



Multiple Sclerosis Update

CLINICAL, ECONOMIC, AND
PATIENT-CENTRIC STRATEGIES FOR
SPECIALTY PHARMACY PROFESSIONALS

Jointly provided by



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Live Webcast

Wednesday, July 1, 2020

12:00pm – 1:30pm ET



Welcome

Michael Zeglinski, RPh

SVP & CEO

Optum Specialty & Infusion Pharmacies

Agenda



12:00-12:05 PM	Opening Comments/Overview Michael Zeglinski, RPh
12:05-12:35 PM	<i>Assessing the Clinical Benefits of Current and Emerging MS Therapies in a Specialty Pharmacy Setting</i> Mitzi Joi Williams, MD
12:35-1:00 PM	<i>Special Pharmacy Management Services for Optimal Outcomes in MS</i> Michael Zeglinski, RPh
1:00-1:15 PM	<i>Shared Decision-Making: Aligning MS Specialty Pharmacy Care with Patient Needs</i> Alexis Crispino
1:15-1:25 PM	Audience Question & Answer Session Faculty Panel
1:25-1:30 PM	Key Takeaways and Closing Comments

Learning Objectives



- Discuss where current and emerging therapies fit into the MS management algorithm
- Review the potential impact of and value of real-world evidence to inform clinical decision making in MS
- Explore how to integrate electronic health technology into MS care management
- Employ treatment optimization approaches to balance costs with improved outcomes in MS management



*Assessing the Clinical Benefits of
Current and Emerging MS Therapies
in a Specialty Pharmacy Setting*

Mitzi Joi Williams, MD

Founding Director, Joi Life Wellness Group
Assistant Professor of Neurology, Emory University

Learning Objectives

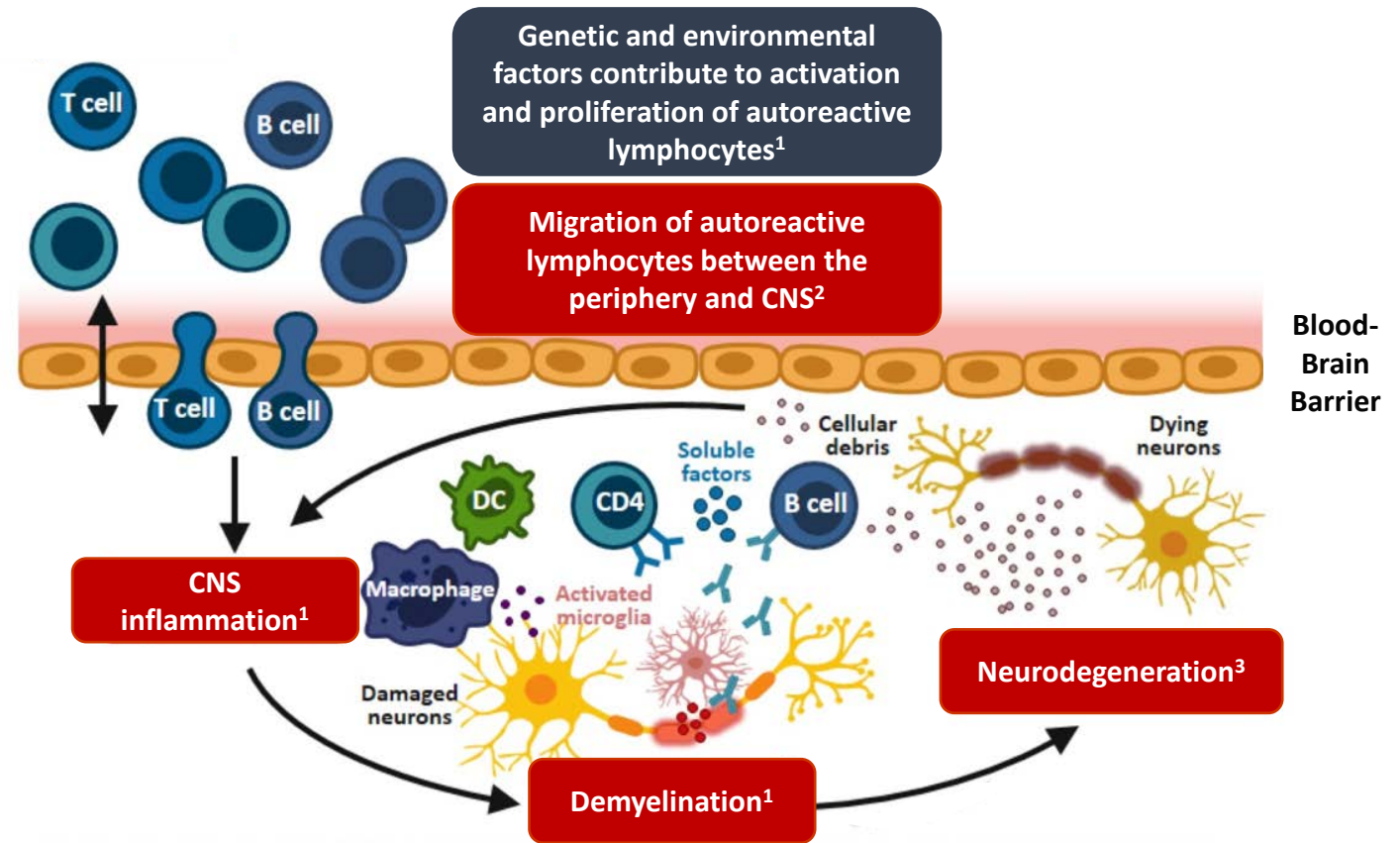


- Discuss where current and emerging therapies fit into the multiple sclerosis (MS) management algorithm
- Review the potential impact of and value of real-world evidence to inform clinical decision making in MS

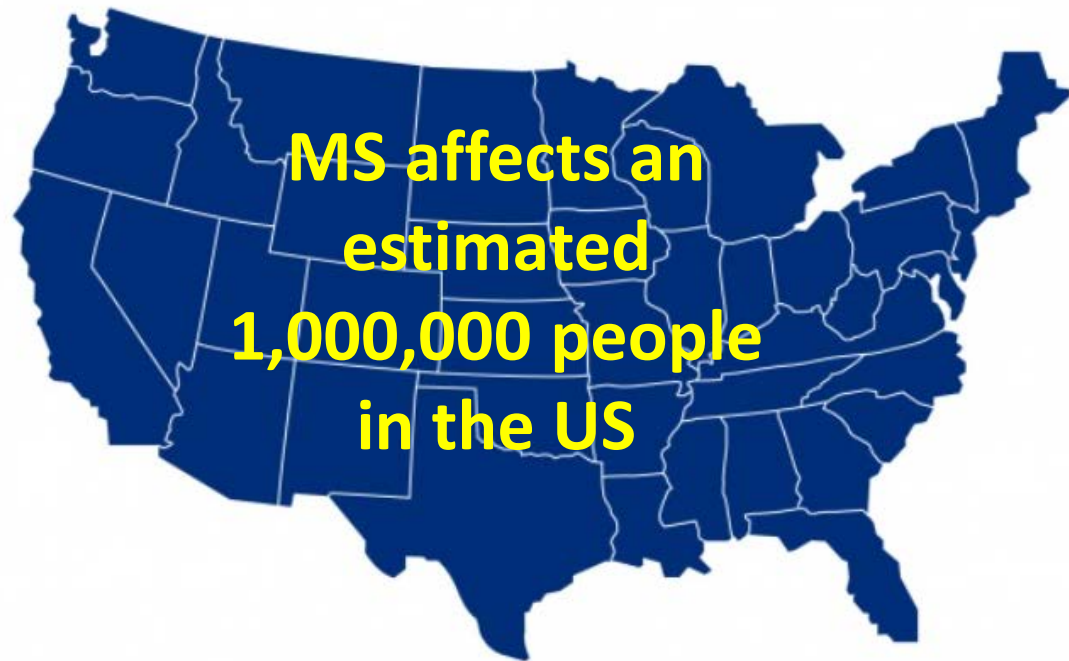


What is Multiple Sclerosis?

- Chronic progressive immune-mediated disease of the CNS
- Associated with demyelination, axonal damage, and subsequent scar or plaque formation
- Associated with significant disability
- Primary etiology unknown, but likely multifactorial



MS Epidemiology

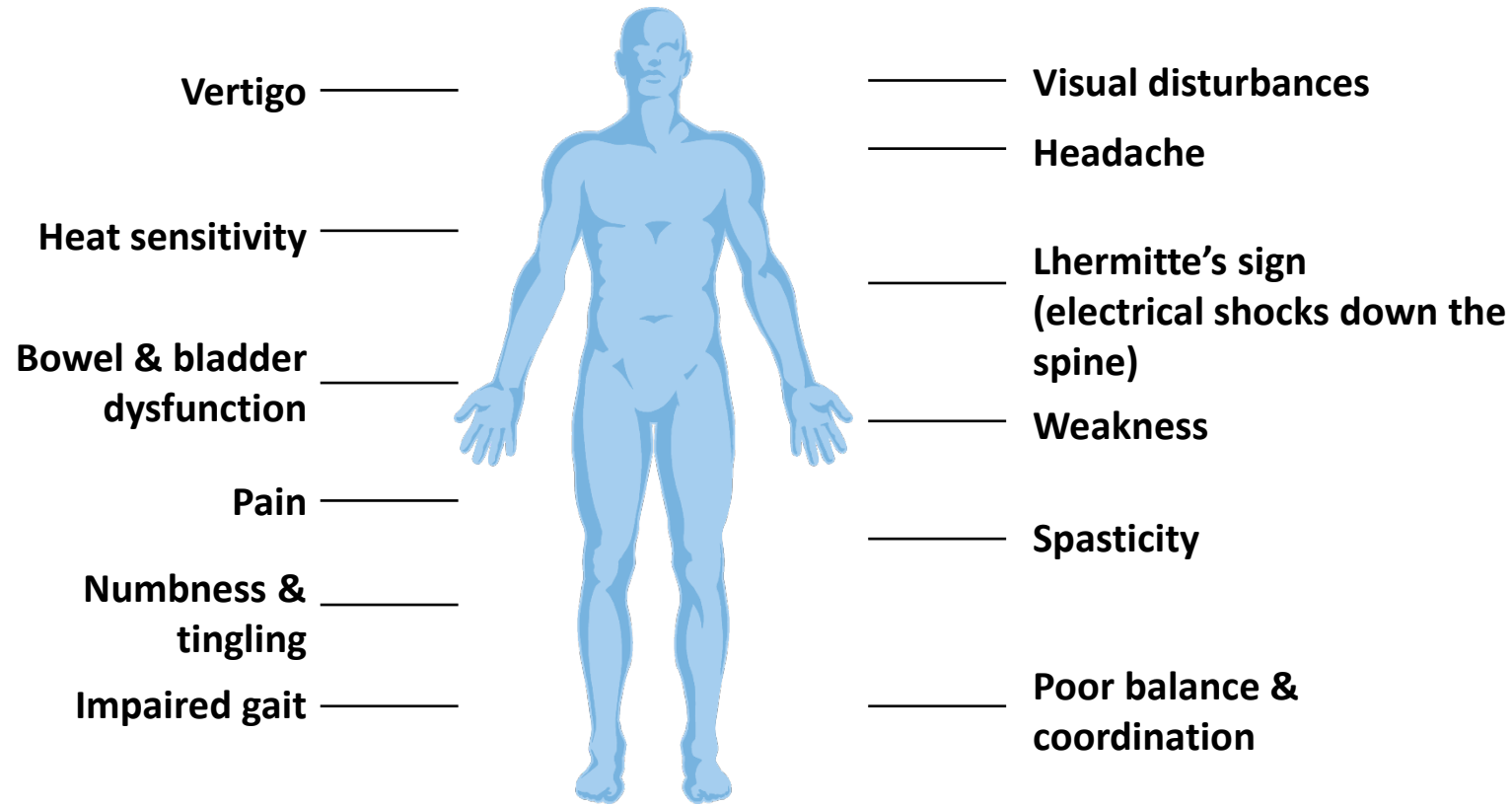


- MS is the most common cause of neurologic disability in the 18- to 60-year-old population
- More prevalent in females
- Peak incidence occurs between 20 and 40 years old
- Annual cost in the US estimated to be \$6.8 to \$11.9 billion

Patients with MS Can Exhibit a Variety of Symptoms and Experience Significant Disability



Physical Symptoms¹⁻⁵



Nonphysical Symptoms

- Cognitive impairment¹
- Depression and mood/emotional changes²
- Pseudobulbar affect⁶

1. Compston A, Coles A. *Lancet*. 2008;372(9648):1502-17; 2. Calabresi PA. *Am Fam Physician*. 2004;70(10):1935-44; 3. Gelfand JM. *Handb Clin Neurol*. 2014;122:269-90; 4. Olek MJ. *Current Clinical Neurology: Multiple Sclerosis*. Totowa, NJ: Humana Press Inc; 2005:15-53; 5. Milo R, Miller A. *Autoimmun Rev*. 2014;13(4-5):518-24; 6. Work SS, Colamonico JA, Bradley WG, Kaye RE. *Adv Ther*. 2011;28(7):586-601.

What is the lowest Extended Disability Status Scale (EDSS) score that indicates severe disability?

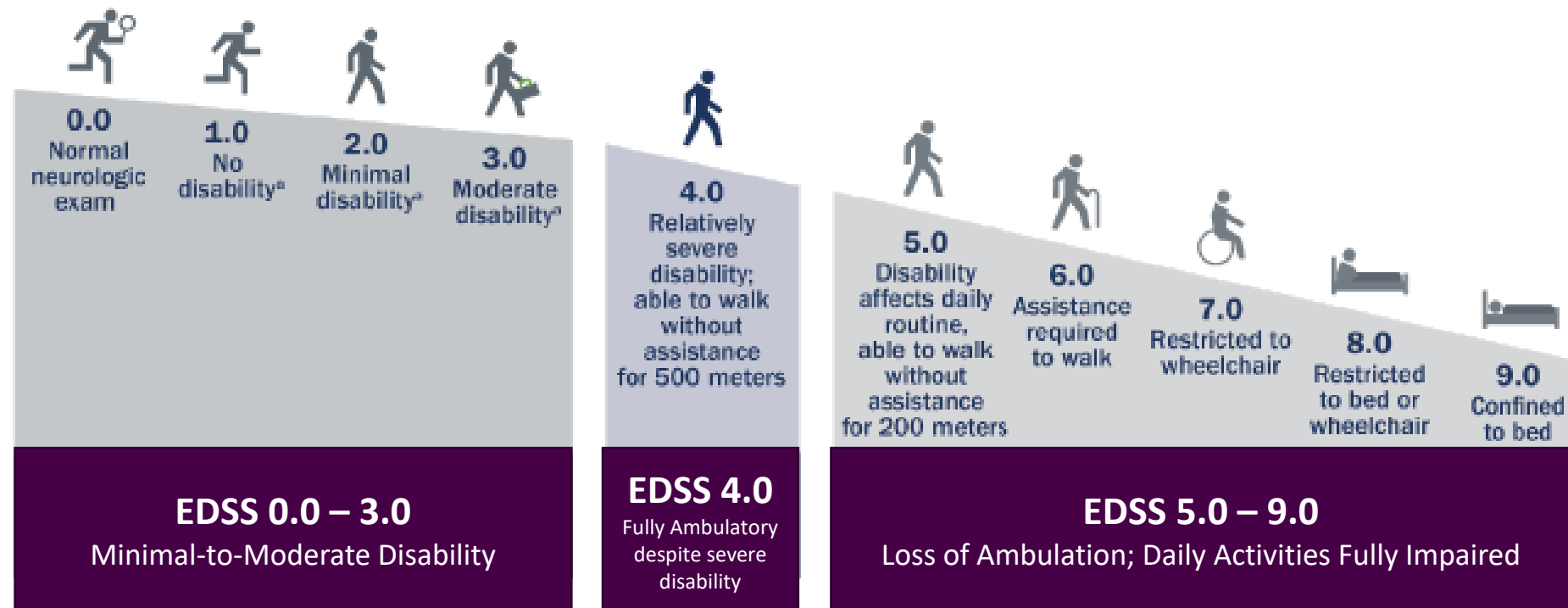


- a) 1.0
- b) 2.0
- c) 3.0
- d) 4.0
- e) 5.0
- f) 6.0
- g) 7.0
- h) 8.0
- i) 9.0

Disability Progression Based on the Extended Disability Status Scale (EDSS)

