



NURSE PRACTITIONER 2021 Virtual CE Summit

Expanding the Role of the Nurse Practitioner in Multiple Sclerosis to Optimize Outcomes: Early Diagnosis, Treatment Advances, and Patient-Centered Care



This CME activity is provided by Integrity Continuing Education.
This CE activity for AANP credit is jointly provided by Global
Education Group and Integrity Continuing Education.



Supporter Acknowledgement

- This activity is supported by an educational grant from Biogen, Inc.

Faculty Presenter

Denise Bruen, ANP-BC, MSN, MSCN

University of Virginia

James Q. Miller Consultative MS Center

Charlottesville, Virginia

Faculty Disclosures

Denise Bruen, ANP-BC, MSN, MSCN

Consulting Fees – Biogen, Viela Bio, Novartis, EMD
Serono, Genentech/Roche, Genzyme, Janssen

Learning Objectives

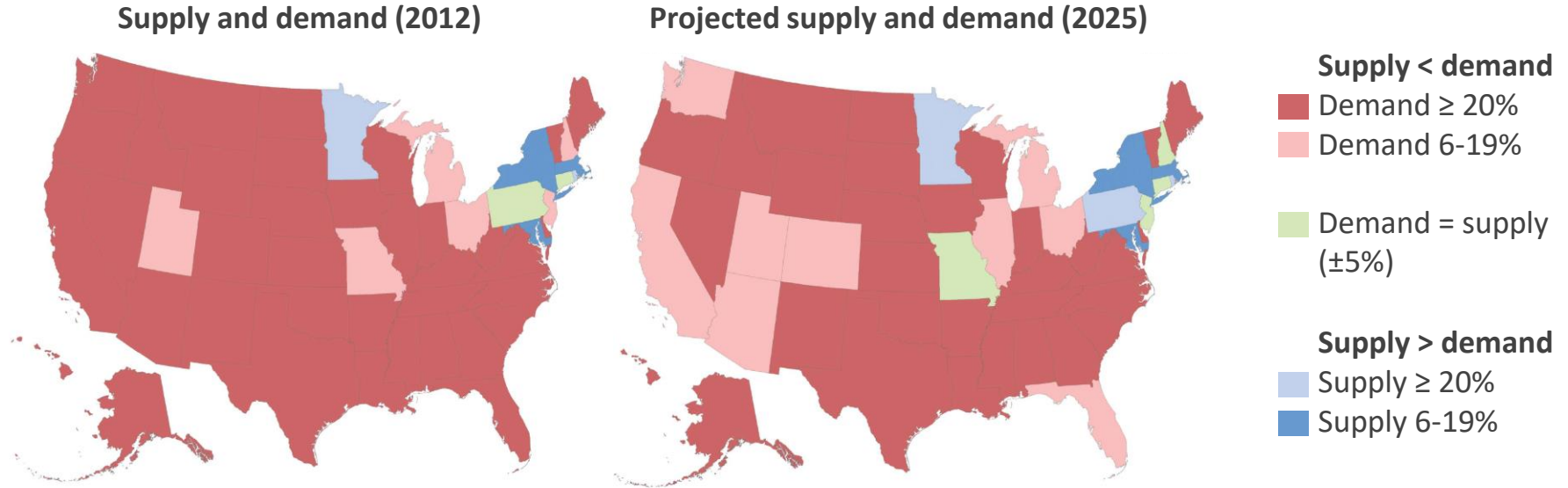
- Define the role of the NP in the healthcare setting, and their role in the diagnosis and treatment of multiple sclerosis (MS)
- Describe how to evaluate patients for signs and symptoms of early MS or relapse, to facilitate prompt referral to specialist care
- Identify available therapies for treatment of MS, and factors to consider in their use in individual patients
- Characterize strategies to address patient education and adherence challenges, and the long-term monitoring of overall wellness in patients with MS



NURSE PRACTITIONER 2021 Virtual CE Summit

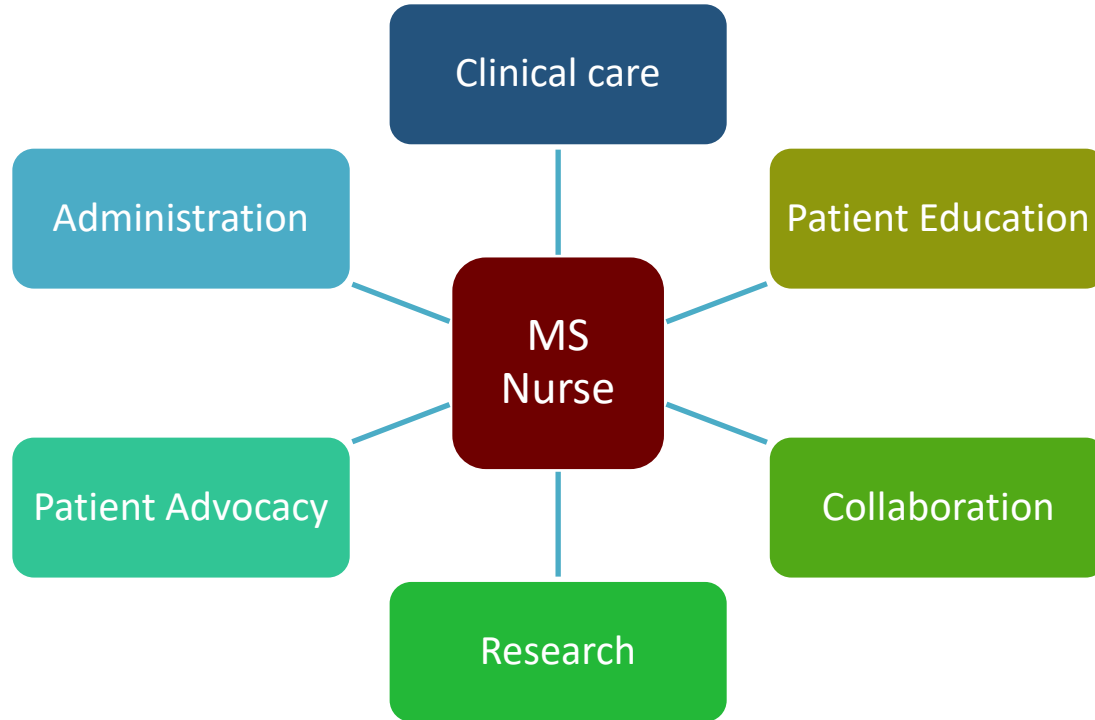
The Evolving Role of NPs in MS

Access to Neurologists in the US



Demand for board-certified neurologists exceeds supply in vast majority of US states, a trend that is projected to persist into the near future.

