Advanced Practice Nursing in Multiple Sclerosis

Advanced Skills, Advancing Responsibilities

3RD EDITION

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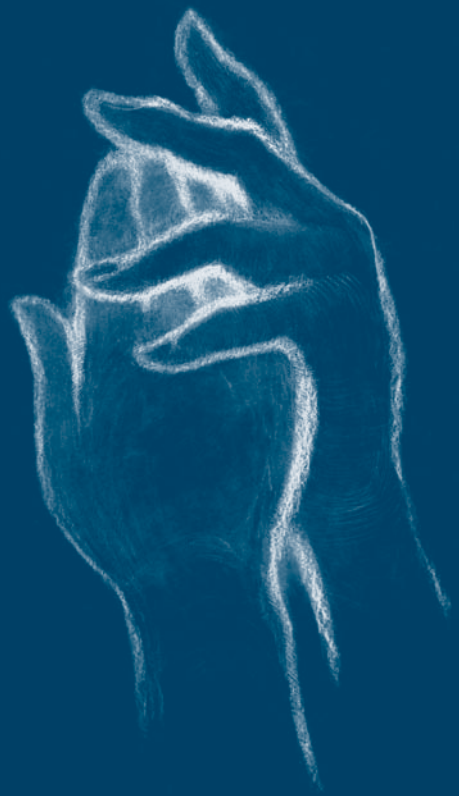

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DISCLOSURES

Ms. Costello has the following relationships to disclose: She has been or is a consultant to Biogen Idec, EMD Serono, and Teva Neuroscience. She has participated in speakers' bureaus and on advisory boards for Biogen Idec, EMD Serono, and Teva Neuroscience.

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Foreword

For nearly 2 decades, basic and clinical research have provided greater insight into the pathophysiology of multiple sclerosis (MS) and the impact of early intervention with disease-modifying therapies. Long-term data regarding most of these therapies indicate that relapse control and delay in disability progression can continue for years with consistent use. Still, for some patients, the effect of disease-modifying therapy is suboptimal—or, for patients with progressive forms of MS, ineffective. In these cases, the disease course results in many symptoms and functional disability. The unpredictability of this illness requires lifelong management that utilizes a multidisciplinary team approach.

The current healthcare environment, with its focus on best practices, evidence-based practice, patient outcomes, and cost-effective care, is suited to the expertise and leadership skills of advanced practice nurses (APNs). APNs can provide specialized skills and knowledge that are an asset in this milieu and are essential in helping patients manage a chronic illness such as MS. The multiple sclerosis advanced practice nurse (MS APN) has emerged as a nursing leader who accepts accountability and responsibility for evidence-based practice and best patient outcomes. As such, the MS APN is best equipped to recognize, understand, practice, and interpret these concepts for the broader community of MS professionals and caregivers. To ensure that MS APNs can continue to provide high-quality, consistent care and add to the body of nursing knowledge, their roles must be well defined, described, and validated through nursing research.

With that goal in mind, the International Organization of Multiple Sclerosis Nurses (IOMSN) convened an Advanced Practice Nurse Advisory Consensus Meeting to define the MS APN's roles and domains and the practice competencies related to MS care, primary-care needs, and patient outcomes. This monograph, the third in a series focusing on MS nursing, builds on earlier works and summarizes the roles, domains, and competencies of the MS APN.

The first monograph described key issues in promoting adherence; detecting, assessing, and maximizing cognitive function; and empowering patients to optimize their quality of life. The second monograph addressed the evolving role of nurses in this field, describing a philosophy and framework, domains and competencies, best practices in disease management and treatment, and opportunities for research. In this monograph, advanced practice nursing in MS is presented as an internationally recognized branch of nursing that is now specialized and certified. This monograph, now in its third edition, expands on this structure and explores the domains and practices of APNs, both in general and specifically in relation to MS.

This monograph is divided into 6 sections: (1) Overview of Multiple Sclerosis, (2) Nursing Care in Multiple Sclerosis, (3) Domains of Practice in Multiple Sclerosis Care, (4) The APN in Treatment Decisions and Symptom Management, (5) Primary-Care Needs in Multiple Sclerosis, and (6) Measuring Outcomes.

This monograph presents an expert consensus on APN role definition and clarification that will help to validate and perpetuate the role of the APN in MS care throughout the world and, ultimately, benefit those people who are affected by MS.

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Introduction

An ever-increasing body of medical, nursing, and scientific knowledge has changed the face of healthcare, demanding advanced training, expanded skills, and specialized certification, along with expanded responsibility and accountability. Because of the way these changes impact the care of patients with multiple sclerosis (MS), advanced practice nurses (APNs) who focus on MS care met at Niagara-on-the-Lake, Ontario, Canada, in September 2002 with 2 goals: (1) to identify and validate the multidimensional nature of the care they provide for patients with MS and (2) to build upon the domains of basic MS nursing recently promulgated by the International Organization of Multiple Sclerosis Nurses (IOMSN).

A monograph capturing the results of discussions at that meeting was published in 2003. It focused on 3 key areas:

1) defining the domains and roles of the APN in MS care,

2) identifying the importance of the primary-care needs of patients and determining the role of the APN in addressing those needs, and

3) measuring the effectiveness of the outcomes of APN care.

Underscoring the advanced training, expertise, and responsibilities of APNs, the monograph explored the ways in which APNs complement the contributions of other nursing specialties and MS healthcare team members. A second edition was published in 2005.

This third edition of the monograph builds on the framework of that initial work and incorporates new findings, actions regarding drug safety, and relevant data published in the literature or reported at scientific sessions since then. It also emphasizes the unique problems related to MS—a lifelong disease that requires a multidisciplinary approach to its overall management. It focuses on issues such as the long-term safety and efficacy of immunomodulators, adherence to therapy to enhance outcomes, and the crucial role of the APN in these challenges to the healthcare system.

This edition contains additional material not included in the original, such as new information on clinical trials involving MS therapies and the APN's role in treatment decisions and symptom management.

As with the previous editions, this monograph is dedicated to our patients and their families, for whom we strive to make things better. It is our hope that one day we will better control or cure MS.

Overview of Multiple Sclerosis

DEFINITION AND DIAGNOSIS

Multiple sclerosis (MS) affects an estimated 300,000 to 400,000 people in the United States and approximately 55,000 to 75,000 in Canada.[1,2,3] MS is typically diagnosed in early adulthood (most commonly between the ages of 20 and 50) and has a variable course, with about half of patients experiencing significant difficulty with ambulation within 15 years after disease onset.[4]

The course of MS varies widely, but may be classified as relapsing-remitting, secondary-progressive, progressive-relapsing, and primary-progressive.[5] Most individuals (approximately 80%) begin with a relapsing-remitting course of MS (RRMS), characterized by episodes of neurological symptoms separated by periods of time with stability of symptoms. Common early symptoms are sensory disturbances, unilateral optic neuritis, double vision, limb-weakness, clumsiness, and bladder and bowel problems; fatigue is also common.[4] Cognitive impairment, depression, emotional lability, progressive quadriparesis, tremors, spasticity, and other symptoms of central nervous system dysfunction may develop and become very disabling.[4]

The diagnosis of MS is based on established clinical and laboratory criteria.[4] The McDonald criteria for diagnosis, originally published in 2001 and revised in 2005, have attempted to simplify the diagnostic process of MS and to integrate magnetic resonance imaging (MRI) into the diagnosis.[6,7] The outcomes of the diagnostic process should yield possible MS, definite MS, or an exclusion of MS.* Diagnosis requires 2 attacks, lasting for at least 24 hours and occurring at least 1 month apart, and clinical evidence of 2 or more lesions. Fewer than 2 attacks and/or clinical evidence of fewer than 2 lesions require additional evidence of disseminated time and space demonstrated by MRI.[7] Cerebrospinal fluid analysis and evoked potential studies may still be incorporated to provide paraclinical evidence of the disease, although their use today is less frequent than in the past. Patients with a single attack and clinical evidence of one lesion are classified as having a clinically isolated syndrome (CIS).[7] By these criteria, MS remains a diagnosis of exclusion. Differential diagnosis of MS is complex, and consensus guidelines have been developed to help clinicians systematically exclude alternative diagnoses.[8]

* The McDonald criteria were developed to replace previous MS diagnostic criteria established by Poser et al (*Ann Neurol.* 1983;13:227-231), which yields 5 possible results: clinically definite MS, laboratory supported definite MS, clinically probable MS, laboratory supported probable MS, and no MS.

EVOLUTION OF MS CARE PATTERNS

MS care patterns have evolved significantly in recent decades. In the 1970s and 1980s, the care pattern was focused primarily on palliative care and alleviation of symptoms. However, in the mid 1990s, disease management options and the scope of useful interventions were greatly expanded with the development of the immunomodulatory therapies, along with refinements in diagnostic and monitoring technologies.

Today, healthcare professionals have a more comprehensive perspective and a more proactive approach toward treating patients with MS. This approach encompasses everything from improving earlier diagnostic efforts to maximizing overall wellness. At the foundation of all MS treatment is the formalized appreciation of the fact that patients and their significant others are active partners in the care process.

According to the Consortium of Multiple Sclerosis Centers' Recommendations for Care, because MS is a lifelong disease for which there is currently no cure, the healthcare team treating patients with MS should seek to provide a comprehensive approach to disease management, which takes into consideration the medical, social, vocational, emotional, and educational needs of the patient and his or her family.[9] The goal of this comprehensive, integrated approach is to empower patients and their families to maximize independent functioning and quality of life and to prepare them for the adaptations that will come with changes in physical and cognitive functioning. The reach of this integrated care extends beyond the walls of the healthcare office(s) and into the patient's centers of living (eg, home and work environments) for the duration of the patient's life.

EVOLUTION OF MS TREATMENT AND EXPECTATIONS

Current goals of MS treatment have expanded beyond management of neurological symptoms to include reducing relapse rates, slowing disease progression, and preventing resulting disability.[10] These expanded goals depend on heightened expectations for medications, which must be safe, effective, and well tolerated over the long term. A brief

review of symptomatic management of MS begins on page 20.

Corticosteroids

Corticosteroids are the accepted standard of care in the treatment of acute MS relapses, as they may accelerate recovery from relapse symptoms.[4,10,11] The long-term use of corticosteroids, in intermittent pulse therapy or other forms, has shown uncertain benefit for reducing relapses and resultant disability.[10,11] Given the risks associated with long-term corticosteroid use, such as cataracts and osteoporosis, the use of corticosteroids is generally recommended only for short courses during acute episodes.

Disease-Modifying Therapies

The disease-modifying therapies (DMTs) approved by the Food and Drug Administration (FDA) in the 1990s fundamentally changed the philosophy of MS care from a paradigm of palliation to a paradigm of relapse reduction and delay in long-term disability.[12,13] In contrast to corticosteroids, the immunologic activities of the DMTs diminish new central nervous system (CNS) inflammatory activity, reduce the number of relapses, and, depending on the agent, demonstrate a positive effect on disability progression. Although DMTs do not constitute cures, they hold significant promise for altering the natural history of MS. In conjunction with ongoing care and support by healthcare professionals, these treatments offer patients options that help sustain hope and facilitate an acceptable quality of life.