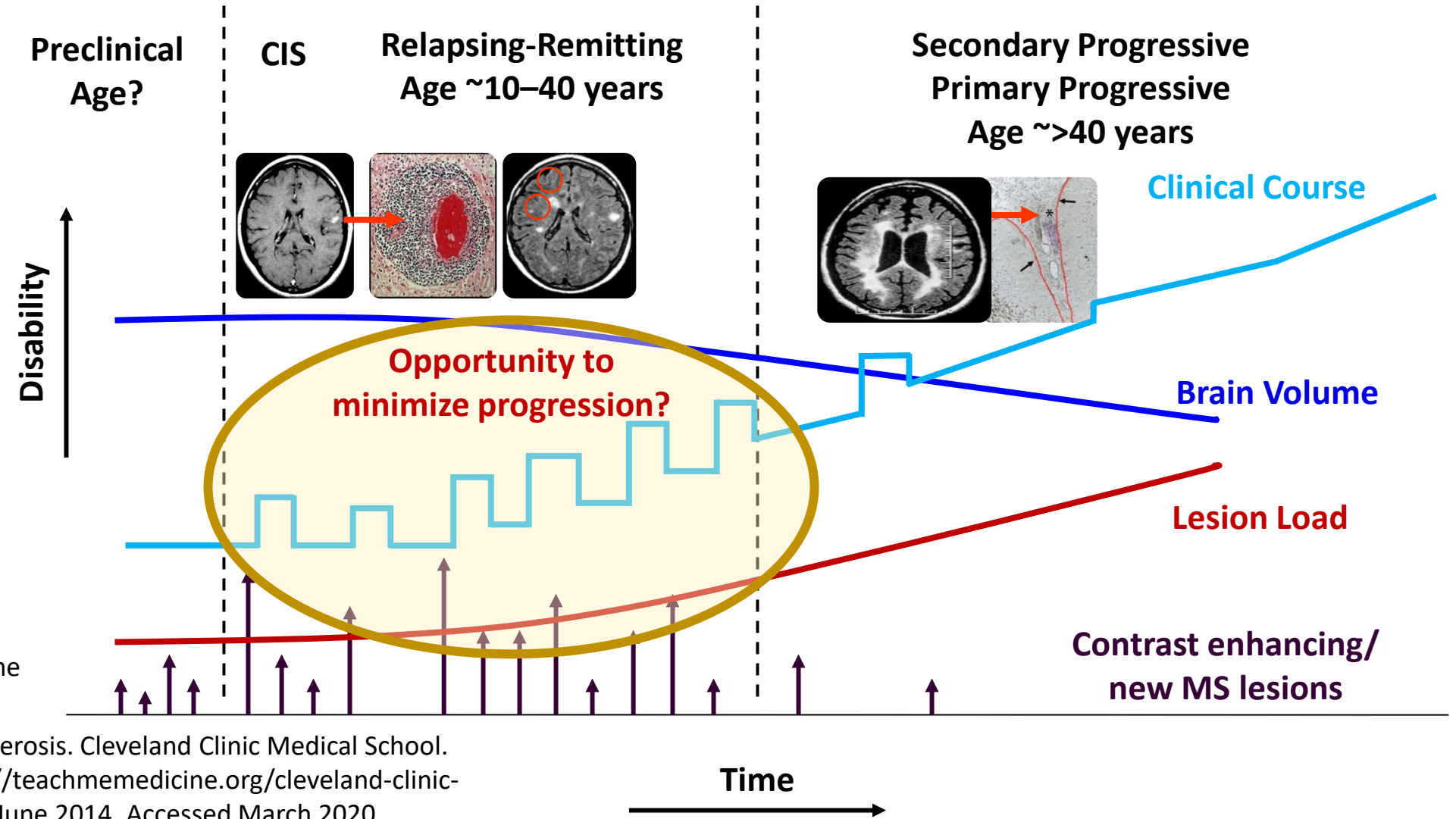


Disability Progression Based on the EDSS^{1,2}





MS Disease Course



CIS: clinically isolated syndrome

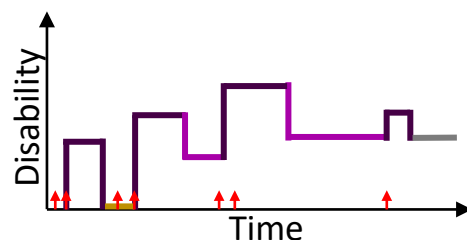


MS Disease Subtypes

Radiologically or Clinically Isolated Syndrome (RIS/CIS)

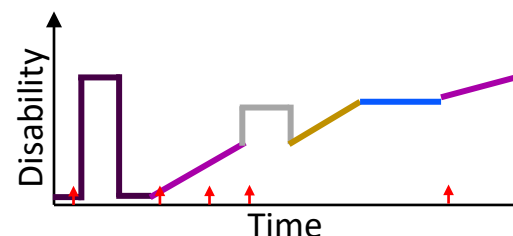
First episode of neurologic symptoms; must last for ≥ 24 hours; may not evolve into MS

Relapsing-Remitting (RRMS)



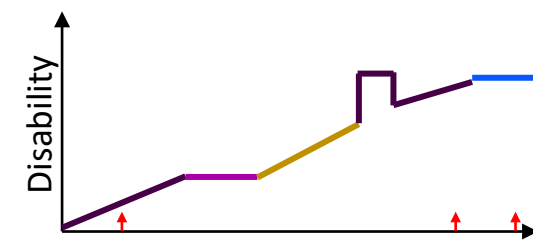
- Relapse
- Active without worsening
- Worsening (incomplete recovery from relapse)
- Stable without activity
- ↑ New MRI activity

Secondary Progressive (SPMS)



- RRMS
- Active (relapse or new MRI activity) with progression
- Active (relapse or MRI activity) without progression
- Not active with progression
- Not active without progression (stable)
- ↑ New MRI activity

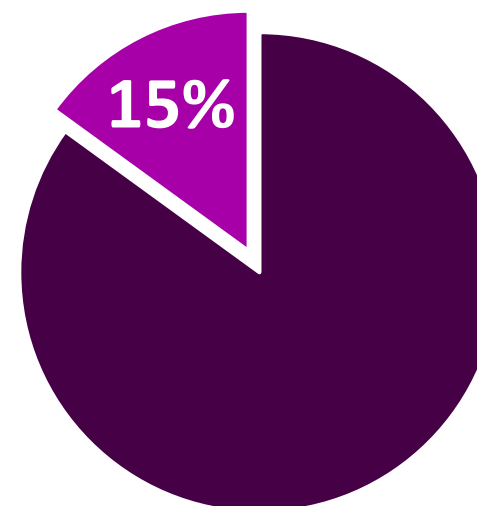
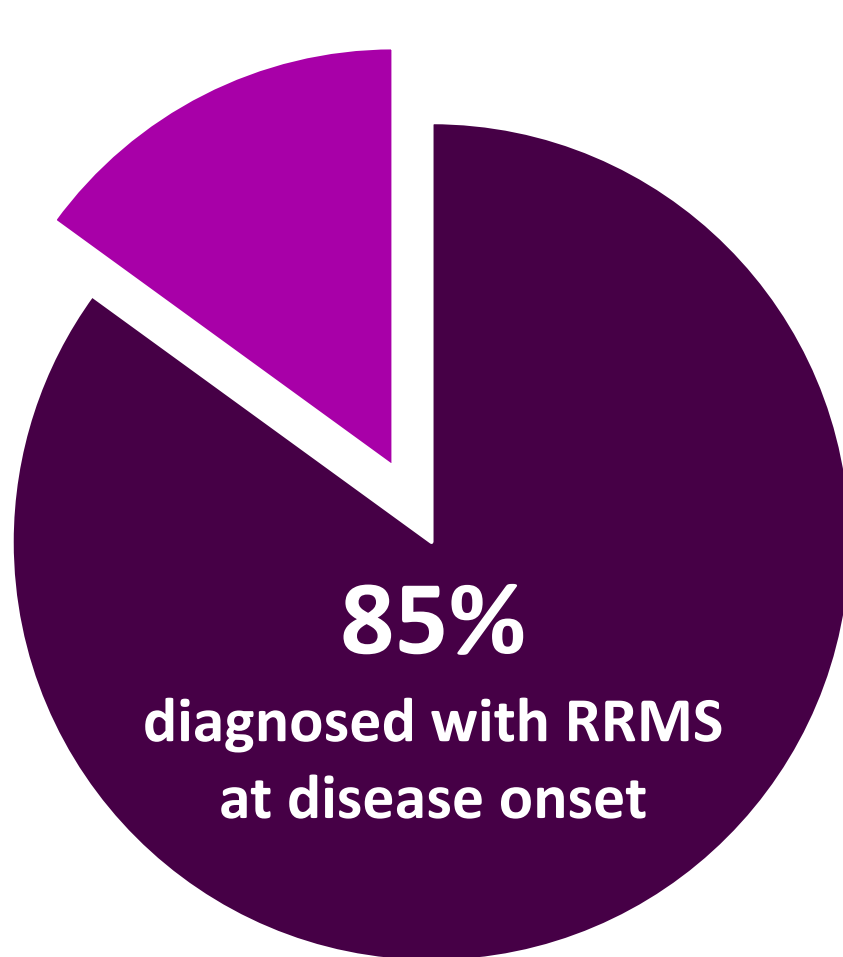
Primary Progressive (PPMS)



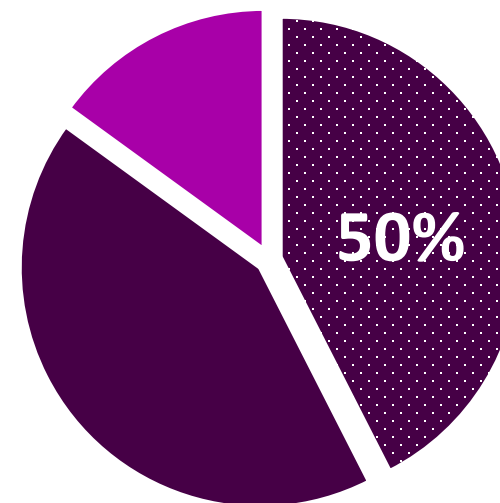
- Active (relapse or new MRI activity) with progression
- Not active without progression (stable)
- Not active with progression
- Active without progression
- ↑ New MRI activity



Frequency of MS Clinical Subtypes



15%
are diagnosed
with PPMS at
disease onset



Left untreated,
~50%
of RRMS cases
transition to SPMS
within 10 years of the
initial diagnosis

Components of the MS Diagnosis



- **Clinical:** symptoms and exam findings suggestive of MS
- **MRI:** objective evidence of CNS white matter lesions disseminated in time and space
- **Lab tests:** blood work to rule out mimics (e.g., antinuclear antibody and neuromyelitis optica)
- **CSF studies:** findings supportive of MS such as cell count, IgG index, and oligoclonal bands
- **Neurophysiology:** evoked potential supportive of MS (e.g., Lhermitte's phenomenon)



Predictors of MS Disability

Clinical¹

- Longer disease duration
- Higher relapse rate
- More frequent early relapses
- Poor recovery from relapses

Imaging^{2,3}

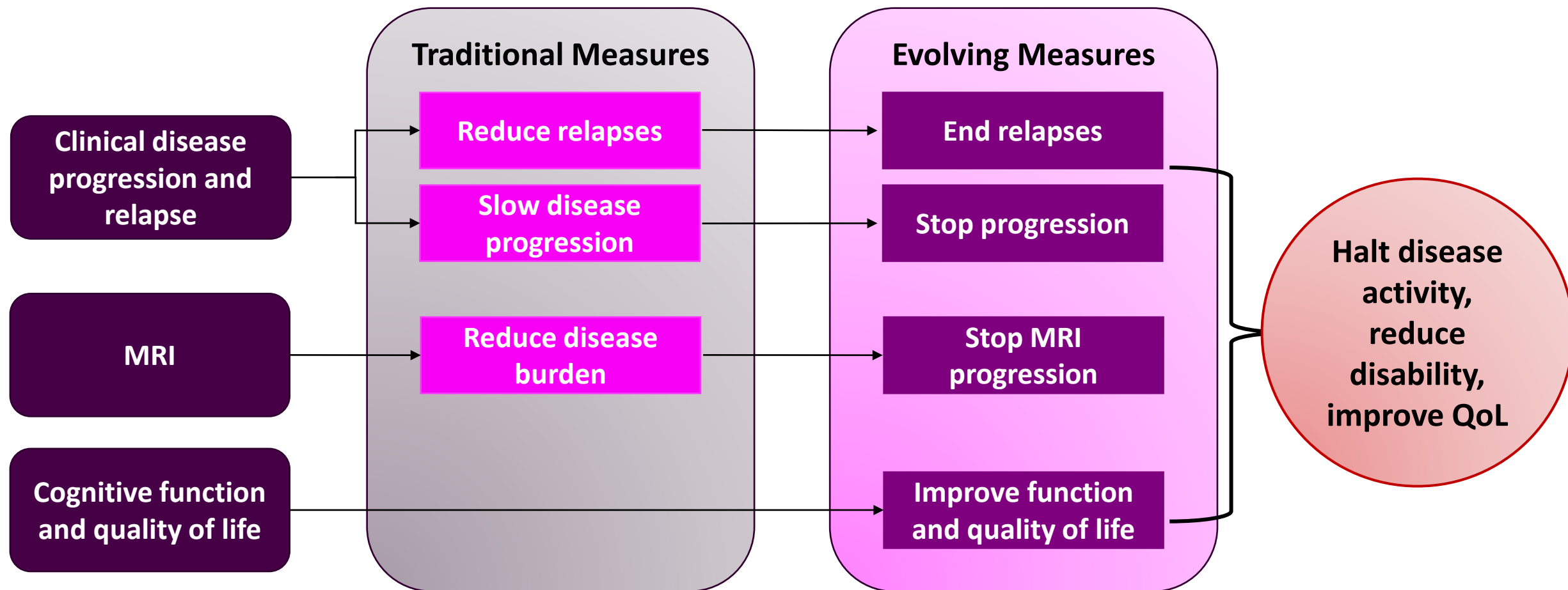
- Spinal cord lesions
- Diffuse abnormalities in the spinal cord
- Cortical lesions and atrophy

Patient^{4,5}

- Age
 - Younger age of disease onset
- Gender
 - Males have increased risk for disability
- Ethnicity
 - Higher Patient-derived MS Severity Score (P-MSSS) in African-American and Hispanics vs. Caucasians



Treatment Goals in MS

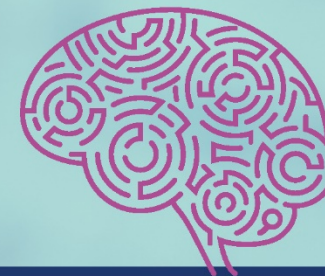




Evolving Clinical Outcome Measures in MS

	Measurement	Conventional Disability	Composite Disability	No Evidence of Disease Activity (NEDA) 3	No Evidence of Disease Progression & Disease Activity	Expanded No Disability Progression & Disease Activity
Assessment of Disability Progression	EDSS	✓	✓	✓	✓	✓
	T25-FW		✓		✓	✓
	9-HPT		✓		✓	✓
	SDMT/cognitive measure					✓
Assessment of Disease Activity	Relapses			✓	✓	✓
	MRI activity			✓	✓	✓
	Atrophy measure					✓

