Multiple Sclerosis Update

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

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SPECIALTY PHARMACY 2020 summit

Welcome

Michael Zeglinski, RPh

SVP & CEO

Optum Specialty & Infusion Pharmacies

Agenda

11:30-11:35 AM	Opening Comments/Overview **Michael Zeglinski, RPh**
11:35 AM-12:05 PM	*Assessing the Clinical Benefits of Current and Emerging MS Therapies in a Specialty Pharmacy Setting* **Mitzi Joi Williams, MD**
12:05-12:30 PM	*Special Pharmacy Management Services for Optimal Outcomes in MS* **Michael Zeglinski, RPh**
12:30-12:45 PM	*Shared Decision-Making: Aligning MS Specialty Pharmacy Care with Patient Needs* **Alexis Crispino**
12:45-12:55 PM	Audience Question & Answer Session Faculty Panel
12:55-1:00 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

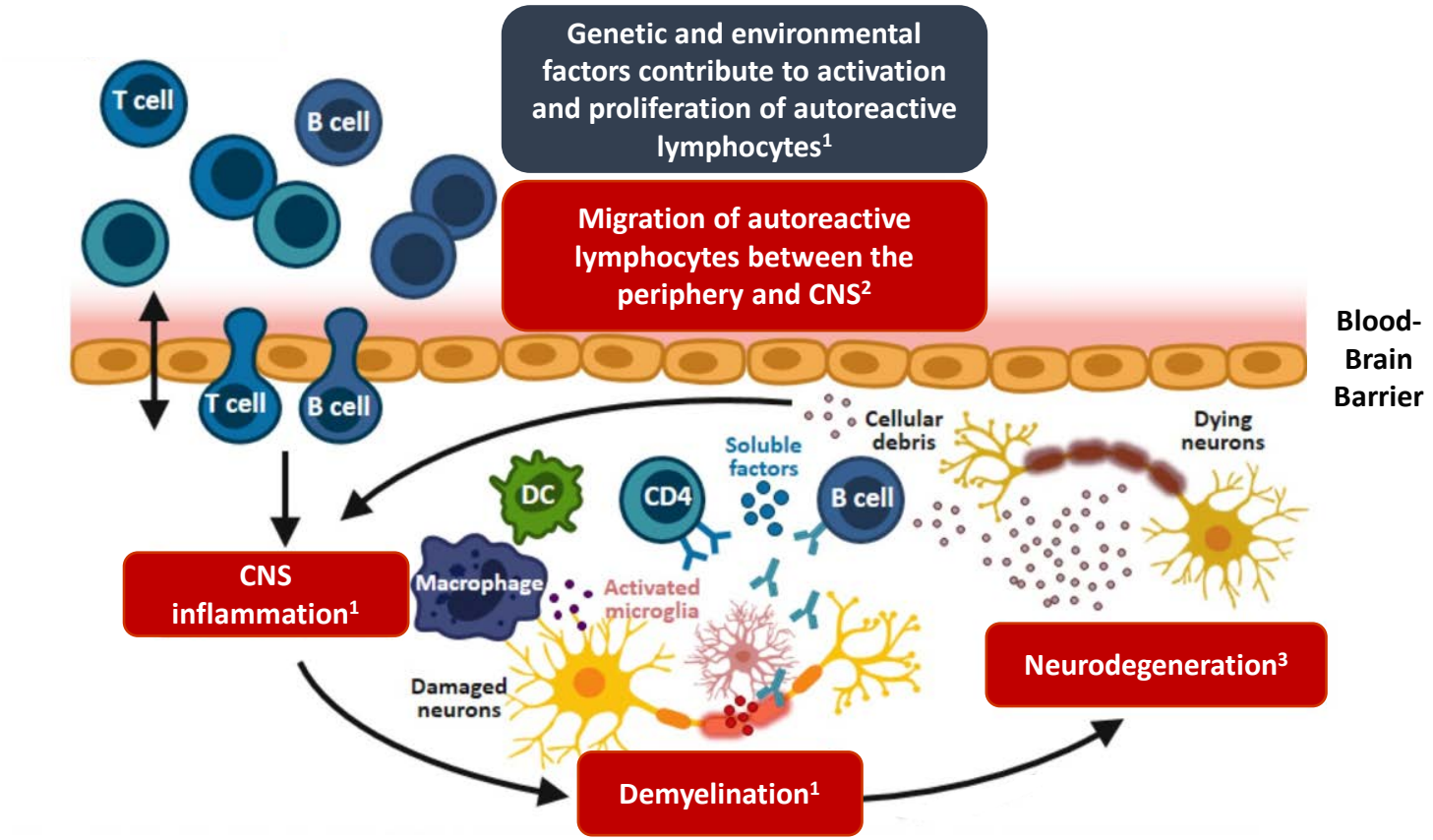
Mitzi Joi Williams, MD
Founder and CEO
Joi Life Wellness Group, LLC

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

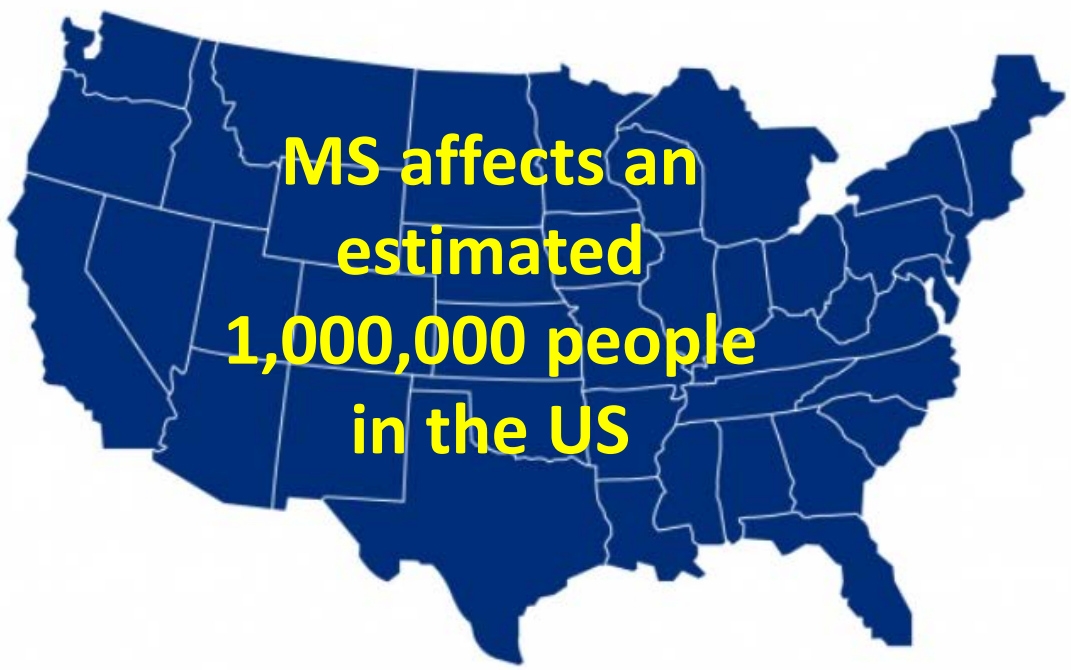
What is Multiple Sclerosis?

- 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



1. Sospedra M, Martin R. *Annu Rev Immunol*. 2005;23:683-747; 2. Larochelle C, Alvarez JI, Prat A. *FEBS Lett*. 2011;585(23):3770-80; 3. Wu GF, Alvarez E. *Neurol Clin*. 2011;29(2):257-78.

MS Epidemiology

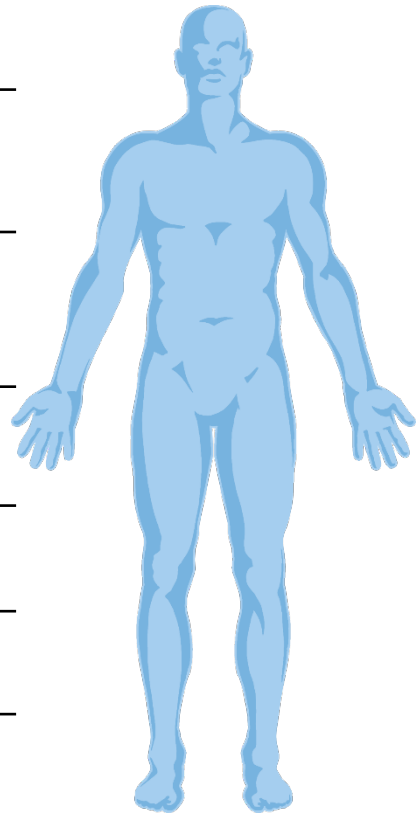


- MS is the most common cause of neurologic disability in the 18- to 60-year-old population
- More prevalent in females
- Peak incidence occurs between 20 and 40 years old
- Annual cost in the US estimated to be $6.8 to $11.9 billion

Calabresi PA, Newsome SD. Multiple sclerosis. In: Weiner WJ et al. *Neurology for the Non-Neurologist*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2010:192-221; Ascherio A. *Expert Rev Neurother*. 2013;13(12 Suppl):3-9; Whetten-goldstein K, Sloan FA, Goldstein LB, Kulas ED. *Mult Scler*. 1998;4(5):419-25; Wallin MT, Culpepper WJ, Campbell JD, et al. *Neurology*. 2019;92(10):e1029-e1040 .

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

Physical Symptoms[1-5]



- Vertigo
- Heat sensitivity
- Bowel & bladder dysfunction
- Pain
- Numbness & tingling
- Impaired gait
- Visual disturbances
- Headache
- Lhermitte's sign (electrical shocks down the spine)
- Weakness
- Spasticity
- Poor balance & coordination

Nonphysical Symptoms

- Cognitive impairment[1]
- Depression and mood/emotional changes[2]
- Pseudobulbar affect[6]

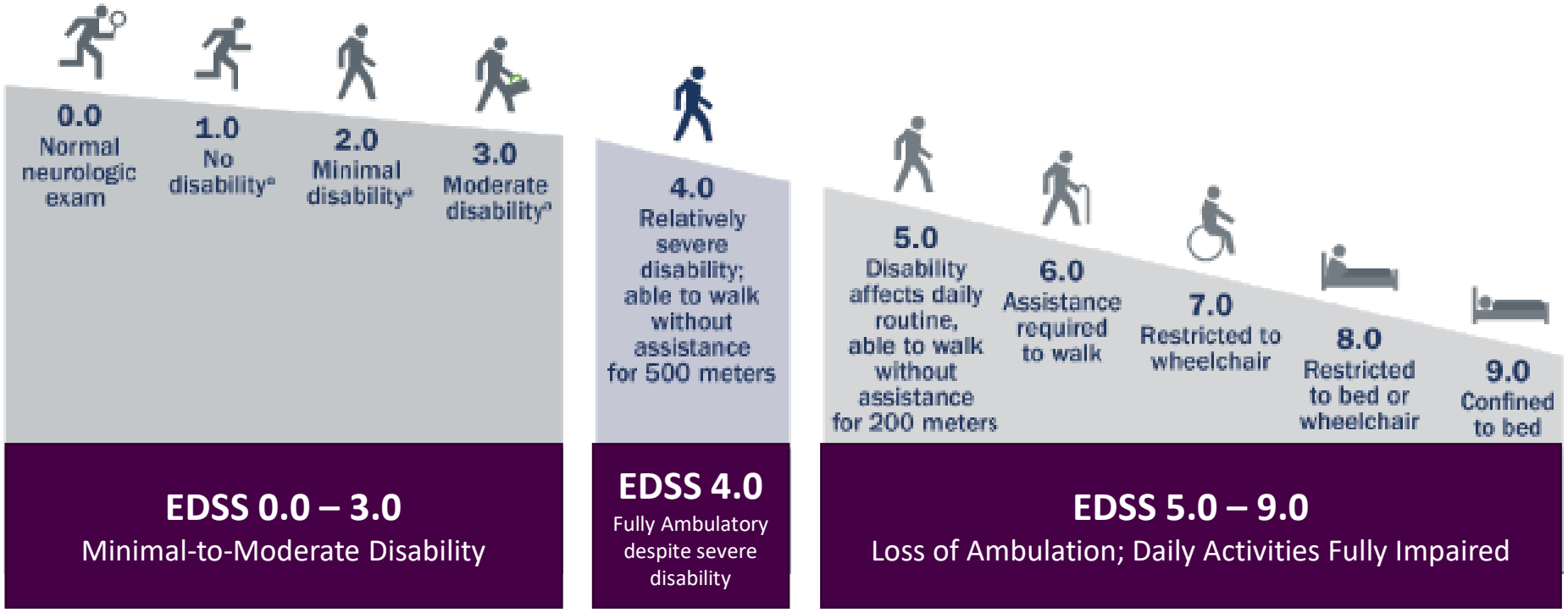
1. Compston A, Coles A. *Lancet*. 2008;372(9648):1502-17; 2. Calabresi PA. *Am Fam Physician*. 2004;70(10):1935-44; 3. Gelfand JM. *Handb Clin Neurol*. 2014;122:269-90; 4. Olek MJ. *Current Clinical Neurology: Multiple Sclerosis*. Totowa, NJ: Humana Press Inc; 2005:15-53; 5. Milo R, Miller A. *Autoimmun 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

