sustaining care focuses on maintaining patient well-being. In sustaining care, MS nurses coordinate referrals, identify community and information resources, and serve as consultants as patients' and families' needs change. Sustaining care also calls for the establishment of collaborative liaisons among MS nurses and other healthcare professionals—for example, neurologists, primary care physicians, speech and language pathologists, rehabilitation specialists, psychologists, and social workers—as dictated by the patients' physical and emotional needs. In addition, MS nurses may establish liaisons outside the healthcare team, to include government services, religious establishments, and other organizations that can provide assistance and support for patients with MS.

**Figure 5. Cohesive Model of Nursing Care in Multiple Sclerosis**



Adapted with kind permission from Marie Namey.

## Practice Areas Across the Disease Trajectory

### Patients with new or probable diagnoses

For patients with a new diagnosis of CIS or MS, or symptoms that strongly suggest MS, the nurse's priority is to establish care. Nurses are aware that patients differ in their reactions to diagnosis.<sup>25,26</sup> Some patients experience grief and shock; some, denial; others may feel relieved to find an explanation for their symptoms. Initially, some patients may be unable to absorb much specific information about the disease and treatment options; others may want as much information as possible. Special attention may be needed for patients who

are awaiting confirmation of a probable diagnosis, a process that may be prolonged and frustrating.<sup>26</sup> Definitive diagnosis can take several years, especially for patients with CIS, and misdiagnosis is not uncommon.<sup>27</sup> As part of building trust and open communication, nurses need to carefully assess patients' reactions, coping mechanisms, and information needs.

### Patients with relapsing forms of MS (RMS) (including relapsing-remitting MS [RRMS])

For patients with RMS, the main focus is on continuing care. Sometimes, however, activities for establishing care apply—for example, when a patient has been symptom-free for months or years and then has a relapse. Research suggests that a relapse represents an “interruption” that precipitates a need for new information to help the patient cope.<sup>28</sup> MS nurses will likely find themselves counseling patients to help them contend with the disappointment and discouragement associated with a relapse. Nurses can reestablish communication and reassess information needs to ensure that the continuing care needs of these patients are met.

As part of continuing care for patients with RMS, nurses seek to emphasize the importance of early and sustained treatment with DMTs. They can help patients establish realistic expectations and explore treatment options. Nurses can also help patients make informed decisions about the use of complementary or alternative therapies.

Nurses also serve as advocates to ensure that patients have timely and adequate access—through insurance or other healthcare programs or through industry-supported programs—to medications, adaptive equipment, supplies, and mental health counseling. Nurses can help patients and families cope with the major responsibilities of managing symptoms and complications of MS while maintaining “normal” lives and dealing with the ordinary events and experiences of living.<sup>24</sup> Encouraging patients to develop support networks (eg, through participation in an MS support group) can help.

In sustaining care of patients with RMS, nurses endeavor to recognize the tremendous burden and responsibility that the disease represents to patients and their families.<sup>24,25</sup> Nurses can advocate for adequate insurance entitlements and appropriate access to care. They may need to defend patient autonomy with regard to treatment decisions and

self-care activities. Sustaining care for patients with RMS requires continuous evaluation of patients' physical, cognitive, and emotional status. Specific changes, for example, in mobility or cognition, need to be assessed and treated when they become evident and when they interfere with activities of daily living. In addition, treatment outcomes and patients' self-care abilities must be monitored. If patients are doing well on treatment, positive reinforcement can help continue that pattern; if patients are not adhering to treatment, nurses can try to determine the impediments to adherence and initiate strategies to reverse this trend. In some cases, this may mean a change in DMT.

### Patients with progressive MS

The nursing care needs of patients with progressive MS are often complex. Sustaining patient trust and maintaining open communication are crucial to effective practice. If the disease worsens, the patient's physical, cognitive, and emotional needs are to be continually reevaluated. Safety issues are the key concern. A caregiver or family member may need to be enlisted to assume responsibilities for activities of daily living and other interventions previously managed by the patient. Nurses can assist with training the caregiver and counseling the patient through this change in status. If disability increases, continued counseling and healthcare interventions can help the patient adapt and adjust. Rehabilitation efforts may be employed to reduce the severity of certain symptoms and improve patient independence.<sup>29</sup>

### Patients with advanced MS

For patients whose disease has become more advanced, nurses must try to redefine therapeutic partnerships with patients and with family members or care partners who ensure that the patient's daily needs are met. If the patient's condition warrants home healthcare or admission to a nursing home, the nurses who provide this care will attempt to establish new therapeutic relationships. For patients with advanced disease, it is especially important for care to be planned and implemented with attention to individual patient preferences, cultural mores, and previous lifestyle. In addition, because case management issues associated with advanced MS are often complex, nurses also often serve as advocates for quality care.

Continuing care needs of patients with advanced MS shift to providing comfort, ensuring safety, and preventing complications. For example, patients with impaired mobility need interventions that prevent pressure sores. For patients who have difficulty speaking, alternate communication methods need to be devised. For patients who have lost the ability to swallow, alternative feeding methods will be necessary. Although these patients may not be able to care for themselves, they require recreation, stimulation, and support of their daily living activities. These requirements are universal for all people and are especially important for those facing daily losses in function, financial and emotional security, and self-esteem.

As part of sustaining care for patients with more advanced disease, these patients and their families require information and counseling on various issues, including the acceptance of progression of their disease and the need for life planning and advance directives, nursing home placement, and hospice care. Patients may need an opportunity to talk openly and honestly about their feelings. Nurses can be alert to signs of despair, helplessness, and hopelessness in their patients and make appropriate referrals. Depression and suicide are real phenomena in MS. Patients with advanced disease and their families are often dealing with end-of-life issues, and nurses will want to consider palliative care options used by other patient populations.

## Domains and Competencies of Multiple Sclerosis Nursing

The purpose of this section is to continue defining a model for MS nursing by identifying domains and competencies that describe the unique specialty of MS nursing. This model also helps to define best practices.

The domains of MS nursing are the particular areas of knowledge, expertise, and influence provided by nurses who care for patients with MS. Competencies are defined as the specific types of knowledge and skills that fit within and support the nursing domains. The domains and competencies described here have been selected to encompass care of patients over the full life-span trajectory of people with MS—that is, across the continuum from the newly diagnosed patient to advanced-stage disease.

Together, these domains and competencies define the standards and scope of MS nursing practice. They can serve

as a guide for nurses who currently specialize in MS care or who plan to pursue this specialty.

### Multiple Sclerosis Nursing Domains

*Establish therapeutic partnerships* with MS patients, their families, and other health professionals on the patient's professional healthcare team.

- *Perform comprehensive assessments* to gauge each patient's level of functioning, identify the patient's needs and preferences, understand the patient's learning style, appreciate the patient's lifestyle, and get to know the patient's family or care partners.
- *Formulate a collaborative treatment plan*, taking into account the patient's symptoms, level of disability, need for DMT, and need for sustained or prolonged care.
- *Initiate and facilitate a treatment regimen* by educating the patient about DMTs; teaching self-injection, oral administration, and infusion protocols; serving as a patient advocate; helping the patient to overcome physical, cognitive, or other obstacles to treatment; and administering treatment when necessary.
- *Educate the patient about the possibility of a relapse* despite treatment with a DMT. This may include relapse management with intravenous (IV) or oral steroids.
- *Monitor the patient's treatment outcomes*, including adherence; self-care, self-efficacy, and responsibility; side effects and adverse effects of medications; lifestyle changes; and quality of life.
- *Sustain therapeutic alliances* with the patient, family members or care partners, and other professionals on the patient's healthcare team.
- *Maintain and broaden nursing competencies* by developing new skills; enhancing MS knowledge; and initiating, coordinating, or participating in MS research.

### Knowledge-Based Competencies

To carry out activities in these various domains, MS nurses require solid, comprehensive, and current knowledge in the following areas:

1. The diagnostic process, courses, and pathology of MS, including the trajectory of MS across the life span
2. Pharmacology of the evolving array of therapeutic agents used for acute, symptomatic, and disease-modifying treatments
3. Use of complementary and alternative therapies in MS

4. Use of evaluation tools for monitoring outcomes
5. Basics of rehabilitation practice
6. Community resources—information and resources for patients and families
7. Educational principles, including age-specific learning techniques
8. Psychosocial issues, such as cultural and ethnic considerations, coping, and gender and sexuality issues
9. Reimbursement processes (eg, insurance and managed care plans, Medicaid, Medicare, pharmaceutical industry programs)
10. Healthcare and education strategies that encourage wellness and health promotion
11. Professional expertise—for example, knowledge of nursing theory and models, assessment tools, current technologies, technical nursing skills, professional organizations, and the comprehensive model of MS care

### Skill-Based Competencies

Skills necessary to professional nursing care of patients with MS include the following:

1. Communication
  - a. Listen to patient, family, other members of the healthcare team
  - b. Collaborate with other healthcare providers
  - c. Perform healthcare visits in person and virtually
  - d. Network with other providers and patient groups
  - e. Negotiate for access to care and patient entitlements
  - f. Delegate tasks as necessary
  - g. Document health assessments, plan of care, and other pertinent healthcare information
2. Assessment
  - a. Recognize physical care requirements
  - b. Perform neurological assessment
  - c. Perform functional assessment
  - d. Perform psychological, sociological, and cognitive assessments
  - e. Recognize culture-specific needs
  - f. Detect acute and chronic changes in health, including comorbidities



3. Counseling
  - a. Provide anticipatory guidance (eg, foresee and forestall problems)
  - b. Define patient's, family's, care partners', and nurse's limits and responsibilities
  - c. Listen, motivate, inspire hope, and put MS "in its place"
  - d. Solve problems
4. Education and teaching
  - a. Serve as a role model for patients, family members, care partners, other nurses, and other members of the professional healthcare team
  - b. Serve as a mentor and preceptor
  - c. Increase awareness about MS in the community
5. Advocacy
  - a. Negotiate within the healthcare system and with outside groups such as insurers
  - b. Promote self-care
6. Participate in research
  - a. Establish benchmarks of nursing care
  - b. Examine outcomes of nursing practice

### Specialized Competencies

The following is a list of skills that may require a unique approach in the care of patients with MS:

1. Management of elimination dysfunction
2. Assessment and control of pain
3. Assessment and reduction of spasticity
4. Skin care and management of injection-site reactions
5. Infusion skills for IV therapies
6. Knowledge of advanced technologies (eg, MRI, optical coherence tomography [OCT], rehabilitation innovations)

### Matching Nursing Competencies to Nursing Domains

**Table 1** shows how specific skill-based competencies can be matched to MS nursing domains, providing a comprehensive and practical illustration of the scope of MS nursing practice. For example, as part of *establishing therapeutic partnerships*, nurses listen to and communicate with patients and other health professionals. Nurses assess the patient's psychological, social, and cognitive abilities and maintain sensitivity to cultural, ethnic, and gender issues. Nurses provide anticipatory guidance; establish limits and responsibilities of care for patients, family members, and healthcare professionals; and listen, motivate, and inspire hope in initiating treatment. Education about the disease and about effective treatment and management of symptoms is an essential component of developing nurse-patient partnerships. Furthermore, as part of establishing therapeutic partnerships, nurses may need to serve as advocates by negotiating within the healthcare system—ensuring that patients get the medications, equipment, and resources they need—and by promoting patient self-care.