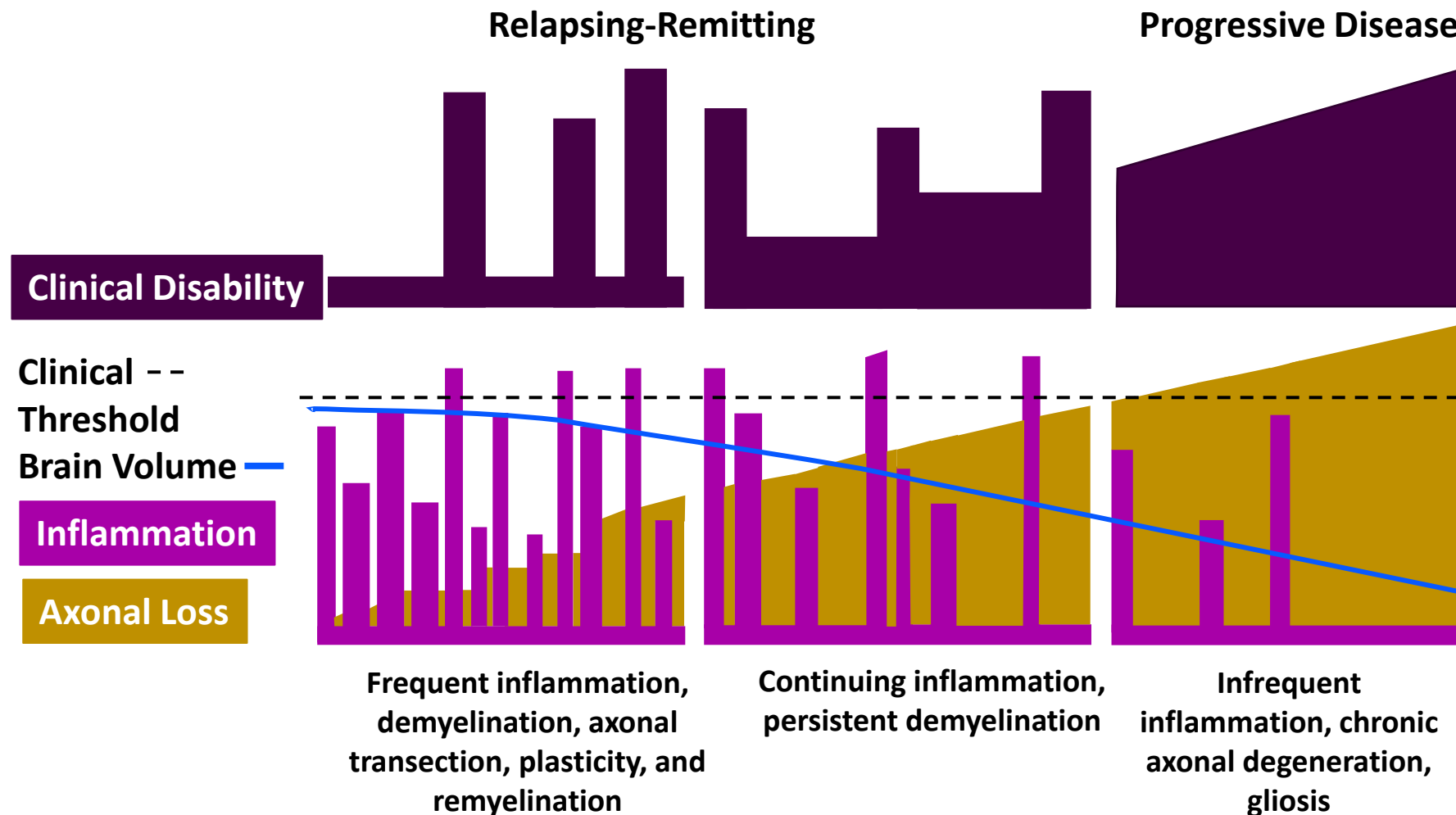
EDSS=extended disability status scale; T25-FW=timed 25-foot walk test; 9-HPT=9-hole peg test; SDMT=symbol digit modalities test; MRI=magnetic resonance imaging



Importance of Early Treatment

Guiding Principles

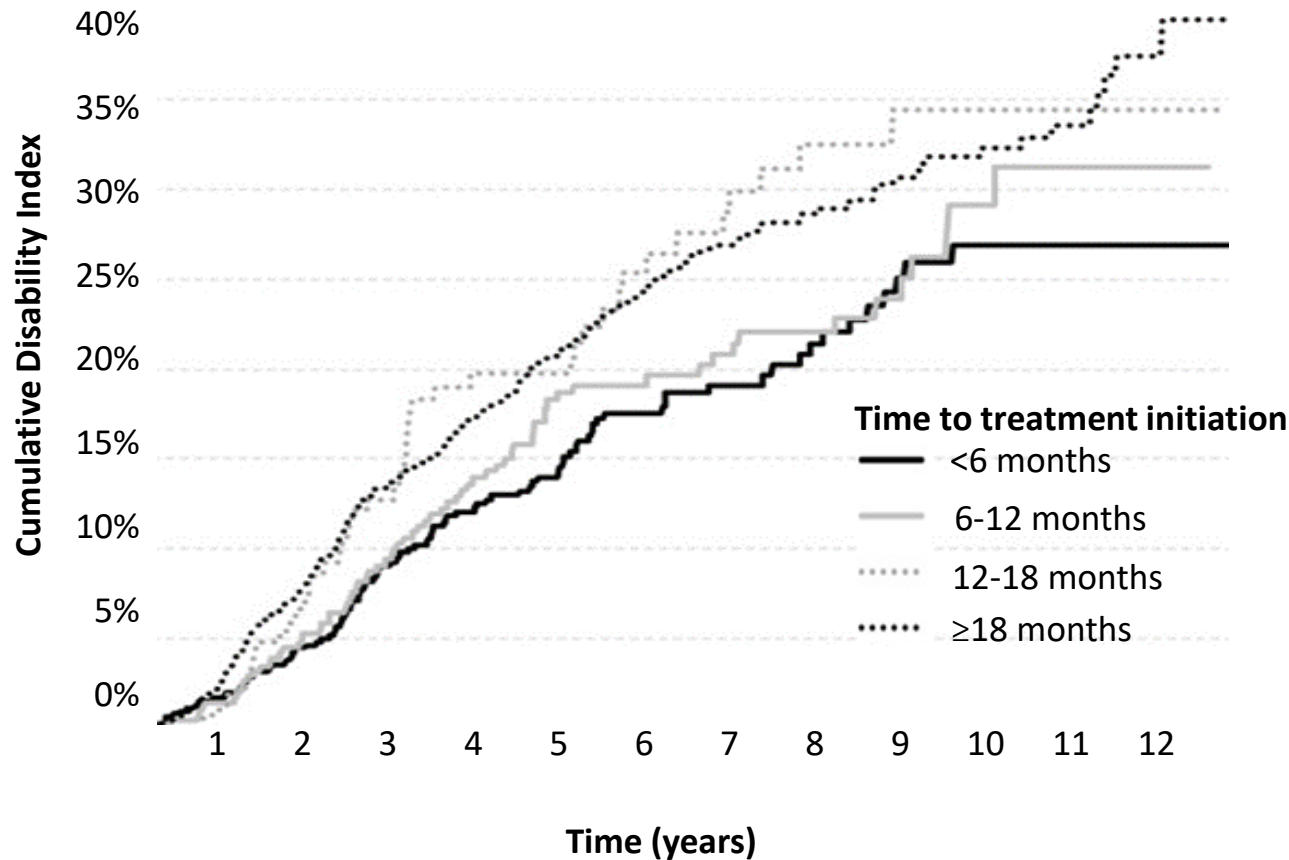
- Start treatment within 12 months after symptom onset if MRI is positive
- Initiate DMT treatment early in the disease course
- Treat-to-target



Early Treatment with Disease Modifying Therapy (DMT) is Associated with Reduced Risk of Disability



Impact of Early Treatment on the Risk of Disability



Patients (n=2477) who started treatment within 6 months after onset had a 36% lower risk (HR 0.74, p = 0.010) of full-time disability during follow-up vs. patients starting treatment after 18 months

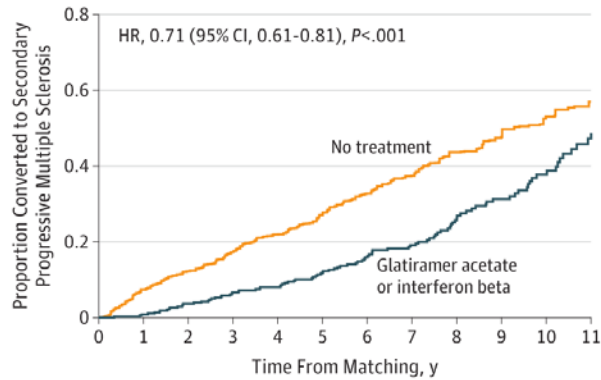
36%

Retrospective, observational study to estimate the long-term impact of early treatment of MS on the risk of disability pension. Patients started DMT treatment between January 1, 2002 and December 31, 2012. The association between time from onset of MS to treatment initiation and full-time disability pension using survival analysis was assessed.

Early Treatment with DMT Associated with Later Conversion to SPMS

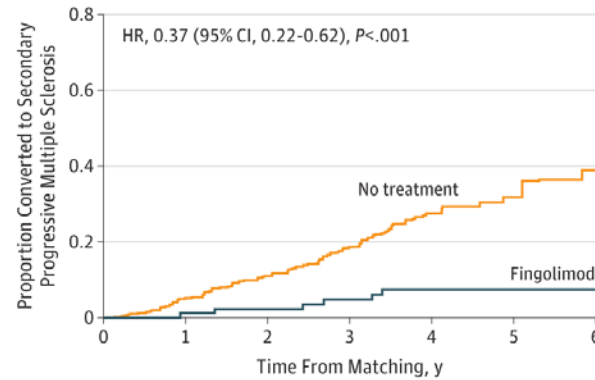


A Glatiramer acetate or interferon beta vs no treatment



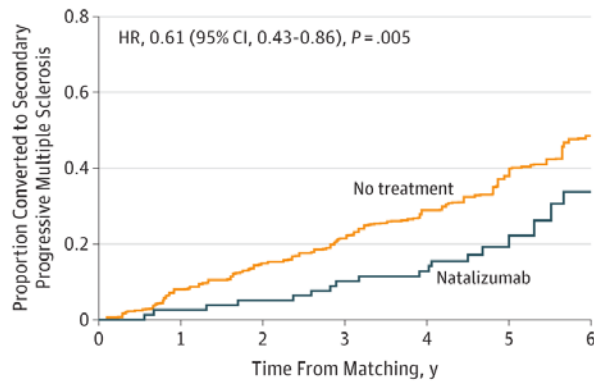
No. with follow-up data	
No treatment	213 213 213 213 213 180 153 126 96 74 51 33
Glatiramer acetate or interferon beta	407 407 407 407 407 355 300 251 191 142 98 62

B Fingolimod vs no treatment



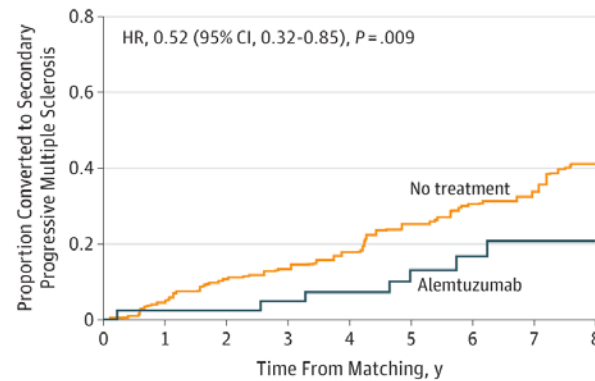
No. with follow-up data	
No treatment	174 174 174 174 174 39 20
Fingolimod	85 85 85 85 85 21 11

C Natalizumab vs no treatment



No. with follow-up data	
No treatment	164 164 164 164 164 77 35
Natalizumab	82 82 82 82 82 36 17

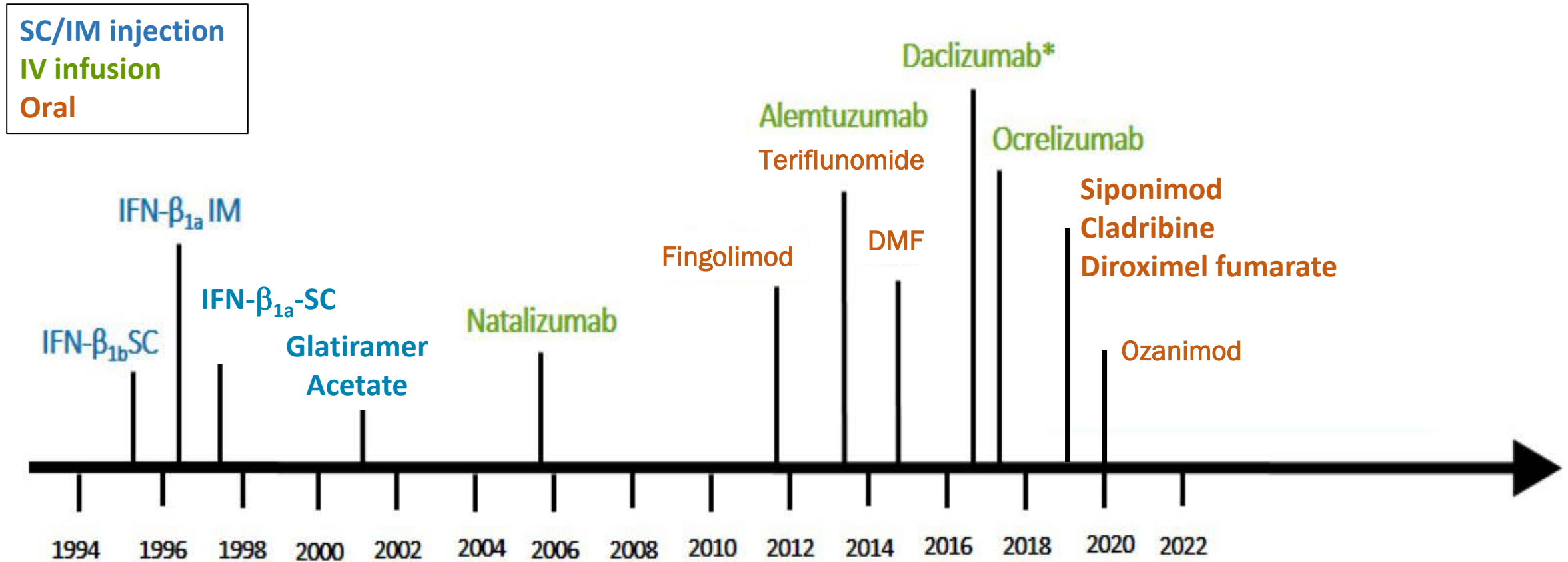
D Alemtuzumab vs no treatment



No. with follow-up data	
No treatment	92 92 92 92 92 77 68 50 36
Alemtuzumab	44 44 44 44 44 37 34 24 17

- Comparison of the cumulative hazard of conversion to SPMS in untreated patients vs. matched treated patients compared by initial treatment
- Median follow-up:
 - A. 7.6 years
 - B. 4.5 years
 - C. 4.9 years
 - D. 7.4 years

MS Treatment Landscape Continues to Expand†



DMF=dimethyl fumarate

*Daclizumab: withdrawn in March 2018 due to reports of AEs including inflammatory encephalitis and meningoencephalitis

†Year of discovery or licensing



FDA Indications for FDA-Approved DMTs

Agent	Approval	CIS	RRMS	PPMS	SPMS
Interferon β-1b (Betaseron; Extavia)	1993	✓	✓		
Interferon β1-a (Avonex)	1996	✓	✓		
Glatiramer acetate (Copaxone)	1996	✓	✓		
Interferon β-1a (Rebif)	1996		✓		
Mitoxantrone (Novantrone)	2000		✓		✓
Alemtuzumab (Lemtrada)	2001		✓		
Natalizumab (Tysabri)	2004		✓		
Fingolimod (Gilenya)	2010		✓		
Teriflunomide (Aubagio)	2012		✓		
Dimethyl fumarate (Tecfidera)	2013		✓		
Peginterferon β-1a (Plegridy)	2014		✓		
Ocrelizumab (Ocrevus)	2017		✓	✓	
Siponimod (Mayzent)	2019	✓	✓		✓
Cladribine (Mavenclad)	2019		✓		✓
Diroximel fumarate (Vumerity)	2019	✓	✓		✓
Ozanimod (Zeposia)	2020		✓		