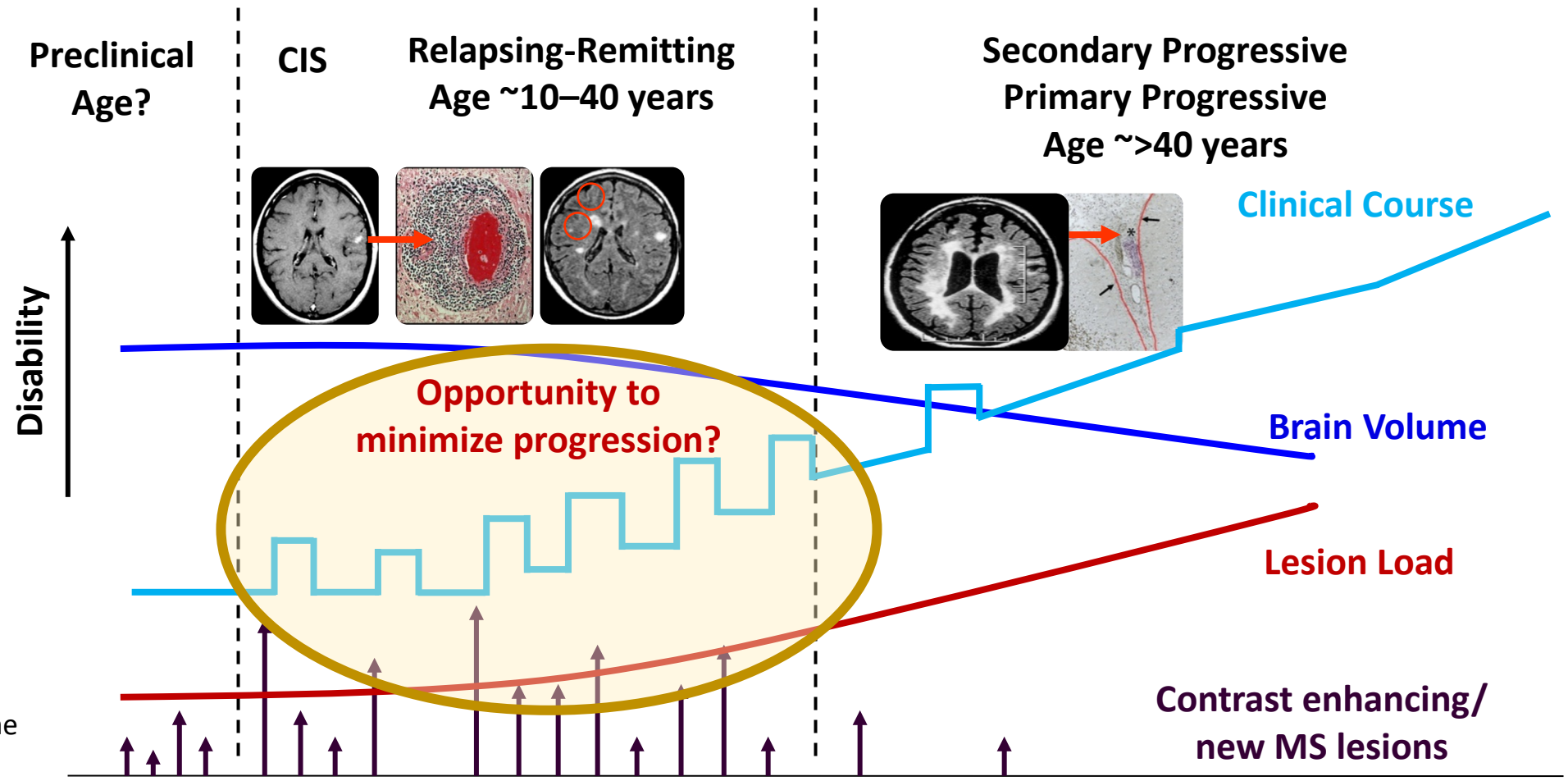
Disability Progression Based on the Extended Disability Status Scale (EDSS)

Disability Progression Based on the EDSS[1,2]



1. Renoux C. *Neurol Clin.* 2011;29(2):293-308. 2. Kurtzke JF. *Neurology*. 1983;33(11):1444-52 .

MS Disease Course



CIS: clinically isolated syndrome

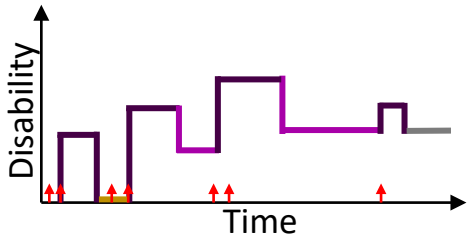
Hersh CM, Fox RJ. Multiple Sclerosis. Cleveland Clinic Medical School. TeachMeMedicine.org. https://teachmemedicine.org/cleveland-clinic-multiple-sclerosis. Published: June 2014. Accessed March 2020.

MS Disease Subtypes

Radiologically or Clinically Isolated Syndrome (RIS/CIS)

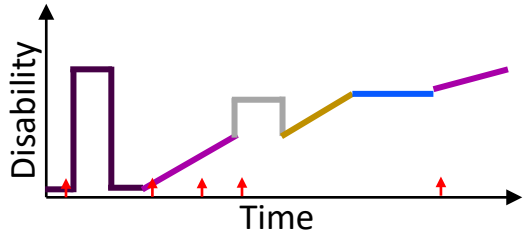
First episode of neurologic symptoms; must last for ≥24 hours; may not evolve into MS

Relapsing-Remitting (RRMS)



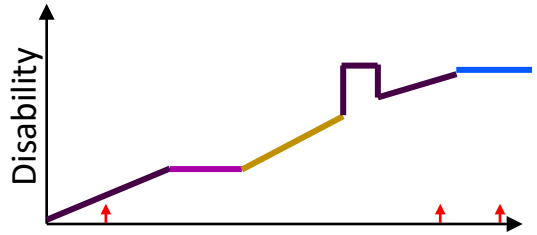
- Relapse
- Active without worsening
- Worsening (incomplete recovery from relapse)
- Stable without activity
- New MRI activity

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

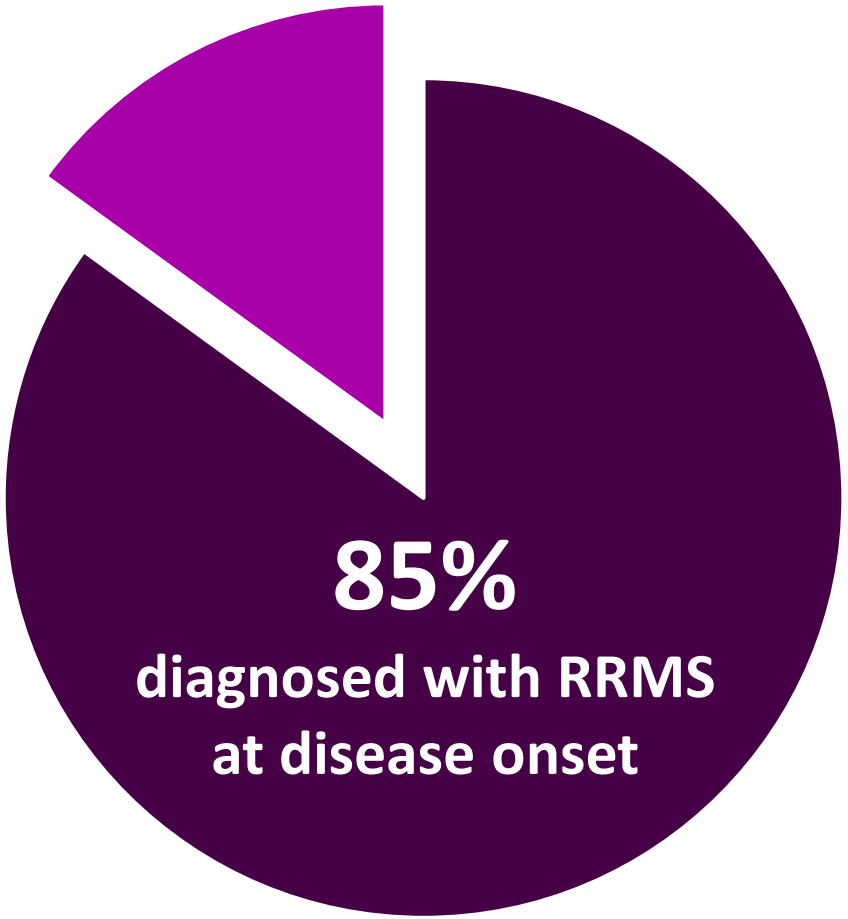
Primary Progressive (PPMS)

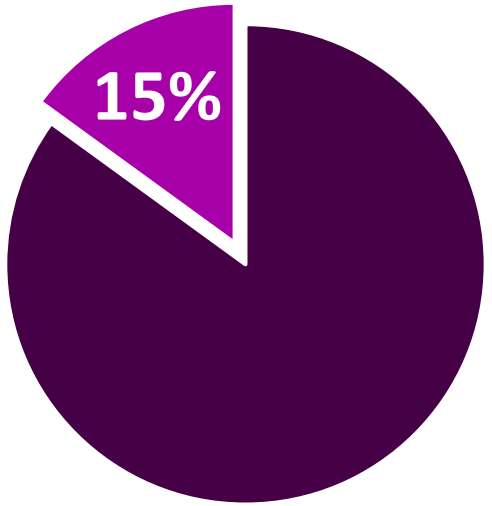


- Active (relapse or new MRI activity) with progression
- Not active without progression (stable)
- Not active with progression
- Active without progression
- New MRI activity

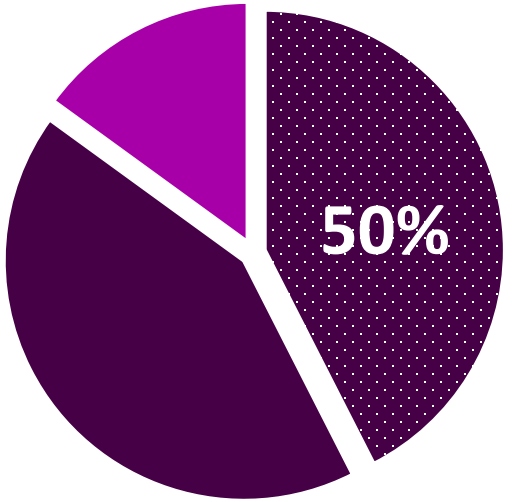
Types of MS. National Multiple Sclerosis Society. www.nationalmssociety.org/What-is-MS/Types-of-MS. Accessed March 2020;
Lublin FD, Reingold SC, Cohen JA, et al. *Neurology*. 2014;83(3):278-86

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

Types of MS. National Multiple Sclerosis Society. www.nationalmssociety.org/What-is-MS/Types-of-MS. Accessed March 2020;
Lublin FD, Reingold SC, Cohen JA, et al. *Neurology*. 2014;83(3):278-86.

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)

Polman CH, Reingold SC, Banwell B, et al. *Ann Neurol*. 2011;69(2):292-302; Polman CH, Reingold SC, Edan G, et al. *Ann Neurol*. 2005;58(6):840-6.