As part of *monitoring outcomes*, MS nurses listen and communicate and must continuously assess and document the patient's functional, psychological, sociological, and cognitive status over time (**Table 1**). In addition to monitoring the patient's general health status, nurses must be acutely aware of the appearance of, or any changes in, symptoms. Nurses also provide counseling to motivate patients and encourage hope and self-care. They provide education about monitoring treatment, recognizing relapses, serving as role models for patients and families and as mentors and preceptors for their less experienced peers.

Many of the specific skills identified in **Table 1** apply across multiple domains. For example, anticipatory guidance is crucial not only for establishing strong therapeutic relationships but also for formulating, initiating, and facilitating treatment. Similarly, the nurse's capacity to listen, motivate, and inspire hope is essential not only to establishing therapeutic partnerships and formulating treatment plans but also to monitoring treatment outcomes and sustaining therapeutic alliances. Recognizing the patient's physical care needs is obviously important to performing a comprehensive assessment, but it is also part of formulating and implementing treatment and monitoring treatment outcomes. These examples illustrate the continuity that exists both within and across domains and competencies.



Table 1. Domains and Competencies of Multiple Sclerosis Nursing

COMPETENCIES	Establish Therapeutic Partnerships	Perform Comprehensive Assessments	Formulate Collaborative Treatment Plan	Initiate and Facilitate Treatment Regimen	Monitor Outcomes	Sustain Therapeutic Alliances	Maintain and Broaden Nursing Competencies
<b>1. Communicate</b>							
a. Listen	X	X			X	X	X
b. Collaborate	X		X			X	X
c. Perform	X	X		X	X	X	X
d. Network			X			X	X
e. Negotiate			X	X		X	X
f. Delegate			X	X		X	X
g. Document		X	X		X		X
<b>2. Assess patient care needs</b>							
a. Recognize physical care requirements		X	X		X		
b. Perform neurological assessment		X			X		X
c. Perform functional assessment		X	X	X	X		X
d. Perform psychological, social, and cognitive assessments		X	X	X	X		X
e. Recognize culture-specific needs	X	X	X				X
f. Detect acute and chronic health changes		X			X		
<b>3. Counsel patients and families</b>							
a. Provide anticipatory guidance	X		X	X		X	
b. Define limits and responsibilities	X		X	X		X	
c. Listen, motivate, inspire hope, put MS "in its place"	X		X	X	X	X	
d. Solve problems			X	X	X	X	
<b>4. Educate</b>							
a. Serve as a role model	X			X	X	X	X
b. Serve as a mentor and preceptor					X	X	X
c. Increase awareness of MS in the community						X	X
<b>5. Advocate</b>							
a. Negotiate within the healthcare system	X		X	X		X	X
b. Promote self-care	X		X	X	X	X	X
<b>6. Participate in research</b>							
a. Establish benchmarks of care							X
b. Examine outcomes of nursing practice							X

### Role of the Nurse in Pharmacologic Therapy of Multiple Sclerosis

As a primary source of information for patients and families affected by MS, nurses are in an optimal position to provide education about medications. Nurses can provide practical information about indications, effectiveness, administration, and side effects, thereby facilitating patients' treatment decisions, clarifying any misconceptions, and ensuring proper use of medications. Shared decision-making occurs when a healthcare provider and a patient work together to make a healthcare decision that is best for the patient. The optimal decision takes into account evidence-based information about available options, the provider's knowledge and experience, and the patient's values and preferences. There are five steps in the shared decision-making process<sup>30</sup>:

1. Engage patient participation
2. Explore and compare treatment options
3. Assess patient values and preferences
4. Reach a decision on treatment with the patient; and
5. Evaluate the patient decision

MS nurses also play a substantial role in monitoring adherence. Once a particular medication or medication regimen is begun, nurses must know how to assess treatment responsiveness and how to monitor for and recognize potential side effects. Nurses also serve as advocates, working with insurance companies, managed care organizations, Medicaid and Medicare, and pharmaceutical support programs to make sure that patients can obtain and receive reimbursement for the treatments prescribed. Medications for MS include:

- Episodic treatments—those used to shorten relapses
- Symptomatic treatments—those used to minimize or control specific symptoms, such as spasticity, bowel and bladder problems, and fatigue
- Disease-modifying treatments (DMTs)—immunomodulatory drugs and other agents developed to reduce the frequency and severity of relapses and slow disease progression

This section lists and discusses many of the medications used for the management of MS, along with specific nursing considerations for each medication.

### Episodic Treatments

In patients with MS, a relapse—also known as an acute attack or an exacerbation—is defined as an episode of new or worsening MS symptoms that lasts more than 24 hours and is not related to metabolic changes (eg, due to fever or intercurrent illness) or steroid withdrawal. Typically, an acute relapse tends to progress over a few days, reaches its peak within a week, and then slowly resolves.<sup>31,32</sup> Relapses often lead to a lasting change in the patient's functional status.<sup>33,34</sup> Relapse rates have been declining over the past decade, presumably due to the efficacy of DMTs; research also suggests that continuous use of DMTs may blunt relapse episodes and symptoms.<sup>33,35</sup>

There is no established standard for management of relapses. Treatment decisions are determined by the healthcare provider on an individual basis. Depending on specific symptoms, no treatment may be suggested—for example, for patients with mild sensory attacks and no functional decline. Most patients who are experiencing acute relapses are given high-dose corticosteroids, either IV or orally,<sup>36</sup> to reduce inflammation in the CNS and potentially help to reestablish the integrity of the BBB, thereby hastening improvement of symptoms.<sup>37</sup>

Treatment is based on the practice patterns of the prescribing provider caring for the patient. Unfortunately, there is a paucity of literature documenting the superiority of one route of administration over the other; however, intravenous methylprednisolone (IVMP) is consistently the treatment of choice. Initially, this anti-inflammatory corticosteroid is given at high, intermittent doses over 3 to 5 days.<sup>38</sup> IVMP can be given in the hospital or at home and may or may not be followed by a gradually tapering dose of an oral corticosteroid.<sup>36</sup> The Canadian model leans toward high-dose oral steroids in place of IV administration. ACTH, previously used for relapses during the mid-20th century, is available but there is no accepted protocol for relapse management, and there are issues related to high cost and access.<sup>32,38</sup> Plasmapheresis is also an option for patients experiencing severe relapses that don't respond to corticosteroids.<sup>32</sup>

During steroid treatment, patients and families need to know what to expect. Nurses can provide education about realistic outcomes and side effects that demand medical intervention. Typical side effects include increased

appetite, gastrointestinal upset, nervousness or anxiety, and insomnia.<sup>36</sup> Facial flushing, urinary frequency, and taste disturbance may also accompany corticosteroid treatment. Patients should be encouraged to call their healthcare provider if they experience anxiety or insomnia. Other side effects that may warrant monitoring and medical treatment include glycosuria and severe mood changes or mood swings. Patients should be advised to limit salt and sugar intake while on corticosteroid treatment, and patients taking DMTs should be instructed not to stop these medications while receiving IVMP or any other treatment for a relapse. During the time of a relapse, it is important to assess whether patients would benefit from other interventions, such as adaptive equipment. For example, for patients who have difficulty walking during an attack, a cane or walker can provide a safe, energy-conserving mobility device. Nurses may also want to discuss temporary modifications to patients' work and physical activities. In these cases, nurses can advocate for patients by providing information on Family Medical Leave (FML) or short-term disability.

## Symptomatic Treatments

Managing the ongoing symptoms of MS is challenging, but effective management can dramatically improve the patient's quality of life. Fatigue, elimination problems, and other common symptoms can be controlled or reduced through education, counseling, and rehabilitation measures.<sup>39</sup> When these strategies are not sufficient, pharmacotherapy may be considered.

**Table 2** lists medications used for symptom management in MS. It gives generic drug names, along with specific nursing implications associated with their use, for treatment of various symptoms. The table is not intended to be exhaustive; the most common or problematic symptoms are discussed here, but others that may be alleviated by nursing intervention include tremor, weakness, vertigo, and sexual dysfunction. Excellent reviews of the strategies and medications used to manage these symptoms are available for guidance, and many can be found on the IOMSN website (<https://iomsn.org>).

The first step in symptom management is to determine the factors that are causing or contributing to symptoms. Concomitant medications and concurrent illnesses or

other medical conditions may produce new symptoms or alter the severity of the symptoms. If pharmacologic treatment is needed to alleviate symptoms, some general "rules of thumb" apply. First, it is essential to determine whether any contraindications, such as other medical conditions or concomitant medications (including over-the-counter medications and alternative treatments such as cannabis), preclude treatment with a particular agent. Second, nurses need to convey what outcomes patients should anticipate and what side effects may occur—this can help reinforce positive therapeutic relationships and can help optimize symptom management. Third, patients need to be encouraged to follow up, so that nurses can confirm that medications are working properly and intervene if unexpected outcomes or intolerable side effects occur. Nursing strategies such as dose escalation and dose titration of DMTs can help patients avoid side effects and increase tolerance of treatment.