Clinical Benefit of Widely Used DMTs: Annual Relapse Rate (ARR)



Agent	Trial/Duration	ARR Reduction vs. Comparator
IFN-β1b 250 µg qod SC	3 years	34% ↓
IFN-β1a 30 µg/wk	2 years (stopped early)	18%-21% ↓
IFN-β1a 44 µg SC tiw	PRISMS/2 years	33% ↓
IFN-β1a 125 µg q2w	ADVANCE/48 weeks	35% ↓
Glatiramer acetate 20 mg	2 years	29% ↓
Glatiramer acetate 40 mg tiw	GALA/1 years	34% ↓
Natalizumab	AFFIRM/2 years	68% ↓
Alemtuzumab 12 or 24 mg/d	CARE MS I-II/2 years	55%, ↓ 49% ↓ vs IFN-β1a
Ocrelizumab	OPERA I-II/96 weeks	46% and 47% ↓ vs IFN-β1a
Fingolimod 5 mg	FREEDOMS I-II/2 years TRANSFORMS/1 years	54% ↓ 48% ↓ vs IFN-β1a
Teriflunomide 14 mg po/day	TOWER/>48 weeks TEMPO/108 weeks	36% ↓ 31% ↓
Dimethyl fumarate	DEFINE, CONFIRM/ 2 years	49% ↓ 44% ↓
Siponimod	EXPAND/3 years	55% ↓
Cladribine	CLARITY/ 2 years	55-57% ↓
Diroximel fumarate	EVOLVE-MS-1/2 years	83% ↓
Ozanimod	SUNBEAM/1 year	48% ↓



Injectable DMTs: Safety and Monitoring

Agent	Minor Side Effects	Serious Side Effects	Monitoring
IFNβ-1a (low dose) ¹	Flu-like symptoms, headache, transaminitis, depression	Suicidal ideation, anaphylaxis, hepatic injury, provoke rheumatic conditions, congestive heart failure, blood dyscrasias, seizures, autoimmune hepatitis	CBC with differential, LFTs, TFTs, interferon neutralizing antibodies (if clinically warranted), skin surveillance
IFNβ-1a (high dose) ²	Same as above; injection-site reactions	Same as above; skin necrosis	Same as above
Peg IFNβ-1a³	Same as above	Same as above	Same as above
IFNβ-1b^{4,5}	Same as above	Same as above	Same as above
Glatiramer acetate⁶	Injection-site reactions; post-injection vasodilatory reaction	Lipoatrophy, skin necrosis, anaphylaxis	No specific labs, skin surveillance

CBC: complete blood count; LFTs: liver function tests; TFTs: thyroid function tests; ALT: alanine amino-transferase; AST: aspartate-aminotransferase

1. IFN β -1a [prescribing information]. Cambridge, MA: Biogen Idec Inc; March 2016; 2. IFN β -1a [prescribing information]. Rockland, MA: EMD Serono, Inc; November 2015; 3. Pegylated IFN β -1a [prescribing information]. Cambridge, MA: Biogen Idec Inc; July 2017; 4. IFN β -1b [prescribing information]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; August 2018; 5. IFN β -1b [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; December 2018; 6. Glatiramer acetate [prescribing information]. Overland Park, KS: TEVA Neuroscience, Inc; January 2018.

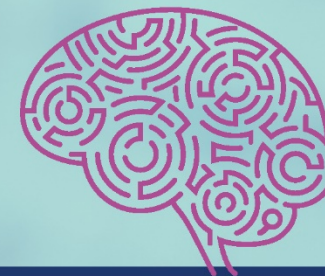


IV DMTs: Safety and Monitoring

Agent	Minor Side Effects	Serious Side Effects	Monitoring
Natalizumab¹	Headaches, joint pain, fatigue, wearing-off phenomenon	Boxed warning for PML, infusion reaction, herpes zoster, other infections, liver failure	CBC with differential, LFTs, serum JCV antibody (every 6 months), MRI, natalizumab antibodies (if clinically warranted)
Alemtuzumab²	Infusion reactions	Boxed warning for autoimmunity, infusion reactions, stroke, and malignancies; autoimmune thyroid disease, ITP, Goodpasture syndrome, infections (HSV, VZV)	Monthly CBC with differential, LFTs, urinalysis with urine cell counts, TFTs every 3 months
Ocrelizumab³	Upper respiratory tract infections and infusion reactions	Severe infusion reactions, reactivation hepatitis, opportunistic infections, malignancies	Hepatitis panel, CBC with differential, LFTs, PPD or Tb spot/QuantiFERON prior to starting

ITP: immune thrombocytopenic purpura

1. Natalizumab [prescribing information]. Cambridge, MA: Biogen Idec Inc; April 2018; 2. Alemtuzumab [package insert]. Cambridge, MA: Genzyme Corporation; January 2019; 3. Ocrelizumab [prescribing information]. Genentech, Inc. November 2018.



Oral DMTs: Safety and Monitoring

Class/Agent(s)	Adverse Events	Serious Side Effects	Monitoring
S1P Receptor Modulators <ul style="list-style-type: none"> Fingolimod¹ Siponimod² Ozanimod³ 	Lymphopenia (absolute lymphocyte count >200), transaminitis	Bradycardia, heart block, hypertension, risk of infections (herpetic, cryptococcal), lymphopenia (absolute lymphocyte count <200), transaminitis, macular edema, skin cancer, reactive airway, PRES, PML, cryptococcal meningitis, rebound	First-dose cardiac monitoring, eye and skin examinations, CBC with differential, LFTs, varicella-zoster virus IgG prior to starting medication, PFTs (if clinically indicated)
Pyrimidine Synthesis Inhibitor <ul style="list-style-type: none"> Teriflunomide⁴ 	Diarrhea, nausea, hair thinning	Boxed warning for hepatotoxicity and risk of teratogenicity, transaminitis, lymphopenia, teratogenic (men and women), latent tuberculosis, neuropathy, hypertension	CBC with differential, LFTs (monthly for first 6 months), PPD or Tb spot/QuantiFERON prior to starting, wash out (if needed)
Dimethyl fumarate⁵	Flushing, gastrointestinal distress	Transaminitis, leukopenia, PML	CBC with differential, LFTs
Purine Antimetabolite <ul style="list-style-type: none"> Cladribine⁶ 	Upper respiratory tract infection, headache, and lymphopenia	Boxed warning for malignancy and risk of teratogenicity Lymphopenia; infection; hematologic toxicity; graft vs. host disease; liver injury	Follow standard cancer screening guidelines Obtain CBC prior to initiation, before 2 nd course, 2 and 6 months after start of treatment, and periodically thereafter
Diroximel fumarate⁷	Flushing, abdominal pain, diarrhea, and nausea	Anaphylaxis and angioedema; PML; Herpes Zoster; Lymphopenia; Liver injury	N/A

CBC: complete blood count; LFT: liver function tests; PFT: pulmonary function tests; PPD: purified protein derivative; PML: progressive multifocal leukoencephalopathy; PRES: posterior reversible encephalopathy syndrome.

1. Fingolimod [package insert]. Novartis Pharmaceuticals Corporation; January 2019; 2. Siponimod [package insert]. Novartis Pharmaceuticals Corporation; March 2019; 3. Ozanimod [package insert]. Celgene Corporation; March 2020; 4. Teriflunomide [package insert]. Genzyme Corporation; November 2016; 5. Dimethyl fumarate [prescribing information]. Biogen Idec Inc; December 2017; 6. Cladribine [package insert]. EMD Serono, Inc. April 2019; 8. Diroximel fumarate [package insert]. Biogen, Inc.; March 2020.



MS Therapies in Late-Phase Development

Agent	Target/ Mechanism of Action	Possible Indication	Administration	Status
Sphingosine-1-Phosphate Receptor Modulators				
Ponesimod	S1P1 receptor modulator	Relapsing MS	Oral	NDA submitted
Monoclonal Antibodies				
Ofatumumab	Anti-CD20 monoclonal antibody	Relapsing MS	SC	BLA submitted
Opicinumab	LINGO-1 (remyelination promoter)	RRMS, SPMS	IV	Phase 2
Rituximab	Anti-CD20 antibody	RRMS, SPMS	IV	Phase 2
Temelimab	Human endogenous retrovirus	Relapsing MS	IV	Phase 2
Ublituximab	Anti-CD20 B cell modulator	Relapsing MS	IV	Phase 3

MS Therapies in Late-Phase Development (cont'd)



Agent	Target/ Mechanism of Action	Possible Indication	Administration	Status
Other Strategies				
Evobrutinib	Bruton tyrosine kinase inhibitor (B cell signal inhibition)	Relapsing MS, SPMS	Oral	Phase 3
Ibudilast	IL-1 β , TNF- α , and IL-6 inhibitor	PPMS, SPMS	Oral	Phase 3
Masitinib	Protein kinase inhibitor of mast cells	PPMS, SPMS	Oral	Phase 3
Biotin	Vitamin involved in fat metabolism	SPMS, PPMS	Oral	Phase 3
Lipoic acid	Antioxidant	SPMS	Oral	Phase 2/3
Simvastatin	HMG-CoA reductase inhibitor	SPMS	Oral	Phase 3

The DMTs Are Not Interchangeable



- **Characteristics of currently available DMTs approved for the treatment of MS are diverse including**
 - **MOA**
 - **Benefit –risk profile**
 - **Route of administration**
 - **Safety**
 - **efficacy**

- **Few head-to-head trials between DMTs have been conducted/published**
- **This limits the ability to compare the safety, efficacy, and value of DMTs**

- **The DMT landscape continues to evolve with several additional agents in development**
 - **SPS-1 receptor modulators**
 - **Monoclonal antibodies**
 - **Remyelination agents**
 - **Antisense oligonucleotides**

Bourdette DN, et al. *Neurol Clin Pract.* 2016;6:1-6;

The Use of Disease-Modifying Therapies in Multiple Sclerosis: Principles and Current Evidence. Multiple Sclerosis Coalition. http://ms-coalition.org/wp-content/uploads/2019/06/MS_CDMT_Paper_062019.pdf. Published July 2014. Updated June 2019. Accessed March 2020;

Ali R, Nicholas RS, Muraro PA. *Drugs.* 2013;73(7):625-50.

What to Consider When Making an Initial MS Treatment Decision



Disease Activity

- Inactive
- Active
- Highly active
- Rapidly evolving
- Severe

Drug-related Issues

- Tolerability
- Safety profile
 - Immunosuppression
 - PML risk
- Monitoring frequency
- Drug effects
 - Drug-drug interactions

Patient Profile

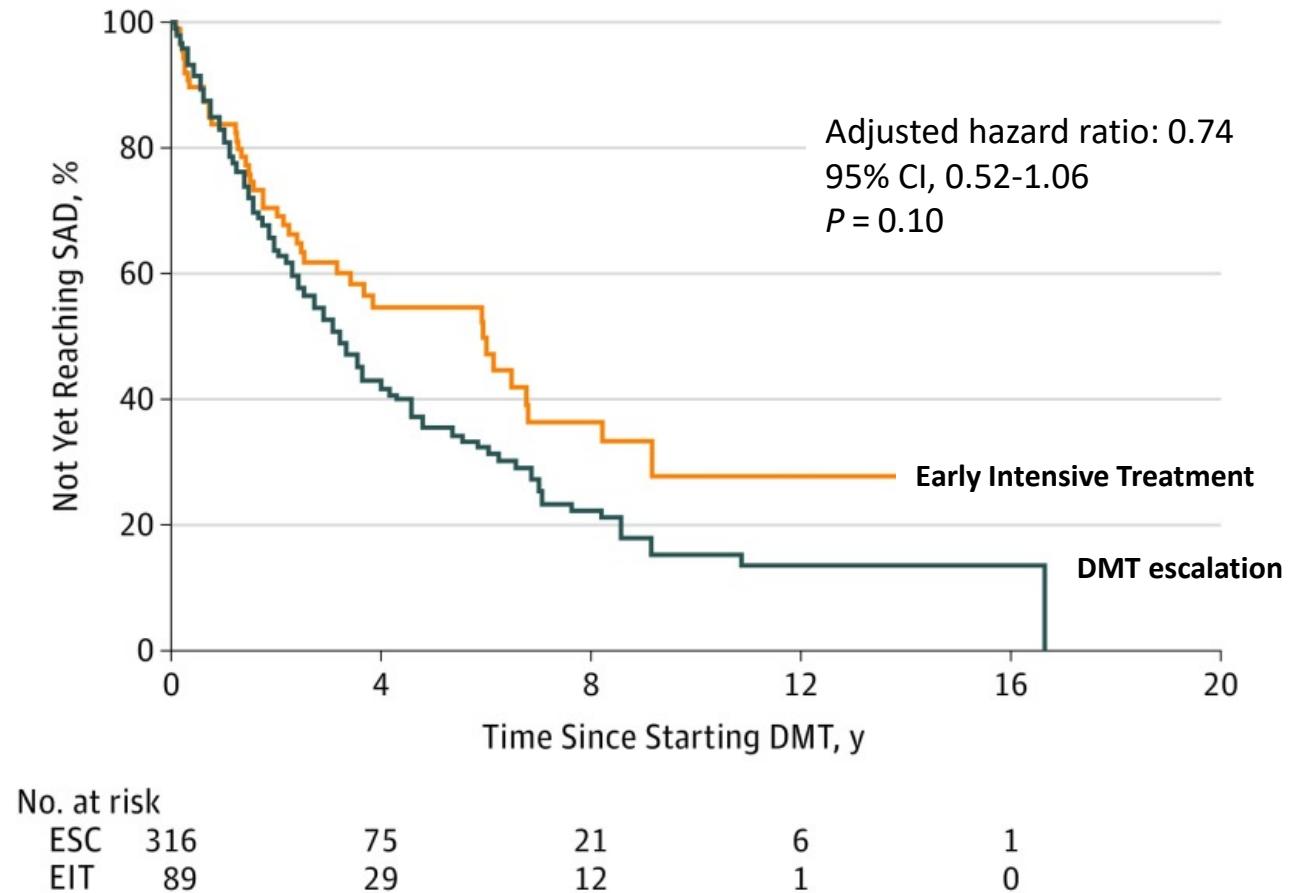
- Adherence
- Comorbidities
- Personal factors
 - Pregnancy
 - Travel
 - Work
 - Treatment expectations

Shared Decision Making

Time to Sustained Accumulation of Disability by Initial Treatment Strategy



- Uncertainty remains about how aggressively to treat early MS
- Analysis of patients (n=592) classified according to first-line treatment strategy
 - High-efficacy early intensive treatment
 - Moderate-efficacy DMT escalation
- Long-term outcomes were more favorable following early intensive therapy vs. first-line moderate-efficacy DMT



DMT indicates disease-modifying therapy; EIT, early intensive treatment; ESC, escalation approach; SAD, sustained accumulation of disability

Which of the following DMTs are considered to be interchangeable?