The DMTs currently approved for use in the United States and Canada to treat RRMS include the immunomodulators glatiramer acetate (Copaxone®) and the interferon beta (IFN β) agents: intramuscular (IM) IFN β-1a (Avonex®), subcutaneous (SC) IFN β-1a (Rebif®), and IFN β-1b (Betaseron®, Extavia® [Extavia is not available in Canada]), and natalizumab (Tysabri®).[14-19] Glatiramer acetate, IFN β-1b, and IM IFN β-1a are also indicated for use in CIS patients. (In Canada, IFN β-1b is also approved to treat secondary-progressive MS [SPMS].[20] Canadian labeling for SC IFN β-1a carries an indication to reduce relapse rate and disease activity on MRI, but not disease progression, in patients with relapsing SPMS.) In the United States, natalizumab can only be prescribed under the TOUCH™ mandatory registration program, described below.[19] The immunosuppressant mitoxantrone (Novantrone®) is approved to treat SPMS, progressive-relapsing MS, or worsening RRMS, and is sometimes used in combination with methylprednisolone.[21]

The interferons, glatiramer acetate, natalizumab, and mitoxantrone achieve their therapeutic effects through different mechanisms of action and consequently produce different side effects. Most of these side effects are mild to moderate, usually subsiding within the first few months after treatment initiation. However, some side effects can be serious and require monitoring or extra caution. For example, treatment with mitoxantrone requires monitoring for signs of cardiotoxicity,[21] while treatment with the interferons requires periodic blood tests to detect blood count or liver abnormalities and observation for signs of depression or suicidal ideation.[15-18] Natalizumab therapy increases the risk of developing progressive multifocal leukoencephalopathy (PML), and due to this risk, natalizumab can only be administered to patients registered in the United States with the TOUCH Prescribing Program.[19] In Canada, patients are advised to register with the Canadian Tysabri Care Program™.[20] Dosing and administration information, side effects, label warnings, and nursing implications for each of these agents are summarized in Table 1.

MS CLINICAL TRIALS

As APNs caring for MS patients, it is important to understand the importance of pivotal clinical trial data and subsequent long-term follow-up studies involving MS therapies. Randomized clinical trials have laid the foundation for current MS drug therapy. First, they established that each of the currently available DMTs has favorable effects on MS relapses and may prolong the time to sustained disability progression in a significant proportion of patients.[21-27] Most DMTs also reduce disease activity as measured by MRI.[22,27-30] Other randomized studies have demonstrated that initiating interferon or glatiramer acetate therapy in CIS patients at the first sign of clinical demyelination can significantly delay the development of clinically definite MS.[31-36] Longer-term data from these pivotal trials and other trials support the sustained safety and clinical benefits of the immunomodulators, with added evidence coming from MRI scans.[30, 37-43] In the most recent and ongoing phase in the evolution of evidence-based drug therapy for MS, head-to-head clinical trials have been conducted to compare disease-modifying agents directly, and other trials have been conducted to explore their use in new combinations.

DMT Clinical Trial Data

Patients enrolled in the phase III pivotal trials of the DMTs—the IFN β agents and glatiramer acetate—had established RRMS for an average of 4 to 8 years, high relapse rates, and mild or no disability at entry. Relapse rates in these trials showed a consistent reduction of approximately 30%.[45] Investigators have continued to elucidate the effects of these agents on measures of progressive disability, various MRI

outcomes, and long-term safety and efficacy, in both RRMS and CIS. Below is a brief review of selected landmark studies for the DMTs.

IFN β-1a IM (Avonex®). The intramuscular preparation of IFN β-1a was investigated in a double-blind, placebo-controlled, multicenter trial (the MSCRG Study) of 301 patients with RRMS, whose main endpoint was time to sustained disability progression of at least 1.0 point on the Kurtzke Expanded Disability Status Scale (EDSS).[24] After 2 years, 34.9% of placebo-treated patients demonstrated progressive disability compared to 21.9% of those treated with 30 μg IFN β-1a (P=0.02), a 37% relative reduction in risk.[15,24] Interferon-treated patients had significantly fewer exacerbations (P=0.03), with an annual relapse rate of 0.61 over 2 years vs 0.90 for placebo. In addition, treated patients had a significantly lower number and volume of gadolinium (Gd)-enhanced brain lesions on MRI (P=0.02–0.05).[24]

Subsequently, the Controlled High Risk Subjects Avonex

TABLE 1. Disease-Modifying Therapies[14-19,21]

	Glatiramer acetate (Copaxone®)	Interferons			Natalizumab (Tysabri®)	Mitoxantrone (Novantrone®)
		Interferon β-1a (Avonex®)	Interferon β-1a (Rebif®)	Interferon β-1a (Betaseron®, Extavia®)		
Type	Polypeptide mixture	Recombinant protein	Recombinant protein	Recombinant protein	Recombinant humanized monoclonal antibody	Antineoplastic anthracenedione
Indication (US)	RRMS and CIS	Relapsing forms of MS and CIS	Relapsing forms of MS	Relapsing forms of MS and CIS	Relapsing forms of MS	SPMS, PRMS, or abnormally worsening RRMS
Route	SC injection	IM injection	SC injection	SC injection	1-hour IV infusion	5- to 15-minute IV infusion
Administration	Daily	Weekly	3x/week	Every other day	Every 4 weeks	Every 3 months
Dosage (US)	20 mg	30 μg	44 μg	0.25 mg	300 mg	12 mg/m^2 (cumulative dose not to exceed 140 mg/m^2)
Common side effects/ warnings	• Injection-site reactions • Vasodilatation • Rash • Dyspnea • Chest pain • Immediate post-injection reaction	• Mild flu-like symptoms • Muscle aches • Decreased peripheral blood counts • Headaches • Anaphylaxis • Depression or suicide ideation • Hepatic injury or failure	• Mild flu-like symptoms • Muscle aches • Anemia • Injection-site reactions • Anaphylaxis • Depression or suicide ideation • Hepatic injury or failure	• Flu-like symptoms • Injection-site reactions and necrosis • Anaphylaxis • Depression or suicide ideation • Menstrual disorders • Mild neutropenia, anemia, and thrombocytopenia • Abnormal liver function (blood testing for leucopenia and liver and thyroid function required)	• Headache • Fatigue • Arthralgia • Urinary tract infection • Hypersensitivity reactions • Liver injury • PML (rare)	• Nausea • Alopecia • Menstrual disorders/ amenorrhea • URI or UTI • Cardiotoxicity, CHF, and decreases in LVEF • Secondary AML
Nursing implications	• Monitor for injection-site reactions • Ensure that drug is given SC only • Educate regarding potential side effects, problem solving, and available resources	• Help patient establish expectations of therapy • Monitor for injection-site reactions, liver and blood abnormalities, neutralizing antibodies • Observe for depression, suicidal ideation • Educate regarding potential side effects, problem solving, and available resources	• Monitor for injection-site reactions, liver and blood abnormalities, neutralizing antibodies • Observe for depression, suicidal ideation • Educate regarding potential side effects, problem solving, and available resources	• Monitor for injection-site reactions, liver and blood abnormalities, neutralizing antibodies • Observe for depression, suicidal ideation • Educate regarding potential side effects, problem solving, and available resources	• Monitor for hypersensitivity reactions, signs of liver injury, and any signs or symptoms of PML • Ensure that drug is never given as an intravenous push or bolus injection. • Educate regarding potential side effects, problem solving, and available resources	• Monitor for evidence of cardiotoxicity, CHF, and decreases in LVEF; evaluation of LVEF by echocardiogram or MUGA prior to each course of treatment • Monitor for IV infusion-site reactions and signs of extravasation • Ensure that drug is never given SC, IM, or intra-arterially • Educate regarding potential side effects, problem solving, and available resources • Test for blood and liver abnormalities before each course of treatment • Pregnancy tests for women prior to each course of treatment

Multiple Sclerosis Prevention Study (CHAMPS) showed that the benefits of IFN β-1a IM therapy could be extended to individuals with an isolated demyelinating event. In this trial of 383 patients, who received IV steroids for their exacerbation and were randomized to 30 μg IFN β-1a IM or placebo, DMT treatment significantly delayed the time to development of a second exacerbation compared to placebo after 3 years (*P*=0.002), and was associated with reduced number and volume of brain lesions at 18 months.[33] Most recently, 10-year data from an open-label extension of CHAMPS (Controlled High Risk Avonex Multiple Sclerosis Prevention Study in Ongoing Neurologic Surveillance [CHAMPIONS]) showed continued benefit from early treatment in reducing disease progression.[46]

IFN β-1a SC (Rebif®). The Prevention of Relapses and Disability by Interferon β-1a Subcutaneously in Multiple Sclerosis (PRISMS) study compared the effects of IFN β-1a SC at 2 doses (44 mcg and 22 mcg, 3 times per week) with placebo in 560 patients with RRMS. After 2 years, both doses were more effective than placebo in reducing the number and frequency of relapses; exacerbations were reduced by 29% and 32% compared to placebo at the lower and higher doses, respectively. Treated patients also demonstrated delayed progression of disability, and a larger proportion were relapse-free with treatment compared to placebo.[22] Analysis of MRI results showed that treatment reduced the burden of disease from brain lesions compared to placebo, an effect confirmed in long-term follow-up.[37]

In the PRISMS-4 extension study, placebo patients were crossed over to IFN β-1a SC while others continued blinded treatment with their originally assigned dose for another 2 years.[30] The benefits of active treatment were maintained in the latter group, while crossover patients had fewer relapses and less disease activity and MRI lesion burden than they exhibited during the placebo-controlled phase. Patients receiving IFN β-1a from the beginning of the original trial had consistently better efficacy outcomes at 4 years than the crossover group. Long-term follow-up extended to 8 years in the PRISMS cohort (including 68.2% of the original study patients, 72% of whom were still receiving IFN β-1a), and continued to demonstrate clinical and MRI benefit from early vs delayed treatment.[38]

The Early Treatment of MS (ETOMS) trial demonstrated benefits of early IFN β-1a SC treatment in patients with a first neurologic event suggestive of MS and abnormal MRI findings.[36] A total of 308 such patients were randomized to receive either weekly IFN β-1a SC (22 μg) or placebo. After 2 years, 34% percent of treated patients and 45% of those on placebo had progressed to clinically definite MS, a relative reduction of 24% (*P*=0.047). Relapse rate was 33% vs 43% on placebo (*P*=0.045), and MRI activity was significantly lower with active treatment.

IFN β-1b (Betaseron®). In the pivotal trial for this DMT, 372 patients with RRMS were randomized either to placebo, or to 1 of 2 doses of IFN β-1b (1.6 MIU or 8 MIU), for 2 years.[23] Compared to placebo, IFN β-1b reduced the annual relapse rate by about 30%. After 2 years, exacerbation rates were significantly reduced for both lower- and higher-dose treatment groups (1.17 and 0.84 respectively) compared with 1.27 for placebo (*P*=0.0001), with a dosage change among groups. A decrease in mean lesion area was observed in the high-dose group.[23] Treatment benefits were sustained for up to 5 years, with a one-third reduction in relapse rate in the higher-dose treatment group compared to placebo for each year.[39] In a report from this pivotal trial's 16-year long-term follow-up study, early and sustained exposure to IFN β-1b treatment was strongly associated with reduced risk of negative outcomes including an EDSS score of 6.0 or higher, wheelchair use, or progression to SPMS.[40]

Early treatment with IFN β-1b was supported by the Betaferon/Betaseron in newly emerging multiple sclerosis for initial treatment (BENEFIT) trial, which randomized 468 patients within 60 days of an isolated demyelinating event to either 0.25 mg or placebo every other day.[31] After 2 years, treated patients had a lower rate of conversion to definite MS. Among patients who entered an open-label follow-up phase, those who received early treatment had a 37% lower risk of progression to MS (*P*=0.003) at 5 years compared with those initially on placebo.[32]

Glatiramer acetate (Copaxone®). In the pivotal trial of glatiramer acetate, 251 patients with RRMS were randomized to either 20 mg a day of glatiramer acetate or placebo for 2 years.[25] Compared to the placebo group, patients on treatment showed a 29% reduction in relapse rate, the study's primary endpoint. The final 2-year relapse rate was 1.19 for treated patients and 1.68 for placebo (*P*=0.007).