The Role of Nurses in the Management of MS



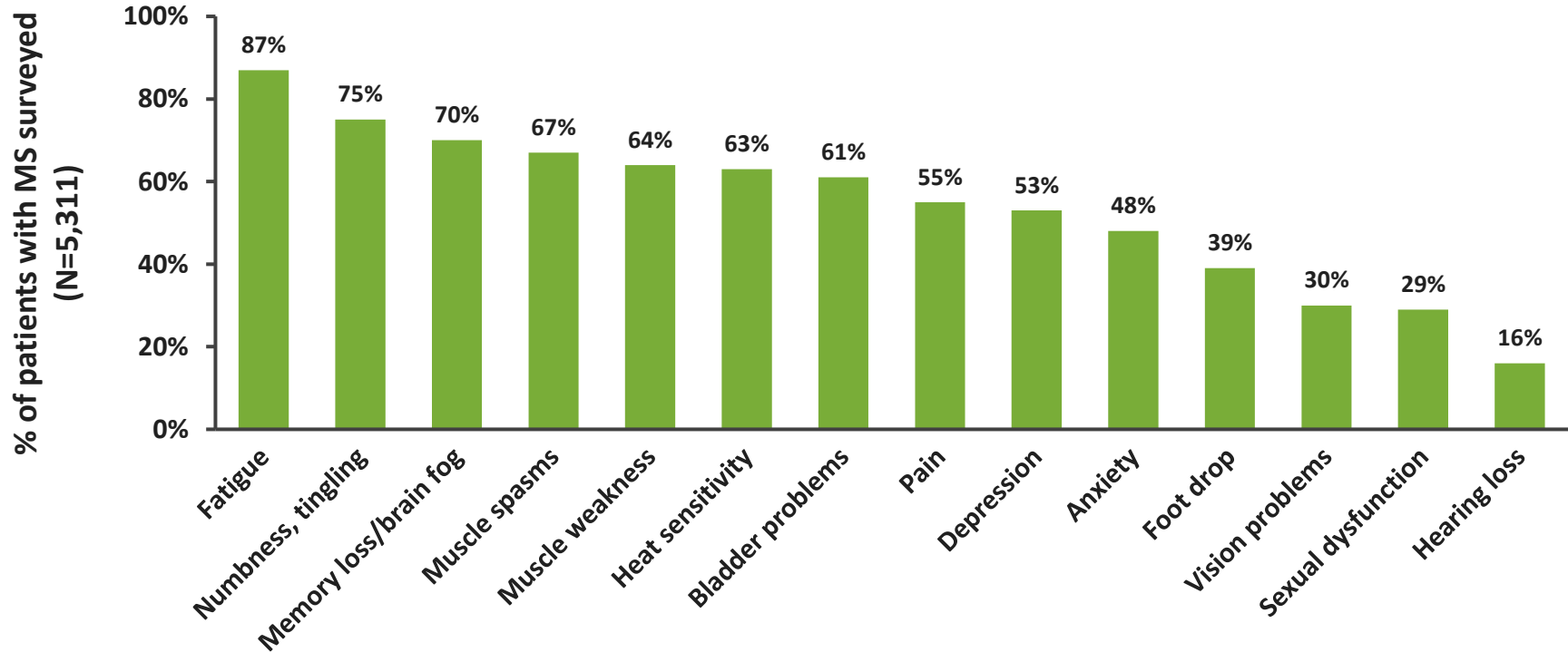


NURSE PRACTITIONER 2021 Virtual CE Summit

Assessment of Multiple Sclerosis

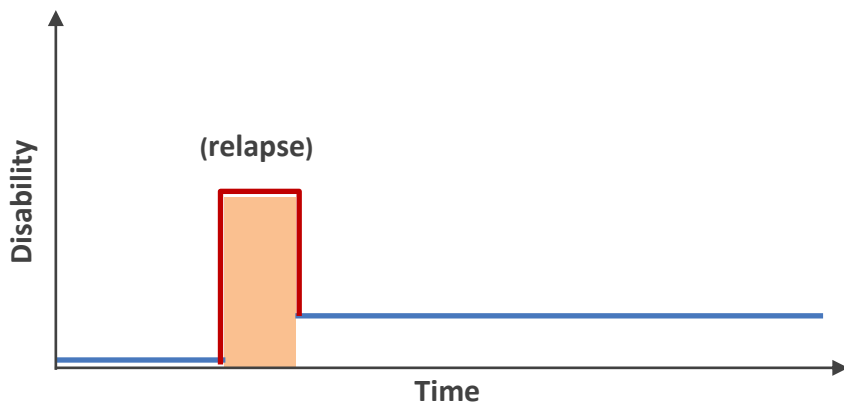
Diagnosis and Evaluation of Disability

Patient-reported Symptoms of MS

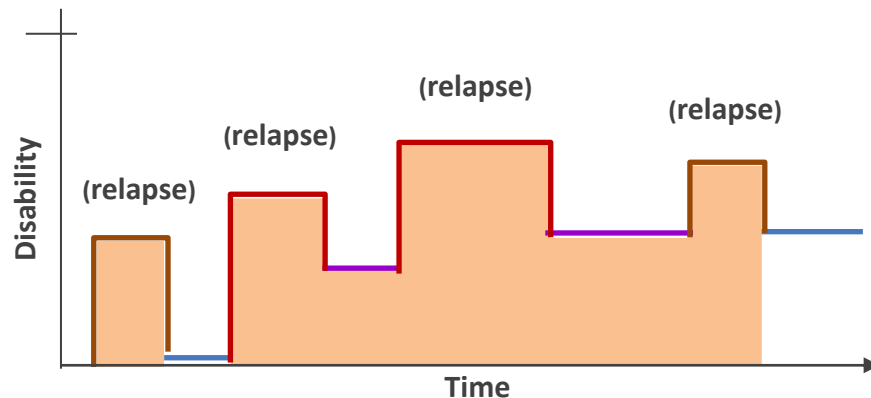


MS Clinical Phenotypes

Clinically Isolated Syndrome (CIS)