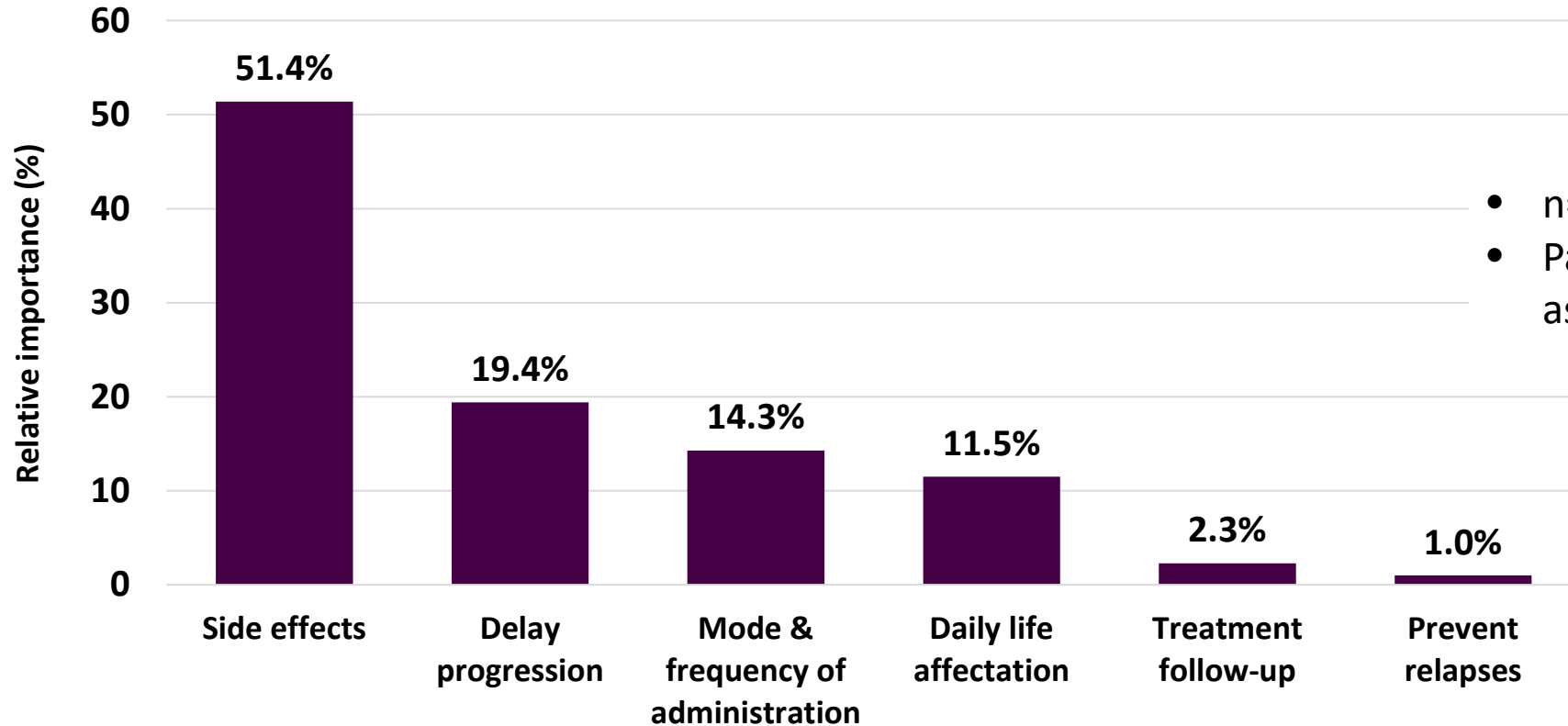
- a) Alemtuzumab and Cladribine
- b) Dimethyl fumarate and Glatiramer acetate
- c) Ocrelizumab and Teriflunomide
- d) Ozanimod and Siponimod
- e) All of the above
- f) None of the above

Factors Influencing a Decision to Switch the DMT



Line of Therapy	Factor Influencing a Switch
First-line DMT to another first line (lateral switch) <i>1st line: IFN; GA; teriflunomide; DMF</i>	<ul style="list-style-type: none"> • Tolerability/safety issues <ul style="list-style-type: none"> • Suboptimal efficacy with suboptimal response but still a low risk for imminent progression
First-line to a second-line DMT (i.e., escalation) <i>2nd line: fingolimod; natalizumab; alemtuzumab; ocrelizumab</i>	<ul style="list-style-type: none"> • Suboptimal response to first-line DMT with a moderate-higher risk for progression (as opposed to low risk) • RRMS patients transitioning to the secondary progressive phase with evidence of relapses or MRI activity
Second-line to a third-line or higher DMT (i.e., these are the patients who moved to a higher risk for progression and the first- and second-line DMTs would not be able to change the risk) <i>3rd line/higher: mitoxantrone; cyclophosphamide; experimental therapy (e.g., cladribine)</i>	<ul style="list-style-type: none"> • RRMS patients continuing to experience relapses on a second-line therapy • Progressive forms of MS with relapses and/or active MRI despite treatment • Safety issues (e.g., patients on natalizumab at high risk of developing progressive multifocal leukoencephalopathy)
Second-line to a first-line DMT	<ul style="list-style-type: none"> • Tolerability/safety issues should the patient maintain the second-line agent AND the perception that the disease is under good control and the patient's risk for imminent progression has been reduced

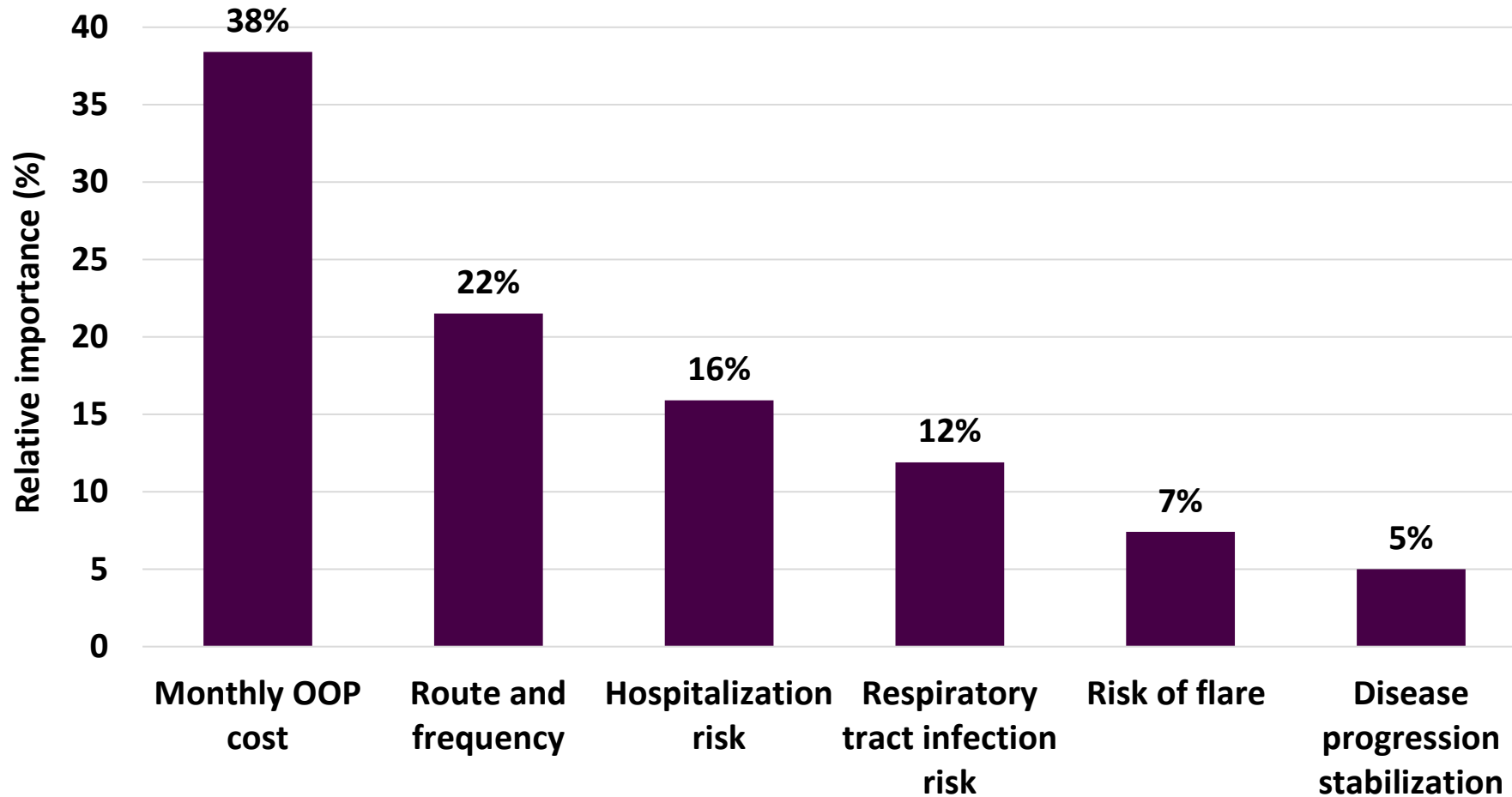
Patients Prefer DMTs That Minimize Side Effects and Delay Disability Progression



- n=125 patients with RRMS or SPMS
- Patients recruited from MS patient associations in Spain

- Preferences measured using a discrete choice experiment
- Multilinear regression used to evaluate the association between preferences for each attribute and patients' demographic and clinical characteristics

Monthly OOP Cost Also Influences Patient Perceptions of DMTs



- Online survey results of 129 patients prescribed DMT for MS recruited from patient advocacy groups in the US
- Patients asked to rank the importance of attributes that influence their satisfaction with a DMT

Using Real-World Evidence in MS Treatment Decision Making



- Randomized controlled clinical trials do not provide all the answers patients, providers, and payers are seeking
- End users are increasingly looking to real-world evidence (RWE) for answers
 - Registries
 - Surveys
 - Patient medical records
 - Claims data
- High-quality real-world studies can fill gaps in evidence



Potential of RWE to Inform MS Treatment Optimization



- RCT data describing patients with an inadequate response to a DMT following dose escalation or a switch to an alternative therapy is limited and/or lacking
- RWE can be used to demonstrate the effectiveness of early treatment optimization
- RWE can also provide insight on clinical questions not answered by RCTs such as the optimal choice for drug switches and sequencing in certain clinical situations

Summary



- MS is a chronic progressive immune-mediated disease of the CNS and is associated with significant disability
- The clinical presentation can be highly variable between patients
- Treatment with disease modifying therapies should be initiated within 12 months of symptom onset to slow disease progression and minimize disability
- Multiple safe and effective DMTs are available with several more in late phase development
- Real-world evidence can provide insights on clinical questions not answered by randomized controlled clinical trials



*Specialty Pharmacy Management
Services for Optimal Outcomes in
MS*

Michael Zeglinski, RPh

SVP and CEO

Optum Specialty & Infusion Pharmacies

Learning Objectives

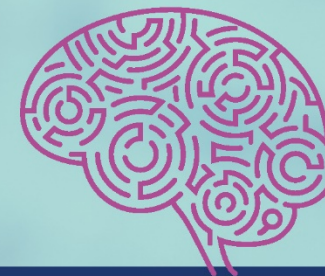


- Employ treatment optimization approaches to balance costs with improved outcomes in multiple sclerosis (MS) management
- Explore how to integrate electronic health technology into MS care management
- Understand the costs associated with MS
- Understand the various challenges of effective MS patient management and potential strategies
- Discuss the importance of pathways in improving outcomes

Which of the following best describes your area of greatest educational need with regards to MS?



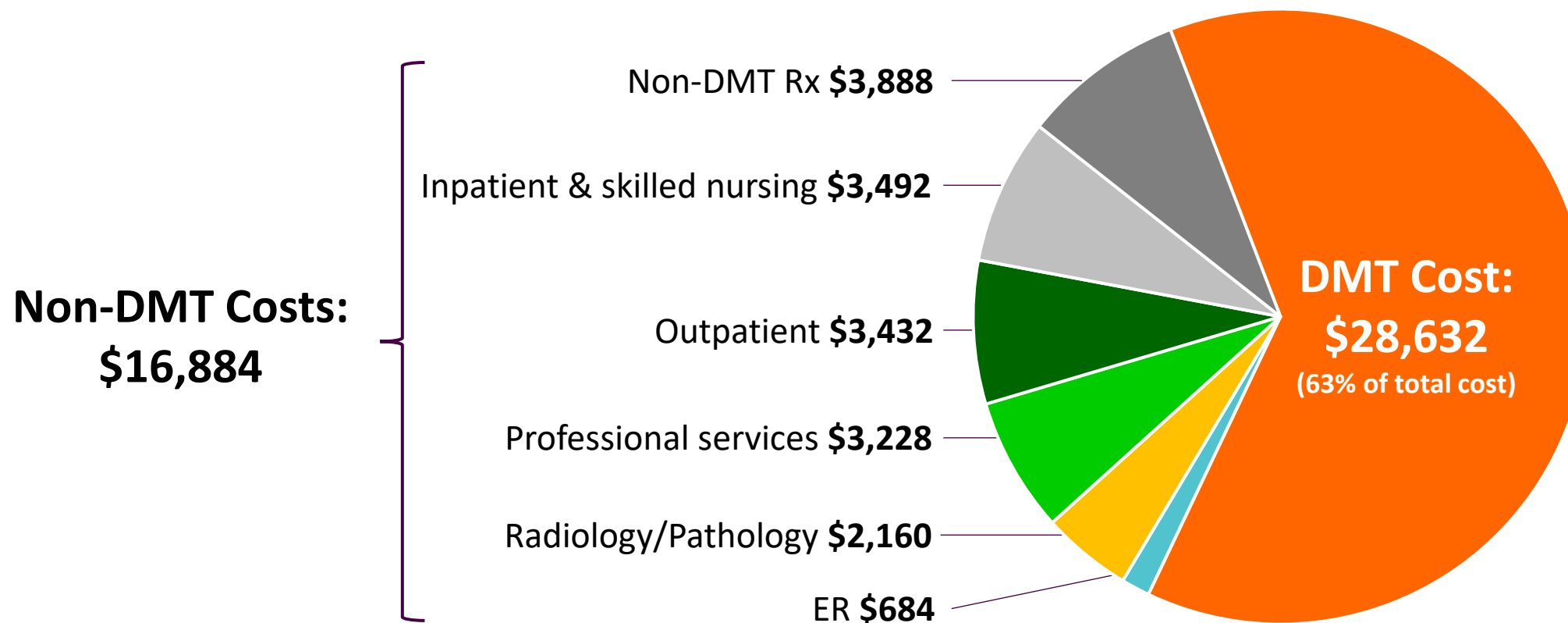
- a) Complex treatment decisions and prolonged treatment duration
- b) Evolving quality performance measures
- c) Expanding treatment armamentarium including novel DMTs and biosimilars
- d) Limited access to specialized, multidisciplinary care
- e) Limited head-to-head and cost-efficacy data
- f) Numerous comorbid conditions
- g) Significant variation in treatment across practice settings
- h) Other



MS is a Costly Disease

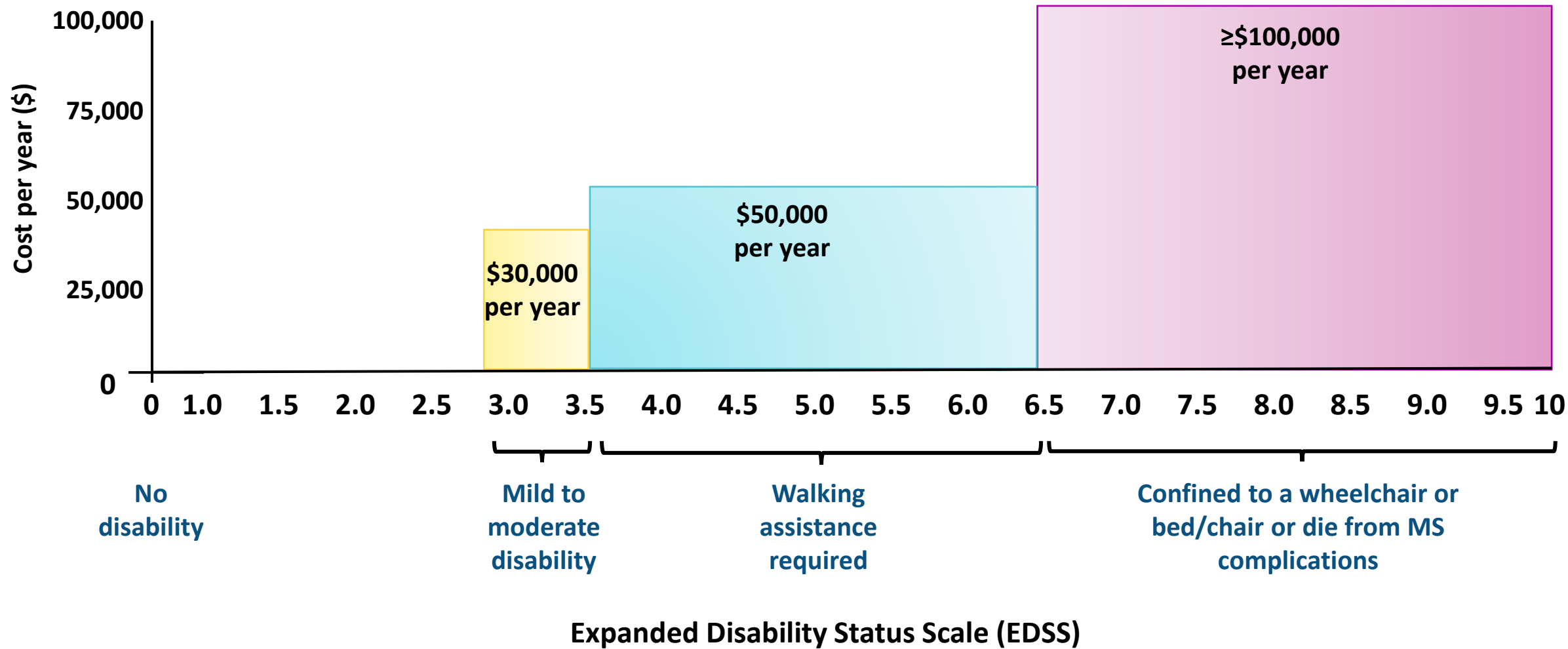
Annual Claim Costs for MS (per patient)