Of the DMTs used to treat MS, glatiramer acetate has the most serially collected data in the clinical trial setting and the longest duration of continuous follow-up, reported at 6, 8, and 10 years.[41-44] At 6 years, during an open-label crossover phase of the trial described above, patients treated with the drug from randomization showed a steady decline in relapse frequency: a mean of 1.5 per year at entry and a mean of 0.42 over all 6 years, a 72% reduction (*P*=0.0001).[41] Those who began with placebo and later switched to active treatment (after a mean of 30 months) showed a lesser decline in relapse frequency and also fared worse in degree of disability compared to those receiving ongoing therapy.[41,42] At 8 years of observation, these results remained consistent, suggesting the importance of early and continued therapy.[43] After a decade, 62% of patients receiving ongoing therapy

with glatiramer acetate had stable or improved EDSS scores, compared to 58% of patients treated for an average of 7 years and 28% of patients who withdrew from the study and returned for evaluation.[44] The open-label extension trial has continued and is now at 15 years.

The European/Canadian MRI Study was a multinational randomized trial that used MRI to document the effect of glatiramer acetate on disease activity in 239 patients with RRMS.[28] After 9 months, treatment significantly reduced MRI measures of MS disease activity and burden: The median cumulative number of T1 Gd-enhancing lesions was 11 in treated patients and 17 in the placebo group (P=0.003).[14,28] The relapse rate was also significantly reduced by 33% for treated patients (P=0.012).[28] In a 9-month open-label extension, investigators found a 54% reduction in the mean number of enhanced lesions for those who switched from placebo to glatiramer acetate, with an additional 24.6% reduction for patients treated from the study's outset.[47]

For treatment in CIS, the PreCISe Study, which randomized 481 such patients to either glatiramer acetate or placebo for up to 3 years, showed that the risk of developing clinically definite MS was reduced by 45% in the treated group vs placebo, and the time to development of definite MS was 386 days longer.[35] The proportion of patients who experienced a second attack at 3 years was 43% in the placebo group vs 25% in the glatiramer acetate group (P<0.001).

Natalizumab (Tysabri®). Natalizumab has a short but eventful history in the treatment of MS due to both its demonstrated efficacy and concerns about its safety. Striking efficacy results on clinical and MRI endpoints were observed in 2 trials: the 2-year natalizumab safety and efficacy in RRMS (AFFIRM) study and the safety and efficacy of natalizumab in combination with IFN β-1a in patients with RRMS (SENTINEL) study.[27,48] Data from AFFIRM revealed a 68% reduction in annual relapse rate compared to placebo and significantly reduced numbers of brain lesions on MRI.[27] Other positive results were reported from SENTINEL, such as a reduction in annual relapse rate of about 54% at years 1 and 2 with natalizumab/IFN β therapy compared to interferon alone.[48]

After being voluntarily withdrawn from the market by its manufacturer in 2005 due to 3 cases of PML and receiving FDA approval to return to the market in 2006, there have been >20 cases of PML worldwide in MS patients taking natalizumab.[49] Research to identify risk factors of PML may help clinicians better identify patients who would benefit from natalizumab treatment. The risk of PML seems to increase with the number of natalizumab infusions,[50] and as the long-term safety of the drug continues to be monitored, it is recommended that the drug be administered to patients who have had an inadequate response to, or are unable to tolerate, other therapies.[19]

Mitoxantrone (Novantrone®). Two-year clinical trial data on mitoxantrone in patients with worsening RRMS, progressive-relapsing MS, or SPMS showed significantly fewer treated relapses in patients treated with mitoxantrone vs those on placebo (24.08 vs 76.77, respectively; P=0.0002).[26] There were also fewer new Gd-enhancing lesions shown on MRI among patients taking mitoxantrone than among those on placebo (0% vs 16%, respectively; P=0.02).

Several trials have suggested that a brief induction of mitoxantrone followed by immunomodulatory therapy may be of benefit. In a trial of 40 patients with RRMS who received either 3 monthly infusions of 12 mg/m^2 mitoxantrone followed by 12 months of 20 mg glatiramer acetate or glatiramer acetate alone, a greater reduction in the number of Gd-enhancing lesions was observed in patients receiving induction therapy than those only on glatiramer acetate (89% reduction at months 6 and 9 [P=0.0001]; 70% reduction at months 12 and 15 [P=0.0147]).[51] Mean relapse rates were also lower in the induction group (0.16) than the glatiramer acetate group (0.32). In another study that also showed the benefit of mitoxantrone induction,[52] 103 patients with very active RRMS were observed for 3 years. One group received 20 mg monthly mitoxantrone plus 1 g monthly methylprednisolone for 6 months, followed by a 3-month therapeutic window, after which they received IFN β-1b for 27 months. A second group received IFN β-1b monthly for 3 years with 1 g methylprednisolone for the first 6 months. Among those receiving the mitoxantrone induction, more patients were relapse free and fewer had fixed disability than among patients who did not receive mitoxantrone.

With regard to long-term safety of mitoxantrone, the registry to evaluate Novantrone effects in worsening MS (RENEW) study evaluated the safety and tolerability of 172 patients receiving mitoxantrone for 5 years. Ten patients experienced congestive heart failure and 3 patients developed leukemia.[53] Researchers determined that the results corroborate with previously reported adverse events experienced with mitoxantrone. Smaller studies, however, suggest that the rates of congestive heart failure and treatment-related leukemia in mitoxantrone-treated patients may be higher than previously reported.[54,55]

Head-to-Head Trial Data

In the past decade, results from several head-to-head trials have offered clinicians direct comparative data for immunomodulatory agents for MS. The randomized, prospective, multicenter INCOMIN (Independent Comparison of Interferon) trial compared treatment with alternate-day IFN β-1b to once-weekly IFN β-1a IM in 188 patients with RRMS. Over 2 years, IFN β-1b appeared significantly

more effective, with 51% of patients in that treatment group remaining relapse-free compared with 36% of those on IFN β-1a IM (*P*=0.03).[56] Development of active lesions on MRI was also strongly reduced by IFN β-1b compared to IFN β-1a.[57]

The EVIDENCE trial in patients with RRMS showed subcutaneous IFN β-1a (44 μg tiw) to be significantly more effective than a lower-dose, lower frequency regimen of intramuscular IFN β-1a (30 μg qw) in reducing relapses and MRI activity, at 24 and 48 weeks of treatment. This advantage was sustained for at least 16 months.[58]

More recently, 3 randomized clinical trials have compared the efficacy and safety of glatiramer acetate with high-dose IFN β therapy in RRMS, all indicating comparable efficacy in relapse reduction and other primary endpoints.[59] In the REbif vs Glatiramer Acetate in Relapsing MS Disease (REGARD) trial, 764 patients were randomized to either IFN β-1a SC or glatiramer acetate for 96 weeks, with no significant difference observed in time to first relapse, the study's primary outcome.[60] For the secondary outcomes, a subset of 460 patients given serial MRI scans showed no significant difference in the number and change in volume of active T2 lesions or in the change in volume of Gd-enhancing lesions, brain-lesion volume or activity; although those on IFN β-1a treatment had fewer Gd-enhancing lesions than those on glatiramer acetate (0.24 vs 0.41, respectively; *P*=0.0002). Tertiary outcomes of the annual relapse rate revealed no significant difference.

In the open-label, multicenter BEYOND (Betaferon Efficacy Yielding Outcomes of a New Dose) trial—the largest of the 3 direct-comparison studies—2,244 patients were randomized to either glatiramer acetate or 1 of 2 doses of IFN β-1b (either the standard 250 μg or 500 μg) for 2 years.[61] In all 3 pair-wise comparisons, the primary outcome of relapse risk did not significantly differ; mean annualized relapse rate over 2 years of treatment declined by about 80% in all 3 arms of the trial, with no significant difference observed among them in EDSS progression or MRI activity. Flu-like symptoms were more common in IFN-treated patients (*P*<0.0001), while injection-site reactions were more common in those given glatiramer acetate (*P*=0.0005).

The relatively small BECOME (Betaseron vs Copaxone in Multiple Sclerosis with Triple-Dose Gadolinium and 3-Tesla MRI Endpoints) study compared IFN β-1b (250 μg, every other day) to glatiramer acetate (20 mg daily) in 75 patients with RRMS.[62] The study relied on an optimized MRI protocol to measure the primary outcome of combined active lesions per scan during 1 year of treatment; the mean number of lesions declined in both treatment groups (0.63 vs 0.58 in the IFN β-1b and glatiramer acetate groups, respectively) but without significant difference between groups (*P*=0.58). Over the study's 2-year duration, there were also no significant differences between the 2 groups in the number of new lesions and clinical relapses.

The Modern MS Clinical Trial

The results of the REGARD, BEYOND, and BECOME trials suggest an efficacy more similar than different on clinical endpoints, and, to a less-certain extent, on MRI activity as well.[63,64] Until new therapeutic alternatives are available, the selection of a first-line agent for RRMS may depend more on adverse effects and adherence issues than on differing efficacy.

It is worth noting that some trials in this second generation of DMT research, or so-called modern MS trials, such as REGARD, have reported markedly lower relapse rates among subjects than relapse rates seen in the earlier DMT pivotal trials.[65] In REGARD, for example, relapse rates were lower than expected in both groups, raising the possibility that populations in later clinical trials have different characteristics, such as a higher proportion of patients at an earlier stage or with lower disease activity. Broader inclusion criteria, earlier diagnosis, and higher awareness of MS among physicians and patients might all contribute to this effect. The REGARD investigators suggested that a trial population with such low disease activity might limit the ability to predict clinical advantage based on earlier trials.[60] To meet the challenge of such low on-study relapse rates, the designers of future clinical trials may need to modify inclusion criteria, increase trial sample size, or otherwise increase the power of clinical trials to reveal distinctions among therapeutic options.[59,60]

Emerging Therapies

Beyond today's DMTs, various novel approaches to MS therapy are under development. These include oral immunomodulatory agents such as cladribine, fingolimod, laquinimod, and teriflunomide. Phase II and phase III trials of these agents have, thus far, proven them to be safe and effective in the short term.[66-69] While oral agents to treat MS would offer a highly sought-after alternative to injectible agents, long-term (≥5 years) safety issues are not yet known and may be of concern. Also under investigation are several monoclonal antibodies, including alemtuzumab and rituximab, and experimental approaches such as hematopoietic stem-cell transplantation.[70] As APNs caring for patients with MS, it is important to be knowledgeable about treatments under study, including potential mechanisms of action, outcome measurements, risks, and expected time to trial completion. As the race for an oral or otherwise new MS therapy quickens, eagerness and excitement should be tempered with accurate and professional guidance that is in the best interest of the patient.