Relapsing Remitting MS (RRMS)

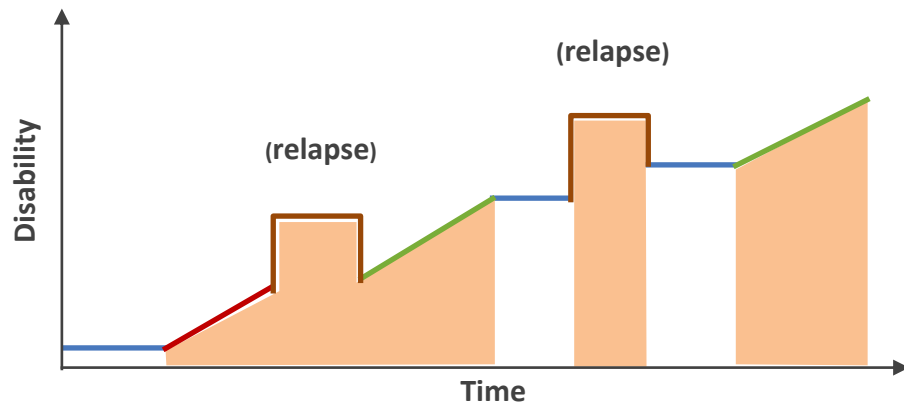


MRI, magnetic resonance imaging.

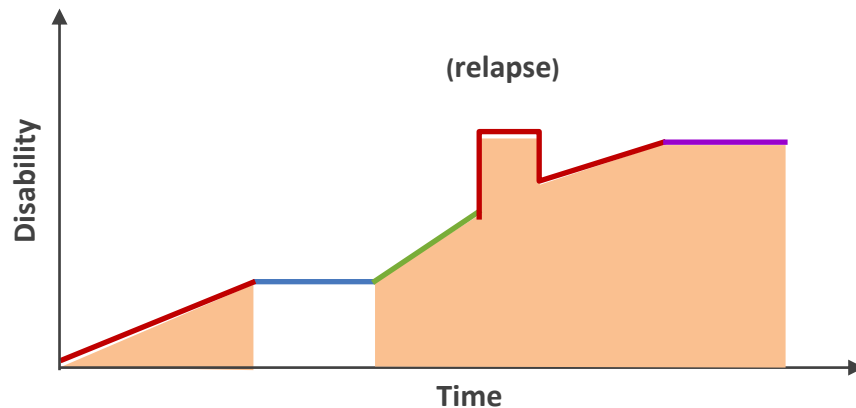
Lublin FD, et al. *Eur Neurol.* 2014;72(Suppl. 1):1-5; image adapted from: <https://www.nationalmssociety.org/What-is-MS/Types-of-MS/Relapsing-remitting-MS>

MS Clinical Phenotypes (Cont'd)

Secondary Progressive MS (SPMS)



Primary Progressive MS (PPMS)



MS Disease Activity

Active vs not active

- Applicable to all phenotypes
- Has there been the following in the *prior year*?
 - A clinical relapse OR
 - A new or enlarging T2 lesion or contrast lesion

Progressing vs not progressing

- Applicable to PPMS and SPMS
- Has the patient gradually **worsened neurologically independent of acute attacks** in the *prior year*?

Diagnosis of Patients With an Attack at Onset

2017 Revised McDonald Criteria

Clinical attack(s)	Lesions with objective clinical evidence	Additional data needed for diagnosis
≥2	≥2	<ul style="list-style-type: none"> • None
≥2	1 (& clear evidence of previous attack involving a lesion in a distinct anatomical location)	<ul style="list-style-type: none"> • None
≥2	1	<ul style="list-style-type: none"> • Dissemination in space demonstrated by an additional clinical attack implicating a different CNS site or by MRI
1	≥2	<ul style="list-style-type: none"> • Dissemination in time demonstrated by an additional clinical attack or by MRIs OR demonstration of CSF-specific oligoclonal bands
1	1	<ul style="list-style-type: none"> • Dissemination in space demonstrated by an additional clinical attack implicating a different CNS site or by MRI AND dissemination in time demonstrated by an additional clinical attack or by MRIs OR demonstration of CSF-specific oligoclonal bands

Diagnosis of Patients With Primary Progressive MS

2017 Revised McDonald Criteria

Criteria
One year of disability progression (retrospectively or prospectively determined) independent of clinical relapse
AND
<u>Two</u> of the following:
<ul style="list-style-type: none">• ≥ 1 T2-hyperintense lesions* characteristic of multiple sclerosis in ≥ 1 of the following brain regions: periventricular, cortical or juxtacortical, or infratentorial• ≥ 2 T2-hyperintense lesions* in the spinal cord• Presence of CSF-specific oligoclonal bands

Definition of MS Relapse



- New symptoms of neurological dysfunction **OR** worsening of existing symptoms in a patient stable for ≥ 30 d