TOTAL: \$45,516





Total MS Costs Rise as Disability Progresses



The MS Drug Benefit Must Be Designed to Optimize Care and Manage Costs



Right Drug

- Preferred products
- Efficacy/safety
- Minimal side effects
- Proper duration of therapy

Right Site of Care

- Hospital (in-/out-patient)
- Provider office
- Retail pharmacy/clinic
- Home nursing care
- Home self-administration

Right Cost

- Utilization management
 - Cost sharing
 - Prior authorization
 - Formulary
 - Specialty tiers
- Contracts/rebates

Selecting the “Right” MS Drug



- Treatment should be individualized using shared decision making between the provider and patient
- None of the approved MS therapies is curative
- Clinicians and patients vary in their tolerance for risk and preference of route-of-administration
 - Multiple mechanisms of action
 - Oral, IV, SC, and IM routes of administration
 - Variable efficacy and safety

Owens GM. *Am J Manag Care*. 2016;22:S151-S158.

The Use of Disease-Modifying Therapies in Multiple Sclerosis: Principles and Current Evidence. Multiple Sclerosis Coalition. http://ms-coalition.org/wp-content/uploads/2019/06/MS_CDMTPaper_062019.pdf. Published July 2014. Updated June 2019. Accessed March 2020



Plan Strategies to Manage Utilization

Tiered formulary

- Generic
- Preferred branded
- Nonpreferred branded specialty
- Non-formulary

Utilization management programs

- Prior authorization
- Step edits

Encouraging appropriate use

- Clinical algorithms/pathways

Cost sharing

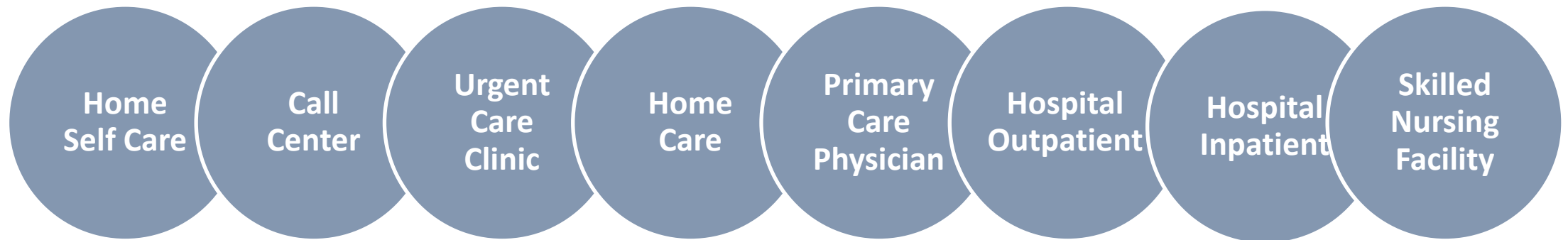
Cost-effectiveness analysis



Site-of-Care Delivery Can Influence Cost and Access



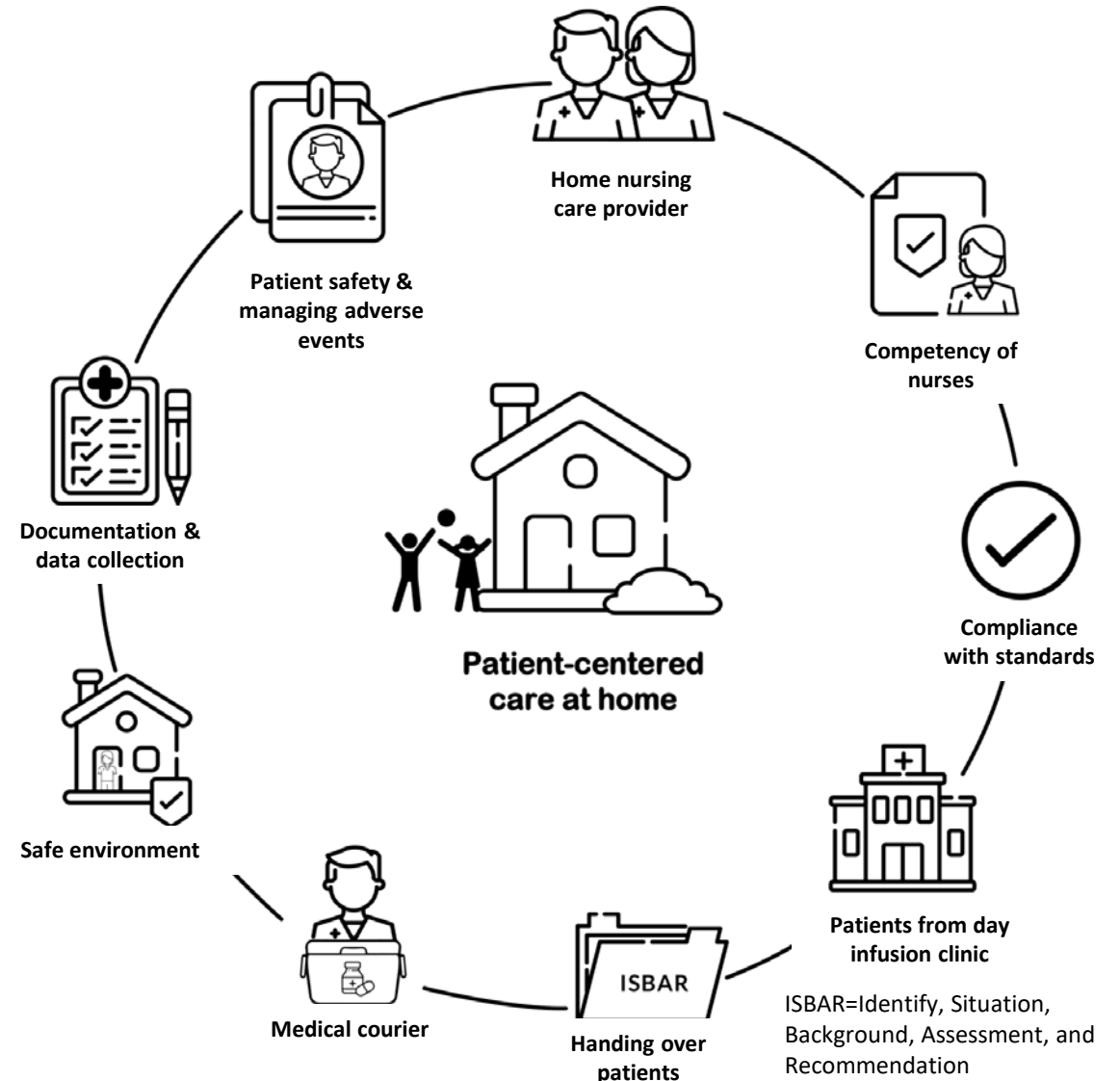
MS Care Continuum



Patient-Centered Care to Guide Home Infusions



- Proposed model of home infusion care
- Implementation can support activities, which enhance patient outcomes including:
 - Appropriate patient selection, patient safety and adverse event management
 - Effective patient education
 - Comprehensive assessment and monitoring
 - Interprofessional communication and collaboration



Managing MS Remains a Challenge



- Providers and payers must effectively manage MS while simultaneously maximizing the value of high-cost treatment options in the face of multiple challenges
 - Significant variation in treatment across practice settings
 - Complex treatment decisions and prolonged treatment duration
 - Limited access to specialized, multidisciplinary care
 - Numerous comorbid conditions
 - Expanding treatment armamentarium including novel DMTs and biosimilars
 - Limited head-to-head and cost-efficacy data
 - Evolving quality performance measures

Using Digital Tools and eHealth Solutions Can Foster Enhanced MS Care Delivery



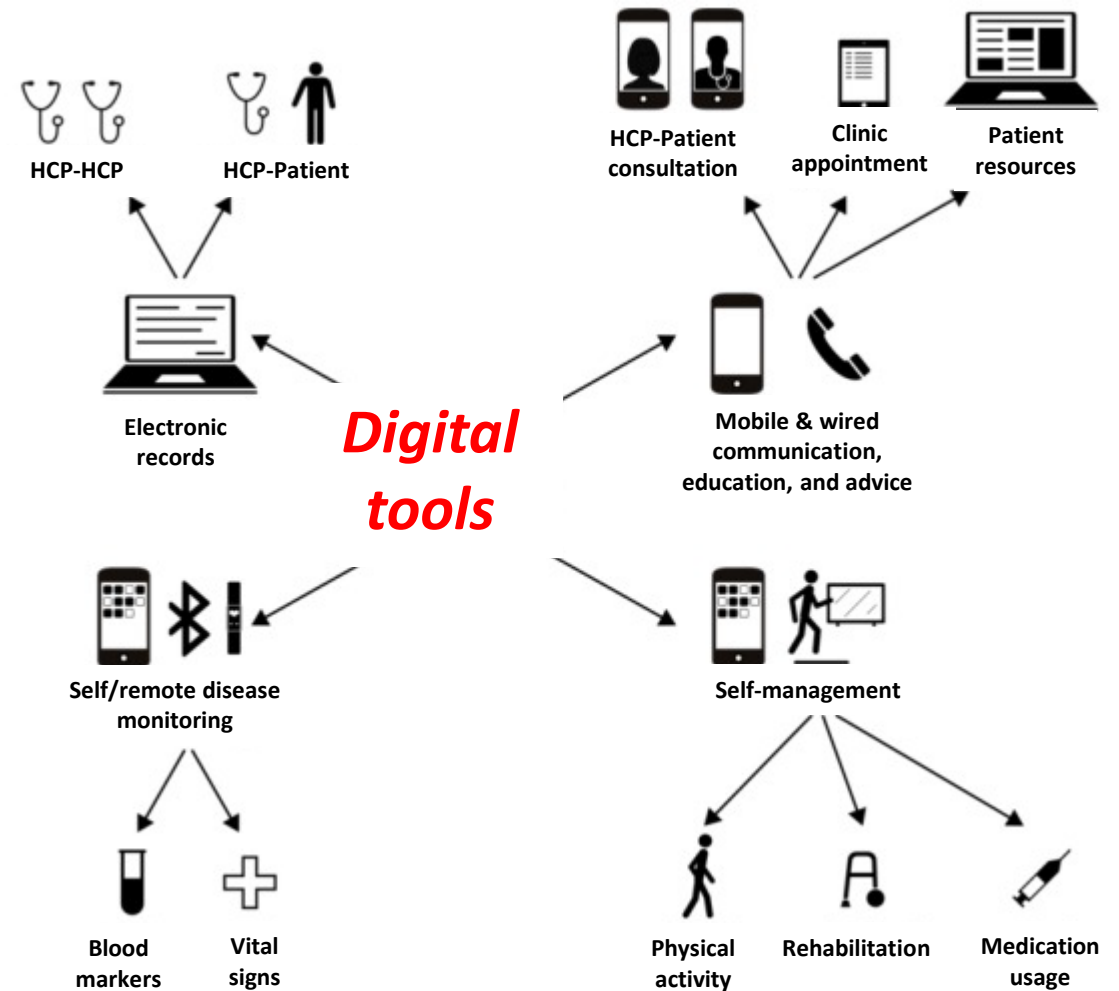
- Digital tools and communication devices are an integral part of everyday life
- Communication and data sharing can enhance face-to-face contact of patient and provider
 - May be especially valuable for long-term treatment of chronic diseases, where successful therapy requires a high level of patient self-management



Advances in Mobile Communication Can Complement Traditional In-Clinic Approaches



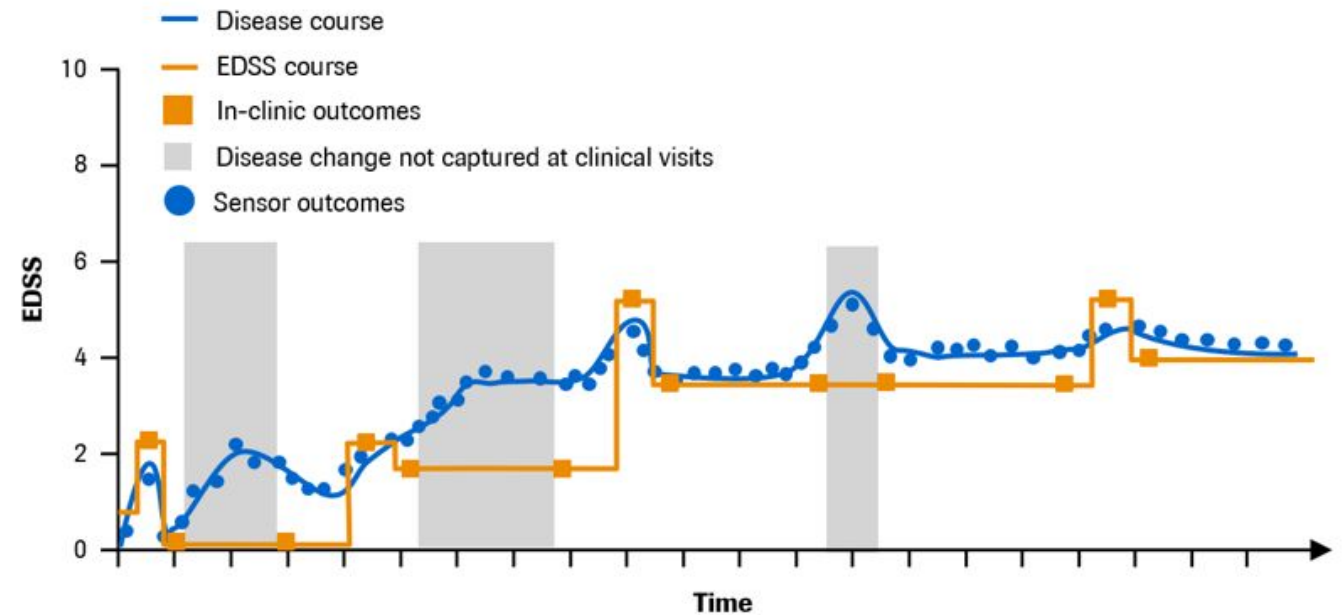
- Benefits for patients include
 - Increased access to care, disease information, and support
 - Monitor/track changes in symptoms, activity, and mood
- Benefits for HCPs include
 - Remote monitoring of symptoms, adverse events, and outcomes
 - More timely intervention vs. face-to-face visits
 - Efficient use of clinic time
 - Supportive of multidisciplinary disease management