Nursing Care in Multiple Sclerosis

EMERGENCE OF MS AS A NURSING SPECIALTY

The expanded strategies and approaches to MS treatment have had dramatic implications for nurses. The role of the nurse has grown in both depth and breadth to accommodate the increased need for education and healthcare management in treating MS. The enhanced spectrum of care requires the abilities of highly skilled nurses who can meet the needs of patients at any point on the health–illness continuum and in a range of settings, including primary, acute, specialized, and rehabilitative care. The variety of MS disease characteristics mandates multidisciplinary care and specialized nursing care for optimal outcomes. This provides the MS nurse with many potential opportunities to play pivotal roles in patient care at many different levels of intervention and interaction. Such opportunities arise because of the broad range of MS signs and symptoms, the unpredictable disease course, the need for long-term treatment and periodic clinical and MRI assessments, the need for consultation and interaction with other health professionals in a variety of specialties and disciplines, and the need for ongoing patient support.[71,72]

To fill this growing need, nurses who specialize in MS have begun to attain higher levels of knowledge and more sophisticated skills. In addition, new roles for the MS nurse have been articulated, new domains defined, and new certification procedures established by the International Organization of Multiple Sclerosis Nurses (IOMSN) to recognize the attainment of expertise and team leadership skills. Founded in 1997, the IOMSN currently has about 2,000 members. It has established a specialized branch of nursing, developed standards of nursing care, supported nursing research, and educated both professionals and laypeople. Progress in these areas is ongoing; the ultimate goal of the IOMSN remains to improve the lives of all those persons affected by MS through the provision of appropriate healthcare services. An international certification board was established as a separate entity in 2001, and the first certification examination was administered in 2002. As of 2005, there are approximately 700 nurses with special certification in MS nursing, up from about 400 nurses in 2002. During the same time, numerous advanced practice nurses (APNs) have become increasingly involved in MS care and research throughout North America.

EVOLUTION OF THE ROLE OF APNS IN NORTH AMERICA

The concept of specialty nursing was introduced in 1900, when an article by Dewitt on the development of specialized clinical practice within the nursing profession appeared in the first issue of the *American Journal of Nursing*.[73] Dewitt's article appeared at a time when hospitals offered their nurses apprenticeship-model postgraduate courses in areas such as anesthesia, tuberculosis, dietetics, and surgery.[74] A nurse who had completed such a course or one who had extensive experience and expertise in a particular clinical area was deemed a specialist.

As new discoveries in science and medicine were incorporated into clinical practice, the need for specialization grew. In the early 1960s, concerns about providing healthcare services for the disadvantaged, along with a push for greater nurse education, spurred the development of the role of the nurse practitioner (NP).[75] By the mid-1970s, more than 500 NP programs existed in the United States. The American Nurses Association published guidelines for NPs in 1974, and a credentialing program was developed in 1976. In Canada, the heavy involvement of the government in the healthcare system and the federation structure of the government impeded the development of the NP. However, by 1993, NP guidelines were established and post-baccalaureate programs developed. The first Extended Class Registered Nurses (RNs; equivalent to NPs) were registered by the Canadian Nurses Association in 1998.

In the 1970s and 1980s, several state nursing practice acts fostered both the continued evolution of the NP role and the contemporary use of the term *advanced practice nursing*. As newly defined, the term was meant to encompass NPs and other advanced nursing specialists, such as certified registered nurse anesthetists (CRNAs), certified nurse-midwives (CNMs), and clinical nurse specialists (CNSs). The state nursing practice acts also served to demonstrate areas of common ground among the various advanced practice specialties.[74]

A growing body of literature attests to the generally positive impact of advanced primary-care nursing roles on patients, nurses, and clinicians.[76] The conceptual basis of advanced practice nursing continues to be elucidated and its core definition refined and clarified—key steps in enhancing

its internal cohesion and increasing its legitimacy and recognition within and beyond the healthcare professions.[77] On a global level, APNs are a critical component of cost-effective healthcare delivery now and in the future. However, many challenges remain in the areas of classification and regulation, with inconsistencies regarding roles and titles persisting across national boundaries.[78]

ROLE OF THE MS APN

The MS APN plays many roles, including:

1) administrator,
2) educator,
3) collaborator,
4) consultant,
5) researcher,
6) advocate, and
7) expert clinician.

Each of these roles is associated with its own set of responsibilities, functions, and skills. Qualifications necessary to fulfill these roles have been identified, along with inherent constraints that exist.

Administrator

Although not all APNs function as administrators, the consensus of the original attendees at the 2002 APN Advisory Consensus Meeting in Ontario, Canada, (see page 36) was that this was potentially an important facet. As an administrator, the MS APN is responsible for staff (including hiring, supervision, and scheduling), budget, policies and procedures, and quality assurance outcomes. The MS APN's responsibilities as an administrator are similar in many important ways to the case management and case-outcomes management responsibilities of the clinical nurse specialist (CNS).[79] As Sparacino points out, the CNS case manager is involved with, and frequently directs, resource management and clinical systems development. In contrast, the CNS case-outcomes manager has even broader responsibilities, including clinical and financial analysis, outcomes for a particular patient population, development and revision of organizational systems, quality assurance, research, provider education, and development and implementation of interdisciplinary practice improvements.

Educator

The MS APN is responsible for teaching a variety of audiences about MS, including patients and their families, physicians and allied health professionals, students, employers, and the community. For the patient and the family in particular, the MS APN provides information about the following.

- Implications of an MS diagnosis
- Pathophysiology and natural history of MS
- Prognostic indicators (both positive and negative)
- Realistic expectations with regard to lifestyle and treatment options
- Pharmacologic management of MS
  - Disease modification using immunomodulators
  - Education about current clinical trials and nursing research in MS care
  - Symptom and side-effect management

Using their highly specialized knowledge and expertise, MS APNs can help dispel misconceptions, interpret research and clinical trial data, help patients make informed decisions about their care, empower patients to participate as full partners, and instill hope in patients and families.

Collaborator

Collaboration is central to the role of any APN and is essential to optimizing outcomes. The MS APN works with a variety of health professionals, including physicians, rehabilitation specialists, and psychologists, to ensure that patients receive appropriate care and follow-up. Collaboration with other nurses also leads to increased recognition of nurses as critical members of the healthcare team.[79] The MS APN collaborates with community-based agencies to facilitate access to services, such as transportation, Meals on Wheels, home care, and other available community support. In addition, the MS APN collaborates with industry to develop tools and strategies related to disease modification and technology, such as intrathecal pumps, assistive devices, and communication aids.

Consultant

The MS APN makes his or her expert knowledge available to others via internal or external consulting. Internal consulting addresses the needs of patients, staff nurses, and other healthcare professionals, whereas external consulting assists the nursing profession, specialty organizations, and health systems outside the practice setting with approaches and solutions for specific problems.[79] Consulting permits the identification and solution of a variety of aspects of patient care,[80] including therapy and treatment options, management of side effects, availability and use of adaptive devices and equipment, use of unapproved therapies, and referrals as necessary. For the MS APN, a crucial aspect of consulting is serving as a liaison to industry, employers, insurance companies, and government agencies that deal with disability issues to clarify MS and its widespread implications.

Researcher

APNs take an active role in clinical practice research, developing practice guidelines, and reviewing outcome and performance measures.[81] Moreover, the MS APN may function as principal investigator for a clinical practice research study, coordinate various aspects of the research effort, examine patients participating in the study, and help evaluate outcomes. Outcomes research may include patient response to pharmaceutical and rehabilitation interventions and may also investigate patient satisfaction, cost of care, or utilization of services.

Advocate

The MS APN serves as an advocate for patients and staff members, and as an agent for change in dealings with healthcare providers, allied health professionals, the community, and healthcare systems. Patient advocacy involves negotiating for the patient with respect to work, legal issues, obtaining appropriate treatment, and making informed choices about treatment. Staff advocacy entails providing emotional and situational support for staff nurses and others to prevent and resolve conflict in their work environment, reduce stress, and improve clinical judgment in the management of patient problems.[80] The MS APN acts as a catalyst in terms of monitoring the standard of patient care, guiding staff in the acquisition of clinical skills and knowledge, interpreting advanced practice nursing for medical professionals and the community, developing innovative approaches to clinical practice, and promoting interdisciplinary collaboration.[80]

Expert Clinician

Many APNs view their most important role—and the heart of advanced practice nursing—as that of the expert clinician.[79,82] In this role, APNs in all areas of specialization have prescriptive authority in all US states and several provinces of Canada and are responsible for assessment, diagnosis, treatment, evaluation, and ongoing management of patients. The MS APN demonstrates an in-depth understanding of the pathophysiology of MS; appropriate interventions, particularly DMTs; symptom management; and diagnostic tests. In addition, the MS APN makes referrals as necessary, counsels patients, promotes wellness, and serves as the coordinator of individualized patient care.

Qualifications

There are unique characteristics required for the role of the MS APN. These are:

- *Autonomy*, which includes practicing without supervision, making decisions independently, and managing one's own time and workload
- *Accountability* for the care provided, including quality of care, patient satisfaction, efficient use of resources, and clinical behavior[81]
- *Authority*, as reflected by the 7 roles of the APN and the 4 domains of advanced practice nursing
- *Accessibility*, which includes being available to patients and easing or eliminating patient barriers to care, such as need for transportation, administrative hurdles, reimbursement, language, and culture[81]
- *Leadership*, as implied by the APN's 7 roles and reflected by the comprehensive care, professional persona, and scholarly inquiry domains of advanced practice nursing

Constraints and Barriers

The following were found to be common constraints or barriers to the development of the APN role.[79,80,82,83]

- Varying education levels upon entry to practice
- The ambiguous role of nursing within the health arena
- Pay scales not commensurate with the degree of responsibility, education, or experience
- Lack of reimbursement by insurance companies for the APN
- Lack of authority and/or autonomy in some settings, underscoring the need for collaborative practice agreements
- Inadequate support from nursing organizations, educational institutions, and fellow nurses
- Gender-specific preconceptions stemming from nursing's history as a female profession
- Paucity of research into the role of APNs and their impact on patients and patient outcomes
- The variety of roles in MS care

Skalia and Hamric suggest several ways to overcome these barriers.[82] These include drafting mutual agreements with the scope of practice defined; developing consensus regarding scheduling and workload; marshaling organizational support for the APN role; forming interdisciplinary networks for collaboration, consultation, and referral; and obtaining and maintaining peer support.

APN PRACTICE PATTERNS IN MS CARE

During the 1960s and 1970s, the terms expanded and extended appeared in the literature to suggest a horizontally structured movement that encompassed expertise in medicine and other disciplines. By comparison, the more contemporary term advanced suggests a more vertically structured movement that encompasses increasing expertise and post-

baccalaureate education in nursing itself rather than in other disciplines.[74]

By consensus, the MS APN is a master's-prepared expert nurse who manages, within the philosophical boundaries of the nursing profession, the complex medical problems and related issues faced by patients with MS and their families across the disease continuum. This includes promotion of wellness, restoration of health, prevention of illness, and management of disease, with the goals of instilling hope and empowering patients to participate in their own care as partners in a therapeutic alliance and not merely as recipients of care.

The evolution of management strategies and treatment options in MS has generated a corresponding evolution in MS APN practice patterns. The MS APN plays a pivotal role in the multifaceted aspects of establishing, continuing, and sustaining care across the health–illness continuum. These areas of care are presented in the monograph for MS nurses entitled *Multiple Sclerosis: Best Practices in Nursing Care*.[72] These aspects of MS care apply to any member of the interdisciplinary team, including the MS APN:

- *Establishing* care is the foundational step and includes building a relationship of trust and partnership with the patient, assessing educational needs and meeting them, and determining the support system available to the patient.