- Acute or subacute onset



- Lasting >24 hours



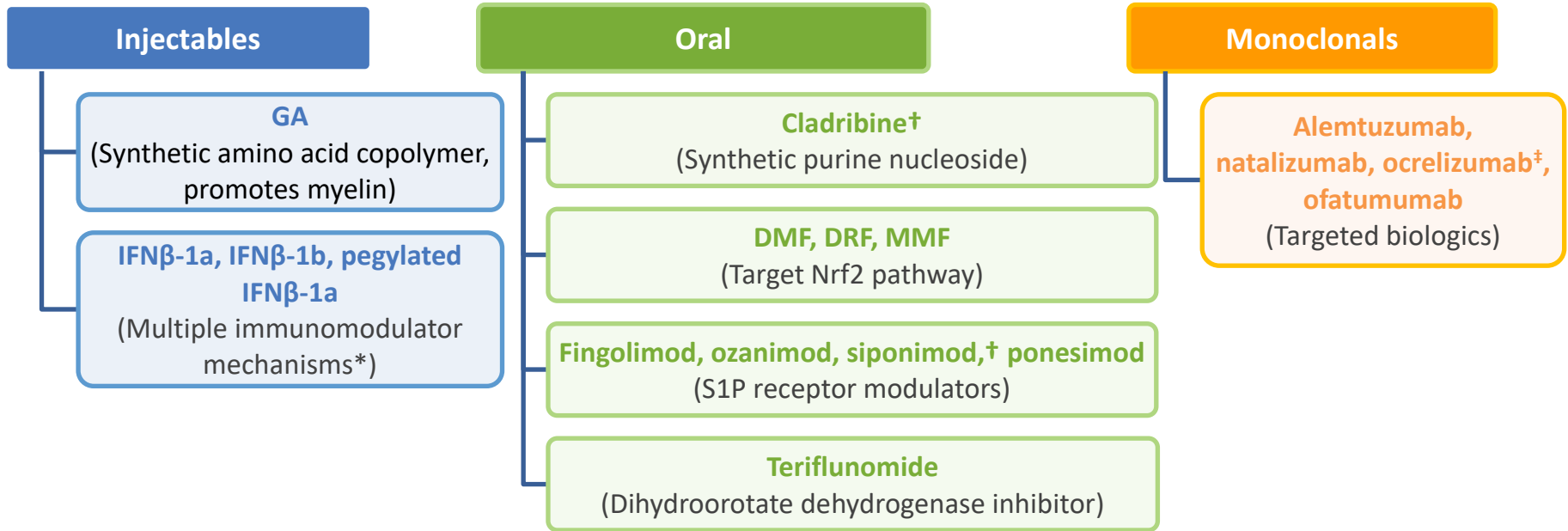
- Not attributable to another cause such as infection (not a pseudo-relapse)



NURSE PRACTITIONER 2021 Virtual CE Summit

A Patient-centered Approach to MS Management Individualizing Treatment

Therapeutic Options: Approved DMTs



*Inhibition of T-cell activation and proliferation, and leukocyte migration across the blood-brain barrier; induction of apoptosis of autoreactive T cells and regulatory T cells; cytokine modulation; †Cladribine and siponimod approved specifically for SPMS.

DMF, dimethyl fumarate; DRF, diroximel fumarate; GA, glatiramer acetate; IFN, interferon; MMF, mycophenolate mofetil; Nrf2, nuclear factor erythroid 2-related factor 2; S1P, Sphingosine-1-phosphate.

DMT Efficacy in Phase 3 Clinical Trials

Therapy	↓ Relapses	↓ MRI Activity	↓ Disability Progression
Injectables	✓	✓	✓ *
Orals	✓	✓	✓
Monoclonals	✓	✓	✓

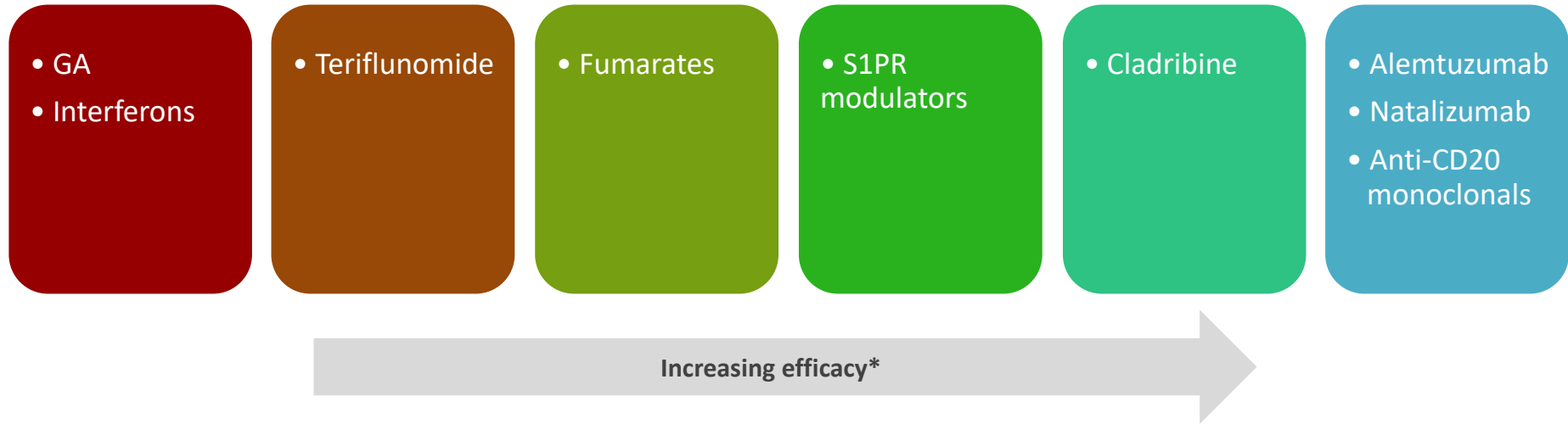
*Outcome not explicitly evaluated for GA and IFNβ-1b .