## Fatigue

Fatigue is the most common—and often the most disabling—symptom associated with MS. Fatigue in patients with MS may occur in several different forms—as activity-related fatigue; as fatigue associated with deconditioning, depression, or neuromuscular exhaustion; or as a lassitude known as "MS fatigue." Treatment of fatigue requires identifying the cause, effective energy management, medications, or both. Nurses can suggest behavioral changes such as conditioning programs, exercise, and improved nutrition.<sup>40,41</sup> Patients can be referred to an occupational therapist who can teach them about and help them implement energy-conservation techniques.

Drugs that can provide relief include CNS stimulants such as methylphenidate (Ritalin®) and modafinil (Provigil®).<sup>41,42</sup> Patients should be advised that these medications may cause nervousness, restlessness, and insomnia. Antidepressants such as fluoxetine (Prozac®) and an antiviral agent, amantadine (Symmetrel®), may also be effective for fatigue.<sup>41,42</sup> Previous literature has also documented the benefit of conditioning programs with graded exercise to reduce fatigue.<sup>41</sup>

## Bladder dysfunction

Bladder dysfunction results from pathology in nerve pathways controlling detrusor function, sphincter function, or both.<sup>43</sup> Symptoms of bladder dysfunction—urinary hesitancy,

frequency, urgency, and/or incontinence—affect many people with MS. Patients may attribute these problems to the effects of aging or childbirth and simply accept them as such rather than see them as modifiable symptoms of MS, but they should be informed that bladder symptoms can be managed. Dysfunction may manifest as failure to store urine, failure to empty urine, or both. Urinary tract infection may be a contributing factor and should be ruled out or treated appropriately before initiating other treatment. Effective pharmacologic treatments include anticholinergic agents such as darifenacin (Enablex®) and solifenacin succinate (Vesicare®); antimuscarinic agents such as tolterodine (Detrol®); alpha-blockers such as terazosin; and newer beta-3 adrenergic receptor agonists, including mirabegron.<sup>43</sup> Onabotulinumtoxin A (Botox®) can be effective in treating failure to store.<sup>44</sup> A bladder training program that includes education, elimination of bladder irritants such as caffeine and aspartame, scheduled voidings, and positive reinforcement can also improve bladder functioning and quality of life. Patients may also require bladder emptying with either intermittent or permanent placement of a catheter.

### Bowel dysfunction

Patients with MS may have bowel problems that range from constipation to bowel urgency and involuntary bowel movements.<sup>45</sup> Constipation is the most common, and involuntary bowel movements are perhaps the most distressing. Constipation is best managed with preventive measures, including a high-fiber diet, adequate fluid intake, exercise, and an established bowel program. The nurse can guide and facilitate a bowel program with education and support. If medication is indicated, bulk formers (such as psyllium) or softeners (such as docusate) may be prescribed.<sup>45</sup> If a stimulating laxative is needed, a mild compound such as milk of magnesia may work best.<sup>45</sup> Stronger stimulants and stimulating suppositories or enemas are to be regarded as occasional treatments or tools to get a bowel program started—their use on a regular basis should be avoided.

Patients with bowel urgency may benefit from treatment with anticholinergic agents.<sup>45</sup> These medications have antispasmodic effects that can ease uninhibited bowel spasms that contribute to urgency. Bulk-forming agents, along with a regular bowel routine, can also reduce bowel urgency.

### Pain

Pain in MS may be neuropathic or neurological in origin and acute or chronic in duration. Pain may also result from poor compensation of weakness—eg, pain in the left hip due to inappropriate compensation for right leg weakness or foot drop. Because the pain associated with MS differs from that typically associated with injury, standard pain medications such as aspirin, nonsteroidal anti-inflammatory agents, and narcotic analgesics do not provide relief.

Types of acute pain that occur frequently in patients with MS are *trigeminal neuralgia*, a sharp, stabbing pain in the face, and a burning, aching sensation known as *burning dysesthesia*. Pharmacologic treatments that can provide relief include the anticonvulsants phenytoin (Dilantin®), carbamazepine (Tegretol®, Carbatrol®), gabapentin (Neurontin®), and lamotrigine (Lamictal®).<sup>46,47</sup> Though often effective for pain, some anticonvulsants may cause sedation; slow titration can minimize this side effect. Tricyclic antidepressants such as amitriptyline may relieve pain and can be especially helpful for dysesthesias; they may act by stopping pain conduction through the nerves.<sup>47</sup> A transdermal delivery system, a lidocaine patch called Lidoderm®, may provide patients with sustained relief if oral medications are partially effective or are ineffective.

Two other medications that are used to treat acute pain due to MS are pregabalin (Lyrica®), an anticonvulsant and analgesic agent also approved to treat neuropathic pain associated with diabetes and fibromyalgia, and duloxetine hydrochloride (Cymbalta®), which is also used to treat depression (see next page).<sup>47</sup> Neither drug has been specifically approved to treat pain associated with MS, but their effectiveness in treating neuropathic pain associated with other diseases make them a suitable option for MS patients.

Chronic pain in patients with MS often manifests as a “pins and needles” sensation or as a burning, aching pain. Chronic pain is often treated with the same medications used for treatment of acute dysesthesias.

Patients with MS also may experience pain as a result of muscle cramping or abnormal musculoskeletal stresses. Musculoskeletal pain can be alleviated by supportive interventions such as an ankle-foot orthosis or by appropriate positioning of seating devices to maintain/sustain appropriate body alignment.

## Spasticity

Another common symptom, spasticity, is a major factor in decreased mobility among patients with MS. Spasticity can manifest as stiffness or spasms, may involve pain and discomfort, and may interfere with daily activities. Regular stretching and exercise can reduce stiffness and improve function, but pharmacologic treatment is often necessary.

Effective antispasmodics include baclofen (Lioresal®, Lyvispah®), a  $\gamma$ -aminobutyric acid (GABA) antagonist, and tizanidine (Zanaflex®), an  $\alpha_2$ -adrenergic agonist.<sup>48</sup> The anticonvulsant medications diazepam (Valium®), clonazepam (Klonopin®), and gabapentin (Neurontin®) may also be helpful in combination with other medications.<sup>48</sup> For many of these medications, it is best to start at low doses, then titrate up, to improve tolerability. Maximizing the dose at bedtime, usually a time of maximal spasticity, is a useful strategy for managing both spasms and the sedative effects of some antispasmodics.

Baclofen is among the most commonly used medications for spasticity, but the drug may cause weakness or sedation. If weakness limits the use of baclofen, tizanidine is a viable alternative. Baclofen and tizanidine may be used in combination as well. For spasticity that is severely disabling and not responsive to oral drug therapy, intrathecal baclofen, delivered via a programmable pump that is surgically inserted into the abdominal wall, may provide relief.<sup>48</sup> For focal muscle spasticity, which may be resistant to systemic treatment, an injection of botulinum toxin (Botox®) can provide temporary relief but may need to be repeated.<sup>49</sup>

Cannabis has entered the discussion of control of spasticity (and pain) in MS, and nurses should be aware of its pros and cons for patients. In addition, cannabis preparations are now legal in many countries and are being used by patients to treat MS symptoms with limited evidence on efficacy. The cannabis-containing compound nabiximols (Sativex®) has been approved for use in countries other than the United States, including Canada, and is poised for approval by the Food and Drug Administration (FDA). It appears to be a safe and effective therapy for spasticity that does not respond to first-line agents.<sup>50</sup>

## Depression

Both clinical depression and a similar, less severe emotional distress are common in patients with MS. About 50% of

patients with MS experience depression at some time during their illness—a rate much higher than that seen in the general population.<sup>51</sup> Rates of suicide among people with MS are also much higher than those seen in the general population.<sup>52</sup> It is important for MS nurses to be aware of the symptoms of depression and assess patients with each contact. Appropriate referrals for counseling or psychiatric therapy and recommendations for pharmacologic treatment can be made as needed. If depression is suspected, certain contributing factors must be considered. Some medications, including baclofen and benzodiazepines, which are used for symptom management, may be associated with depression. Patients are to be screened for depression before starting treatment with a DMT, and any depressive symptoms should be treated before or during therapy. Note that other medical conditions, such as hypothyroidism, can contribute to a depressed affect and need to be ruled out or treated, as appropriate.

An array of medications is available to alleviate depression. Selective serotonin reuptake inhibitors (SSRIs) and serotonin and norepinephrine reuptake inhibitors (SNRIs), such as fluoxetine (Prozac®), sertraline (Zoloft®), escitalopram oxalate (Lexapro®), citalopram hydrobromide (Celexa®), paroxetine (Paxil® or Paxil CR®), and duloxetine (Cymbalta®), are frequently prescribed.<sup>53,54</sup> Tricyclic antidepressants, including amitriptyline and nortriptyline, are useful,<sup>54</sup> especially if sleep disturbance accompanies depression. Atypical antidepressants such as venlafaxine (Effexor®) and bupropion (Wellbutrin®) may also be prescribed.<sup>54</sup> It is important to review any interactions of depression treatment with DMTs, as some DMTs have been shown to reduce the effectiveness of the antidepressants.