- *Continuing* care builds on this foundation and fosters the partnership through the provision of information to the patient on disease and medication management, adherence to the regimen, self-care and wellness strategies, and family involvement and support.

- *Sustaining* care involves approaches to maximize the patient's well-being through coordination of community, public, and private resources, and through coordination of care with appropriate specialists in multiple disciplines.

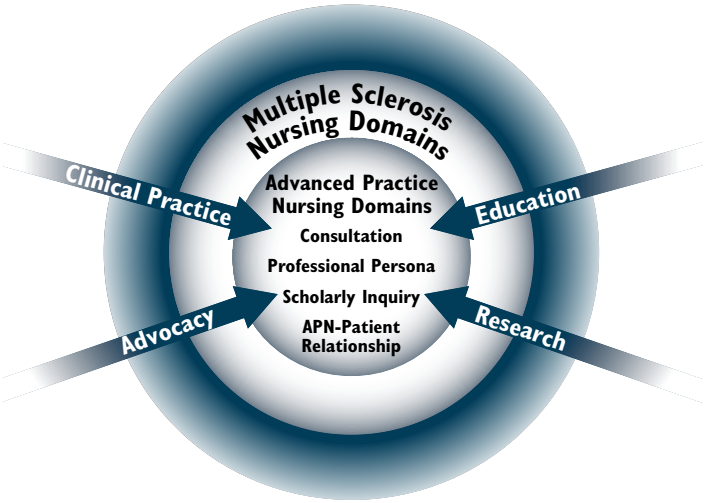
The advanced MS nursing practice can be found in hospitals, neurology offices, MS centers, rehabilitation units, and patients' homes. As care patterns evolve, these practice settings may expand to primary care settings and into other specialty units.

Notes

Domains of Practice in Multiple Sclerosis Care

Domains are realms of accountability and responsibility for the performance of identified tasks. The 4 MS nursing domains include clinical practice, education, advocacy, and research. These domains serve as the foundations for the more specialized domains of the APN. Conceptual frameworks and models for advanced practice nursing guide the development of MS advanced practice domains.[77] A schematic conceptualization of how these domains interrelate within the field of MS nursing is presented in Figure 1.

FIGURE 1. Multiple Sclerosis Nursing Domains



MODELS AND FRAMEWORKS OF ADVANCED PRACTICE NURSING

Of the advanced practice nursing models and frameworks described in the literature, 4 have emerged as relevant to advanced practice nursing in MS: (1) Benner, (2) Fenton, (3) Brykczynski, and (4) Hixon. Benner's seminal contribution to nursing was the novice-to-expert model.[84] Her practical model continues to guide the development of nurse competency through a clinical judgment process and is drawn on by nurse leaders to further refine and define the advanced practice nursing domains.

Benner's Domains of Expert Practice

Because nursing is a practice discipline, Benner undertook to identify and define clinical knowledge competencies that nurses could draw on to improve practice. Benner defines competency as "an interpretively defined area of skilled performance identified and described by its intent, functions, and meaning."[84] She identifies 7 domains of nursing practice that can provide direction for APNs (Figure 2).[85] She expands on a model of skill acquisition termed the Dreyfus model (Dreyfus S, Dreyfus H. A 5-stage model of the mental activities involved in directed skill acquisition. Unpublished study; 1980).

Expanding on Benner

The Dreyfus model was utilized by several APNs to enhance knowledge and skill acquisition. Hixon, in describing the transition of the APN from novice to expert practitioner, developed a model incorporating the Benner domains (Table 2).[86] Applying Benner's expert practice model to advanced practice NP skills acquisition, Brykczynski identified additional domains and competencies to be used by NPs in ambulatory care settings.[87] Four competencies are necessary in the management of patient health–illness status: (1) assessing, monitoring, and coordinating patient care over time; (2) detecting acute or chronic disease while attending to illness; (3) scheduling follow-up patient visits to monitor care; and (4) selecting and recommending diagnostic and therapeutic interventions.

Brykczynski identified 4 competencies in monitoring and

FIGURE 2. Benner's Domains of Expert Practice

Diagnostic/ patient monitoring functions	Administering/ monitoring therapeutic interventions and regimens	Monitoring/ ensuring the quality of health-care practices	Organization and work role competencies	Healing role of the nurse	Teaching/ coaching function	Effective management of rapidly changing situations

Reprinted from Hamric AB, Spross JA, Hanson CM, eds. *Advanced Nursing Practice: An Integrated Approach*. Philadelphia, PA: Saunders; 1996:33-51.[85]

TABLE 2. Novice-to-Expert Characteristics of Performance

NOVICE
- Has a narrow scope of practice
- Develops diagnostic reasoning and clinical decision-making skills
- Needs frequent consultation and validation of clinical skills
- Needs and identifies mentor
- Establishes credibility
- Develops confidence

ADVANCED BEGINNER
- Enhances clinical competence in weak areas
- Enhances diagnostic reasoning and clinical decision-making skills
- Begins to develop the educator and consultant roles
- Incorporates research findings into practice
- Sets priorities
- Develops a reference group
- Builds confidence

COMPETENT
- Has an expanded scope of practice
- Feels competent in diagnostic reasoning and clinical decision-making skills
- Begins to develop administrator role
- Develops organizational skills
- Views situations in multifaceted ways
- Senses nuances
- Relies on maxims to guide practice
- Feels efficient and organized
- Networks

PROFICIENT
- Incorporates direct and indirect role activities into daily practice
- Enhances clinical expertise
- Conducts or directs research projects
- Is an effective change agent
- Uses holistic approach to care
- Interprets nuances

EXPERT
- Has a global scope of practice
- Cohesively integrates direct and indirect roles
- Has an intuitive grasp
- Has a greater sense of salience
- Is a reflective practitioner
- Empowers patients, families, and colleagues
- Serves as a role model and mentor

Adapted with permission from Hixon ME. Professional development: socialization in advanced practice nursing. In: Hickey JV, Ouimette RM, Venegoni SL, eds. *Advanced Practice Nursing: Roles and Clinical Applications*. 2nd ed. Philadelphia, PA: Lippincott; 2000:46-65.[86]

ensuring quality health care practices: (1) developing strategies for dealing with concerns over consultation, (2) self-monitoring and seeking consultation as necessary, (3) using physician consultation effectively, and (4) giving constructive feedback to ensure safe practices. Other competencies used by Brykczynski, adapted from Benner, included broad domains of organization and work role competencies, teaching/mentoring/coaching, and consulting.[87]

Advanced practice CNS competencies are also grounded in the Benner expert model. Fenton expanded on the Benner model to develop CNS competencies.[88] The additional competencies identified by Fenton, in brief, are:

- Recognizing recurrent generic problems resolvable by policy change
- Coping with staff and organizational resistance to change
- Grooming staff to see their roles as part of the organization
- Providing support for nursing staff
- Making the bureaucracy respond to patient/family needs
- Providing emotional and informational support for patients' families
- Providing patient advocacy by sensitizing staff to patient dilemmas
- Interpreting the role of nursing to others

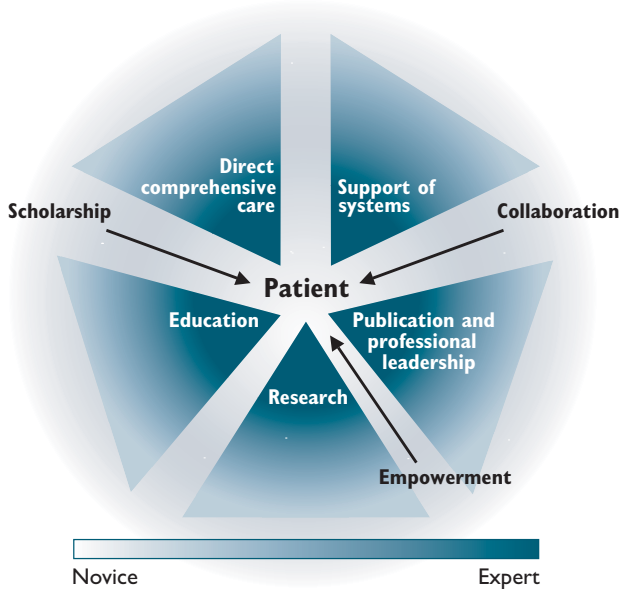
Strong Model of Advanced Practice

The Strong Model of Advanced Practice was developed in 1994 by APNs and faculty members at Strong Memorial Hospital of the Rochester Medical Center in Rochester, New York (Figure 3).[89] This model defines and identifies 5 domains of advanced practice and describes the activities in each domain. The domains include (1) direct comprehensive care, (2) support of systems, (3) education, (4) research, and (5) publication and professional leadership. Each domain incorporates the direct and indirect care activities of the APN. Unifying the domains and activities of the Strong model are the conceptual strands of collaboration, scholarship, and empowerment that describe the attributes of advanced practice nursing, the approach to care, and the professional attitude that defines practice.

Brown Model

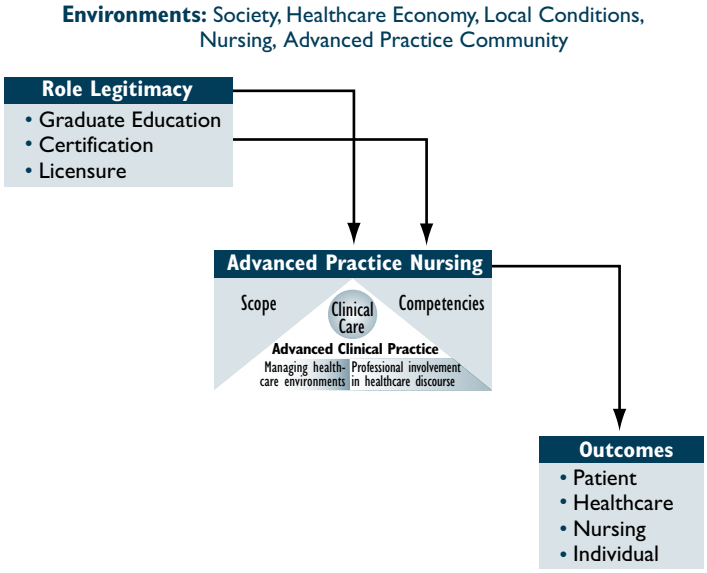
In contrast to the models of advanced practice nursing that primarily address the direct care practice of APNs, Brown proposed a broad, comprehensive conceptual framework for advanced practice nursing to guide the development of curricula, shape role descriptions and practice agreements, and provide direction for research.[90] The framework, shown in Figure 4, consolidates and integrates the defining elements, competencies, characteristics, outcomes,

FIGURE 3. The Strong Model of Advanced Practice



Reprinted from Mick DJ, Ackerman MH. Advanced practice nursing role delineation in acute and critical care: application of the Strong Model of Advanced Practice. *Heart Lung*. 2000;29:210-221.[89] ©2000, with permission from Elsevier.