IFNB Multiple Sclerosis Study Group. *Neurology*. 1993;43(4):655-661.; PRISMS Study Group. *Lancet*. 1998;352(9139):1498-1504.; Calabresi PA, et al. *Lancet Neurol*. 2014;13(7):657-665.; Calabresi PA, et al. *Lancet Neurol*. 2014;13(6):545-556.; Cohen JA, et al. *Lancet*. 2012;380(9856):1819-1828.; Coles AJ, et al. *Lancet*. 2012;380(9856):1829-1839.; Comi G, et al. *Lancet Neurol*. 2012;11(1):33-41.; Comi G, et al. *Lancet*. 2009;374(9700):1503-1511.; Confavreux C, et al. *Lancet Neurol*. 2014;13(3):247-256.; Fox RJ, et al. *N Engl J Med*. 2012;367(12):1087-1097.; Giovannoni G, et al. *N Engl J Med*. 2010;362(5):416-426.; Gold R, et al. *N Engl J Med*. 2012;367(12):1098-1107.; Hauser SL, et al. *N Engl J Med*. 2017;376(3):221-234.; Jacobs LD, et al. *N Engl J Med*. 2000;343(13):898-904.; Jacobs LD, et al. *Ann Neurol*. 1996;39(3):285-294.; Kappos L, et al. *JAMA Neurol*. 2016;73(9):1089-1098.; Kappos L, et al. *Neurology*. 2006;67(7):1242-1249.; Kappos L, et al. *N Engl J Med*. 2010;362(5):387-401.; Lublin FD, *European Neurology*. 2014; 72(suppl 1)(Suppl. 1):1-5.; Miller AE, et al. *Lancet Neurol*. 2014;13(10):977-986.; O'Connor P, et al. *N Engl J Med*. 2011;365(14):1293-1303.; Rammohan K, et al. *Mult Scler Relat Disord*. 2012;1(1):49-54.; Selmaj K, et al. *Lancet Neurol*. 2013;12(8):756-767.

Patient-centered Treatment Selection



Relative Efficacy of Select DMTs for RRMS



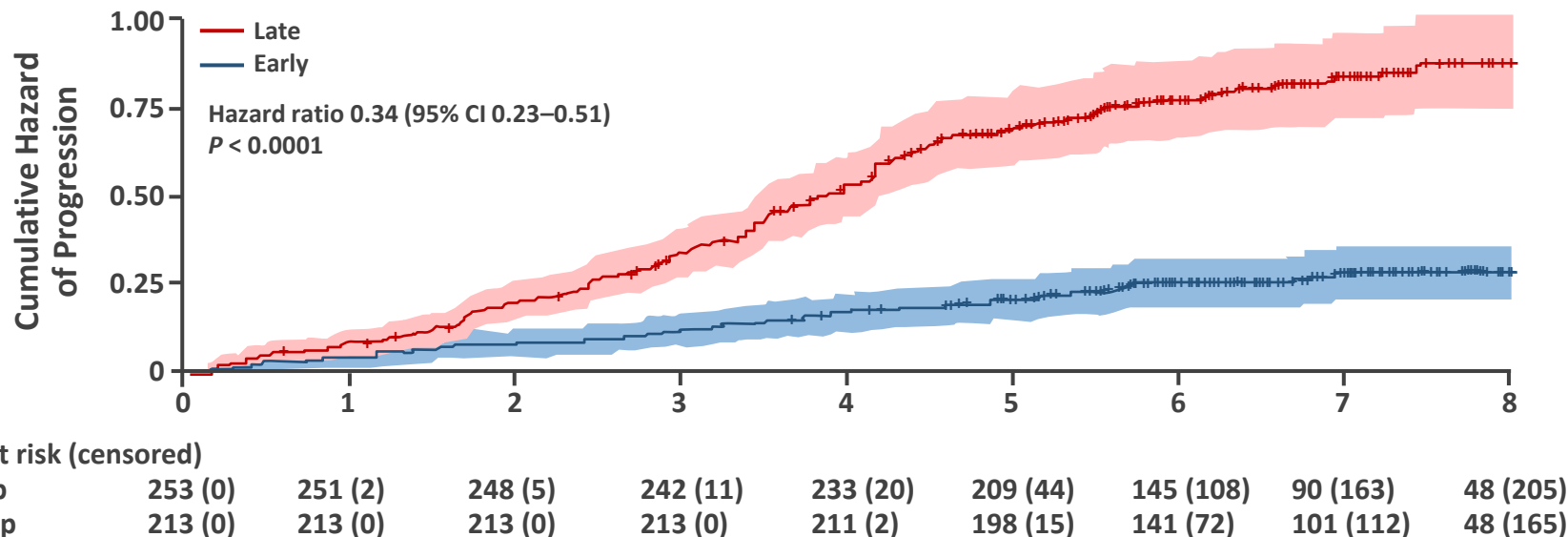
*Efficacy range within DMT class.

S1PR, sphingosine-1-phosphate receptor 1.

Lucchetta RC, et al. *CNS Drugs*. 2018;32(9):813-826; Hauser SL, et al. *Am J Med*. 2020;133:1380-1390.e2; Giovannoni G, et al. *Neurol Ther*. 2020;9:359-374. http://icerorg.wpengine.com/wp-content/uploads/2020/10/CTAF_MS_RAAG_030617.pdf

Impact of Early High-efficacy Treatment on MS Disability

Commencement of High-Efficacy Therapy



High-efficacy therapy commenced within 2 years of disease onset is associated with less disability after 6–10 years than when commenced later in the disease course.

Safety and Tolerability: Injectable Therapies

Agent	Adverse Events
GA	<ul style="list-style-type: none">• Injection site reactions, systemic/immediate post-injection reaction
IFNβ-1a	<ul style="list-style-type: none">• Headache, flu-like symptoms, injection site pain and inflammation
IFNβ-1b	<ul style="list-style-type: none">• Flu-like symptoms, headache, injection site reactions, injection site skin breakdown, low white blood cell count
Pegylated IFNβ-1a	<ul style="list-style-type: none">• Flu-like symptoms, headache, injection site reactions

Available at: <http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Brochure-The-MS-Disease-Modifying-Medications.pdf>; Vumerity [package insert]. Cambridge, MA: Biogen, Inc. ;2019.