eHealth Tools Can Provide Real-Time Monitoring of MS Disease Activity



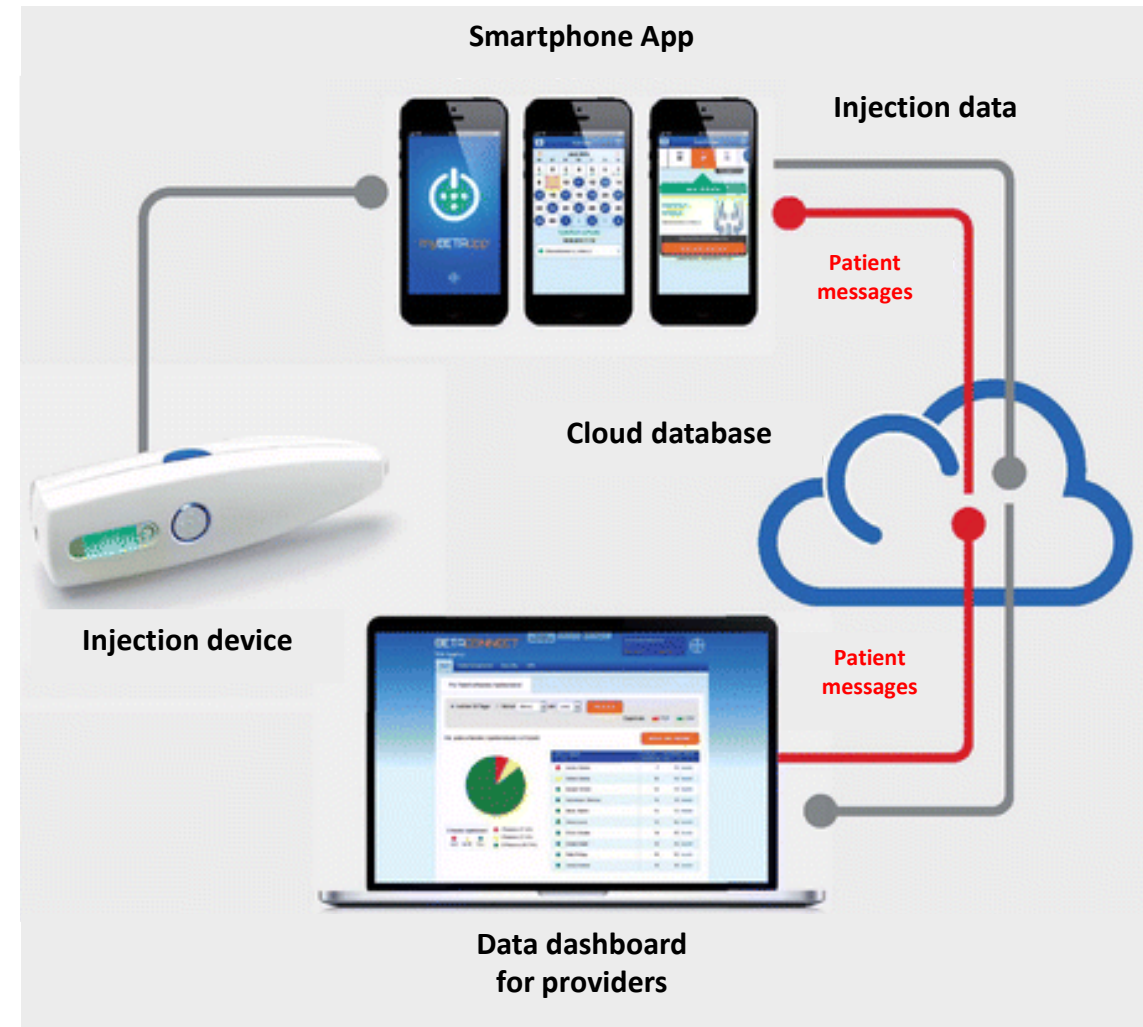
- The EDSS and other tools commonly used in the clinic can detect large changes in functionality
 - However, in-clinic assessment techniques often fail to capture subtle changes in disease course
- Many changes are also missed due to the infrequency of clinic visits
- Digital tools and applications allow continual real-time capture of disease-related changes



eHealth Tools Can Assist in Real-Time Monitoring of Treatment Adherence



- Adherence to long-term treatment in MS can be challenging
- Digital tools can assist in real-time monitoring of adherence
 - Example: combining autoinjector technology with digital monitoring/reporting tools
- Can be used to support patient self-management and facilitate communication between patients and healthcare providers



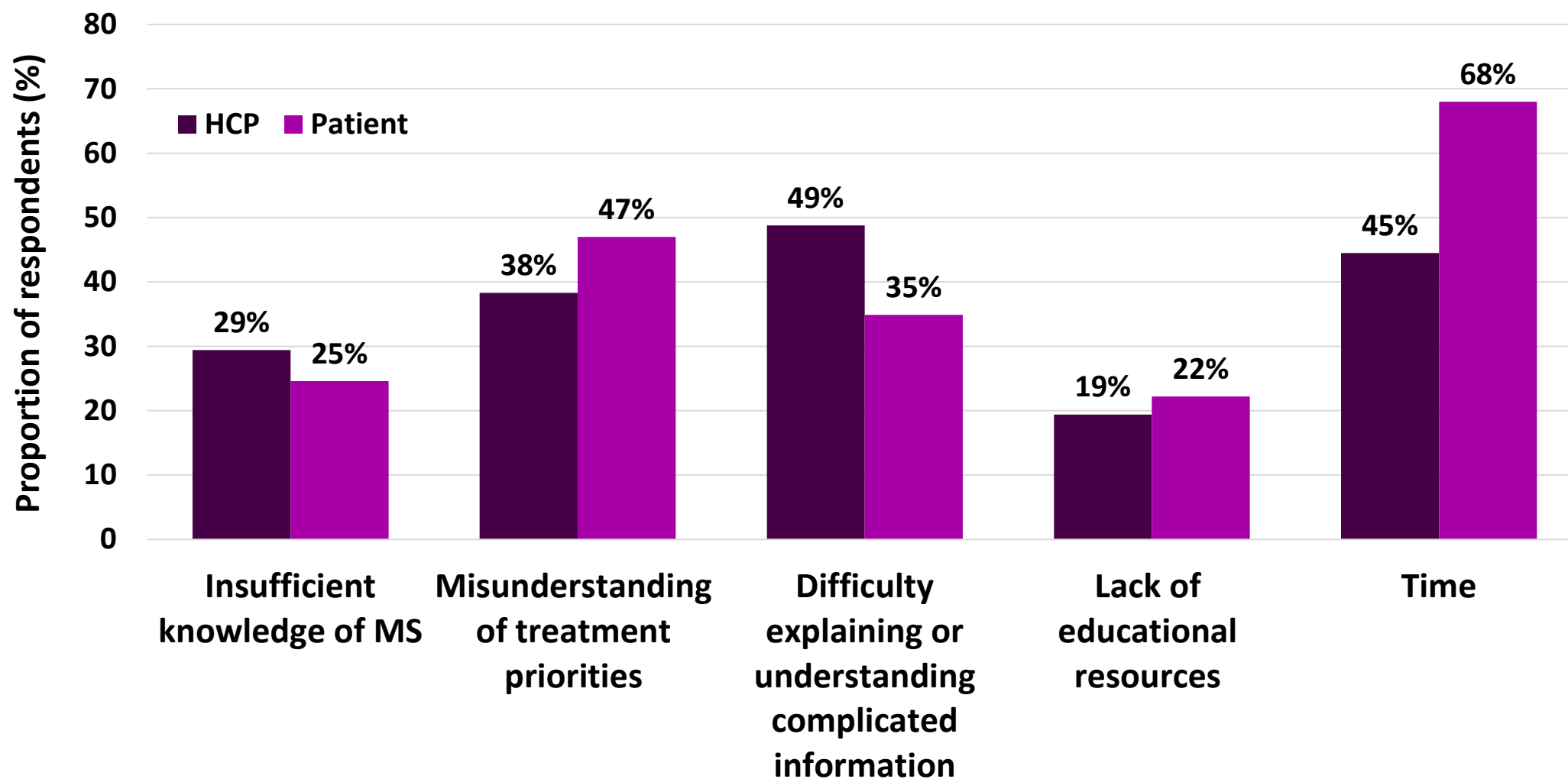
eHealth Tools Can Assist Patients in Gaining Access to Specialty Drugs



- As specialty pharmacy becomes an increasing focus for cost management, digital tools are making it easier for patients to access specialty drugs
- One large national specialty pharmacy developed 2 smart phone apps to facilitate access
 - **Provider-facing:** designed to minimize the prior authorization and onboarding process with the goal of achieving these milestone within three days
 - **Patient-facing:** allows patients to select where and how they want to receive their specialty drugs—at the pharmacy or through mail order
 - The app also allows the specialty pharmacy to keep patients up to date on required insurance information and financial supports



Barriers to Effectiveness of eHealth Solutions



Use of Care Pathways Can Be An Effective Approach to Lowering Barriers to Appropriate MS Care



- Enhance multidisciplinary collaboration
- Reinforce patient-centered care
- Incorporate local and national guidelines into routine clinical practice
- Support alignment with evidence-based standards of care
- Reduce unnecessary variation in patient care
- Optimize management of health care resources



Successful Pathway Implementation Depends on Evidence-Based Care





Specialty Pharmacy's Role in Care Pathways

Role	Activities
Medication therapy management	<ul style="list-style-type: none">• Medication selection and review
Medication assistance	<ul style="list-style-type: none">• Assist in obtaining medication during transitions of care
Education	<ul style="list-style-type: none">• Family and patient on medication efficacy, safety, and expected outcomes• Providers and health care staff on medication place in therapy, duplications, optimal timing, drug interactions; assist in creation of educational materials
Revise and establish policies and protocols	<ul style="list-style-type: none">• Review current policies in place and recommend amendment based upon changes in evidence-based medicine or to reflect clinical pathway management
Research and evaluate outcomes	<ul style="list-style-type: none">• Complete medication use evaluations; create reports and present to leadership

What barrier to appropriate MS care has the highest potential for improvement from the use of Care Pathways?



- a) Enhance multidisciplinary collaboration
- b) Incorporate local and national guidelines into routine clinical practice
- c) Reduce unnecessary variation in patient care
- d) Reinforce patient-centered care
- e) Optimize management of health care resources
- f) Support alignment with evidence-based standards of care
- g) Other

Care Pathways Can Be Used to Enhance MS Management



- Increase awareness of MS among patients, primary care providers and neurologists



Pre-Diagnosis

- Promote use of screening tools to identify early symptoms and ensure timely referral and diagnosis
- Develop referral pathways



Referral & Diagnosis

- Perform regular monitoring of disease activity and patient progress
- Manage comorbidities
- Document outcome



Treatment Initiation & Management

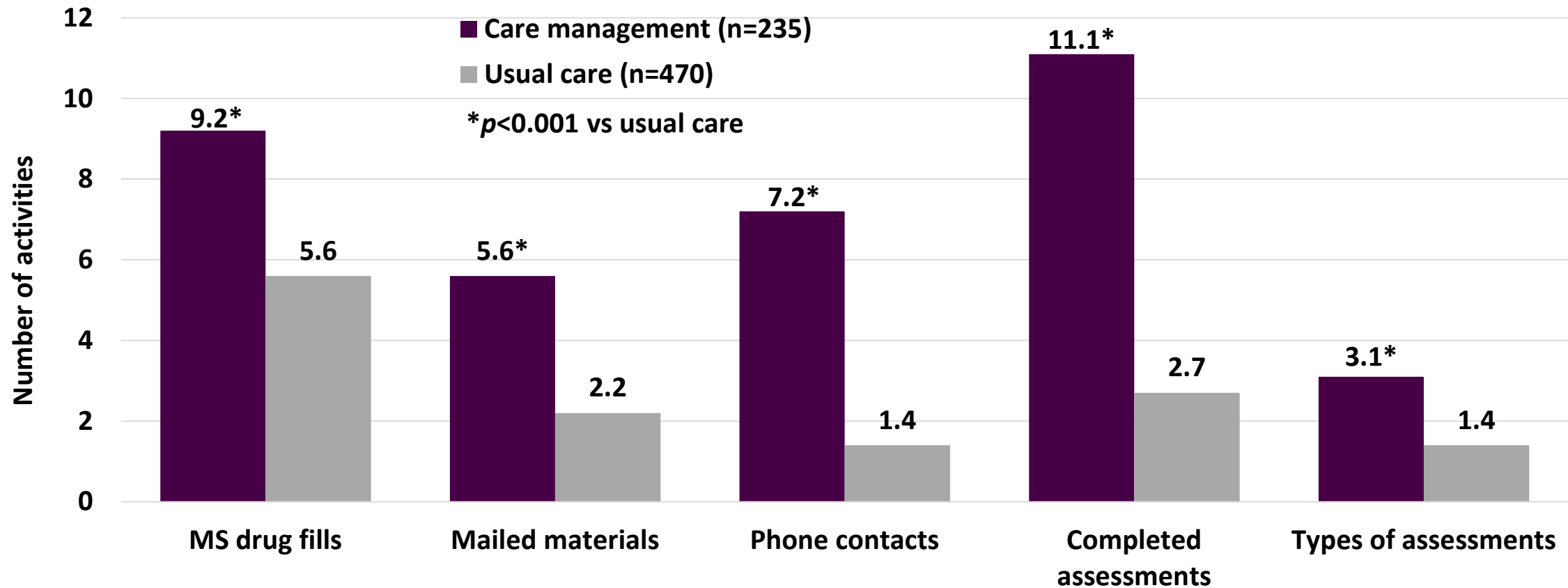


Follow Up

- Promote collaboration between the multidisciplinary care team to provide comprehensive care

- Provide evidence-based care
- Optimize treatment based on response to therapy
- Engage patients in their care

Comprehensive Care Pathways Increased Delivery of Appropriate MS Care

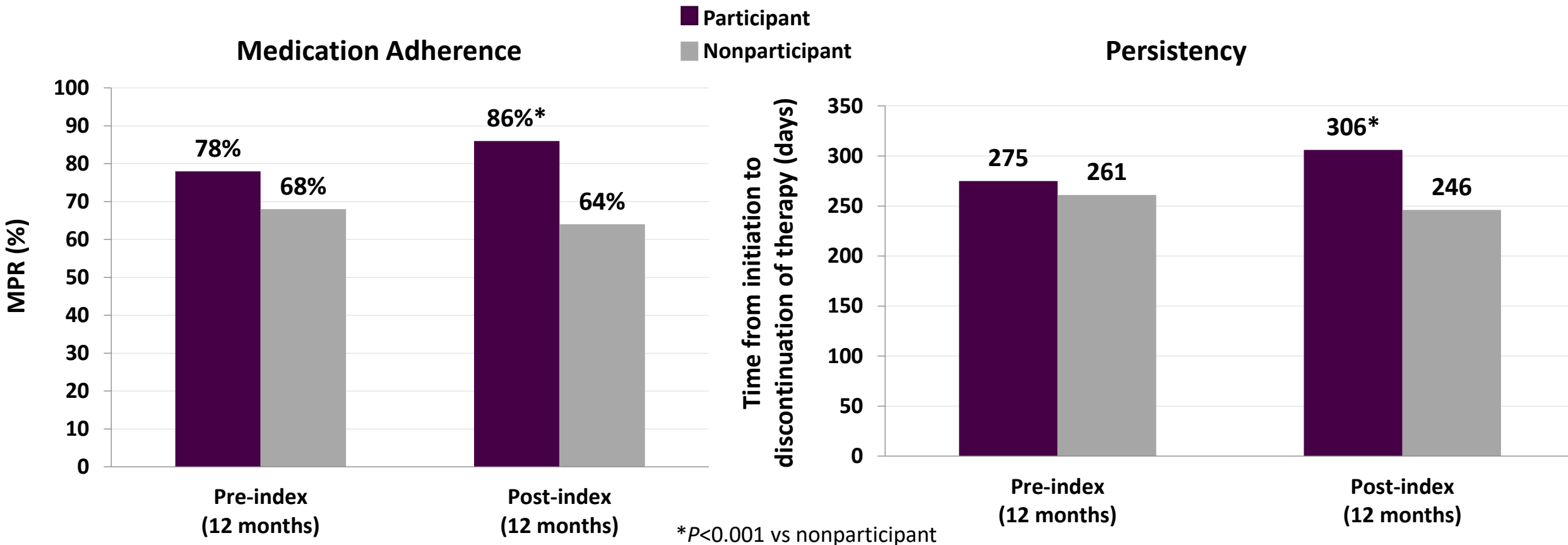


Data source: Walgreens Connected Care MS Treatment Management Program

Intervention: Patients received services beyond standard medication fulfillment, including individualized therapy management; education about disease progression, dosing and administration, and managing adverse effects; adherence support and assistance; recommendations regarding supportive care; and advice about overall health and wellness.