FIGURE 4. Brown's Framework on Advanced Practice Nursing



Reprinted from Brown SJ. A framework for advanced practice nursing. *J Prof Nurs*. 1998;14:157-164.[90] ©1998, with permission from Elsevier.

and multiple contexts of advanced practice nursing into a broad comprehensive model. Specifically, this model includes a holistic perspective, partnership with patients, use of expert clinical reasoning, and diverse approaches to patient management. It comprises the 4 main concepts of environments, role legitimacy, advanced practice nursing, and outcomes, in addition to 17 more specific concepts. Advanced practice nursing itself is defined by its 5 attributes: focus, domains of activity, orientation, scope, and competencies (Table 3).[91]

Common Elements of Advanced Practice Nursing

Advanced practice care is provided across the spectrum of healthcare: acute, chronic, long-term, and rehabilitative services with substantial positive outcomes in terms of health, wellness, and cost of care. A recent study published in the *Journal of the American Academy of Nurse Practitioners* concluded that employer-sponsored nurse practitioner primary healthcare services afforded enhanced wellness, health promotion, increased access to care, reduced illness, and employee productivity.[92] DeVries et al described the benefit of group medical appointments with a chronic care team in terms of health outcomes and patient satisfaction coordinated and directed by an advanced practice nurse.[93]

Although these and other models and frameworks differ in several important ways, they all reflect common elements shared by APNs.[91]

- APNs are RNs with a master's or doctoral degree in a specialized area of advanced practice nursing
- APNs have had supervised practice during their graduate training and ongoing clinical experiences
- APNs are committed to ongoing learning and acquisition of new knowledge, skills, and competencies

The models and frameworks underscore how APNs differ from RNs without advanced training who are involved in basic or standard nursing practice (Table 4).[91]

DOMAINS OF ADVANCED PRACTICE NURSING IN MS

Important differences exist between APNs in other areas of specialization and APNs specializing in the care of patients with MS (MS APNs). The unpredictability of the progression of MS and the lack of uniformity of disease presentation require a keen ability to assess and manage the care of MS patients and their families. The MS nurse, particularly the certified MS nurse, has knowledge and skills adequate to establish, continue, and sustain the care of patients and families.

MS APNs have a considerable impact on the health and well-being of patients with MS. The competencies required to sustain care are described below through delineation of the domains specific to MS APN practice.

TABLE 3. Elements of Advanced Practice Nursing

Attributes:	Focus	Domains of Activity	Orientation	Scope	Competencies
Elements:	Clinical care	• Advanced clinical practice • Managing healthcare environments • Professional involvement in healthcare discourse	• Holism • Partnership • Expert clinical reasoning • Reliance on research • Diverse ways of assisting	• Specialization • Expansion • Autonomy • Accountability	• Core • Role emphasis

Reprinted from Brown SJ. A framework for advanced practice nursing. *J Prof Nurs*. 1998;14:157-164.[90] © 1998, with permission from Elsevier.

Domain Definitions

Domains are realms of accountability and responsibility for the performance of explicit competencies. The domains identified and defined in the Benner, Strong, and Brown models are antecedents of the 4 domains of MS advanced practice nursing:

- The nurse–patient partnership
- Comprehensive care throughout the health–illness continuum
- Professional persona
- Scholarly inquiry

These 4 domains, unique to advanced practice MS nursing, and their qualities or tasks are normally exclusive and exhaust all areas of practice or scope of practice, attitudes, knowledge, and skills. The major focus of the domains of MS advanced practice nursing centers on how the MS APN interacts with patients, their families, and others who provide care. Each domain, along with its qualities, is discussed in further detail below.

TABLE 4. How Does the APN Role Differ From the RN Role?

- APNs have an advanced education beyond basic nursing program
- APNs engage in complex clinical reasoning and decision-making related to complex patient problems
- APNs possess advanced skills in managing organizations, systems, and environments
- APNs practice with greater autonomy
- APNs exercise a higher degree of independent judgment
- APNs use well-developed communications skills with multidisciplinary teams and systems across complex healthcare environments

Adapted with permission from Hickey JV. Advanced practice nursing at the dawn of the 21st century: practice, education, research. In Hickey JV, Ouimette RM, Venegoni SL, eds. *Advanced Practice Nursing: Roles and Clinical Applications*. 2nd ed. Philadelphia, PA: Lippincott; 2000:3-8.[91]

The Nurse–Patient Partnership

The nurse–patient partnership domain describes the depth and breadth of the MS APN relationship to patients. This domain's qualities include:

- Therapeutic alliance built on mutual trust and respect, with the patient as partner-participant
- Education and teaching
- Promotion of health and well-being
- Social and family interactions
- Empowerment
- Autonomy
- Expert clinicianship
- Collaboration
- Advocacy
- Flexibility
- Coaching
- Holistic care

Comprehensive Care Throughout the Health–Illness Continuum

Given the unpredictability of MS and the relapsing-remitting nature of the disease, the domain of comprehensive care across the health-illness continuum is of particular relevance to sustaining the care of patients with MS and their families. Within this domain, the biological, psychological, social, and spiritual needs of patients and their partners and families must be met holistically. Specifically, this involves the following:

- Assessment of the response to chronic illness, emotional status, support networks, environment, culture-specific needs, vocational issues, financial and insurance resources, transportation needs, lifestyle, activities of daily living, potential for abuse and neglect, and gender-specific issues

- Interventions such as educating patient and family about MS, managing crises, counseling, referring to support groups, enhancing self-esteem, guiding, and providing hope
- Evaluation and follow-up of treatment, referrals, and adherence to therapy and plan of care, as well as knowledge of community resources, government services, insurance and reimbursement practices, and other issues necessary to implement biopsychosocial tasks

Other qualities and tasks in this domain are as follows.

- Direct and indirect care, including assessing, monitoring, coordinating, managing the patient's health status, and referring to specialists
- Patient–family outcomes, including assessment of patient–family response to treatment interventions and modification of plan of care as necessary
- Promotion of health and well-being
- Innovative practice and problem-solving strategies
- Collaboration with other members of an interdisciplinary team and with other services to optimize the patient's health status
- Consultation with others and for others
- Education of patient and family with regard to MS disease course, treatment, symptom management, psychological and coping skills, and vocational and recreational needs
- Leadership within the team responsible for the patient's care
- Case management
- Evidence-based practice
- Quality assurance
- Advocating self-care strategies and skills and negotiating for the patient with regard to the healthcare system, the health policy arena, and access to care
- Health policy and legislation
- Economic accountability
- Teaching patients, families, and colleagues about MS and modifying teaching for special populations
- Ethical accountability

Professional Persona

This domain involves the skills and sense of professional identity that distinguish advanced practice nursing in MS. The MS APN incorporates the norms, values, and ethical standards of advanced practice nursing in MS into his or her professional behavior and maintains the professional persona by performing the identified tasks in this domain, which include the following.

- Upholding ethical standards of practice and facilitating the process of ethical decision making in patient care
- Maintaining autonomy
- Adhering to all aspects of professional accountability
- Serving as an expert in MS for patients, families, colleagues, allied health professionals, and community groups
- Promoting health and well-being
- Suggesting innovative practices and problem-solving strategies to answer clinical questions
- Collaborating with other health professionals, departments, and services to optimize patient care, improve strategic planning, and recommend policy changes
- Serving as a consultant to improve patient care and nursing practice
- Educating colleagues, community groups, special interest groups, and professional groups about MS
- Maintaining competencies in oneself and colleagues
- Providing and sustaining leadership for patients and colleagues
- Developing, implementing, and evaluating standards of practice, policies, and procedures
- Evaluating quality assurance measures
- Serving as an advocate to increase awareness of MS—and the MS APN—among community and professional groups
- Obtaining and maintaining professional recognition via specialty certification and other means
- Participating in efforts to influence health policy and legislation
- Being flexible to possible changes in MS treatment paradigms and to changes in healthcare environments and policies
- Increasing professional involvement in administration, policy issues, continuing education, MS organizations and conferences, and the larger medical community
- Serving as a mentor, coach, teacher, and/or role model for patients, colleagues, students, and other medical professionals

Scholarly Inquiry

The domain of scholarly inquiry provides the MS APN with numerous opportunities to strengthen the professional persona and go beyond the boundaries of patient care while providing comprehensive and holistic care and nurturing the nurse–patient partnership. The MS APN can fulfill the identified tasks/qualities of the scholarly inquiry domain by doing the following.

- Providing authoritative information on all aspects of care for patients with MS
- Exercising critical thinking in reviewing research-study designs, methodologies, and findings
- Incorporating theory into practice
- Educating professionals and nonprofessionals about MS through public speaking and written work, and by serving as a preceptor, mentor, and role model
- Regularly evaluating competencies, modifying as necessary, with regard to their applicability to patient care
- Providing leadership by adding to MS nursing knowledge
- Shaping public policy on MS healthcare
- Analyzing data pertaining to MS, MS nursing knowledge, and MS nursing performance
- Participating in patient-centered research studies, evidence-based research, and outcomes research
- Disseminating research findings
- Keeping current with evidence-based practices
- Evaluating quality assurance measures
- Showing intellectual curiosity and eagerness to expand and develop nursing knowledge
- Increasing professional involvement in lecturing, writing, and serving on advisory councils and editorial boards
- Coaching colleagues and other medical professionals in their scholarly inquiries

Notes

The APN in Treatment Decisions and Symptom Management

An ever-growing armamentarium of MS agents and their associated treatment protocols has important implications for advanced practice nursing in MS, starting with the APN's role in therapeutic decision-making. The need to provide patients with relevant, up-to-date information and guidance on new therapies (such as oral DMTs) or advances in existing therapies (such as novel IFN formulations or enhanced delivery systems using thinner needles) speaks directly to the APN's roles as educator, counselor, and consultant. In the age of the Internet, the APN can act as expert, collaborator, and advocate to help patients interpret the vast flow of health information (and misinformation) and thereby participate meaningfully in their own treatment decision-making process.

The use of DMTs requires that nurses master a complex skill set that includes both medical knowledge and interpersonal skills. The MS APN should be familiar with the short-term and long-term efficacy data regarding DMTs and participate in the drug selection process. This calls for an understanding of the various agents' mechanisms of action, diverse effects on the neurological system, and relative advantages and disadvantages (to the extent that they have been established by clinical trials). The MS APN should be able to explain side effects and demonstrate the facility to help patients manage them. As the primary source of information for the patient and family members, the MS APN is in the best position to involve them in the care continuum and reinforce their understanding of their specific regimen and the importance of adherence to it.

Because adherence to DMTs is vital in promoting their clinical effectiveness, it is extremely helpful to identify predictors of adherence and implement effective interventions. In one study—in which 66% of patients with RRMS treated with glatiramer acetate were adherent and 43% were not—there were 4 significant predictors of adherence: (1) self-efficacy, (2) hope, (3) perceived support of the physician, and (4) no previous use of other immunomodulators.[94] Level of disability and sociodemographic factors such as duration of MS, time on glatiramer acetate treatment, age, gender, race, education, and income were not significant predictors. The study investigators concluded that providing greater support for patients who have previously taken immunomodulators, enhancing self-efficacy, and inspiring hope are important in promoting adherence to therapy. All of these interventions are consistent with the advanced practice nursing domain of comprehensive care across the health–illness continuum discussed earlier.

A central focus of the MS APN practice is the evaluation and management of neurologic symptoms directly associated with MS exacerbations and progression. Symptomatic treatments for MS include those used to control or alleviate specific symptoms such as fatigue, bladder and bowel problems, spasticity, depression, and pain. Other MS-related symptoms may include tremor, sexual dysfunction, vertigo, or weakness. Effective management of MS symptoms through education, counseling, and rehabilitation—and, when indicated, pharmacotherapy—can significantly enhance patients' functioning and quality of life. Table 5 gives a brief synopsis of some of the most common symptoms associated with MS and the treatment options available.