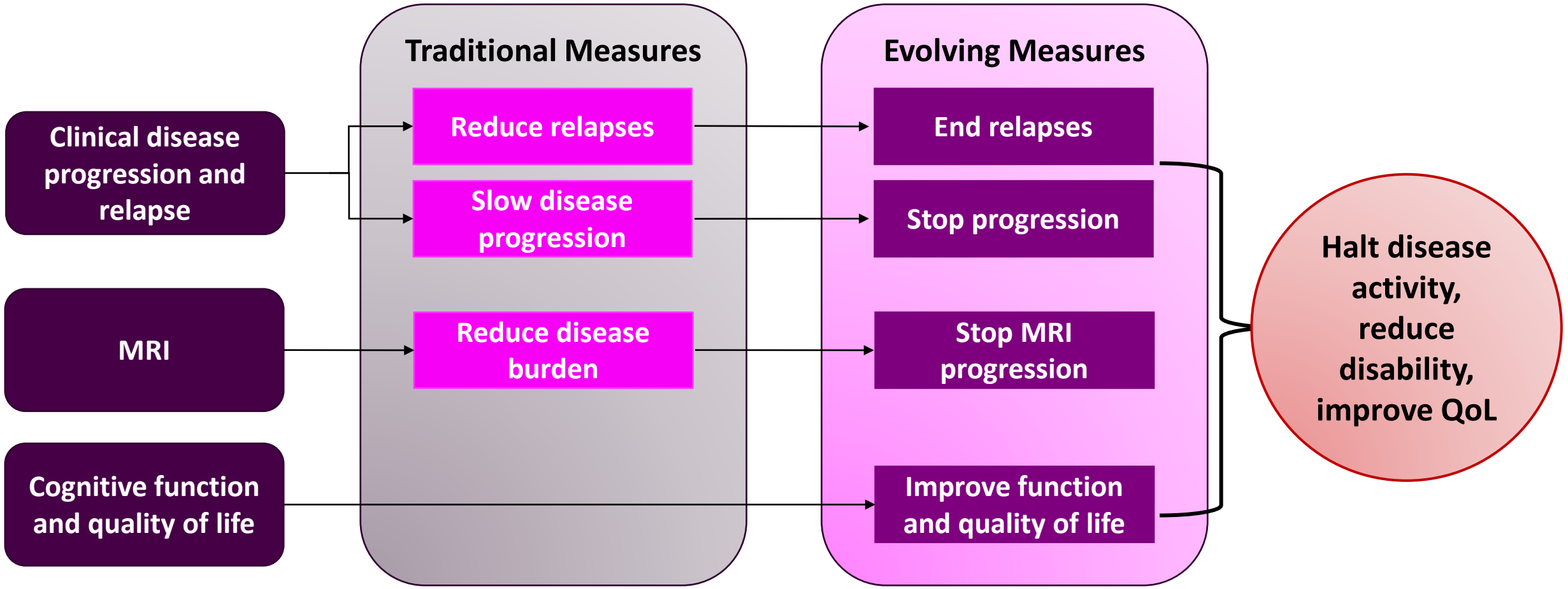
Predictors of MS Disability

Clinical[1]	Imaging[2,3]	Patient[4,5]

• Longer disease duration
• Higher relapse rate
• More frequent early relapses
• Poor recovery from relapses
	• Spinal cord lesions
	• Diffuse abnormalities in the spinal cord
	• Cortical lesions and atrophy
		• 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

1.Jokubaitis VG, Spelman T, Kalincik T, et al. *Ann Neurol*. 2016;80(1):89-100; 2. Kearney H, Miszkiel KA, Yiannakas MC, Altmann DR, Ciccarelli O, Miller DH. *Mult Scler*. 2016;22(7):910-20; 3. Scalfari A, Romualdi C, Nicholas RS, et al. *Neurology*. 2018;90(24):e2107-e2118; 4. Ventura RE, Antezana AO, Bacon T, Kister I. *Mult Scler*. 2017;23(11):1554-1557; 5. Jokubaitis VG, Spelman T, Kalincik T, et al. *Ann Neurol*. 2016;80(1):89-100.

Treatment Goals in MS



Smith AL, et al. *Neurotherapeutics*. 2017;14:952-960; Rotstein DL, Healy BC, Malik MT, Chitnis T, Weiner HL. *JAMA Neurol*. 2015;72(2):152-8; Lazibat I, Šamija RK, Rotim K. *Acta Clin Croat*. 2016;55(1):125-33.

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					✓

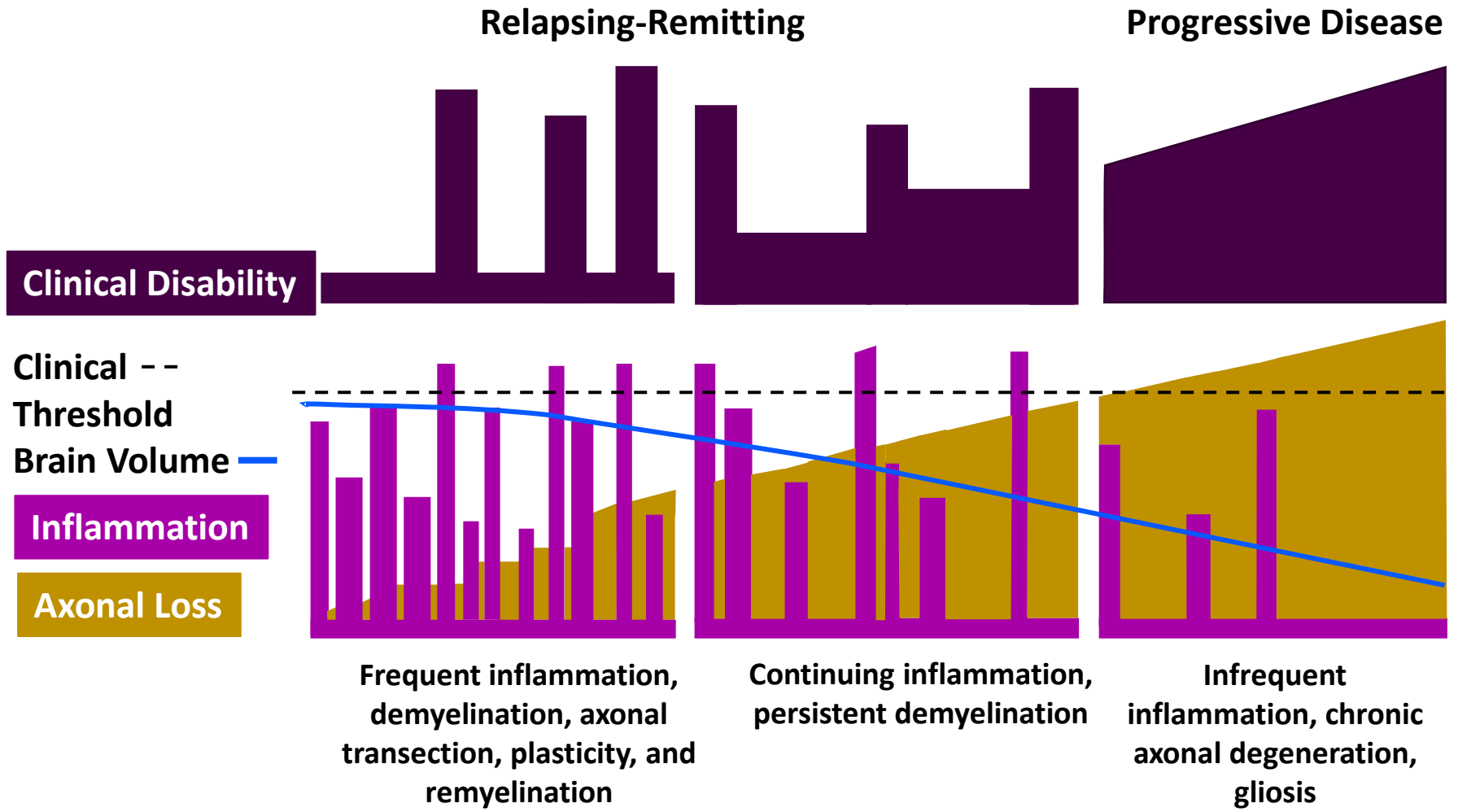
EDSS=extended disability status scale; T25-FW=timed 25-foot walk test; 9-HPT=9-hole peg test; SDMT=symbol digit modalities test; MRI=magnetic resonance imaging

Van munster CE, Uitdehaag BM. *CNS Drugs*. 2017;31(3):217-236.

Importance of Early Treatment

Guiding Principles

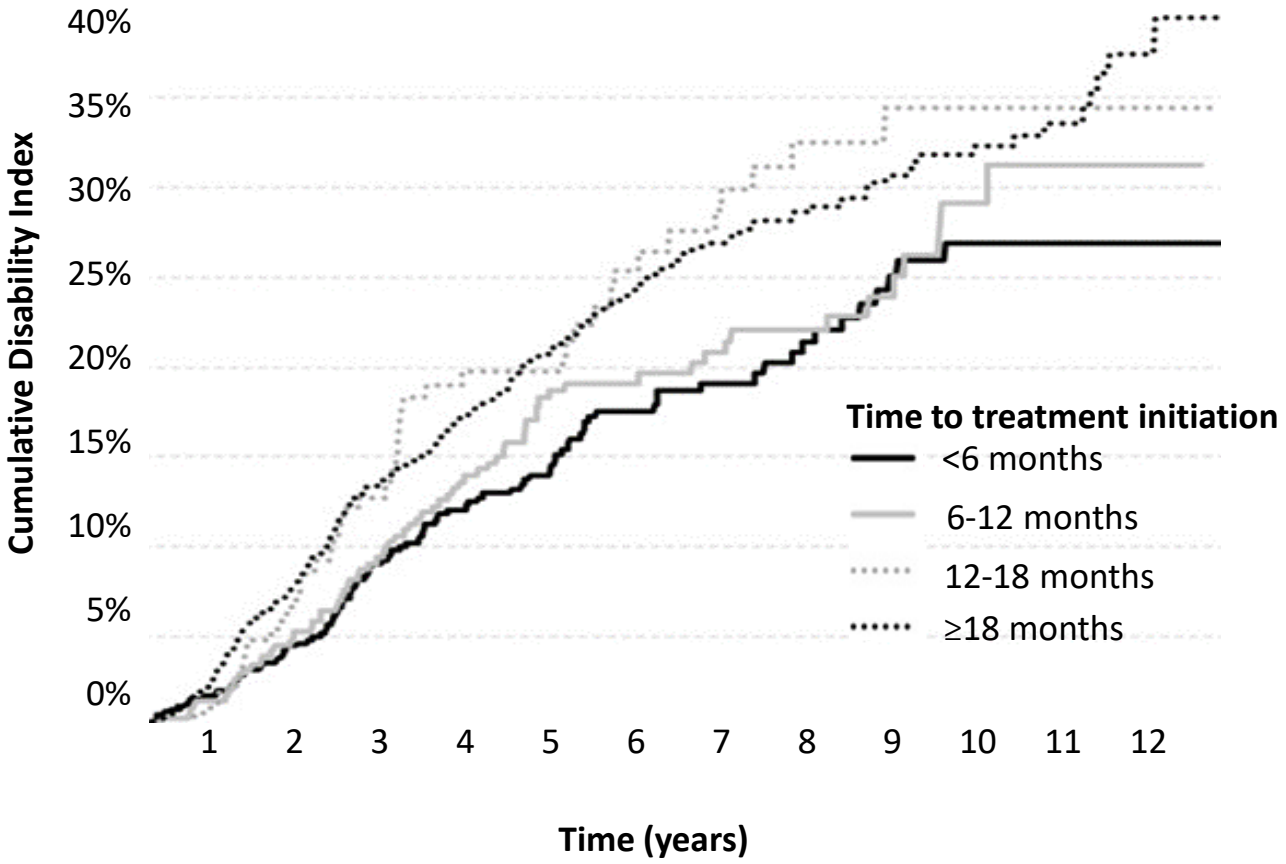
- Start treatment within 12 months after symptom onset if MRI is positive
- Initiate DMT treatment early in the disease course
- Treat-to-target



Cerqueira JJ, Compston DAS, Geraldes R, et al. *J Neurol Neurosurg Psychiatry*. 2018;89(8):844-850; Smith AL, et al. *Neurotherapeutics*. 2017;14:952-960; Dendrou CA, Fugger L, Friese MA. *Nat Rev Immunol*. 2015;15(9):545-58.