Outcomes assessed: Clinical services received and adherence at 12 months

Care Pathways Improved Adherence and Persistence



Data source: Retrospective claims analysis of MS patients ≥ 18 years ($n=3993$) from the HealthCore Integrated Research Database (January 2004-April 2008)

Intervention: Regular phone calls by nurses to provide a liaison to the pharmacy, medical information, adherence support, AE management, and refill reminders

Outcomes assessed: Adherence and persistence; MS-related hospitalization; total MS-related cost of care during the 12 months post-index period

Results of a 12 Month Disease Management Program in Patients with MS



	Before (mean)	After (mean)	Change (mean)	<i>P value</i>
MS medication adherence	0.85	0.87	0.025	0.010
MS relapse	0.45	0.25	-0.20	0.110
mEDSS scores	3.76	3.77	0.08	0.190
MS-related outpatient visit	2.93	2.66	-0.28	0.276
MS-related hospitalization	0.04	0.02	-0.02	0.304

Retrospective analysis using prescription drug claims, medical claims, and electronic medical record information (2013-2015) 1 year before and after enrollment in the disease management program for members (n=377) with 24 months of continuous health plan coverage.

- Disease management program staffed by clinical pharmacists trained in MS management
- Potential benefits of the program were diminished by high adherence at baseline
- Increased adherence drives subsequent increases in health plan paid amount on MS medications

Use of Multiple Modalities to Assess Adherence in Patients with MS



- Adherence in MS is usually measured using a single measure –typically electronic pharmacy records
- However, the level of medication adherence can depend on how it is measured
- A study of patients with MS suggested use of PROs in addition to the MPR provides a more comprehensive view of adherence
- Based on these findings, adherence should be assessed repeatedly and addressed during clinical encounters with patients

Adherence Across Time as Assessed by the Medication Possession Ratio and Patient-Reported Outcomes

Measure	% of Patients Adherent at 6 Months	% of Patients Adherent at 12 Months
MPR	81	82
PRO 1*	96	94
PRO 2 [†]	72	70

Patients with MS (n=194) were surveyed *prospectively* at baseline, 6 and 12 months later and their health records and medication claims were *retrospectively* obtained.

*PRO 1=Multiple Sclerosis Treatment Adherence Questionnaire (MS-TAQ)

[†]PRO 2=Probabilistic Medication Adherence Scale (ProMas)

Factors Associated with Suboptimal Adherence to DMTs



- Assessment of adherence to MS DMTs in a cross-sectional cohort of MS patients receiving care at VA medical centers (n=2,939; 79.7% male)
- Less than 70% of patients with MS refilled their medications at least 80% of the time over two years
- Missed appointments, mood disorders, and traumatic brain injuries are among the risk factors for poor adherence
- There is an urgent need for interventions aimed at person-level barriers
- DMT adherence should be discussed at every visit, whether it is MS-related or not in order to improve self-management abilities

Summary



- Management of MS can be complex and requires lifelong care, ideally delivered by a coordinated multidisciplinary team
- Coverage decision makers are challenged to find a balance between effectively managing the disease and maximizing the value of high-cost DMTs
- Treatment of MS should be individualized, and shared decision making between patients and healthcare providers is critical for successful management
- Care management via the use of care pathways, digital tools, and other techniques is associated with greater adherence, decreased risk for disease relapse, and lower cost of care



Shared Decision Making: Aligning MS Specialty Care with Patient Needs

Alexis Crispino

Director of Education & Healthcare Relations
Multiple Sclerosis Association of America (MSAA)

Learning Objective



- Discuss strategies to align treatment decision making with patient preferences and therapeutic goals

Patient Case 1



- **Patient:** 40-year-old female diagnosed with MS 7 years ago after experiencing numbness in her legs
 - MRI revealed characteristic brain lesions of demyelinating disease
- **Current treatment:** DMT; struggles with adherence
- **Social history:** single mother of 2 boys
- **Current complaint:** MS now affects every aspect of her life and she worries she may no longer be able to work and support her kids

Discussion



- What are your biggest concerns with this patient?
- What steps would you take to help improve the overall care of this patient?
- Where can this patient find the support needed to develop additional self-management skills?

Primary Challenges for People Living with MS



- **Chronicity:** most individuals will live with MS for decades
- **Unpredictability:** each individual experience with MS will be unique, but all will be uncertain
- **Change:** MS will require all individuals and their caregivers to make unanticipated changes to their lives to accommodate the disease
- **Expense:** appropriate management of the disease, its symptoms, and related comorbidities will have large direct and indirect costs

Patient Case 2



- **Patient:** 35-year old male seen in the Neurology Clinic
- **Diagnosis:** Laboratory and imaging studies confirm a diagnosis of multiple sclerosis
- **Family history:** Mother died following a diagnosis of breast cancer; father had an MI at 59
- **Comorbidities:** Diabetes (controlled on medication)
- **Current complaints:** Stumbling gait, diminishing visual acuity, tremors, fatigue, tendency to aspirate liquids and solids, continuous tinnitus, decreased finger dexterity, bilateral weakness of the hands, impaired short-term memory, irritability

Discussion



- What are your biggest concerns with this patient?
- What steps would you take to help improve the overall care of this patient?
- Where can this patient find the support needed to develop additional self-management skills?

Foundational Elements of Successful MS Management



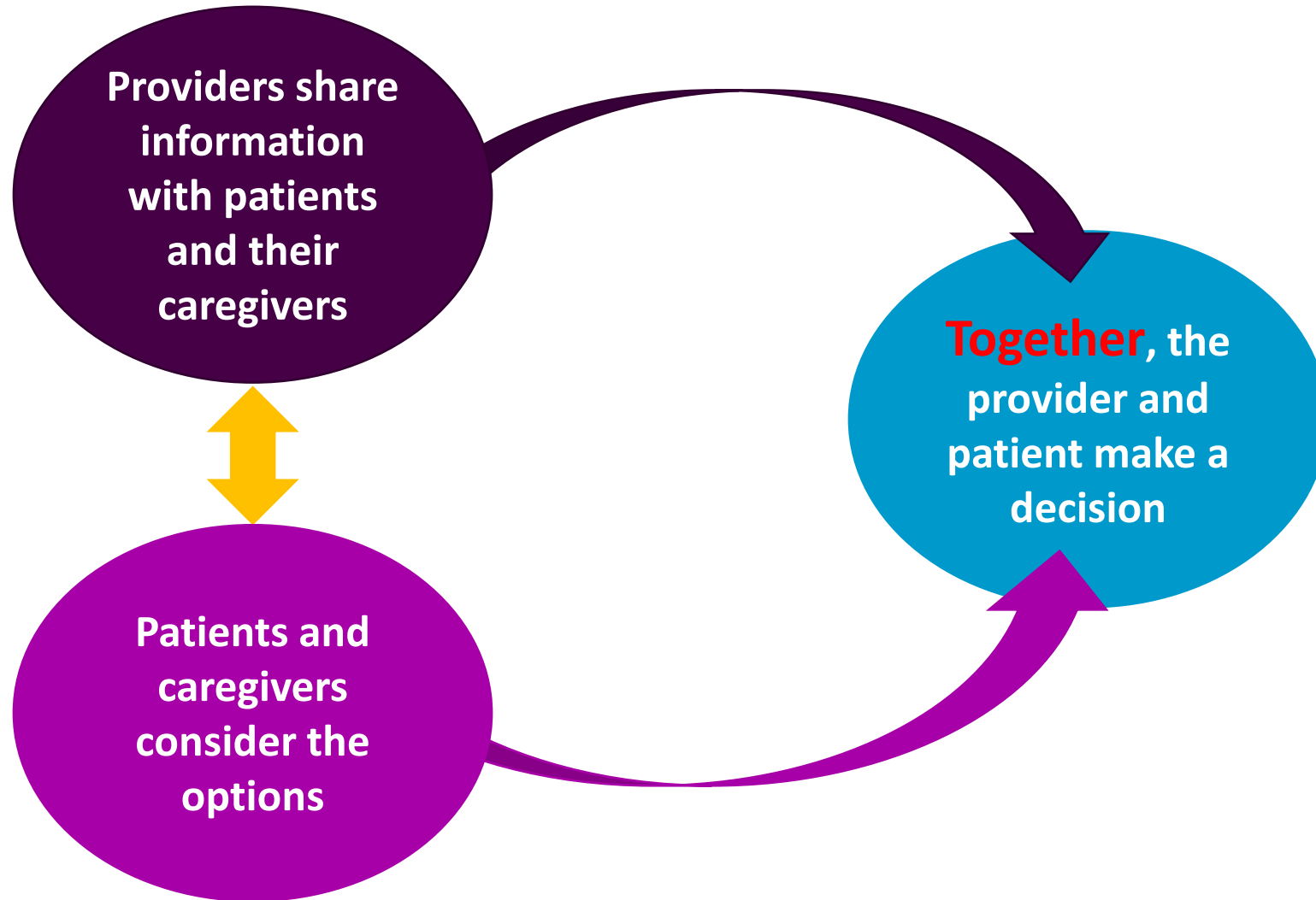
Providers

- Must...
 - Foster ongoing interactive relationships between patients and the medical care team
 - Strive for integration of therapeutics to obtain and maintain disease control, symptom management, and psychological well-being

Patients

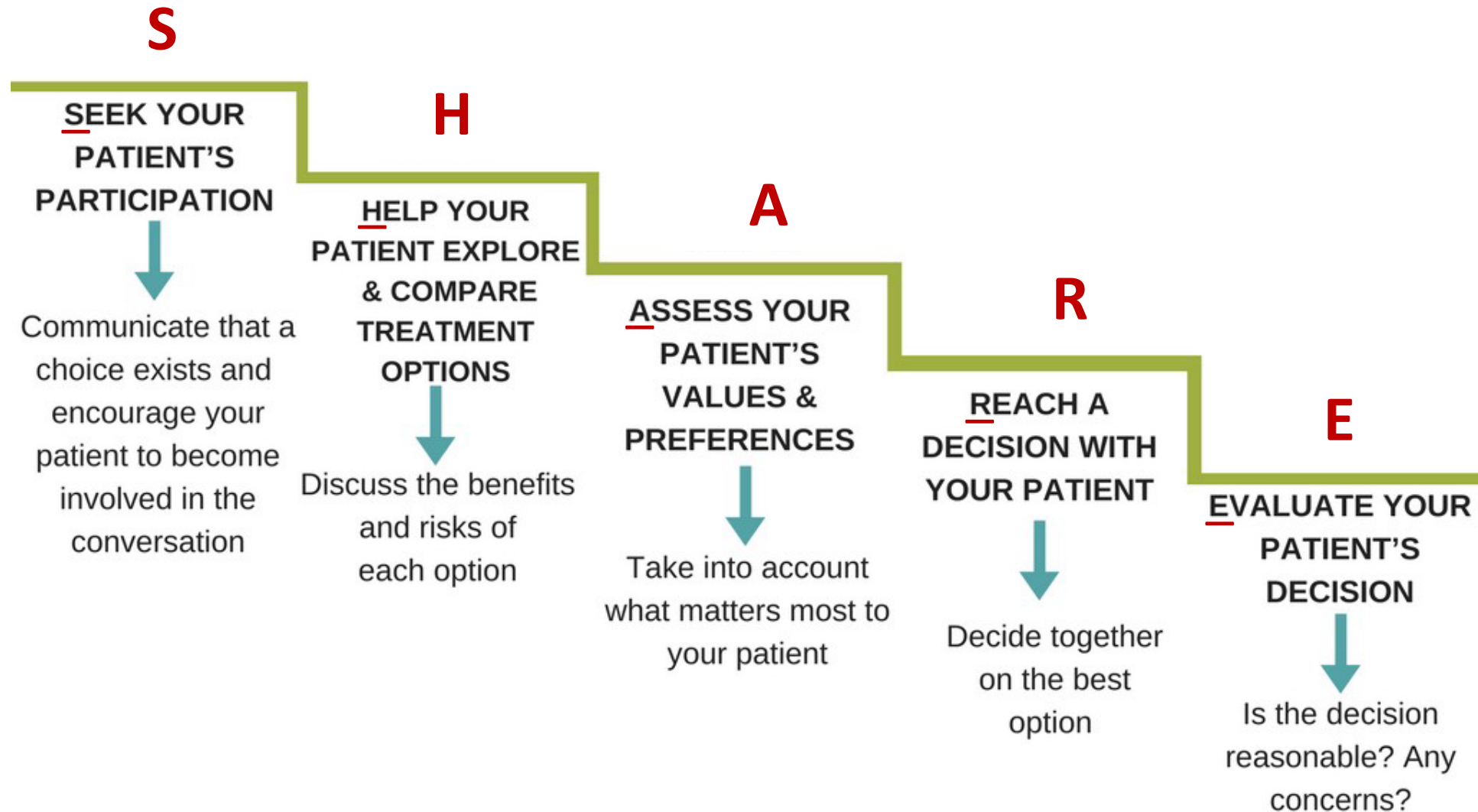
- Must...
 - Be willing and ready to begin therapy
 - Believe therapy can make a difference
 - Willing to make a commitment to be adherent
 - Educated regarding the disease and its treatment

Shared Decision Making





Steps Involved in Shared Decision Making



When is Shared Decision Making Most Useful?



**When more than one
safe and effective
treatment option is
available**



**To identify and
accommodate
patient preference**



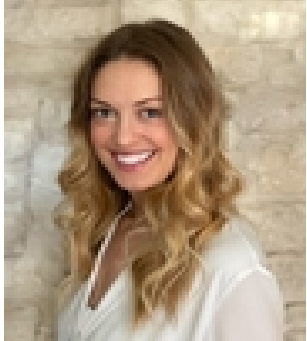
**When there is little
evidence to favor
one choice over
another**

Summary



- Management of MS can be complex and requires lifelong care
- Treatment of MS should be individualized, and shared decision making between patients and healthcare providers is critical for successful management

Faculty Idea Exchange and Q&A Session



Alexis Crispino

Director of Education & Healthcare
Relations
MSAA



Mitzi Joi Williams, MD

Founding Director
Joi Life Wellness Group
Assistant Professor of
Neurology
Emory University



Michael Zeglinski, RPh

SVP & CEO
Optum Specialty &
Infusion Pharmacies



How to Claim Credit

Option 1: Complete the online post-survey and evaluation form immediately following the live webcast. The link to the survey will appear on your screen at the conclusion of the webcast. If you are unable to fill out the evaluation immediately following the webcast, please note that a personalized evaluation link will be emailed to you following the webcast at the account you registered with. Once you fill out your evaluation, your certificate will be emailed to you.

For Pharmacists, in order to submit your credit to the CPE Monitor:

Please go to www.impactedu.net/cpe

Enter code: **0701**

You will then need to log in or create an account ensuring your NABP information is entered and correct. Be sure to enter today's date, **July 1, 2020**, as the date of participation. You will be immediately notified if your submission has been accepted or if there are any issues. Once accepted, the record of your participation will appear in the CPE Monitor within 48 hours. **Credit must be uploaded to CPE Monitor within 30 days.**

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Multiple Sclerosis Update

CLINICAL, ECONOMIC, AND
PATIENT-CENTRIC STRATEGIES FOR
SPECIALTY PHARMACY PROFESSIONALS

Jointly provided by



This activity is supported by an independent educational grant from Sanofi Genzyme and Bristol-Myers Squibb.

Live Webcast

Wednesday, July 1, 2020

12:00pm – 1:30pm ET