## Walking problems

Walking and overall mobility can be affected by MS to a greater or lesser extent based on the nature of the disease course, problems with stamina and fatigue, environmental factors such as climate and structural issues (stairs, length of halls, etc) and demands of activities of daily living. Dalfampridine (Ampyra®) has been approved by the FDA to improve walking speed in MS but it is important that the nurse also ensure that the patient receives appropriate rehabilitative and exercise training to enhance the effect of the medication.<sup>55</sup>



### Emotional lability (pseudobulbar affect [PBA])

Patients with MS can experience a wide range of emotions related to coping with this disorder. One stressful and embarrassing problem is pseudobulbar affect or inappropriate laughing or crying. The associated stress of this problem is obvious and embarrassing. The FDA has approved Nuedexta®, an oral medication that is a combination of the generic drug quinidine, which prevents cardiac arrhythmia, and the cough suppressant dextromethorphan. The most common side effects include diarrhea, dizziness, cough, emesis, urinary tract infections, elevated liver enzymes, and flatulence. This medication can interact with other medications (see [Table 2](#)).<sup>56</sup>

### Medications Used for Disease Modification

#### Immunomodulatory agents

Evidence that MS is more than a demyelinating disease—that axonal transection is the pathology underlying permanent disability, occurs early in the disease course, and causes irreversible damage—gave rise to a major impetus to early and aggressive treatment with immunomodulatory agents.<sup>2</sup>

The introduction of injectable DMTs in the 1990s, including IFN  $\beta$ -1a (intramuscular [IM] and subcutaneous [SC]), IFN  $\beta$ -1b, and glatiramer acetate, changed the disease course for RMS. Along with nonpharmacologic strategies, including appropriate exercise and nutrition, it is no longer inevitable

that a patient diagnosed with RMS will eventually end up in a wheelchair.

Because of the rapidity of development of new DMTs and so as not to outdate this monograph, it is beyond the scope to detail the evidence behind each of the DMTs available for use in MS. Suffice it to say that extensive data definitively support the early and continued use of these immunomodulatory agents to modify disease progression, reduce future disability, and improve quality of life for patients with RMS.<sup>57,58</sup> For instance, a recent modeling study assessing the effect of DMTs on 14,717 patients followed for up to 15 years found treated patients were less likely to have relapses (reduced by 40%-41%), worsening of disability (reduced by 19%-44%), and progression to needing a walking aid (reduced by 67%) compared with untreated patients.<sup>59</sup>

Both the American Academy of Neurology and the MS Coalition of MS-related organizations, including Accelerated Cure, Can Do Multiple Sclerosis, The Consortium of Multiple Sclerosis Centers, International Organization of Multiple Sclerosis Nurses, Multiple Sclerosis Association of America, Multiple Sclerosis Foundation, National Multiple Sclerosis Society, and United Spinal Association, offer information on the data behind the use of DMTs, including clinical trial results, proposed mechanisms of action (MOA), side effects, and warnings and precautions.<sup>57,58</sup>



Table 2. Pharmacologic Management of Selected Symptoms in Multiple Sclerosis

Symptoms	Treatment	Nursing Considerations
Fatigue	<ul style="list-style-type: none"> <li>CNS stimulants (pemoline, modafinil, armodafinil, methylphenidate)</li> <li>Amantadine</li> <li>Selective serotonin reuptake inhibitors (SSRIs), eg, fluoxetine</li> </ul>	<ul style="list-style-type: none"> <li>Restlessness or sleep disturbance may occur</li> <li>Help patients with dosing schedule, titrate doses up</li> </ul>
Bladder dysfunction	<ul style="list-style-type: none"> <li>Anticholinergics (eg, oxybutynin, darifenacin, solifenacin succinate)</li> <li>Antimuscarinics (eg, tolterodine)</li> <li>Beta-blockers (eg, terazosin)</li> <li>Onabotulinumtoxin A (Botox®)</li> </ul>	<ul style="list-style-type: none"> <li>Determine if urinary tract infection is present</li> <li>Monitor retention</li> <li>Monitor fluid balance</li> <li>Follow overall elimination pattern</li> <li>Consider contribution of other medications</li> <li>Provide strategies to avoid side effects (eg, dry mouth)</li> </ul>
Bowel dysfunction	<div> <div> <b>Constipation</b> <ul style="list-style-type: none"> <li>Stool softeners</li> <li>Bulk-forming agents</li> <li>Mini-enemas</li> <li>Stimulants</li> <li>Suppositories</li> </ul> </div> <div> <b>Urgency/Diarrhea</b> <ul style="list-style-type: none"> <li>Bulk-forming agents</li> <li>Anticholinergics</li> </ul> </div> </div>	<ul style="list-style-type: none"> <li>Provide bowel training regimens; many of the medications should not be used long-term</li> <li>Consider contributory effects of other medications (eg, steroids or antibiotics)</li> <li>Consider lifestyle issues</li> <li>Encourage exercise</li> <li>Provide diet counseling</li> </ul>
Pain	<ul style="list-style-type: none"> <li>Anticonvulsants (phenytoin, carbamazepine, gabapentin, pregabalin, lamotrigine)</li> <li>Tricyclic antidepressants (amitriptyline)</li> <li>Duloxetine hydrochloride</li> </ul>	<ul style="list-style-type: none"> <li>Watch for sedation</li> <li>Start with low doses and titrate up</li> <li>Monitor outcomes; alter treatment as necessary; supportive measures can help</li> </ul>
Spasticity	<ul style="list-style-type: none"> <li>GABA antagonists (oral or intrathecal baclofen)</li> <li>α-Agonists (tizanidine)</li> <li>Anticonvulsants (diazepam, clonazepam, gabapentin)</li> <li>Botulinum toxin</li> </ul>	<ul style="list-style-type: none"> <li>Time doses to maintain therapeutic blood levels</li> <li>Titrate doses up (especially with baclofen)</li> <li>Watch for sedation or cognitive symptoms; may require a change in dosage or medication</li> <li>Combination treatments may help</li> <li>Intrathecal baclofen requires surgical insertion of programmable pump</li> </ul>
Depression	<ul style="list-style-type: none"> <li>SSRIs and SNRIs (eg, fluoxetine, sertraline, paroxetine, citalopram, duloxetine, escitalopram)</li> <li>Tricyclic antidepressants (eg, amitriptyline, nortriptyline)</li> <li>Atypical antidepressants (eg, venlafaxine, bupropion)</li> </ul>	<ul style="list-style-type: none"> <li>Evaluate type and degree of depression</li> <li>Consider contribution of medications (eg, with interferons)</li> <li>Assess family situation/support network</li> <li>Consider suicide risk</li> <li>Promote use of psychiatric services</li> <li>Advise patient that medication effects may take several weeks</li> <li>Advise patient not to stop medications suddenly</li> <li>Reassess patient regularly</li> <li>Paroxetine can be taken in the morning or at night, can help with anxiety</li> <li>Monitor urinary function with venlafaxine (may cause fluid retention)</li> </ul>
Walking difficulty	<ul style="list-style-type: none"> <li>Dalfampridine www.ampyra.com</li> </ul>	<ul style="list-style-type: none"> <li>10 mg every 12 hours</li> <li>Do not crush</li> <li>Consider seizure risk</li> <li>Monitor for infections</li> <li>Advise not to increase dosage</li> <li>Do not take with compounded 4-AP</li> </ul>
Pseudobulbar affect	<ul style="list-style-type: none"> <li>Nuedexta® (dextromethorphan hydrobromide and quinidine sulfate) www.nuedexta.com</li> </ul>	<ul style="list-style-type: none"> <li>Use for MS or ALS</li> <li>May be used for other types of emotional lability</li> <li>Not restricted to any types of MS</li> <li>Dose once daily for 7 days, 1 capsule every 12 hours</li> <li>Should not be used with quinine, quinidine, mefloquine, or MAO inhibitors</li> <li>Do not use with other drugs that prolong Q-T interval</li> </ul>

### DMT Resources

*CMSC Practical Guidelines for the Selection of Disease-Modifying Therapies in Multiple Sclerosis.*

CMSC DMT Guideline Writing Group

DMT Consensus Committee Program Chairs:

Corey C. Ford, MD, PhD, and Sarah A. Morrow, MD, MS, FRCPC

The Consortium of Multiple Sclerosis Centers.

Glen Rock, NJ: Delaware Media Group. 2019.

<https://cmscscholar.org/cmssc-practical-guidelines-for-the-selection-of-disease-modifying-therapies-in-ms/>

*The Use of Disease-Modifying Therapies in Multiple Sclerosis: Principles and Current Evidence.*

2014; updated 2019

MS Coalition

[https://www.nationalmssociety.org/NationalMS-Society/media/MSNationalFiles/Brochures/DMT\\_Consensus\\_MS\\_Coalition.pdf](https://www.nationalmssociety.org/NationalMS-Society/media/MSNationalFiles/Brochures/DMT_Consensus_MS_Coalition.pdf)

*American Academy of Neurology Practice Guideline: Disease-modifying Therapies for Adults with Multiple Sclerosis.* April 2018; reaffirmed September 2021

Alexander Rae-Grant, Gregory S. Day, Ruth Ann Marrie, Alejandro Rabinstein, Bruce A.C. Cree, Gary S. Gronseth, Michael Haboubi, June Halper, Jonathan P. Hosey, David E. Jones, Robert Lisak, Daniel Pelletier, Sonja Potrebic, Cynthia Sitcov, Rick Sommers, Julie Stachowiak, Thomas S.D. Getchius, Shannon A. Merillat, Tamara Pringsheim *Neurology*. 2018;90:777-788

<https://www.aan.com/Guidelines/home/GuidelineDetail/898>

As of the writing of this monograph, over 20 DMTs are available to manage RMS, falling into the following categories:

**Interferons** are injectable medications approved by the FDA for the treatment of RMS and active SPMS. IFN  $\beta$ -1a and IFN  $\beta$ -1b are recombinant proteins that may exert their effects by inhibiting inflammation and the migration of white blood cells across the BBB. This class of drugs includes Avonex<sup>®</sup> and Rebif<sup>®</sup>, interferon  $\beta$ -1a injectables, and Betase-

ron<sup>®</sup> and Extavia<sup>®</sup>, interferon  $\beta$ -1b injectables.<sup>60-63</sup> Plegridy<sup>®64</sup> (peginterferon beta-1a) is a newer agent in this class.