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

Impact of Early Treatment on the Risk of Disability



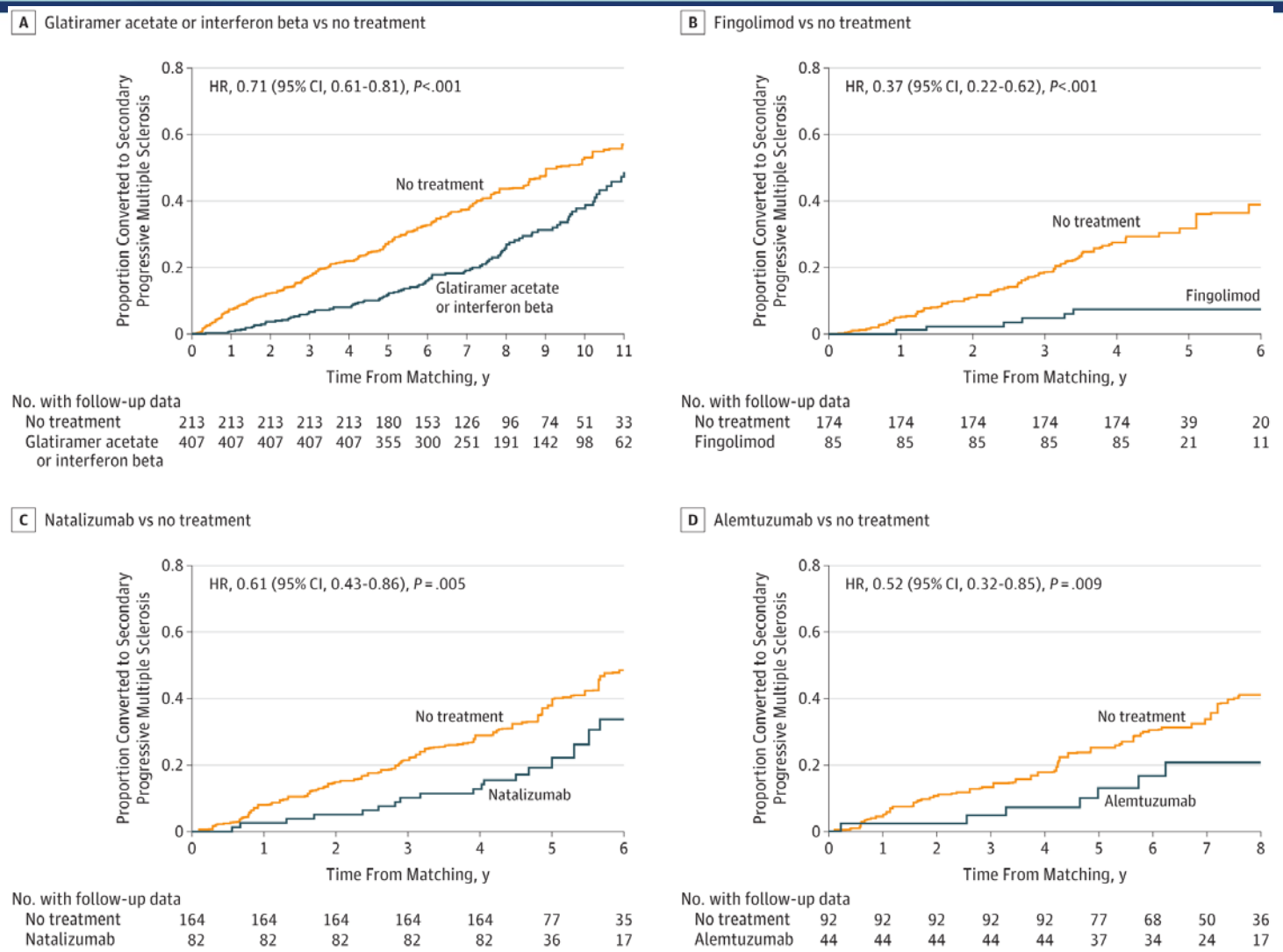
Patients (n=2477) who started treatment within 6 months after onset had a 36% lower risk (HR 0.74, p = 0.010) of full-time disability during follow-up vs. patients starting treatment after 18 months

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.

Landfeldt E, Castelo-branco A, Svedbom A, Löfroth E, Kavaliunas A, Hillert J. *J Neurol*. 2018;265(3):701-707.

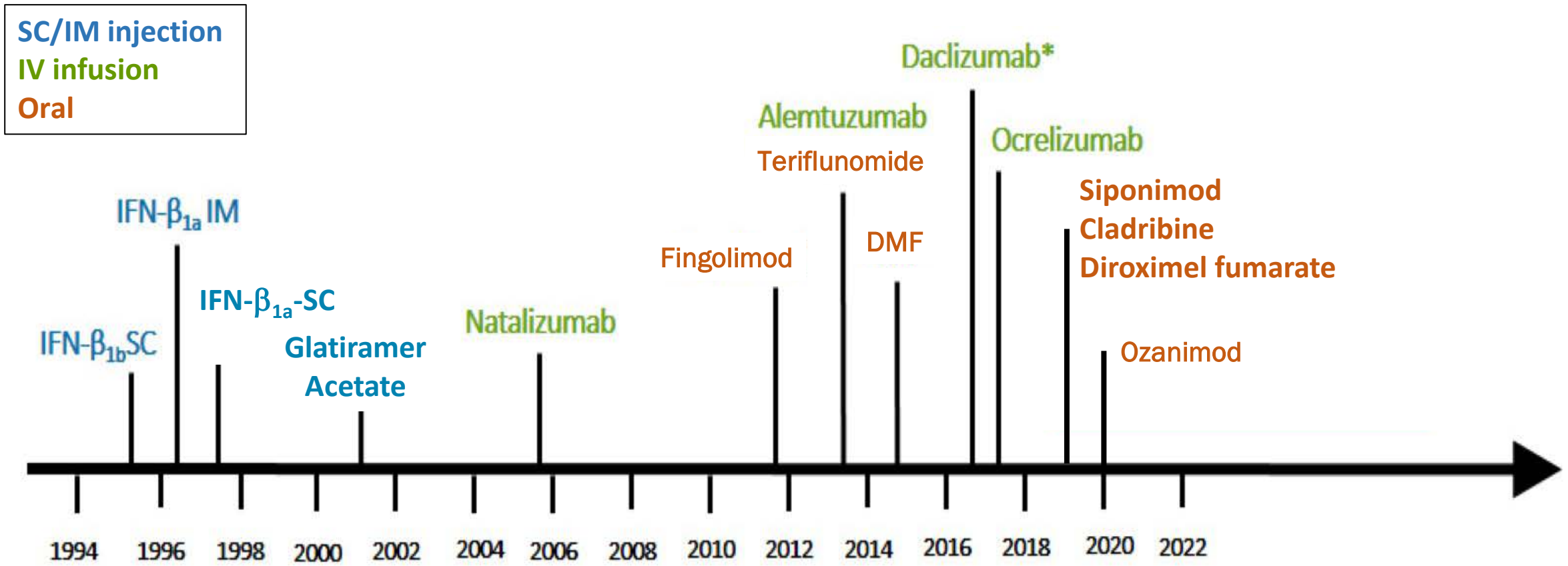
Early Treatment with DMT Associated with Later Conversion to SPMS



- 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

Brown JWL, Coles A, Horakova D, et al. *JAMA*. 2019;321(2):175-187.

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

Thompson AJ, Baranzini SE, Geurts J, Hemmer B, Ciccarelli O. *Lancet*. 2018;391(10130):1622-1636.

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 TEMSO/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% ↓

Smith AL, Cohen JA, Hua LH. *Neurotherapeutics*. 2017;14(4):952-960.

Bold: >50% reduction vs. placebo/comparator

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-1a[3]	Same as above	Same as above	Same as above
IFNβ-1b[4,5]	Same as above	Same as above	Same as above
Glatiramer acetate[6]	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. IFNβ-1a [prescribing information]. Cambridge, MA: Biogen Idec Inc; March 2016; 2. IFNβ-1a [prescribing information]. Rockland, MA: EMD Serono, Inc; November 2015; 3. Pegylated IFNβ-1a [prescribing information]. Cambridge, MA: Biogen Idec Inc; July 2017; 4. IFNβ-1b [prescribing information]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; August 2018; 5. IFNβ-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
Natalizumab[1]	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)
Alemtuzumab[2]	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
Ocrelizumab[3]	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 • Fingolimod[1] • Siponimod[2] • Ozanimod[3]	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 • Teriflunomide[4]	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 fumarate[5]	Flushing, gastrointestinal distress	Transaminitis, leukopenia, PML	CBC with differential, LFTs
Purine Antimetabolite • Cladribine[6]	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 2nd course, 2 and 6 months after start of treatment, and periodically thereafter
Diroximel fumarate[7]	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.

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/MSC_DMTPaper_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

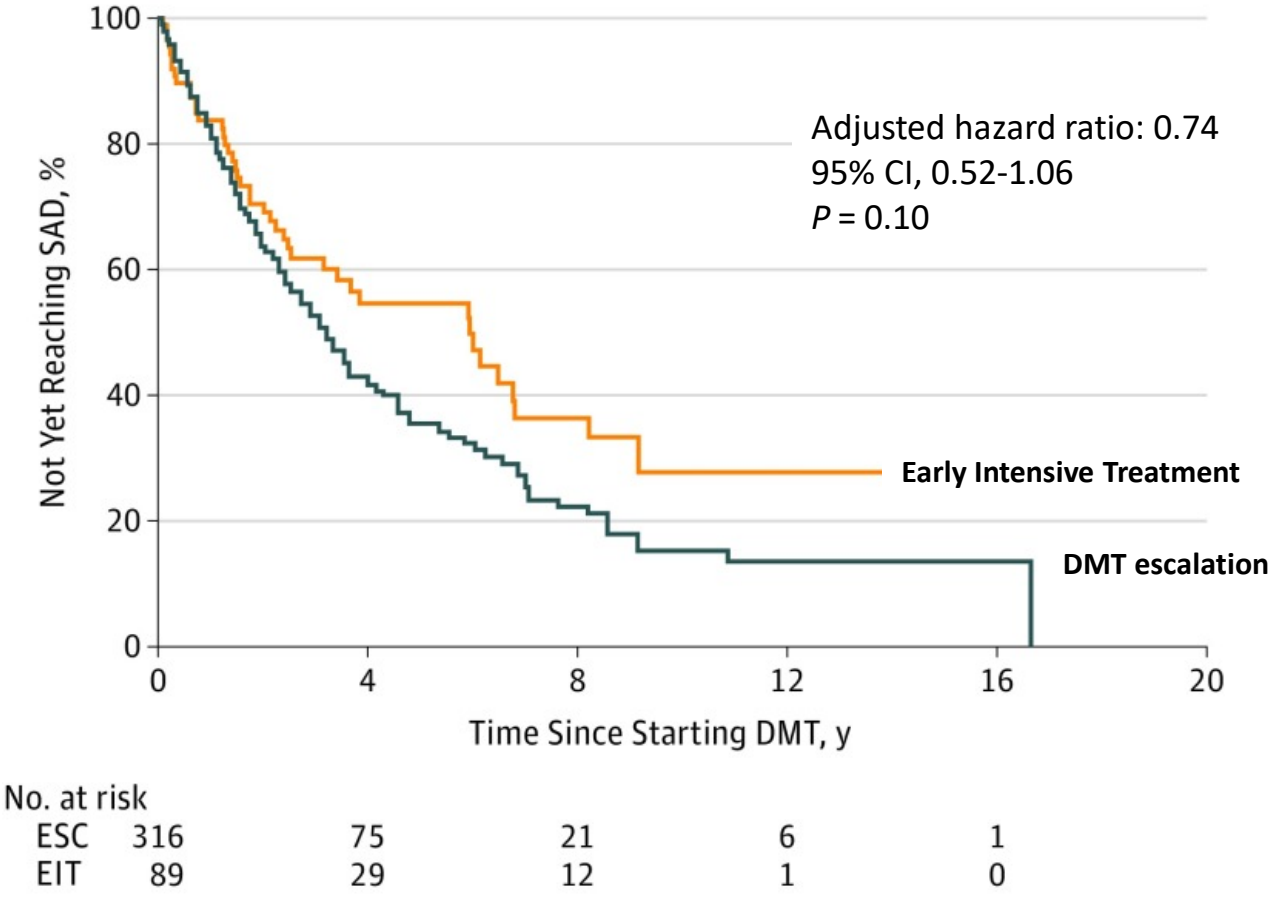
- Adherence
- Comorbidities
- Personal factors
  - Pregnancy
  - Travel
  - Work
  - Treatment expectations

Shared Decision Making

Wingerchuk DM, Weinshenker BG. *BMJ*. 2016;354:i3518; Colligan E, Metzler A, Tiryaki E. *Mult Scler*. 2017;23(2):185-190.