Safety and Tolerability: Oral Therapies

Agent	Adverse Events
Cladribine	<ul style="list-style-type: none"> • URI, headache, lymphopenia; black box warning for potential malignancy and teratogenicity risks in treated patients
MMF, DMF, DRF	<ul style="list-style-type: none"> • Flushing, GI-related (nausea, diarrhea, abdominal pain)
Fingolimod	<ul style="list-style-type: none"> • Headache, flu, diarrhea, back pain, liver enzyme elevations, sinusitis, abdominal pain, pain in extremities and cough
Ozanimod	<ul style="list-style-type: none"> • Back pain, BP changes, URI, frequent and painful urination
Siponimod	<ul style="list-style-type: none"> • Headache, HTN, and liver enzyme elevations
Teriflunomide	<ul style="list-style-type: none"> • Headache, hair thinning, diarrhea, nausea, abnormal liver tests; black box warning for potential hepatotoxicity and teratogenicity risks in treated patients

Teriflunomide carries a black box warning for potential hepatotoxicity and teratogenicity risks in treated patients; Cladribine carries a black box warning for potential malignancy and teratogenicity risks in treated patients. BP, blood pressure; HTN, hypertension; GI, gastrointestinal.

Available at: <http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Brochure-The-MS-Disease-Modifying-Medications.pdf>; Vumerity [package insert]. Cambridge, MA: Biogen, Inc. ;2019.

Safety and Tolerability: Monoclonals

Agent	Adverse Events
Alemtuzumab	<ul style="list-style-type: none"> Rash, headache, fever, nasal congestion, nausea, UTI, fatigue, insomnia, upper RTI, herpes viral infections, hives, itching, thyroid gland disorders, fungal infection, pain in joints, extremities and back, diarrhea, vomiting, flushing Infusion reactions (eg, nausea, hives, itching, insomnia, chills, flushing, fatigue, shortness of breath, changes in the sense of taste, indigestion, dizziness, pain) common during and for 24 hours or more after infusion PML has occurred (1 case).
Natalizumab	<ul style="list-style-type: none"> Headache, fatigue, joint pain, chest discomfort, UTI, lower RTI, gastroenteritis, vaginitis, depression, pain in extremity, abdominal discomfort, diarrhea, rash PML (over 800 cases)
Ocrelizumab	<ul style="list-style-type: none"> Infusion reactions (most commonly itchy skin, rash, throat irritation, flushed face or fever, headache), which in rare instances may be life-threatening; increased risk of infections, including RTI and herpes infections; possible increase in malignancies, including breast cancer
Ofatumumab	<ul style="list-style-type: none"> Upper RTIs, injection-related (systemic) and injection-site (local) reactions, headache, UTIs, back pain As expected with B-cell depletion, decreased immunoglobulin levels have been observed

NOTE: Monitoring for hypogammaglobulinemia recommended with anti-CD20s (based on rituximab data).

PML, progressive multifocal leukoencephalopathy.

Recommended Monitoring During Treatment: Oral and Self-Injectable Therapies

DMT	CBC w/ diff	LFT	Thyroid Function Tests	BP	Cardiac Exam*	Eye Exam	Skin Exam
GA							
IFNβ-1	✓	✓	✓		✓		
Teriflunomide	✓	ALT monthly for first 6 mos		✓			
Fingolimod, siponimod, ozanimod	✓	✓		✓	✓ **	✓	✓
DMF, DRF	6 mos after initiation, then every 6–12 mos	As clinically indicated					
Cladribine	At 2 mos, then every 6 mos after initiation	As clinically indicated					

*In patients with certain preexisting cardiac conditions; **For ozanimod.

ALT, alanine transaminase; CBC, complete blood count; LFT, liver function tests.

Gross RH, et al. *Continuum (Minneap Minn)*. 2019;25(3):715-735; Vumerity. Prescribing Information. Biogen, Inc; 2019.

Zeposia. Prescribing Information. Celgene Corp.

Recommended Monitoring During Treatment: Monoclonal Therapies

Alemtuzumab

- Skin exams & HPV screening annually
- CBC, serum creatinine, & urinalysis monthly until 48 mos after last infusion
- TFTs every 3 mos until 48 mos after last infusion
- HIV

Natalizumab

- JCV antibody testing every 3 months
- CBC & LFTs every 6 months

Ocrelizumab

- CBC
Lymphocyte subsets every 6 months
- Immunoglobulins every 6–12 months
- Comprehensive metabolic profile
- HBV*

Ofatumumab

- Immunoglobulins (especially in patients with opportunistic or recurrent infections, & after discontinuation)
- HBV*

*If indicated.

HBV, hepatitis B virus; HPV, human papillomavirus; JCV, John Cunningham virus or human polyomavirus 2; TFT, thyroid function test.

Gross RH, et al. *Continuum* (Minneap Minn). 2019;25(3):715-735.

Real-world Differences in Disability and DMT Use Among Patients With RRMS by Race and Ethnicity

- NARCRMS registry December 2016–May 2020
- MS patients aged 18-50 years across 24 sites in the US and Canada (N = 722)

Disability

- Patients with EDSS ≥ 4.0
 - Blacks/AAs: **20%**
 - Whites: **9.7%**

DMT Use

- 57% of patients treated with DMTs
 - 50% using injectables
 - 37% using oral DMTs
- Hispanic patients *less likely to use DMTs* vs non-Hispanics (**43% vs 62%**)
- Black/AA-Hispanics *least likely to use DMTs* among groups evaluated (**26%**)



NURSE PRACTITIONER 2021 Virtual CE Summit

A Patient-centered Approach to MS Management

The Importance of Patient
Education and Engagement

Patient and Care Partner Education

Goals of Education

- Active patient participation (informed choices about health behaviors & competent, confident self-care)
- Maximal wellness (coping, adaptation, & empowerment toward better QoL & greater hope)
- Specific goals:
 - ✓ Understanding diagnosis & coping with life impact
 - ✓ Critical planning (eg, relationships, parenting, employment, and lifestyle)
 - ✓ Preventing disabling outcomes, with specific goals related to new symptoms

Role of the Nurse

- Assist with activities promoting health or recovery that patients can later perform unaided
- Help individuals carry out prescribed therapy
- Contribute to behavior changes that provide knowledge & skills to maintain & improve health
- Repeatedly assess patient understanding & behavioral change
- Promote & encourage treatment adherence

Real-world DMT Adherence and Persistence in Patients With MS

- Systematic review of 31 studies published between January 2010 and April 2018
- 31 studies of patients with MS treated with once- and twice-daily oral DMDs (N=16,398)

Outcome	No. of studies	Mean (%)	95% CI
Overall 1-year MPR	4	83.3	74.5–92.1
Overall 1-year PDC	4	76.5	72.0–81.1
Pooled 1-year MPR $\geq 80\%$	6	78.5	63.5–88.5
Pooled 1-year PDC $\geq 80\%$	5	71.8	59.1–81.9
Pooled 1-year discontinuation	20	25.4	21.6–29.7

At one year, approximately one in five patients with MS do not adhere to, and one in four discontinue, daily oral DMDs.