**Glatiramer acetate** (Copaxone<sup>®65</sup>, Glatopa<sup>®66</sup>, generic) is a synthetic polypeptide thought to resemble myelin basic protein and may act by stimulating immune suppressor lymphocytes that then release anti-inflammatory cytokines. Glatiramer acetate may also compete with myelin antigens for binding to antigen-presenting cells, thereby preventing autoimmune reactions that lead to demyelination. Glatiramer acetate is approved for RMS and active SPMS and is delivered via injection.

**Sphingosine 1-phosphate (S1-P) receptor modulators** are oral agents indicated for treatment of RMS and active SPMS. There are currently four SP-1 receptor modulators that are approved by the FDA: fingolimod (Gilenya<sup>®</sup>),<sup>67</sup> ozanimod (Zeposia<sup>®</sup>),<sup>68</sup> ponesidmod (Ponvory<sup>™</sup>),<sup>69</sup> and siponimod (Mayzent<sup>®</sup>).<sup>70</sup> The drugs trap lymphocytes in the lymph nodes and other tissue reservoirs, thereby reducing the number of lymphocytes in the circulation that can then enter the CNS.<sup>57,58</sup> Fingolimod was the first oral medication approved by the FDA—in 2010—to modify the disease course in MS.

**Monoclonal antibodies.** Alemtuzumab (Lemtrada<sup>®</sup>),<sup>71</sup> natalizumab (Tysabri<sup>®</sup>),<sup>72</sup> and ofatumumab (Kesimpta<sup>®</sup>)<sup>73</sup> are approved for RMS and active SPMS. Ocrelizumab (Ocrevus<sup>®</sup>)<sup>74</sup> is the only drug that is approved for PPMS as well as RMS and active SPMS. Alemtuzumab, ocrelizumab, and natalizumab are delivered via infusion; ofatumumab is administered by injection. The purported MOA of monoclonal antibodies is that they target T and/or B cells and prevent the migration of activated lymphocytes, which cause damage to the brain and spinal cord, across the BBB.

Natalizumab was the first monoclonal antibody to be approved as a DMT for MS. There were striking efficacy results on both clinical and MRI endpoints from two clinical trials,<sup>72</sup> but also safety concerns due to the occurrence of a rare opportunistic infection due to compromise of the immune system, progressive multifocal leukoencephalopathy (PML), which resulted in the temporary withdrawal of the therapy in 2004. When it was approved to re-enter the treatment paradigm, the FDA required that it be available only through restricted distribution via the so-called TOUCH program to monitor for symptoms of PML. Candidates for natalizumab are to be tested for antibodies to John Cunningham (JC)

**Table 3. Immunomodulatory Disease-Modifying Therapies Approved by the FDA Circa 2022**

Injectable Agents	Infusible Agents	Oral Agents
Glatiramer acetate (Copaxone®, Glatopa®, generic)	Alemtuzumab (Lemtrada®)	Cladribine (Mavenclad®)
Interferon beta-1a (Avonex®, Rebif®)	Natalizumab (Tysabri®)	Dimethyl fumarate (Tecfidera®, generic)
Interferon beta-1b (Betaseron®, Extavia®)	Ocrelizumab (Ocrevus®)	Diroximel fumarate (Vumerity®)
Ofatumumab (Kesimpta®)		Fingolimod (Gilenya®)
Peginterferon beta-1a (Plegridy®)		Monomethyl fumarate (Bafiertam®)
		Ozanimod (Zeposia®)
		Ponesidmod (Ponvory™)
		Siponimod (Mayzent®)
		Teriflunimide (Aubagio®)

virus, which causes PML, prior to starting the DMT as well as while they are on the drug, and then evaluated yearly for their individualized risk of PML.<sup>72,75</sup>

**Purine antimetabolite.** Cladribine (Mavenclad®)<sup>76</sup> is the only drug in this category and is approved for RMS and active SPMS. An oral agent, its unique MOA is believed to be that it destroys activated lymphocytes, which are then replaced by immune cells that do not attack the CNS.

**Enzyme blocker.** Teriflunimide (Aubagio®)<sup>77</sup> is approved for RMS and active SPMS. It inhibits the enzyme dihydroorotate dehydrogenase (DHODH), which the immune system needs to reproduce T and B cells. It also appears to decrease the number of abnormal and dysfunctional T and B cells.

**Fumarates.** Three drugs are currently available in this category and are all oral agents approved to treat RMS and active SPMS: dimethyl fumarate (Tecfidera®<sup>78</sup> and a generic), diroximel fumarate (Vumerity®)<sup>79</sup>, and monomethyl fumarate (Bafiertam®).<sup>80</sup> All of these medications break down to the same active metabolite, monomethyl fumarate. Fumarates appear to work by stimulating the Nrf-2 pathway, which plays a role in reducing the byproducts of inflammation in the body, thus helping to prevent MS-induced damage to the CNS.

**Table 3** lists the currently available immunomodulatory agents in the United States. **Table 4** categorizes agents by their general immunotherapeutic mechanisms, and **Table 5** provides contact information for patient support programs for these drugs.

Data from long-term follow-up studies involving the randomized populations in the pivotal trials of glatiramer acetate, IFN  $\beta$ -1b, and SC IFN  $\beta$ -1a reveal that these therapies benefit patients with MS in the long term.<sup>81-84</sup>

As research continues to reveal the benefits of DMTs, new and unique DMTs are being researched, and currently approved agents are being compared with one another in different patient populations and using more advanced imaging techniques. Although it is exciting to have so many effective and safe therapies available to offer to patients, this availability has greatly complicated clinical management for MS nurses and other clinicians who must expand their role to include extensive knowledge of potential side effects, monitoring requirements, and administration and adherence issues to appropriately counsel patients in making the decision of when to initiate a DMT and also switch up DMTs if necessary.<sup>85</sup>

For most patients with a confirmed diagnosis of MS (that is, patients who have experienced two or more attacks

**Table 4. General Immunotherapeutic Mechanisms of MS Therapies**

<ul style="list-style-type: none"> <li>Immunomodulation/alteration of cell function               <ul style="list-style-type: none"> <li>Glatiramer acetate (SC)</li> <li>Interferon <math>\beta</math> (SC or IM)</li> <li>Dimethyl fumarate (oral)</li> <li>Monomethyl fumarate (oral)</li> <li>Diroximel fumarate (oral)</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>Cell trafficking               <ul style="list-style-type: none"> <li>Natalizumab (IV)</li> <li>Fingolimod (oral)</li> <li>Siponimod (oral)</li> <li>Ozanimod (oral)</li> <li>Ponesimod (oral)</li> </ul> </li> </ul>
<ul style="list-style-type: none"> <li>Cell depletion (B cell targeted therapies)               <ul style="list-style-type: none"> <li>Alemtuzumab (IV)</li> <li>Cladribine (oral)</li> <li>Ocrelizumab (IV)</li> <li>Ofatumumab (SC)</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>Cell replication/proliferation               <ul style="list-style-type: none"> <li>Mitoxantrone (IV)</li> <li>Teriflunimide (oral)</li> </ul> </li> </ul>

IV=intravenous; SC=subcutaneous.

Used with kind permission of Marie Namey.

**Table 5. Patient Support Programs for MS DMTs**

Drug	Telephone No.	Website
Aubagio® (teriflunomide)	855-MSONE2ONE (855-676-6326)	www.aubagio.com
Avonex® (interferon beta-1a)	800-456-2255	www.avonex.com
Bafiertam® (monomethyl fumarate)	855-3BANNER (855-322-6637)	www.bafiertam.com
Betaseron® (interferon beta-1b)	844-788-1470	www.betaseron.com
Copaxone® (glatiramer acetate)	800-887-8100	http://copaxone.com
Extavia® (interferon beta-1b)	888-NOW-NOVA (888-669-6682)	www.extavia.com
Gilenya® (fingolimod)	800-GILENYA (800-445-3692)	www.gilenya.com
Glatiramer acetate injection	844-695-2667	www.glatirameracetate.com
Glatopa® (glatiramer acetate)	855-452-8672	www.glatopa.com
Kesimpta® (ofatumumab)	855-KESIMPTA (855-537-4678)	www.kesimpta.com
Lemtrada® (alemtuzumab)	855-MSONE2ONE (855-676-6326)	www.lemtrada.com
Mavenclad® (cladribine)	877-447-3243	www.mavenclad.com
Mayzent® (Siponimod)	877-MAYZENT (877-629-9368)	www.mayzent.com
Ocrevus® (ocrelizumab)	844-OCREVUS (844-627-3887)	www.ocrevus.com
Plegridy® (peginterferon beta-1a)	800-456-2255	www.plegridy.com
Ponvory™ (ponesidmod)	877MyCarePath (877-227-3728)	www.ponvory.com
Rebif® (interferon beta-1a)	877-447-3243	www.rebif.com
Tecfidera® (dimethyl fumarate)	800-456-2255	www.tecfidera.com
Tysabri® (natalizumab)	800-456-2255	www.tysabri.com
Vumerity® (diroximel fumarate)	800-456-2255	www.vumerity.com
Zeposia® (ozanimod)	833-ZEPOSIA (833-937-6742)	www.zeposia.com

separated by time and space, have clinical evidence of two or more lesions in the CNS, or otherwise fulfill the McDonald MRI criteria described earlier<sup>71</sup>), the question is not *whether* to treat with an immunomodulatory agent but rather *which* agent to use and how to best use it. **Tables 6** and **7** summarize recommendations from the MS Coalition and the AAN on DMT use. Currently, there is also ongoing discussion of how aggressive to be with therapy, and both the MS Coalition and the AAN recommend that patients with highly active MS be treated with a so-called high-efficacy medication such as cladribine, fingolimod, natalizumab, or ocrelizumab.<sup>57,58</sup> Patients who have breakthrough activity while on another DMT are also candidates for high-efficacy DMTs, according to the MS Coalition.<sup>57</sup> In the past, the best approach for most patients was believed to be to start with a moderately effective DMT that had less risk of incurring PML and other serious side effects, and switching to a higher-efficacy DMT as needed if

there was clinical and/or radiologic evidence of active disease. That strategy is known as the escalation approach. Emerging data are showing that starting on higher-efficacy therapies early in the disease course can have long-term benefits over escalation, an approach known as early, aggressive therapy.<sup>86</sup> Results of a European study comparing an older high-efficacy infusible drug, a newer high-efficacy infusible medication, and a high-efficacy oral drug showed that all three slowed disease progression better compared with older injectable DMTs and with low-to-moderately effective oral therapy. Patients who were initiated at diagnosis on a higher-efficacy DMT also required fewer drug changes and exhibited more stability of disease progression.<sup>87</sup> The results of two trials are currently underway comparing these treatment approaches: The Traditional versus Early Aggressive Therapy for MS (TREAT-MS) trial and the Determining the Effectiveness of early Intensive Versus Escalation approaches for the treatment of

**Table 6. Recommendations of the MS Coalition on DMT Use<sup>57</sup>**

A coalition of MS-related organizations, including Accelerated Cure, Can Do Multiple Sclerosis, The Consortium of Multiple Sclerosis Centers, International Organization of Multiple Sclerosis Nurses, Multiple Sclerosis Association of America, Multiple Sclerosis Foundation, National Multiple Sclerosis Society, and United Spinal Association, have joined to form the MS Coalition. This collaborative group reviewed the current evidence and released the following guidelines on the use of DMTs in MS.