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

Harding K, Williams O, Willis M, et al. *JAMA Neurol*. 2019.

Which of the following DMTs are considered to be interchangeable?

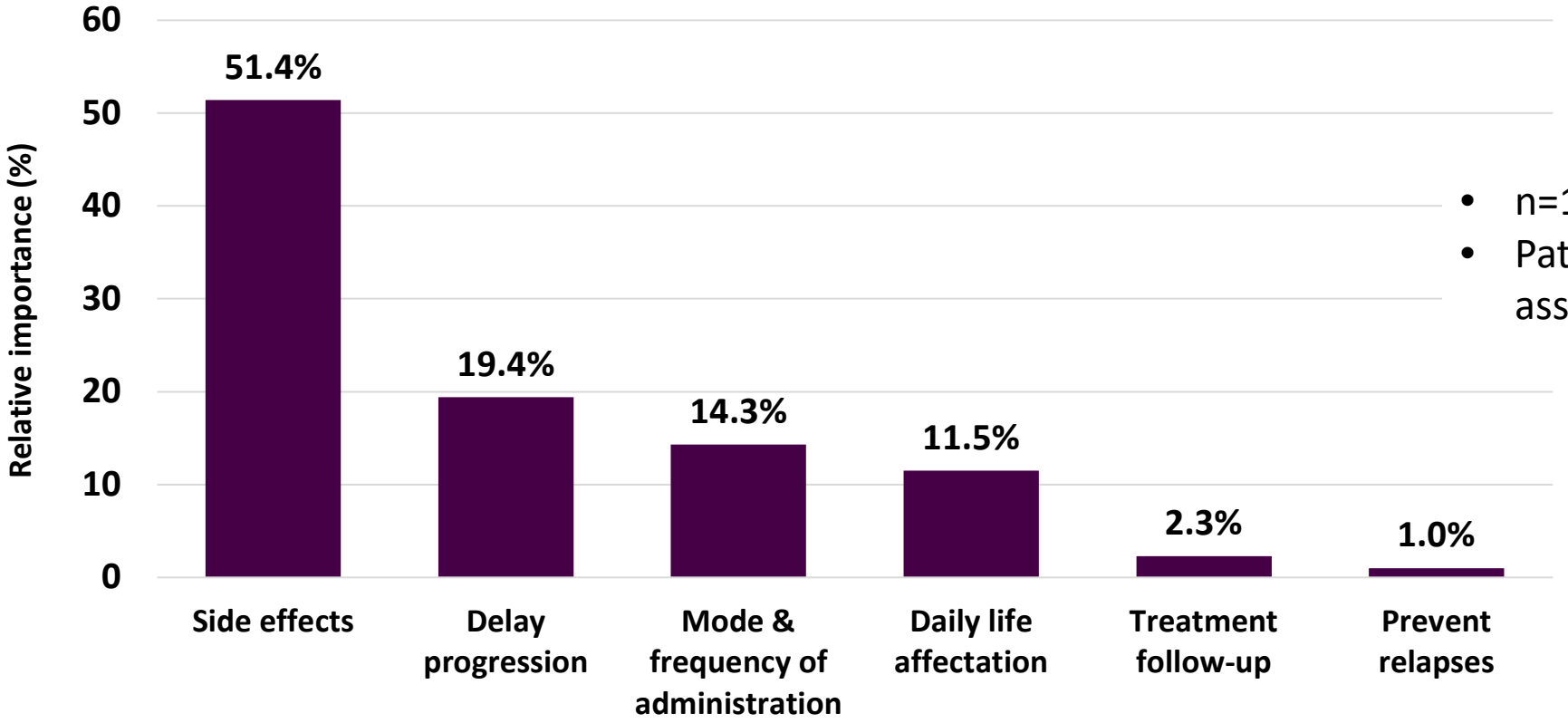
a) Alemtuzumab and Cladribine
b) Dimethyl fumarate and Glatiramer acetate
c) Ocrelizumab and Teriflunomide
d) Ozanimod and Siponimod
e) All of the above
f) None of the above

Factors Influencing a Decision to Switch the DMT

Line of Therapy	Factor Influencing a Switch
First-line DMT to another first line (lateral switch) *1st line: IFN; GA; teriflunomide; DMF*	• Tolerability/safety issues • Suboptimal efficacy with suboptimal response but still a low risk for imminent progression
First-line to a second-line DMT (i.e., escalation) *2nd line: fingolimod; natalizumab; alemtuzumab; ocrelizumab*	• 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) *3rd line/higher: mitoxantrone; cyclophosphamide; experimental therapy (e.g., cladribine)*	• 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	• 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

Freedman MS, Selchen D, Arnold DL, et al. *Can J Neurol Sci*. 2013;40(3):307-23.

Patients Prefer DMTs That Minimize Side Effects and Delay Disability Progression

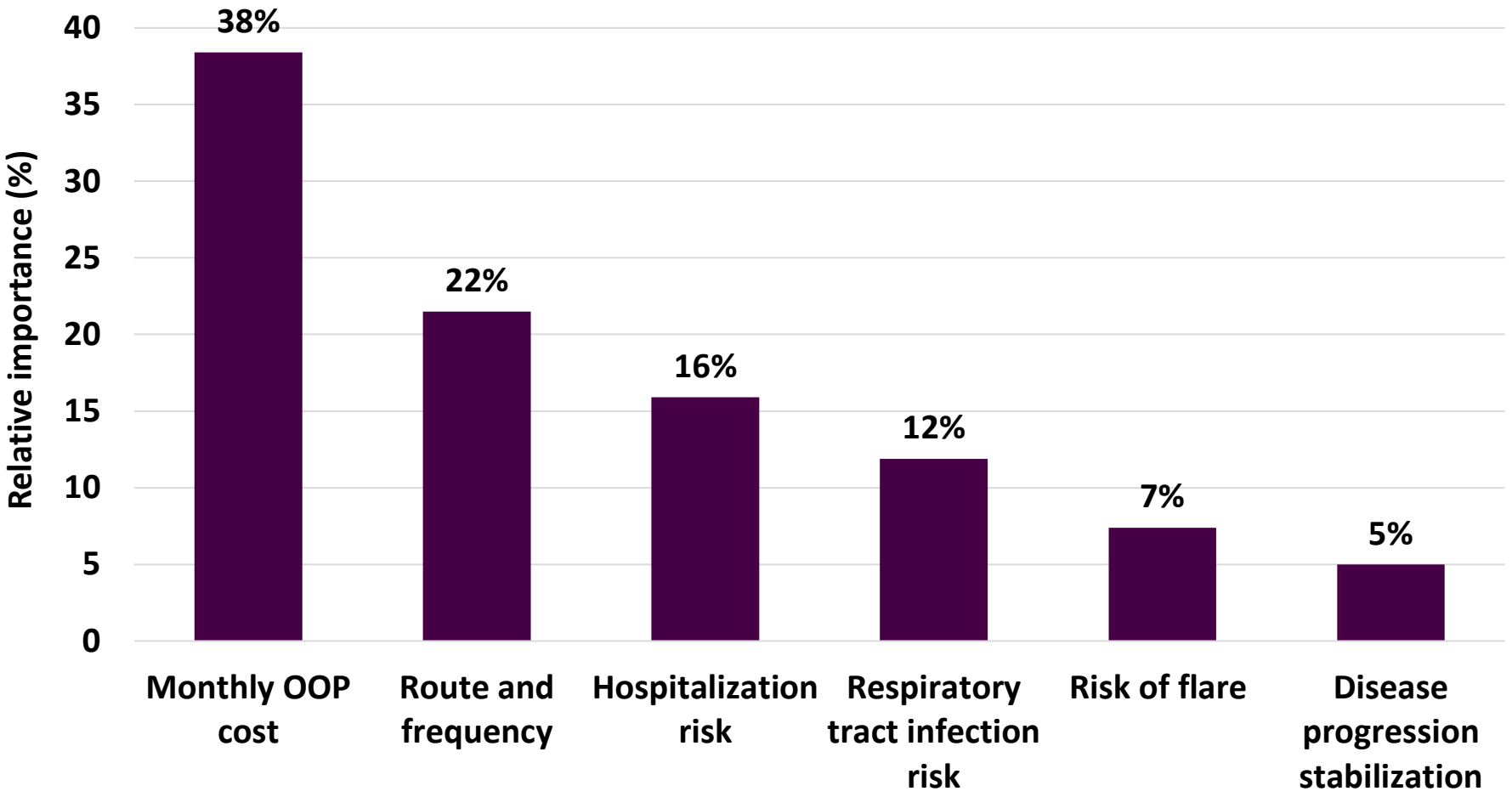


- n=125 patients with RRMS or SPMS
- Patients recruited from MS patient associations in Spain

- 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

Garcia-dominguez JM, Muñoz D, Comellas M, Gonzalbo I, Lizán L, Polanco sánchez C. Patient Prefer Adherence. 2016;10:1945-1956.

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

Hincapie AL, Penm J, Burns CF. *J Manag Care Spec Pharm*. 2017;23(8):822-830.

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

Caffrey M. *Am J Manag Care*. September 11, 2019. https://www.ajmc.com/conferences/ectrims-2019/bringing-realworld-data-to-multiple-sclerosis-treatment-decisions. Accessed March 2020.

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

Brown JL, et al. Abstract 128. Presented at: ECTRIMS 2017; October 26, 2017; Paris France. https://onlinelibrary.ectrims-congress.eu/ectrims/2017/ACTRIMS-ECTRIMS2017/202481/j.william.l.brown.the.effect.of.disease-modifying.treatments.on.conversion.to.html?f=media=3*speaker=546949. Accessed March 2020.