Complex protocols for symptom assessment and management also require high skill levels. Bladder management interventions, for example, may include education on diagnostic procedures and strategies to improve the management of urinary dysfunction. MS APNs provide bladder training and positive reinforcement, instruction in self-catheterization or explanation of an indwelling catheter, and information on possible surgical options.[95,96] Bowel elimination and continence interventions include establishment of goals, instruction on managing dysfunction, advice on nonpharmacologic interventions, nutritional guidance, bowel training, and treatment of constipation and impaction (Table 5).[96-98]

Symptom management begins with evaluating the causative factors, which may be produced or worsened by MS or may arise from concurrent illness, medication, or other conditions. Medication for symptom relief (including over-the-counter agents and alternative therapies) must be assessed for any contraindications suggested by MS itself or by DMT or other concomitant medication use. Patients must be counseled on realistic expectations for symptom treatment and possible side effects, and supported in follow-up care.[72]

One further component of the therapeutic decision-making process is ideally suited to the roles and competencies of the APN: the inclusion of holistic wellness strategies in the overall program of MS management. Given the long-term natural history of MS and its potential impact on physical and psychosocial functioning, the importance of optimal adherence to fundamental health-promoting behaviors such as diet, exercise, smoking cessation, and social and spiritual connectedness cannot be overstated. MS APNs must stress

TABLE 5. Managing MS Symptoms

Symptoms	Management	Nursing issues
Fatigue	• Conditioning programs of graded exercise • Optimal nutrition • CNS stimulants (modafinil, pemoline) • Amantadine • SSRIs (eg, fluoxetine)	• Counsel on risk of restlessness/sleep disturbance • Supervise dosing schedule and titration
Bladder dysfunction	• Bladder training program • Anticholinergics (eg, oxybutynin) • Antimuscarinics (eg, tolterodine) • α-blockers (eg, terazosin) • Catheterization	• Rule out UTI • Monitor retention and fluid balance • Consider role of other medications • Manage side effects (eg, dry mouth)
Bowel dysfunction	*Constipation:* • Prevention strategies (fiber, fluids, exercise) • Education and support for bowel program • Stool softeners • Bulk-forming agents • Stimulants (occasional use only) • Lubiprostone *Urgency/diarrhea:* • Bulk-forming agents • Anticholinergics • Antimuscarinics	• Provide bowel training regimens • Consider effects of other medications (eg, steroids, antibiotics) • Counsel on diet, exercise, lifestyle issues
Depression	• Cognitive-behavioral therapy or other psychotherapeutic options • SSRIs and SNRIs (eg, fluoxetine, sertraline, paroxetine, citalopram) • Tricyclic antidepressants (eg, amitriptyline, nortriptyline) • Atypical antidepressants (eg, venlafaxine, bupropion)	• Evaluate type and degree of depression; assess suicide risk • Consider contribution of other medications (eg, interferons) • Assess family and social support network • Facilitate use of psychiatric care • Counsel on medications (eg, delayed efficacy and side effects of antidepressants) • Re-assess at follow-up
Pain	• Supportive measures • Anticonvulsants (phenytoin, carbamazepine, gabapentin, lamotrigine, pregabalin) • Tricyclic antidepressants • Duloxetine hydrochloride	• Watch for sedation • Start with low doses, titrate up • Monitor outcomes and alter treatment as necessary
Spasticity	• GABA antagonists (oral/intrathecal baclofen) • α-agonists (tizanidine) • Anticonvulsants (diazepam, clonazepam, gabapentin) • Botulinum toxin • Surgical intervention	• Time doses to maintain therapeutic levels • Titrate doses up • Watch for sedation or cognitive symptoms • Consider combination therapy

wellness-focused lifestyles. Weight control and regular exercise are important to cardiac health, bone health, flexibility, and muscle strength—all important to maximize mobility. Smoking has been found to be a risk factor in the development of MS as well as a factor linked to a more progressive MS disease course.[99-102]

Despite advances in pharmacologic therapy, many patients will contend with symptoms, relapses, and progressive disability that will negatively affect their quality of life. The MS APN should be able to refer patients affected by mental and physical disabilities brought on by MS to allied health professionals, such as occupational therapists, speech pathologists, physical therapists, social workers, and psychologists. The proactive involvement of the MS APN can raise patients' and their care partners' awareness of, and access to, complementary non-drug modalities and resources, such as support groups, that may ameliorate some of the burden of disease.

Notes

Primary-Care Needs in Multiple Sclerosis

Primary care of patients with MS is the promotion of general health and wellness across their life span. Whereas the primary care provider (PCP) may see the patient only once a year or for acute episodic care, the MS APN typically sees the patient 3 or more times a year. Because of this, the MS APN is in a unique position to identify primary care issues and make appropriate referrals.

Although many primary care problems are directly related to MS, others are not. However, all health concerns have an impact on MS and may contribute to symptoms and relapses. The important thing is to identify the issue and either treat it (if appropriate or feasible) or refer the patient to primary care services. For the MS APN, primary care encompasses the following.[103]

- Identifying and addressing the patient's primary care needs along a continuum of health as part of holistic care
- Recognizing and assessing (but not necessarily treating) the patient's symptoms and non-MS-related conditions
- Referring the patient to appropriate providers
- Assessing outcomes, including adherence to recommendations, during subsequent visits
- Educating both patients and other healthcare providers about primary care needs within the context of MS

The MS APN and the PCP should both be alert for deficits that often occur with MS, factors that contribute to these deficits and/or exacerbate MS, and physical and mental conditions and changes directly related to MS (Table 6). Assessment of the patient's health beliefs regarding MS is important, as these beliefs often influence willingness to accept advice, participate in care, and adhere to therapy.

Optimal delivery of primary care requires that patients be fully involved in the care process, but this is not always the case. Social psychologists and health researchers have developed several models to describe why patients may or may not choose to become fully engaged in the process. For example, the Health Belief Model indicates that patients are more likely to participate if they are aware that (1) they are susceptible to a potentially serious health problem, (2) taking action may decrease their susceptibility, and (3) the likely benefits of acting outweigh the costs.[104-106] This model and others serve as useful guides to the MS APN in establishing the care relationship, providing effective education and support, and coordinating diverse aspects of care with appropriate specialists.

In addition to determining the patient's health beliefs, the MS APN should assess the patient's personal characteristics and situations, barriers to care, existing support systems, and implications for polypharmacy and complementary therapies. Having MS increases the possibility of known disease-related risk factors that can alter the course of MS, and patients with MS must understand that they face the same health risks as patients without MS, with routine health screenings a continued necessity.

MS-specific needs to consider when promoting wellness in patients with MS are listed in Table 7.[107-120] Certain special needs apply to all patients, whereas others apply specifically to women, men, or those with advanced disease.

Time management and productivity are additional challenges that can limit the amount of nursing care that MS APNs provide for patients. In addition, limitations due to arbitrary regional and geographic differences may exist in many practice settings. Another significant issue for the MS APN is the cost of chronic care, medications, and hospital admissions for long-term sequelae and comorbidities, all of which tend to increase with the level of the patient's disability. The economic realities of treating a chronic illness are ever-present concerns.

TABLE 6. Primary Care Problems in Patients With MS

KEY CHALLENGES (MS directly*, general health issues†)

Pressure ulcers*	Hypertension†	Dental problems†
Osteoporosis†	Pneumonia†	Hearing changes/loss†
Thyroid disease†	Sexual dissatisfaction†	Preventive immunizations†
Diabetes†	Mental health problems†	Disease-related immunizations†
Cancer†	Vision problems†	Urinary tract infections*
Deep vein thrombosis†		

MS-RELATED RISK FACTORS

Biological Factors (that contribute to the key challenges)

Genetic predisposition	Comorbid conditions	Polypharmacy

High-risk medications (antiepileptics, chemotherapy, steroids, interferon beta, antidepressants)

Lifestyle and Behavioral Factors (that contribute to the key challenges)

Inadequate diet	Nicotine use	Sedentary lifestyle
Poor hydration	Alcohol abuse	Inadequate personal hygiene
Obesity		

Physical Conditions (caused by MS)

Muscle weakness	Spasticity	Incontinence (bowel and bladder)	Fatigue
Myalgia	Paresthesia/sensory loss	Vertigo	Sleep disturbances
Tremor	Pain	Seizures	

Dependent edema (related to autonomic nervous system changes, obesity, sedentary lifestyle)

Impaired mobility (gait disturbance, ataxia, paraplegia, quadriplegia)

Mental Changes (caused by MS)

Depression	Anxiety

Cognitive changes (short-term memory loss, impaired executive function and/or judgment)

Social/Environmental Factors (resulting from MS or contributing to stress-related MS relapses)

Isolation	Inadequate support system	Financial restraints
Lack of transportation	Inaccessible facilities	Environmental pollutants
Biased attitudes of providers	Lack of adaptable medical equipment	

RECOMMENDED SCREENING TESTS

Mammogram/clinical breast exam for breast cancer
Pap smear for cervical cancer
PSA/clinical testicular and rectal exam for prostate and testicular cancer
Hemoccult/colonoscopy for colon and rectal cancer
Visual inspection of the skin for signs of pressure ulcers, melanoma
Bone densitometry (DEXA) for osteoporosis
Chest x-ray
Cardiogram
Comprehensive metabolic profile (random glucose, liver enzymes, random cholesterol) annually
CBC with differential annually
Thyroid function testing annually

TABLE 7. Special Primary Care Needs of Patients with MS[107-121]

All Patients With MS

- Osteoporosis prevention and treatment strategies
- Coping skills for certain issues
  - Sexual dissatisfaction
  - Incontinence
- Effects of exercise on reducing risk of
  - Cardiovascular disease
  - Osteoporosis
- Vaccinations/immunizations
  - Hepatitis A
  - Hepatitis B
  - Influenza
  - Tetanus
  - Other infectious diseases
- Strategies to improve quality of life
  - Improve diet and nutrition
  - Stress management
  - T'ai chi
  - Yoga
- Physical therapy for general mobility and functional independence

Patients With Advanced MS

- Prevention and treatment of pressure ulcers
- Prevention and treatment of respiratory complications
- Occupational and speech therapies to aid in adaptation to physical and mental limitations

Women With MS

- Reproductive issues
  - Contraception
  - Pregnancy
- Access to facilities for women with disabilities
  - Pap smears
  - Mammograms
- Thyroid disorders

Men With MS

- Routine screening for prostate cancer
- Concerns about erectile dysfunction

Notes

Measuring Outcomes

In today's changing healthcare environment, it has become increasingly important to employ evidence-based approaches to practice, and to identify and measure the outcomes of various healthcare interventions. Whereas older paradigms of clinical practice were based on clinical experience, training and education, and expertise, the newer paradigm maintains that rules of scientific evidence are needed to guide clinical practice correctly.[121] For the APN, protocols developed to shape practice to achieve successful outcomes provide a unique opportunity to promote an evidence-based practice model, particularly in the area of patient assessment. However, despite the emphasis on evidence in advanced practice nursing, there is a gap in outcomes research that specifically targets the effects of interventions by APNs and the care they provide for patients.[122]

As Oermann and Floyd point out, early outcomes studies in nursing focused on costs and length of stay but neglected to consider outcomes of APN practice such as symptom resolution, functional status, quality of life, adherence to therapy, knowledge of patients and families, and patient and family satisfaction.[122] These outcomes are considered as important as cost in a comprehensive model that includes 4 types of outcomes: clinical, functional, costs, and satisfaction. Adherence is particularly important because it is essential for the effectiveness of therapy and overall outcome and is an area in which APNs can have direct influence.