**Treatment Considerations**

- Initiation of therapy with an immunomodulator is advised as soon as possible following a definite diagnosis of relapsing or progressive MS and may be considered for selected patients with a first attack who are at high risk for MS (eg, who are diagnosed with CIS).
- Patients with highly active MS should be prescribed a high-efficacy medication such as alemtuzumab, cladribine, fingolimod, natalizumab, or ocrelizumab.
- Clinicians should also consider a high-efficacy DMT for patients who have breakthrough activity on another DMT, regardless of the number of agents they've previously used.
- Treatment should be continued indefinitely unless any of the following occur, in which case an alternative DMT should be considered:
  - Suboptimal treatment response
  - Intolerable side effects
  - Poor adherence
  - Availability of a more-appropriate treatment option
  - Benefits of the DMT no longer outweigh the risks according to assessment by the provider and patient
- Movement from one immunomodulatory drug to another for medically approved reasons should be permitted.
- If there is a suboptimal treatment response as suggested by clinical or MRI activity while on consistent treatment, a switch to a DMT with a different mechanism of action should be considered.
- Providers and patients should engage in shared decision-making to choose a DMT. An arbitrary restriction of choice or a mandatory escalation therapy approach are not supported by current data.

**Access Considerations**

- Patients' access to medication should not be limited by frequency of relapses, age, or level of disability, or personal characteristics.
- Treatment should not be stopped while insurers evaluate the case for continuing coverage of treatment.
- Therapy should continue indefinitely.
- All of the FDA-approved immunomodulatory agents should be included in formularies and covered by third-party payers so that physicians and patients can determine the most appropriate agent on an individual basis.

CIS=clinically isolated syndrome; DMT=disease-modifying therapy; FDA=Food and Drug Administration.

Adapted from The Use of Disease-Modifying Therapies in Multiple Sclerosis: Principles and Current Evidence. 2014; updated 2019. Multiple Sclerosis Coalition. Available at: [https://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/DMT\\_Consensus\\_MS\\_Coalition.pdf](https://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/DMT_Consensus_MS_Coalition.pdf). Accessed April 15, 2022.

Relapsing-remitting MS (DELIVER-MS) trial.<sup>88,89</sup>

**Clinically isolated syndrome.** Currently, patients with CIS—those who have experienced only one neurological episode suggestive of MS along with MRI data indicative of MS—are considered to be at high risk for a diagnosis of MS, and immunomodulatory therapy is strongly suggested for them. Data from several trials exploring the potential value of initiating treatment at the first sign of clinical demyelination demonstrate that DMTs can significantly delay the development of clinically definite MS in patients who have had only one clinical episode, sometimes referred to as “monosymptomatic” presentation.<sup>90–95</sup> Most DMTs include an indication for CIS.<sup>57,60–74,76–80</sup>

All of the available immunomodulatory agents have side effects.<sup>96</sup> For example, the injectables and infusions can cause skin reactions, which usually are mild and self-limiting. Some side effects, however, such as the flu-like symptoms seen with the interferons, may persist for several months.<sup>60,62</sup> Although most of the side effects associated with the immu-

nomodulatory agents diminish as treatment continues, they can undermine treatment adherence. A survey of participants in the CMSC/NARCOMS Registry—the registry of The Consortium of Multiple Sclerosis Centers/North American Research Consortium on Multiple Sclerosis—demonstrated discontinuation rates ranging from 22% for patients treated with glatiramer acetate to 41% and 70% for patients treated with IFN  $\beta$ -1a administered via intramuscular injection and those treated with IFN  $\beta$ -1b, respectively.<sup>97</sup> Key factors leading to the discontinuation of immunomodulatory therapies included increases in MS symptoms and flu-like symptoms associated with treatment. Fewer than 10% of registrants reported depression and skin reactions as reasons for discontinuing treatment. Interestingly, factors that were not considered adequate reasons for discontinuation included injection-site pain and self-injection or needing assistance with injection.<sup>97</sup> Now that disease modification in MS has expanded to regular infusions and oral therapies, research is revealing different issues and concerns with DMTs, such as the need to remember to take a pill and side effects such as flushing



**Table 7. Recommendations of American Academy of Neurology on the Use of Immunomodulators<sup>58</sup>**

- Patients with newly diagnosed MS should be counseled about their DMT options at a dedicated treatment visit.
- Patient preferences in regard to safety, route of administration, lifestyle, cost, efficacy, common adverse effects, and tolerability should be considered when prescribing a DMT.
- Clinicians should discuss the benefits and risks of DMTs with people with CIS.
- DMTs should be offered to people with relapsing forms of MS with recent clinical relapses or MRI activity.
- Patients on DMTs should be monitored for adherence, adverse events, tolerability, safety, and effectiveness.
- Follow up should be annually or more often depending on the DMT the patient is taking.
- Because DMTs have potential risks for pregnant women, clinicians should monitor the reproductive plans of female patients of childbearing age with MS and counsel them about reproductive risks and use of contraception during DMT use.
- Due to a high rate of severe adverse effects, mitoxantrone should not be prescribed for patients with MS unless the therapeutic benefits greatly outweigh the risks.
- Patients with highly active MS should be prescribed alemtuzumab, fingolimod, or natalizumab.
- Natalizumab can be considered in people with MS who have positive anti-JCV-antibody indexes above 0.9 if there is a reasonable chance of benefit compared with the low but serious risk of PML.
- Ocrelizumab should be offered to patients with PPMS unless the risks of treatment outweigh the benefits.
- Patients who are candidates for DMTs but who cannot afford the medication should be directed to support programs.
- Switching from one immunomodulatory drug to another should be discussed with patients who have breakthrough disease.
- Continuing DMT use should be advocated for all patients with relapsing MS, even those who are stable.
- Discontinuation of DMT may be considered in patients with SPMS who have not had ongoing relapses or MRI activity and have not been ambulatory for at least 2 years.

CIS=clinically isolated syndrome; DMT=disease-modifying therapy; MRI=magnetic resonance imaging; PML= progressive multifocal leukoencephalopathy.

Adapted from Rae-Grant A, Day GS, Marrie RA, et al. American Academy of Neurology Practice Guideline: Disease-modifying Therapies for Adults with Multiple Sclerosis. April 2018; reaffirmed September 2021. Available at: <https://www.aan.com/Guidelines/home/GuidelineDetail/898>. Accessed April 15, 2022.

and gastrointestinal symptoms, headache, and dizziness that may discourage consistent and continuing use.<sup>57,58</sup>

### Nursing roles

With regard to nursing roles in immunomodulatory treatment of MS, probably the most important nursing interventions are education and skill development. Patients and their families or care partners need to have a thorough understanding of the treatment options available to them, along with clear and realistic expectations of what the immunomodulatory agents can and cannot be expected to do. They also need to understand what side effects are associated with treatment and how these side effects can be managed. Nurses may want to use a checklist of questions for patients to consider when selecting an immunomodulatory treatment (**Table 8**).

Once a specific immunomodulatory agent has been chosen, patients need to know how to carry out the self-care aspects of their MS management plan. If an injectable medication is chosen, they will need training in reconstituting and injecting medication. They may need help with overcoming a fear of needles and self-injecting. For those on injectables and oral medications, they may need instruction in the use of specific memory cues to

help them take their medication on schedule. For those on infusibles, they may need help with transportation and access issues.

Nurses play a key role in enhancing treatment adherence through patient education and by developing supportive relationships with patients, as mentioned earlier. A great benefit of these drugs has been the hope they have brought to patients with MS—hope that can help to motivate self-care and adherence to treatment.

Nurses are also monitors of the patient's response to immunomodulatory therapy, both initially and over time. If patients are having trouble adhering to treatment, the nurse can determine the source of the problem. If adherence problems are related to side effects, nurses can make practical suggestions for managing these effects. If side effects are intolerable, the patient may need to try a different immunomodulatory agent.

In addition, MS nurses often serve as advocates for patients who need immunomodulatory treatment. Nurses may interact with managed care organizations, insurance companies, and other health-benefit programs to help patients obtain treatment. As part of this advocacy effort, nurses may need to complete prior authorizations or write letters describing



the medical necessity of the immunomodulatory agents and may need to assist with appeals against denial of benefits.

### Other Therapies

A number of medications that are not specifically indicated for MS are sometimes used to treat the disease. Although used much less frequently than the DMTs described above, these novel and innovative strategies may offer hope to patients who have not responded to conventional treatments.