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

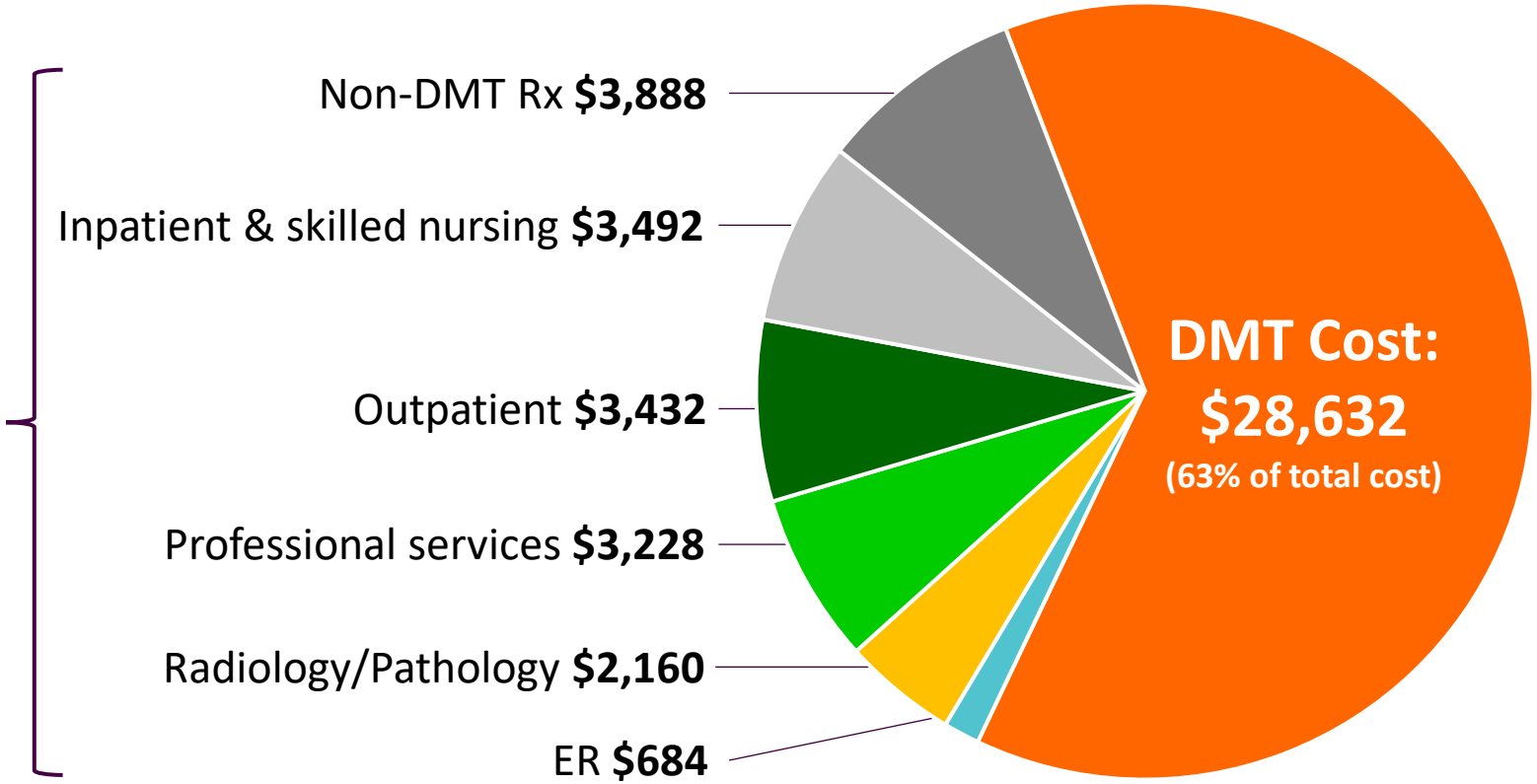
h) Other

MS is a Costly Disease

Annual Claim Costs for MS (per patient)

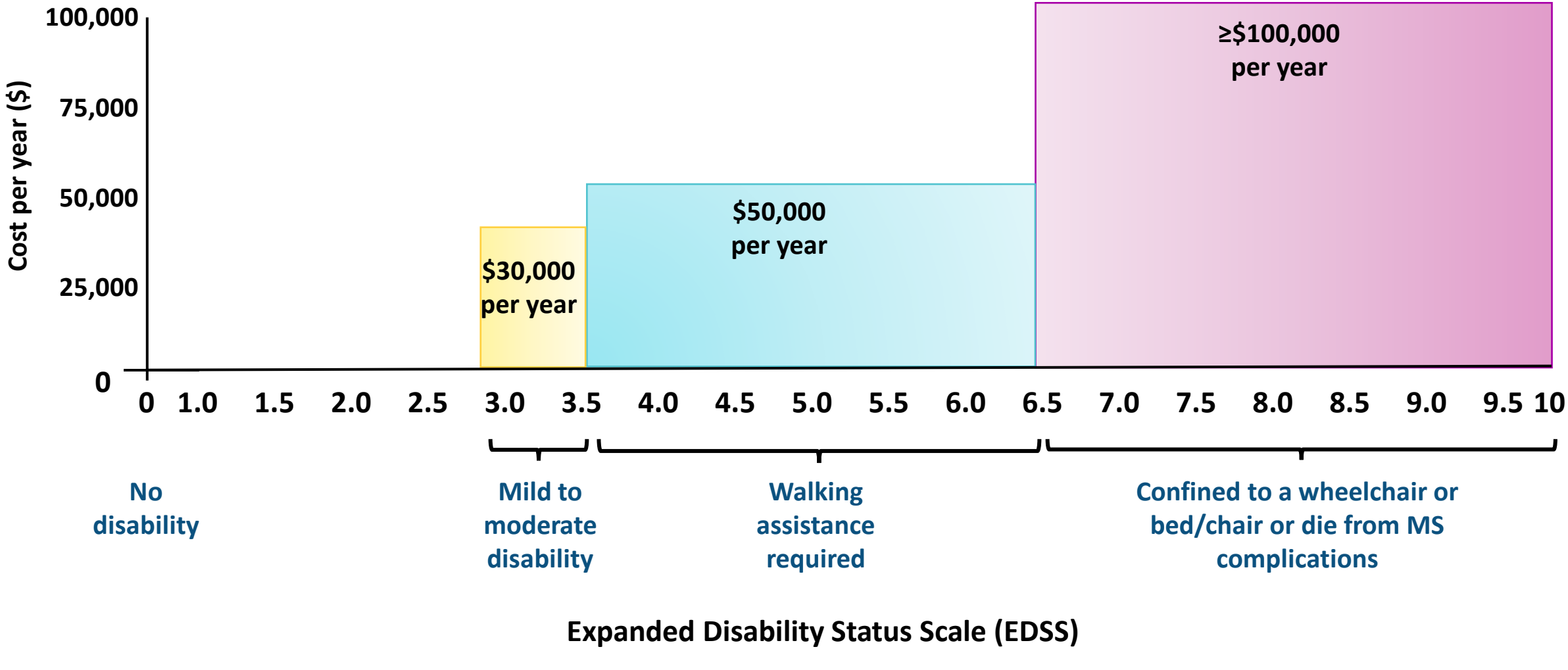
TOTAL: $45,516

Non-DMT Costs: $16,884



Six cost drivers of multiple sclerosis. Optum website. https://www.optum.com/resources/library/ms-cost-drivers.html. Accessed March 2020.

Total MS Costs Rise as Disability Progresses



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

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

EMD Serono Specialty Digest. 14th edition. 2018.

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/MSC_DMTPaper_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

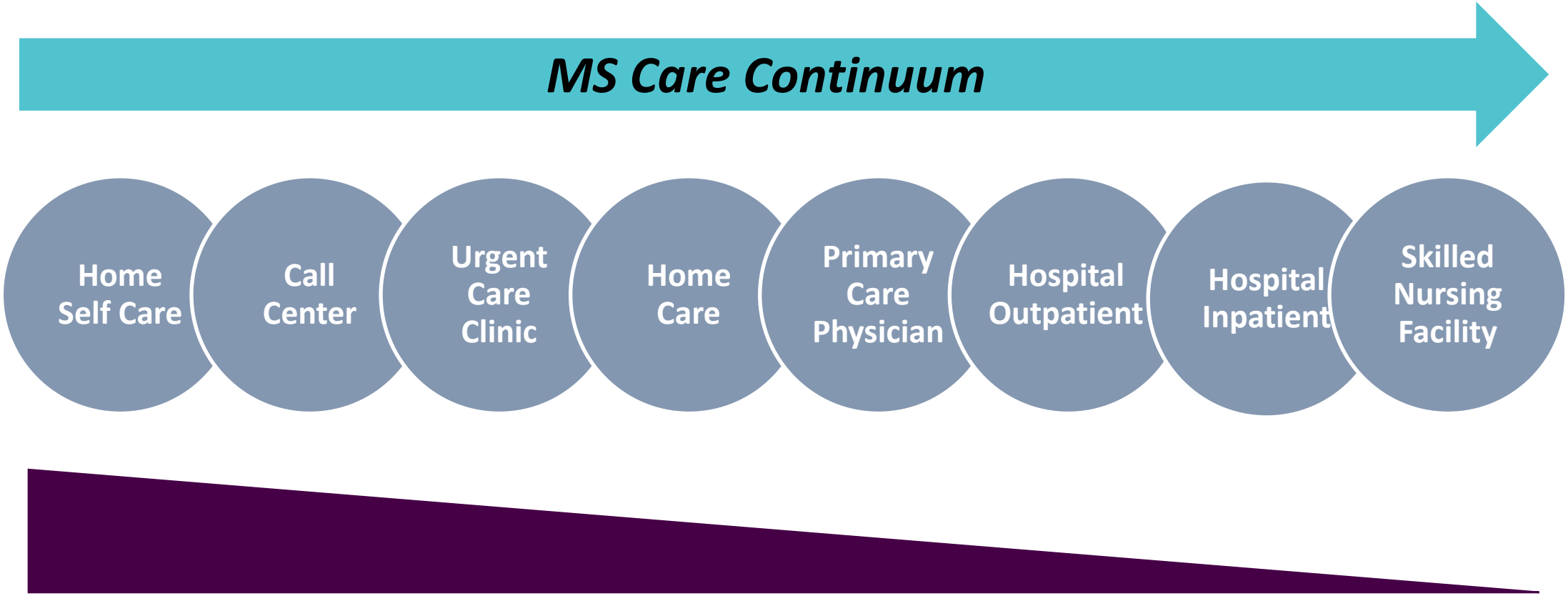
- Clinical algorithms/pathways

Cost sharing

Cost-effectiveness analysis

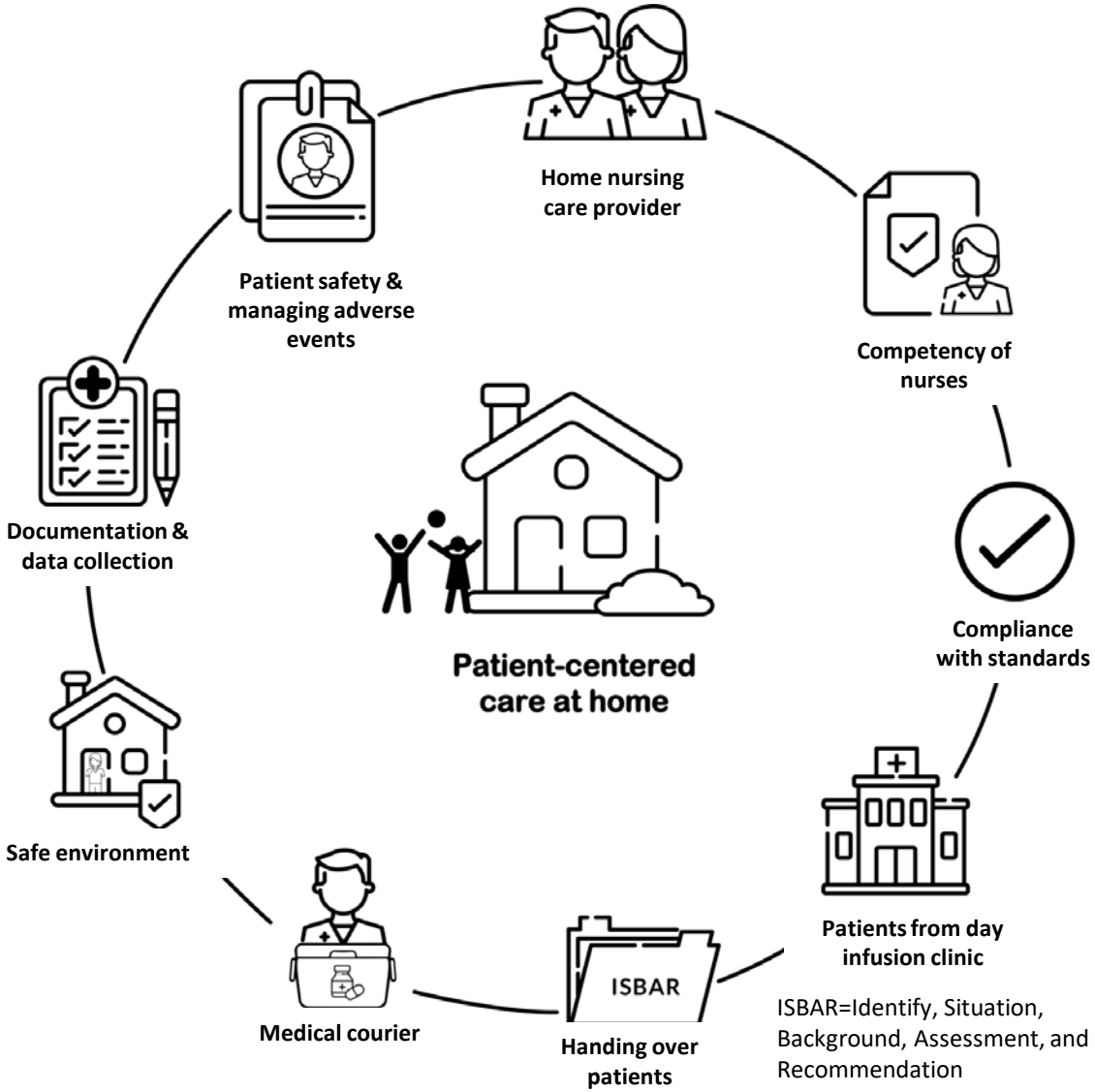
Owens G. *Am J Manag Care.* 2013;19:S307-S312.