Barriers to Adherence Among Patients With MS

DMT characteristics

- Injection-related reasons (anxiety, skin reaction, pain)
- Coping with adverse events

Ability to take DMTs as prescribed

- Disease symptoms (impaired vision, poor manual dexterity, spasticity)
- Forgetting to take medication
- Cognitive impairment, depression, anxiety

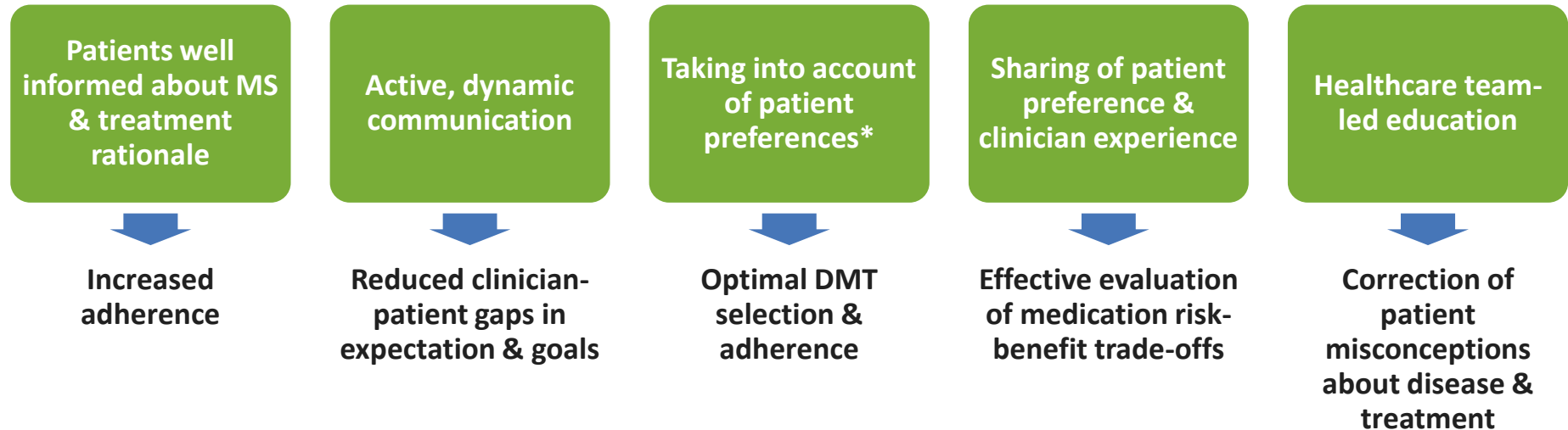
Patient perceptions

- Perceived lack of medication efficacy
- Complacency

HCP-patient relationship

- Lack of comfort in the context of the dynamic
- Ineffective communication

Key Factors Associated With Successful Shared Decision-Making in MS



*This should include route of administration, tolerance, work environment, lifestyle.



NURSE PRACTITIONER 2021 Virtual CE Summit

MS Management During the Era of COVID-19

Recommendations for DMT During COVID-19

- 1 Patients should generally be advised to continue their current DMT
- 2 Discuss therapies with patients if COVID symptoms develop or a positive test result is obtained
- 3 Before starting a new DMT, discuss optimal choice based on individual circumstances:
 - MS course and activity
 - Risks and benefits normally associated with treatment options
 - Individual COVID-19 risk:
 - Other risk factors for more severe COVID-19 (eg, age, medical comorbidities, current DMT)
 - Current and anticipated COVID-19 risk in the local area
 - Risk of exposure due to lifestyle
 - Emerging evidence on potential treatment interactions

The Impact of DMTs on COVID-19 Severity: Current Evidence

Agents	Impact on COVID-19 severity	Comments
IFNs, GA,& teriflunomide	<ul style="list-style-type: none"> • <u>Unlikely</u> to increase severity 	<ul style="list-style-type: none"> • Some evidence of reduced COVID-related hospitalization for GA
Fumarates, TER, S1PR modulators, & NTZ	<ul style="list-style-type: none"> • <u>Not linked</u> to increased severity 	
Monoclonal antibodies & CLA	<ul style="list-style-type: none"> • OCR and RIX <u>linked</u> to increased severity • More data needed on ALZ & CLA 	<ul style="list-style-type: none"> • Growing evidence of risk (greater with RIX); patients on anti-CD20's should be especially vigilant about advice on reducing risk of COVID-19 infection • Treated patients living in close proximity to an outbreak with low lymphocyte counts should isolate to reduce risk • Patients due for additional ALZ, CLA, OCR or RIX dosing should consult HCP about risks & benefits of postponing treatment

ALZ, alemtuzumab; CLA, cladribine; NTZ, natalizumab; OFA, ofatumumab; RIX, rituximab; TER, teriflunomide.

Zrzavy T, et al. Eur J Neurol. 2020; National Multiple Sclerosis Society. MS treatment guidelines during coronavirus.