Azathioprine (Imuran®) is an oral immunosuppressive agent often used in transplant patients but also useful for the treatment of rheumatoid arthritis, lupus nephritis, and psoriatic arthritis. It appears to reduce relapse frequency and decrease brain inflammation and lesion accumulation in patients with MS. However, some clinical trials have shown mixed results, along with severe side effects, such as anemia and liver damage.<sup>98</sup>

Mitoxantrone (Novantrone®), an antineoplastic agent given intravenously, has shown promise in treatment of MS.<sup>98</sup> With long-term use, however, mitoxantrone has dose-dependent cardiotoxic effects, and its lifetime dosage is limited. For this reason, the AAN does not recommend use of mitoxantrone unless the therapeutic benefits greatly outweigh the risks.<sup>58</sup>

Cyclophosphamide (Cytoxan®), a potent IV immunosuppressive drug, has been used to treat MS for many years. Although cyclophosphamide sometimes improves the

condition of patients with PPMS, recent studies have shown that any benefit is modest.<sup>98</sup> In addition, cyclophosphamide can affect blood clotting and increase susceptibility to infection.

Autologous hematopoietic stem cell transplantation is one of the most promising future therapies and has been investigated in small clinical trials. For well-selected patients with aggressive disease, it offers the hope of long-term suppression of disease activity and even improvement in disability.<sup>99,100</sup> The procedure is being refined but is still risky, requiring that the over-reactive immune system be destroyed via high-dose immunoablative chemotherapy in order to infuse autologous adult hematopoietic stem cells into the bloodstream, which over time will build a new immune system. This procedure leaves the patient extremely vulnerable to infection due to the nascent immune system.

### Administration of Vaccines in Conjunction with DMTs

Routine vaccinations, including COVID-19 immunizations, for a variety of infectious diseases are a cornerstone of preventive care and are indicated for patients with MS (Table 9). Optimal timing of vaccines for patients who are using DMTs is critical, however, as there is some evidence that certain DMTs may interfere with effectiveness of the vaccines.

The American Academy of Neurology (AAN)<sup>101</sup> offers guidance on vaccine-preventable infections and immunizations

**Table 8. Checklist of Patient Questions**

**Patients need to consider many factors when making a decision about disease-modifying treatment. This list of questions may be a useful tool for patients.**

- ✓ What can I expect in terms of disease activity while taking the medication? How will the treatment affect relapses and disease progression?
- ✓ How will I feel when taking the medication?
- ✓ What are the effects of treatment over a long period of time?
- ✓ How many studies have been done to show efficacy? Do studies of the different medications have similar results?
- ✓ What if I got pregnant while on the medication? Would my baby be safe?
- ✓ Can I breastfeed my baby while on the medication?
- ✓ What are the side effects of the medication? Are they manageable? Will they affect my lifestyle?
- ✓ If I don't experience side effects, does that mean my therapy is not working?
- ✓ Will I have a skin reaction after injection or infusion?
- ✓ Are there specific reasons why I should not take the medication (for example, spasticity, depression, other medical conditions)?
- ✓ Does the severity of the side effects influence the way the medication works?
- ✓ Will the treatment affect my menstrual cycle? How?
- ✓ Does the treatment require periodic blood tests, MRI scans, or any other follow-up?
- ✓ Aside from the frequency and route of administration, what are the major differences between the therapies?

for people with MS (<https://www.aan.com/Guidelines/home/GuidelineDetail/974>) in a guideline that has been endorsed by MS organizations such as The Consortium of Multiple Sclerosis Centers (CMSC) and the Multiple Sclerosis Association of America (MSAA). In general, AAN recommends that people with MS receive non-live vaccinations recommended by the Centers for Disease Control and Prevention<sup>102</sup> (CDC, <https://www.cdc.gov/vaccines/schedules/hcp/imz/adult.html>), which include an annual flu shot and COVID-19 immunizations.

The AAN performed a systematic review of the evidence on the effects of vaccines on people with MS and found that although there is a lack of data, people with MS have the same risk of infection as people who don't have MS; they also found no association between vaccinations and the development or worsening of MS.<sup>101</sup> There is some suggestion that vaccines may reduce the risk of relapses by preventing infections that can precipitate clinical attacks.

A 2017 review of 51 studies found no association between relapses in people with MS and non-live immunizations against hepatitis B virus, H1N1 flu virus, tetanus, BCG, or tick-borne-encephalitis.<sup>103</sup> However, there was some indication that vaccination against yellow fever (a live vaccine) might increase the risk of an MS relapse.

The NMSS recommends the following regarding vaccinations:<sup>104</sup>

- Follow AAN and CDC guidelines.
- Delay vaccinations in patients experiencing relapses.
- Avoid live vaccines, particularly in patients using immunosuppressive/immunomodulating agents.
- Consult the product insert for individual DMTs to ascertain the best timing for vaccines related to each specific agent.
- Do a blood workup to determine a patient's immunity to viruses before starting a new DMT, treat infections, and advise on vaccinations as needed.
- Counsel patients about the risk of infection related to certain immunosuppressant/immunomodulating therapies.
- Discuss the risks and benefits of vaccines with patients on a regular basis, and at least annually.

Table 9. Vaccines for People with MS

Vaccines Considered Safe for People with MS
Chickenpox (varicella)
COVID-19
Flu (inactivated formulations only, which excludes nasal and high-dose flu vaccines)
Human papillomavirus
Hepatitis B
Measles-Mumps-Rubella (MMR)*
Pneumonia vaccines
Polio
Shingles
Smallpox
Tetanus
Tuberculosis (Bacillus Calmette-Guérin)

\*Should not be given to people on immunosuppressant medications.  
Sources: American Academy of Neurology,<sup>101</sup> Centers for Disease Control and Prevention,<sup>102</sup> National MS Society.<sup>104</sup>

## Supporting Multiple Sclerosis Nursing Practice Through Research

With the challenges presented by the ground-breaking advances in technology and new therapeutic agents for MS, along with the continuous changes in the roles and responsibilities of MS nurses, nursing research is essential to documenting the effectiveness of nursing practice outcomes for patients with MS.<sup>105</sup>

Nursing research, performed as a systematic investigation or inquiry to generate new knowledge or validate existing knowledge, can contribute to the understanding of MS and its effects, guide nursing practice, and identify outcomes of effective nursing interventions. Nursing research may be quantitative or qualitative. It does not focus on an illness or condition purely as a health problem; rather, it examines the physical, emotional, and psychosocial responses of patients and their families to that illness or condition. Nursing research in MS may investigate patient and family

responses anywhere along the illness trajectory and seeks to contribute in positive ways to shaping and managing the course of MS.

Nursing research has provided valuable information about caring for patients with MS and the evolving role of MS nurses.<sup>106,107</sup> For example, studies have shown how patients experience and manage fatigue,<sup>108</sup> the impact of illness uncertainty associated with MS on family life,<sup>109</sup> the effects of COVID-19 on people with MS,<sup>110</sup> the interplay of comorbidities and MS,<sup>111</sup> how patients make decisions about DMTs,<sup>112</sup> and interventions that can help care partners manage stress.<sup>109,113</sup> MS nurses can use this information in practical ways to gain perspective on their patients' physical and emotional status and to encourage wellness, health-seeking strategies, and empowerment.<sup>114,115</sup>

Several studies have examined factors that contribute to quality of life among people with MS. One investigation found that marriage, work, health status, and involvement in recreation or social activities are major contributors to a positive outlook.<sup>116</sup> An investigation by Fraser and colleagues has found that self-efficacy is a positive force in sustained adherence to complex therapies, and have noted that a belief that one can make a difference can sustain continued care.<sup>116,117</sup> Others have found that factors significantly related to perceived quality of life among patients with MS include involvement in health-promoting behaviors, including exercise, nutrition, and stress management, taking responsibility for their health, and feeling free and independent in daily living.<sup>118,119</sup> An additional study revealed that engaging in a creative art program can improve self-esteem, hope, perceived social support, and self-efficacy in people with MS.<sup>120</sup>

Qualitative studies have examined patient experiences surrounding the diagnosis of MS and living with relapsing MS.<sup>26,121</sup> Both studies employed phenomenological research methods—approaches used to understand people and their everyday lives under certain circumstances without including preconceived ideas.<sup>26</sup> In the first study, researchers explored what five people experienced before, at the time of, and after diagnosis of MS.<sup>26</sup> Before diagnosis, these people recalled searching for the reasons for their symptoms and creating possible explanations as a coping mechanism to protect themselves and others from undue anxiety. As symptoms recurred or worsened, patients experienced increasing concern about what might be wrong and entered a phase of worrying, wondering, and waiting for outcomes

of consultations and testing. Once an MS diagnosis was confirmed, patients described feelings of shock and numbness that lasted only a few moments for some but days to weeks for others. Afterward, there was the process of informing family members and others of the diagnosis, an experience that was not always positive. Finally, patients described “claiming” the diagnosis as part of adjusting and refocusing on plans and hopes for the future.

The second study examined the experiences of seven women and three men diagnosed with relapsing MS.<sup>121</sup> With analysis of interview data, several themes emerged to describe patient experiences:

- Reliance on social networks
- Adjustment to MS
- Coping with symptoms and inconveniences
- Feelings of hope and hopelessness
- Need for control and independence
- Conflict with physicians, insurance companies, employers, family members
- Relief associated with confirmed diagnosis
- Uncertainty related to the unpredictability of MS
- Loss of independence, employment, relationships, function
- Fear of loss of health, life, support system
- Becoming informed about MS
- Struggle over revealing or concealing MS

Phenomenological studies such as these provide practical, “real-life” information that promotes empathy and understanding among healthcare professionals, thereby facilitating appropriate patient support.