Site-of-Care Delivery Can Influence Cost and Access



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



Schultz TJ, Thomas A, Georgiou P, et al. *J Infus Nurs*. 2019;42(6):289-296.

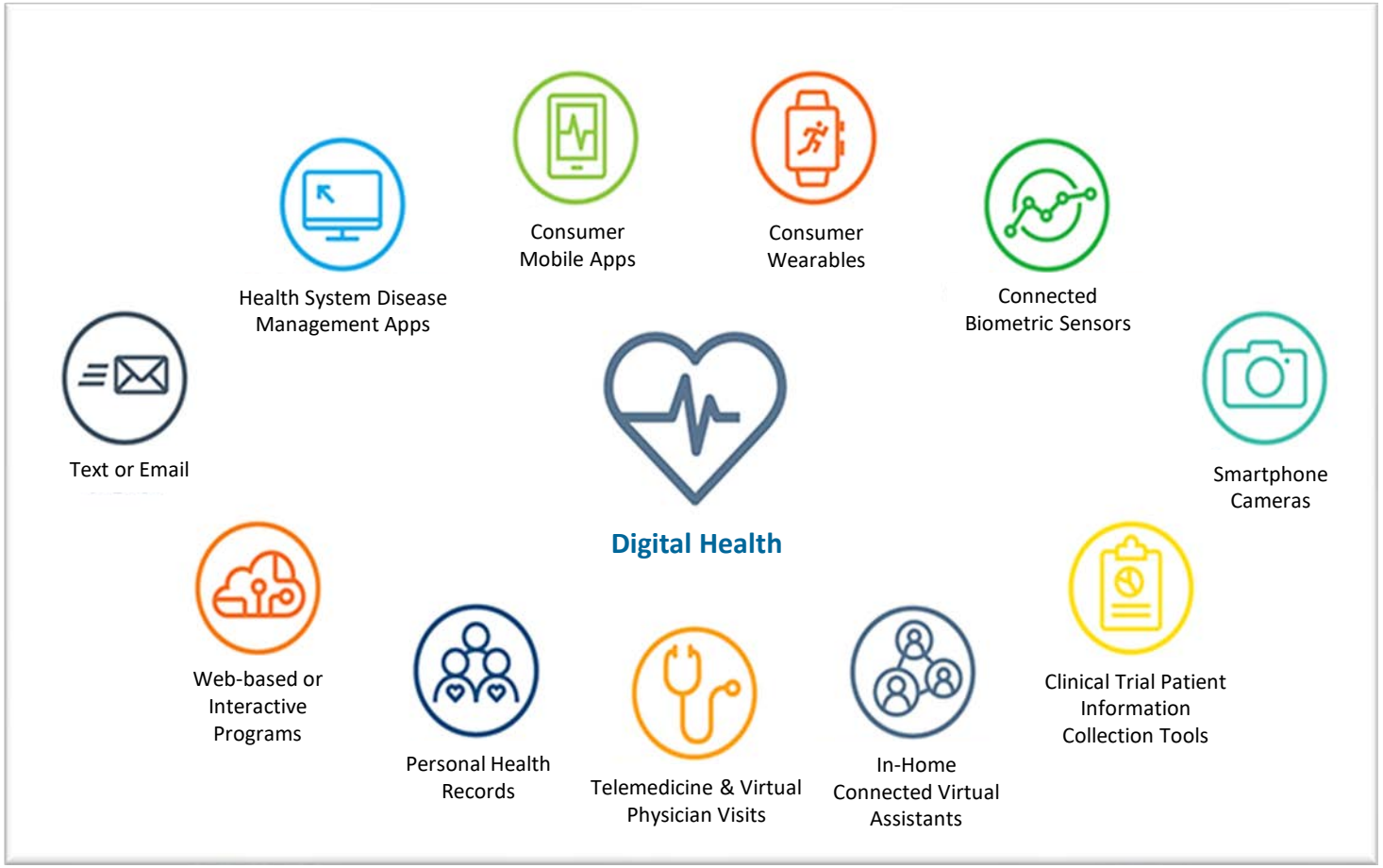
Managing MS Remains a Challenge

- 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

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

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

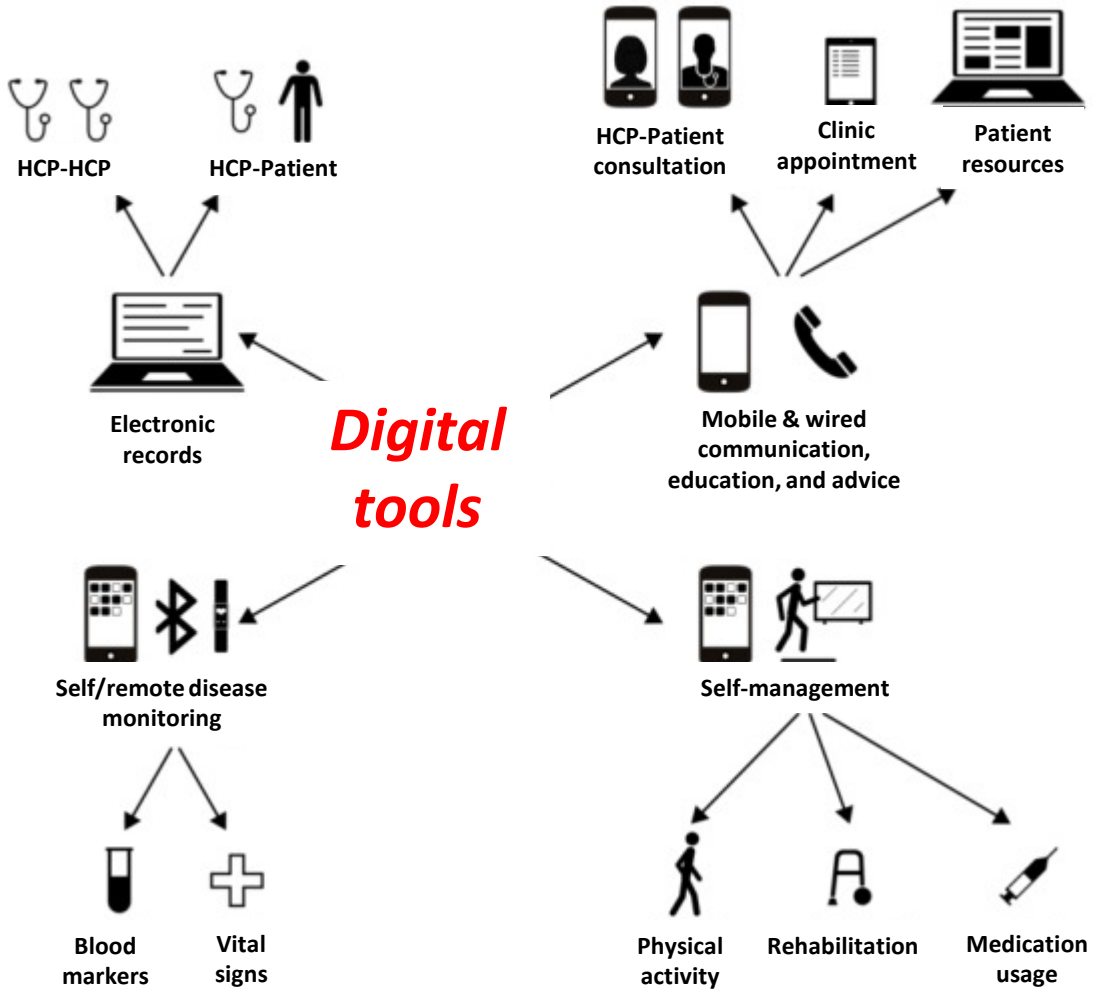
- Digital tools and communication devices are an integral part of everyday life
- Communication and data sharing can enhance face-to-face contact of patient and provider
    - May be especially valuable for long-term treatment of chronic diseases, where successful therapy requires a high level of patient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



Limroth V, et al. *Neurodegenerative Dis Manag*. 2018;8:6. https://www.futuremedicine.com/doi/10.2217/nmt-2018-0030. Accessed March 2020.

Advances in Mobile Communication Can Complement Traditional In-Clinic Approaches

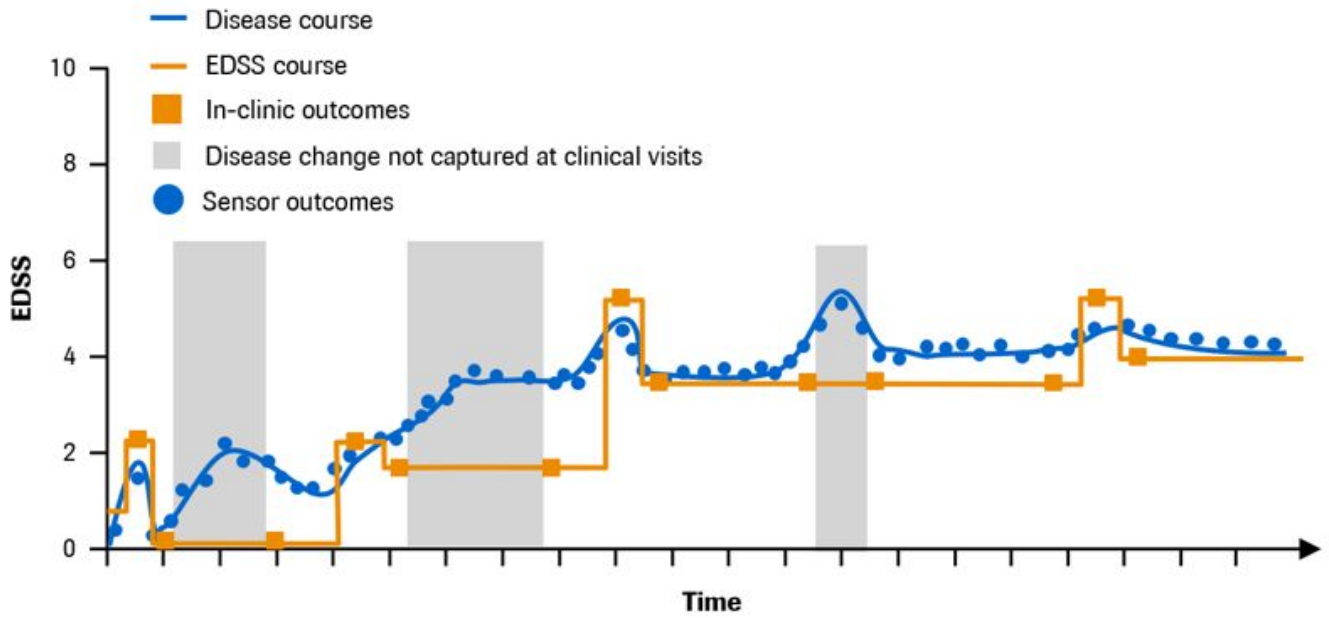
- Benefits for patients include
  - Increased access to care, disease information, and support
  - Monitor/track changes in symptoms, activity, and mood
- Benefits for HCPs include
  - Remote monitoring of symptoms, adverse events, and outcomes
  - More timely intervention vs. face-to-face visits
  -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



Marziniak M, Brichetto G, Feys P, Meyding-lamadé U, Vernon K, Meuth SG. *JMIR Rehabil Assist Technol*. 2018;5(1):e5.