<https://www.nationalmssociety.org/coronavirus-covid-19-information/multiple-sclerosis-and-coronavirus/ms-treatment-guidelines-during-coronavirus>; MS International Federation. Global COVID-19 advice for people with MS. Jan 2021. <http://www.msif.org/wp-content/uploads/2021/01/Jan-2021-MSIF-Global-advice-on-COVID-19-for-people-with-MS-FINAL.pdf>

Impact of DMT on COVID Vaccination

- Direct data remains lacking
- Previous studies of DMT impact on immune responses:

DMT	Impact on immune response
IFN β and DMF*	Seroprotection preserved with multiple vaccine types
GA, TER, S1PR modulators [†] , & NTZ	Seroprotection rates reduced with multiple vaccine types
CLA	Protective antibody levels maintained: <ul style="list-style-type: none">• ≥ 6m after influenza and varicella zoster vaccines, irrespective of timing relative to treatment• Independent of lymphocyte count
ALZ	Timing is important: <ul style="list-style-type: none">• Response to prior vaccinations maintained following treatment• Delay of vaccination ≥ 6m after alemtuzumab treatment recommended
Anti-CD20s	Humoral vaccine responses significantly impaired

*Limited data on DMF; [†]Based on studies of fingolimod and siponimod

Ciotti et al. Mult Scler Relat Disord. 2020;45:102439; Bar-Or. ACTRIMS 2021; CE1.2; Wu et al. ACTRIMS 2021; P071; Roy et al. ACTRIMS 2021; P059.

COVID-19 Therapy for Patients with MS

- Remdesivir is indicated for adults and pediatric patients (≥ 12 YOA and weighing ≥ 40 kg) for treatment of COVID-19 requiring hospitalization
- Other treatments given EUA by the FDA for patients meeting specific criteria, including MS
 - Monoclonal therapies: casirivimab + imdevimab and bamlanivimab
 - Accumulating data in support of positive impact on outcomes
- For patients with MS who become infected with COVID-19 and meet criteria for pharmacologic treatment, individual risk factors (including current DMT use) will drive therapeutic decision-making

EUA, emergency use authorization

National MS Society. COVID-19 vaccine guidance for people living with MS. <https://www.nationalmssociety.org/coronavirus-covid-19-information/multiple-sclerosis-and-coronavirus/covid-19-vaccine-guidance#section-0> ; Centers for Disease Control and Prevention. Information for clinicians on investigational therapeutics for patients with COVID-19. <https://www.cdc.gov/coronavirus/2019-ncov/hcp/therapeutic-options.html>



NURSE PRACTITIONER 2021 Virtual CE Summit

Case Evaluations

Case Study # 1: Patient Description

Kevin is 35-year-old high school teacher. He lives with his wife and twin 4-year-old sons. He is generally very active and participates in road races several times a year. He is in the office today for symptoms that include a noticeable increase in fatigue over the past several weeks, blurred vision in his left eye, and tingling in his hands and feet. He has no prior medical history that would appear to account for his symptoms.

Case Study # 1: Discussion Question

Which of the following should be included as part of Kevin's workup?

- A. MRI
- B. CSF analysis
- C. JCV antibody test
- D. CBC
- E. BMP

Case Study # 1: Discussion Question

Kevin's MRI and labs reveal a total of 3 T2 lesions (1 on his spine and 1 of which was Gd-enhancing). CSF analysis reveals the presence of oligoclonal bands and OCT confirms optic neuritis. His other labs are within normal limits. Based on these findings, he is diagnosed with RRMS. How would you characterize his risk for aggressive disease?

- A. Low
- B. Moderate
- C. High
- D. Not sure

Case Study # 1: Discussion Question

During your conversation about his diagnosis, Kevin confides that he feels overwhelmed by the number of treatment options and has several questions about their effectiveness and safety. After assuring him that this is not at all unexpected, how do you address his concerns?

- A.** Attempt to allay his anxiety by answering his questions in detail
- B.** Provide him with a broad overview of the different therapies
- C.** Schedule a dedicated follow-up appointment to discuss treatments

Case Study # 1: Discussion Question

Which of the following do you think is an appropriate DMT for Kevin?

- A. Glatiramer acetate
- B. An interferon-based therapy
- C. DRF or DMF
- D. A S1P receptor modulator
- E. A targeted biologic

Case Study #2: Patient Description

Marisol is 45-year-old woman with a 12-year history of RRMS. She is currently being treated with GA. She is the manager of a local grocery store and lives with her adult niece. During her regular follow-up visit, she reports that over the last 6 months, she has experienced a gradual increase in difficulty with her endurance and balance. Exam reveals new proximal leg weakness, mild tandem unsteadiness.

Case Study #2: Discussion Question

After further evaluation, you diagnose Marisol with SPMS. Which of the following DMTs is an appropriate treatment in light of this new diagnosis?

- A. DMF
- B. Teriflunomide
- C. Cladribine
- D. Siponimod

Case Study #2: Discussion Question

Given the current pandemic, would you elect to begin a new therapy immediately?

- A. Yes. Evidence indicates little additional COVID-related risk associated with treatments for SPMS.
- B. No. Evidence suggests that switching therapies would engender additional risk of infection.
- C. No. There is insufficient evidence to support the safety of switching therapies during the pandemic.

Case Study #2: Discussion Question

Once Marisol begins a new treatment regimen. How long would you wait before scheduling a follow-up visit to evaluate her treatment response?

- A. 1 month
- B. 2 months
- C. 3 months
- D. 6 months

Program Summary

- Nurses involved in the care of patients with MS shoulder a broad range of responsibilities beyond clinical care, including patient advocacy, research, collaboration with the multidisciplinary healthcare team, and patient and care partner education
- Primary care nurses are often the first point of contact for patients with any type of motor, sensory, or cognitive deficit, and are thus well situated to facilitate early recognition of an MS attack
- This is especially important in light of growing recognition of the need for early effective treatment, and the recent expansion of DMTs with the potential to reduce disease progression as well as improve symptoms
- By providing patient-centered care that includes education and management guidance, nurses can help ensure that patients are equipped to participate in decision-making and achieve optimal therapeutic success



NURSE PRACTITIONER 2021 Virtual CE Summit

Thank You!