There is evidence demonstrating positive APN outcomes with some populations, such as caregivers of the elderly, those experiencing heart failure and stroke, and women pregnant with twins.[123-127] To date, there is still little evidence of outcomes of the practice of the MS APN. Contributing to the gap is the difficulty of measuring nurse-sensitive outcomes in chronic progressive diseases, like MS, that are not characterized by a sudden, distinct event with severe consequences. Rather, they involve a continuous diminution of physical and/or mental abilities, affecting several functions and producing a number of different symptoms over a long period of time.[128]

In a review of the literature reported in 2001,[129] De Broe, Christopher, and Waugh found only 1 study evaluating the benefits of MS APNs (Kirker, Young, and Warlow, 1995)[130] and 2 research studies involving MS APN nursing outcomes: 1 funded by the South Bank University in London and the MS (Research) Charitable Trust,[131] the other funded by the MS Society of Great Britain and Northern Ireland. In the study by Kirker et al, patients found MS APNs to be helpful in improving their knowledge, ability to cope, mood, and confidence about the future, whereas general practitioners found them to be helpful with their MS patients.[130] In the South Bank University and MS Charitable Trust study, new insights were gained into MS specialist nurses' role in emotionally and practically supporting people with MS.[131] Employment of APNs also lead to significant cost and resource savings, as reported to the National Health Survey (NHS).[131]

Nurses at all levels of practice spend substantial amounts of time with patients, usually more time than any other health provider. Intuitively, nurses know that the areas in which they provide care—support, comfort, mobility, hygiene, symptom management, health promotion—are crucial to positive health outcomes. MS APNs also provide care in areas that affect the patient's quality of life, such as pain, suffering, grief, anxiety, and social handicaps. Research demonstrating the outcomes of this care not only is sparse but in many cases would be better measured by quality-of-life instruments than in dollars.[128,132] There is a need to document the value of APNs and the benefits of their interventions with regard to multifaceted outcomes, such as improved health, reduced costs, improved patient satisfaction, and increased efficiency.[133]

Measuring the clinical and economic impact of MS APN interventions is further limited when different studies use different criteria to assess treatment outcomes. For example, treatment outcomes may be assessed on the number and severity of relapses, the number of active lesions on an MRI scan, changes in the Expanded Disability Status Scale (EDSS) score, or other criteria.[128]

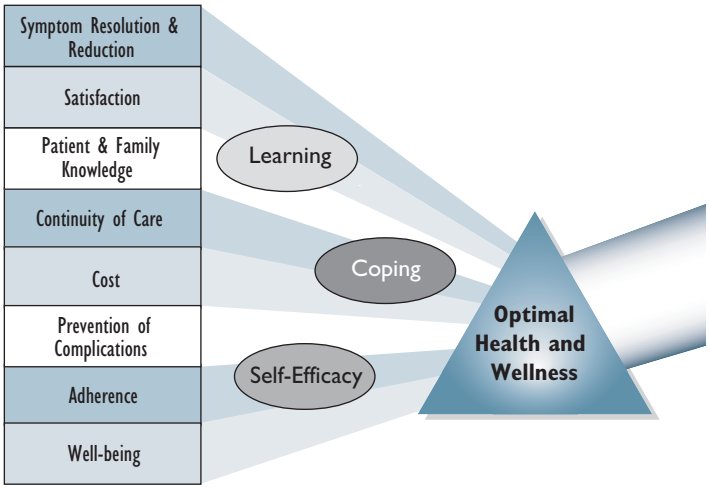
Byers and Brunell have pointed out that quality of care and its outcomes are valued differently by patients and families, MS APNs, physicians, managed care organizations, healthcare systems, payers, regulatory agencies, and society.[134] For example, patients may place a high value on education provided by the MS APN because it improves their ability to cope with MS, whereas payers may value it less highly unless it reduces costs.

MS APN OUTCOME MEASURES

Outcome measures used to assess the effectiveness of advanced practice nursing are care-related, patient-related, and performance-related. However, because no single set of

outcomes is appropriate for all APN outcome evaluations, selected outcomes should be easily identifiable and measurable and directed toward meeting the goals of the outcome assessment. Regardless of the outcome measures chosen, the goal should be to obtain valid and reliable results.[135] In a consensus-based study, 8 outcomes have been identified for the APN to attain the primary goal of optimal health and wellness for those living with MS (Figure 5). Three common elements—learning, coping, and self-efficacy—have been identified as being integral to the attainment of the eight outcomes. For each outcome, factors specific to MS APNs and relevant outcome measures are addressed in greater detail in Table 8.[136-141]

FIGURE 5. Advanced Practice Nursing Outcomes in MS



Notes

TABLE 8. Measuring Outcomes in MS[98-103]

OUTCOMES	MS APN–SPECIFIC FACTORS	MS APN INTERVENTIONS
ADHERENCE	• Treatment and rehabilitation • Follow-up	The MS APN can improve adherence to the therapeutic regimen by providing support, encouragement, information about side effects and adherence, and follow-up.
COST	• Length of office visit • Days in the hospital • Use of equipment • Medications • Use of resources • Home healthcare • Incidentals • Lost workdays • Post-hospitalization costs	MS APNs can influence costs by controlling where and to whom a patient is referred, by preventing certain costly MS-related complications, and by lobbying for reimbursement of MS APN interventions.
SYMPTOM RESOLUTION AND REDUCTION	This specifically includes resolution or reduction of spasticity, fatigue, bladder symptoms, and pain, and improvement in mood and mobility.	MS APNs promote symptom resolution and reduction by interventions such as appropriate diagnosis of symptoms, assessment of contributing factors, prescription of appropriate treatments, and focusing on functional outcomes. Other interventions include educating the patient about symptom management, modifying the treatment plan as necessary, including the family in the patient's care, implementing preventive measures and instructing the patient and family in symptom prevention and reduction, and referring the patient to an appropriate specialist when necessary.
PREVENTION AND REDUCTION OF COMPLICATIONS	• Injection-site reactions • Urinary tract infections • Altered or impaired skin integrity that can increase the risk for pressure ulcers • Pneumonia	MS APNs can prevent or reduce complications by identifying the risk factors for these complications, educating patients and families to recognize the first signs and institute preventive measures, and implementing appropriate compensatory strategies.
WELL-BEING	• Positive health perceptions • Improved satisfaction with life • Improved mood • Stress reduction • Improved ability to cope • Enhanced self-efficacy • Sense of hope	MS APNs influence well-being by utilizing a holistic approach to care, including the family in the patient's care, and focusing on aspects of health and wellness in addition to coping with disease.
PATIENT AND FAMILY SATISFACTION WITH CARE	• Access to care and available services • Comprehensiveness of care • Care delivery • Perception of being well cared for[98]	MS APNs influence patient and family satisfaction with care by fostering communication, encouraging patients and families to express satisfaction or dissatisfaction with care, reviewing and revising treatment goals and their attainment, and clarifying needs and expectations as necessary.
CONTINUITY OF CARE AND CARE MANAGEMENT	Factors include utilization of related disciplines, reduced number of visits to the emergency room and office or clinic, and reduced number of admissions for long-term care.	MS APNs affect continuity of care and care management by making follow-up visits and phone calls, including the family in the patient's care, making referrals as necessary and following up, and using clinical pathways that include multiple providers as a guide through the entire course of treatment.
PATIENT AND FAMILY KNOWLEDGE	• MS • The MS disease process • Medications • MS-related symptoms • The plan of care • The role of the multidisciplinary team involved in MS care • What to expect during the disease course • Supports and resources	MS APNs educate the patient and family about MS, providing appropriate educational materials, encouraging patients and families to ask for any additional information they feel they need, and ascertaining whether the education and/or educational materials provided were adequately understood.

OUTCOME MEASURES

- Chart review
- Patient and family reports
- Drug renewal sheets
- Consultation sheets for rehabilitation services and physical and occupational therapy
- Follow-up on appointments kept

Direct costs
- Departmental tracking
- Chart reviews of interventions
- Utilization of resources

Indirect costs
- Lost wages of the patient
- Lost wages of family members who take time off to provide care

- Documented patient reports
- Visual analog scale, which measures pain intensity on a 0-to-10 scale
- Fatigue Impact Scale, which measures the impact of MS fatigue on various aspects of the patient's life
- SF-36, a multidimensional instrument that is part of the Medical Outcomes Survey; it measures 36 items in 8 subscales:
  - Physical functioning
  - Role limitations due to physical problems
  - Social functioning
  - Bodily pain
  - General mental health
  - Role limitations due to emotional problems
  - Vitality
  - General health perceptions
- MS Quality of Life scale, a multidimensional, patient-reported, MS-specific instrument that includes the SF-36 plus 4 items on health distress, 4 on sexual function, 1 on satisfaction with sexual function, 2 on overall quality of life, 4 on cognitive function, and 1 each for energy, pain, and social function

- Chart review
- Patient reports
- Hospital admission/emergency room visit rates

- Jalowiec Coping Scale, which reflects the ability to cope, the degree of self-reliance or reliance on others, and the coping strategies employed[99]
- Mishel Uncertainty Scale, also known as the Mishel Uncertainty in Illness Scale (MUIS), a self-administered questionnaire that assesses the inability to determine the meaning of illness-related events[100]
- Beck Depression Scale, also known as the Beck Depression Inventory, a 21-item self-report used in many illness states to measure the severity of depression[101]
- Herth Hope Index, a 12-point abbreviated version of the Herth Hope Scale, assesses a patient's overall hope level[102]
- Multiple Sclerosis Self-Efficacy Scale, an 18-item instrument specifically designed for individuals with MS that asks them to rate on a scale of 10 (very uncertain) to 100 (very certain) how certain they are that they will be able to perform specific behaviors[103]

- Questionnaire designed to address areas of satisfaction/dissatisfaction with care

- Hospital admission/emergency room visit rates
- Self-reports of support systems and resources
- Referrals

- Pretests and posttests
- Determinations of perceived knowledge
- Assessment of how well self-care skills are being performed
- Review of logs documenting patient and family calls and reasons for the calls

Conclusion

This monograph is the third in a series devoted to the examination of advances in treatment options that have dramatically altered the roles of nurses providing care for patients with MS. The availability of DMTs, in conjunction with the refinements in diagnostic and monitoring technologies and the advent of complex treatment protocols, mandates a pivotal place for nurses in the development and provision of comprehensive care strategies. With this third edition, all 3 monographs in the series have been revised to provide current clinical data and current perspectives on MS nursing practice.

Key Issues in Nursing Management explores strategies to assess and overcome the cognitive changes experienced by patients over their lifetimes, thus empowering patients to optimize their quality of life. Its third edition revisited these key issues, with a sharper focus on adherence to long-term treatment regimens and the nursing skills requisite to establish and nurture relationships with patients. *Best Practices in Nursing Care* addresses the evolving role of nurses in this field, describing a philosophy and framework, domains and competencies, and best practices in MS nursing. Its third edition provides valuable new information to enhance MS nursing care, particularly with regard to disease management, pharmacologic treatment, and nursing research.

The present updated monograph defines the roles and responsibilities of the MS APN and the APN's domains of practice. It examines the tools used to validate the effectiveness of this model of care and describes the evolution of advanced practice nursing, specifically MS advanced practice nursing. This monograph also provides recent evidence substantiating the effectiveness of DMTs and lauds and emphasizes the value of a multidisciplinary approach to the complex spectrum of MS care.

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