Two exploratory nursing studies by Fawcett et al<sup>122,123</sup> have examined the use of alternative therapies—including nutritional therapy, massage therapy, acupuncture, chiropractic treatment, and homeopathy—in small groups of patients who were not taking disease-modifying agents. The first study identified reasons why patients accessed alternative therapies, finding that most patients turned to these treatments because traditional medicine offered no cure. The second study examined relationships between the use of alternative therapies and differences in symptom severity and functional status. All patients reported reduction in MS symptom severity and improvement in functional status with the use of alternative therapies; however, the greater the number of therapies used, the lower the patients'

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functional status scores. People with MS are often interested in alternative therapies, and findings from studies such as these can help nurses in their roles as counselors who help patients make appropriate treatment decisions. Jacqueline Fawcett has also published a series of essays on nursing issues, including her thoughts on the meanings of the words compliance, adherence, and concordance and the nurse-patient relationship.<sup>124</sup>

A qualitative study investigation identified the information needs of patients experiencing relapses. The study found that these patients had significant gaps in their understanding of the physical symptoms they were experiencing and the drugs used to treat an acute relapse. Barriers to information access included both external barriers, such as limited computer or Internet access or difficulties accessing libraries, and internal barriers, such as denial, uncertainty, and fear. Results from this study and others suggest that patients with MS need relevant, specific, and current information to help them remain independent and to empower them to make informed decisions regarding relapse treatment.<sup>28,125</sup>

Nursing research has identified specific physiological and psychological needs of care partners of patients with MS.<sup>126</sup> Among the strongest needs identified by caregivers (who were usually spouses) was for regular, brief breaks from caregiving to allow for rest and relaxation. In addition, all caregivers in the study reported that they received no help from community organizations. The same study asked caregivers how nurses can provide support. Caregivers stated that they needed more education about the disease process and the technical aspects of care and more current information on new developments in MS. Caregivers also wanted nurses to listen to and understand them.

### Research Priorities

Published MS nursing research is sparse. A PubMed search conducted using the term “multiple sclerosis/nursing” yields only 519 articles. There are many gaps and, clearly, no shortage of studies to pursue.

Suggested areas for further study include the following:

- Barriers to use of early therapy
- Barriers to aggressive therapy with immunosuppressant/immunomodulating agents
- Responses to illness and treatment

- Factors that influence patients’ view of treatment
- Factors that influence adherence to treatment
- Barriers to receiving vaccines
- Use of alternative therapies, including cannabis
- Women’s health issues, eg, MS-related issues in pregnancy, breastfeeding, osteoporosis, and hormone replacement therapy with menopause
- Men’s health issues, eg, relationships between MS or MS treatments and prostate cancer, reproductive concerns
- Impact of MS on parenting and professional roles
- Studies of symptom management using specific measurable outcomes to determine the most effective interventions
- Identification of the needs of patients newly diagnosed with MS (and their families)
- Identification of the needs of patients with advanced MS (and their families)
- Cultural influences on and cultural responses to diagnosis, treatment, stresses, and coping
- Effect of MS on personal and family relationships (eg, children, couples) regarding issues such as disclosure of diagnosis
- Safety issues in MS, eg, in relation to assistive technology, the home and work environment, and the ability to drive

Findings from nursing studies can help broaden nurses’ knowledge and improve professional practice. A wealth of information is available within the environment of MS nursing practice, and research has the potential to provide valuable, practical information that can enhance the lives of patients affected by MS. Development of research skills could help improve nurses’ opportunities to obtain funding, design studies carefully, and conduct systematic qualitative and quantitative investigations.

### Limitations of Multiple Sclerosis Nursing Research

To date, nursing research provides better understanding for MS nursing practice. However, nursing research is hampered by a variety of limitations. For example, there are no standardized definitions for terms such as *caregiver* or *quality of life*, and there are few tools with established validity or reliability for measuring outcomes of nursing interventions. Nursing research is also beset by minimal use of conceptual frameworks, small sample sizes, and lack of sample het-

**Table 10. Funding Sources for Nursing Research**

Organization	Contact Information
Agency for Healthcare Research and Quality	540 Fishers Lane, Rockville, MD 20857 301-427-1364 www.ahrq.gov
American Academy of Nurse Practitioners	P.O. Box 12846, Austin, TX 78711 512-442-4262 www.aanp.org
American Association of Colleges of Nursing	655 K Street, NW, Suite 750, Washington, DC 20001 202-463-6930 www.aacnnursing.org
American Nurses Association	8515 Georgia Avenue, Suite 400, Silver Spring, MD 20910 301-628-5000 www.nursingworld.org/foundation
International Organization of Multiple Sclerosis Nurses	3 University Plaza Drive, Suite 116, Hackensack, NJ 07601 201-487-1050 info@iomsn.org www.iomsn.org
Midwest Nursing Research Society	5034A Thoroughbred Lane, Brentwood, TN 37064 615-432-0098 info@mnrns.org www.mnrns.org
National Institute of Nursing Research	31 Center Drive, Room 5B03, Bethesda, MD 20892-2178 301-496-0207 info@ninr.nih.gov https://ninr.nih.gov
National Institutes of Health	9000 Rockville Pike, Bethesda, MD 20892 866-504-9552, 301-402-7469 https://grants.nih.gov
National League for Nursing	The Watergate, 2600 Virginia Avenue, NW Eighth Floor Washington, DC 20037 800-669-1656 https://www.nln.org/
National Multiple Sclerosis Society	Research Programs Department, 733 Third Avenue, Suite 3, New York, NY 10017 800-344-4867 www.nationalmssociety.org
Sigma Theta Tau International	550 West North Street, Indianapolis, IN 46202 888-634-7575 (US/Canada) or 317-634-8171 (international) https://www.sigmanursing.org/personas/researcher
Canadian Health Services Research Foundation Canadian Foundation for Healthcare Improvement	150 Kent Street, Suite 200 Ottawa, Ontario, K1P 0E4, Canada 613-728-2238 info@cfhi-fcass.ca https://www.cfhi-fcass.ca

erogeneity. Many studies have been performed only once; confirmatory studies are needed. These issues mean that even for the research that has been done, interpretation across studies is difficult.

### Strategies to Facilitate Nursing Research: Buying Time

Many nurses are overburdened with day-to-day responsibilities and are not expected or encouraged to take the time and effort that careful research would require. However, those nurses who wish to investigate a research question can begin to seek funding and support by:

- Identifying funding sources
- Developing grant-writing skills
- Identifying and developing collaborative relationships with other practitioners

Research funds are available from a variety of public and private sources, including those listed in **Table 10**. Candid (comprised of The Foundation Center and GuideStar) also provides information about how to find grant support through its website (<https://candid.org>).

Applying for grants is a necessary aspect of obtaining funds for research. Writing a grant application can be an intimi-



dating prospect, but a variety of instructional programs and materials—including courses at colleges and universities, books, and websites—are helpful. The National Institutes of Health provide guidance on grant application procedures through its website (<http://www.grants.nih.gov>), as does the Binghamton University Libraries' website (<http://library.lib.binghamton.edu/subjects/nursing/nursresearch.html>).

Another challenge in nursing research is patient recruitment. There are various approaches to patient recruitment, one of which is the CMSC/NARCOMS database. More information about access to this database can be obtained through The Consortium of Multiple Sclerosis Centers website (<http://www.ms-care.org>).

An important benefit of nursing research is the professional recognition that comes with publication, whether in nursing journals or in other health-related journals. Publication not only serves to release information valuable to the care of patients with MS but can enhance researchers' chances of obtaining additional funding.

Often, collaborative relationships are necessary to performing research. Nurses may need to form liaisons with other nurse researchers and with other professionals within or outside their practice or department to increase sample size, facilitate study design, acquire funding, and perform statistical analyses. In addition, collaborative efforts can facilitate clearance of research proposals through institutional review boards or research committees at hospitals or universities—often a necessary step in initiating research in many academic and medical school settings.

### Recommendations for Multiple Sclerosis Nursing Research

In conducting research, nurses need to be aware of certain practical issues. For example, they will need to identify appropriate statistical tests to validate and enhance data. Consultation with a statistician and the use of computer programs for statistical analysis will be beneficial. To ensure scientific rigor, investigators should use standardized assessment tools

and outcomes measures that are objective and specific to nursing practice. Patients selected for a study should form balanced, homogeneous sample populations that are large enough to allow reasonable conclusions to be drawn. When appropriate, theoretical frameworks should guide study design. Replication studies can be important for confirming findings that have been published only once. Nurses also should follow ethical standards with regard to patient consent and confidentiality, conflict of interest issues, patent and copyright laws, and responsibilities of authorship when the time comes to prepare a manuscript.

### Enhancing the Professional Practice

While participating in MS research is important, especially research of interest to the nursing practice, many nurses are unable to do so. Funding sources are limited, and the resources and facilities needed to conduct research may not be readily available in a nurse's area of practice. When circumstances hinder the ability to participate in research, it is critical for MS nurses to enhance their professional practice by becoming well versed in the latest research being conducted in the field.

Every month, literature on MS pathogenesis, treatments, and patient care is published. To keep abreast of the latest publications, nurses can make use of searchable databases such as PubMed (<https://pubmed.ncbi.nlm.nih.gov/>), a medical literature database maintained by the US National Library of Medicine and the National Institutes of Health. Conducting regular searches in databases to find MS literature and reading articles of interest and importance build upon knowledge and skills that can be translated into changes in practice that may improve patient care. Patients with MS are becoming increasingly knowledgeable about therapies under investigation and new techniques, and they often look to their nursing team to provide more information. In order to supply their patients with accurate information, it is imperative for nurses to continue to educate themselves by keeping up with research that has been published in peer-reviewed journals.



## Conclusion

Rapid advances in technology and an ever-increasing range of effective medications, along with escalating healthcare costs, shorter hospital stays, and an increased emphasis on home care and patient self-care, have altered the practice environment significantly. With these changes has come a considerable increase in responsibility for nurses who care for patients with MS.

Clearly, nurses have an essential role to play in MS care, one that will continue to evolve. As the mechanisms underlying the development and progression of this disease are further understood, there will be more novel treatment strategies to optimize patient outcomes. Therefore, it is vital for nurses to constantly update their knowledge of MS care, research, and best practices in patient assessment and interventions. Collaboration, expertise, and optimal access to care on the part of nurses will support the MS team's effort to fight the effects of this challenging and complex disease.

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