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

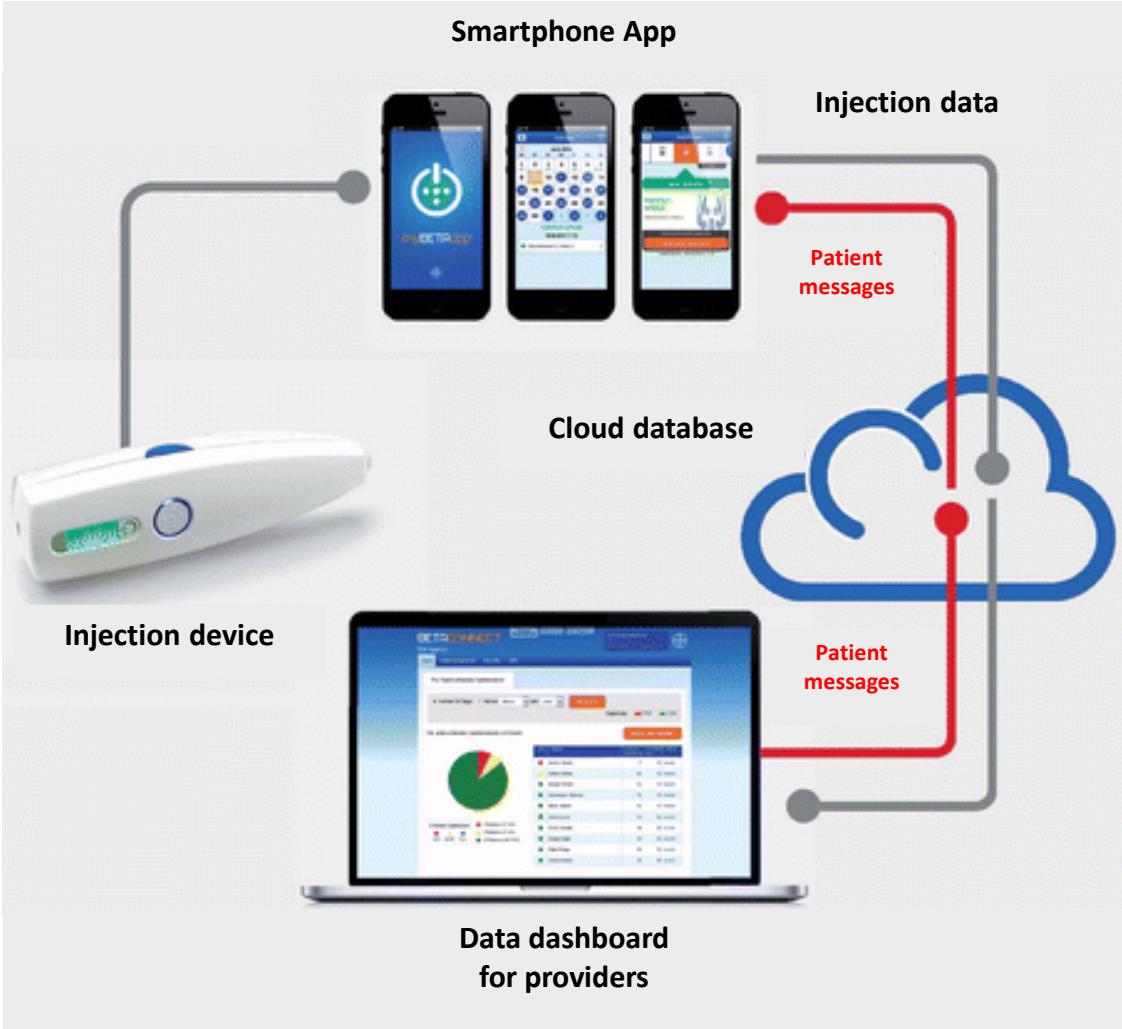


EDSS=Expanded Disability Status Scale

Baker M, van Beek J, Gossens C. *Nature Res.* 2019. https://www.nature.com/articles/d42473-019-00412-0. Accessed March 2020.

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



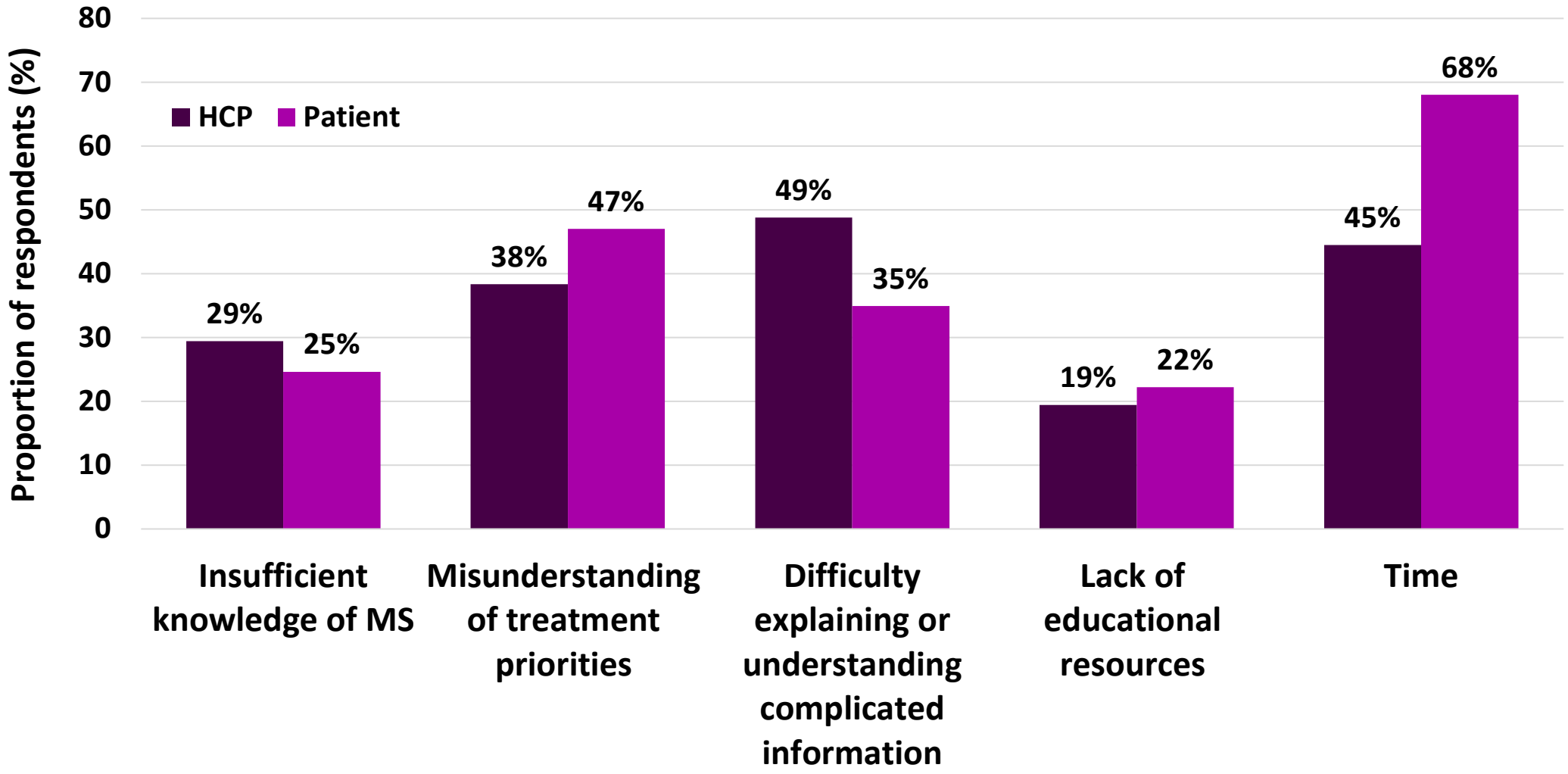
Limroth V, et al. *Neurodegenerative Dis Manag*. 2018;8:6. https://www.futuremedicine.com/doi/10.2217/nmt-2018-0030. Accessed March 2020.

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

Minemyer P. *FierceHealthcare.* https://www.fiercehealthcare.com/payer/cvs-launching-new-pharmacy-solution-aimed-at-making-it-easier-for-patients-to-get-specialty. Published September 25, 2019. Accessed March 2020.

Barriers to Effectiveness of eHealth Solutions



Oreja-guevara C, Potra S, Bauer B, et al. *Adv Ther*. 2019;36(11):3238-3252.

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

Baxter S, Johnson M, Chambers D, Sutton A, Goyder E, Booth A. *BMC Health Serv Res*. 2018;18(1):350.

Successful Pathway Implementation Depends on Evidence-Based Care

Kuntz G. *J Clin Pathways.* 2019;5(2):35-37.

Specialty Pharmacy's Role in Care Pathways

Role	Activities
Medication therapy management	• Medication selection and review
Medication assistance	• Assist in obtaining medication during transitions of care
Education	• 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	• 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	• Complete medication use evaluations; create reports and present to leadership

Hipp R, Abel E, Weber RJ. *Hosp Pharm*. 2016;51(5):416-21.

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

Treatment Initiation & Management

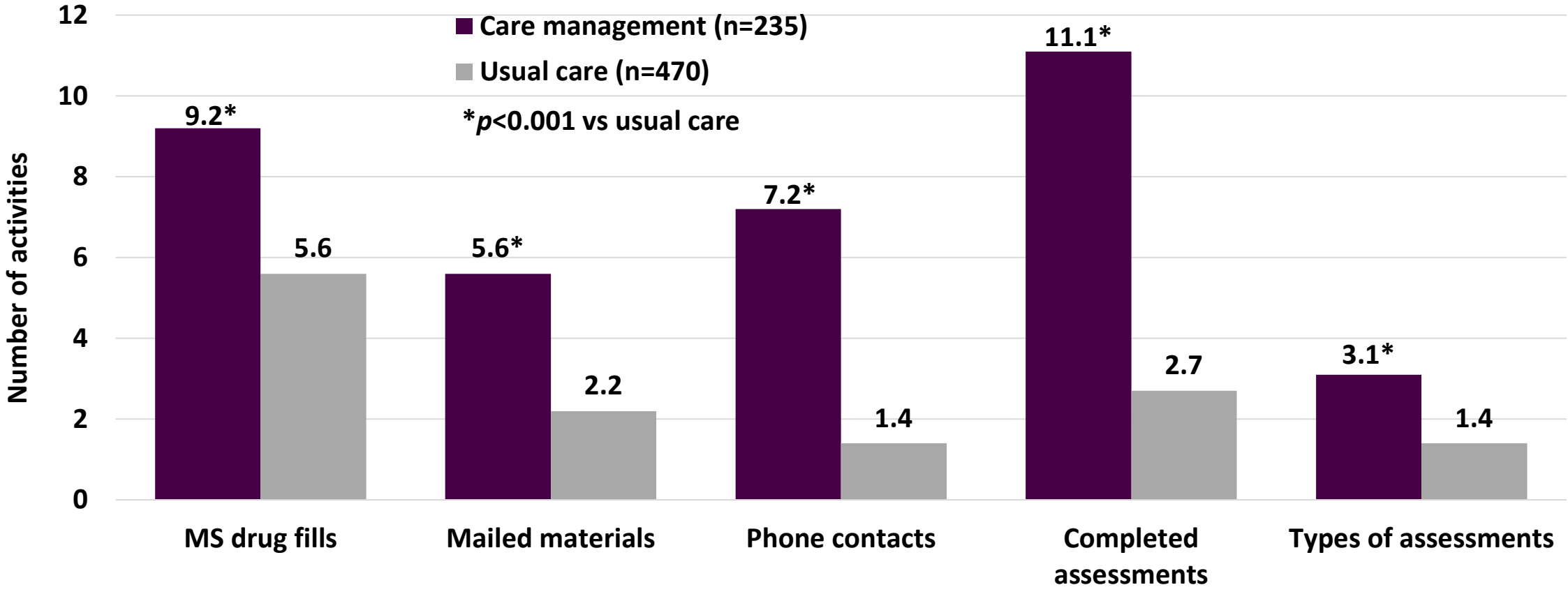
- Perform regular monitoring of disease activity and patient progress
- Manage comorbidities
- Document outcome

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



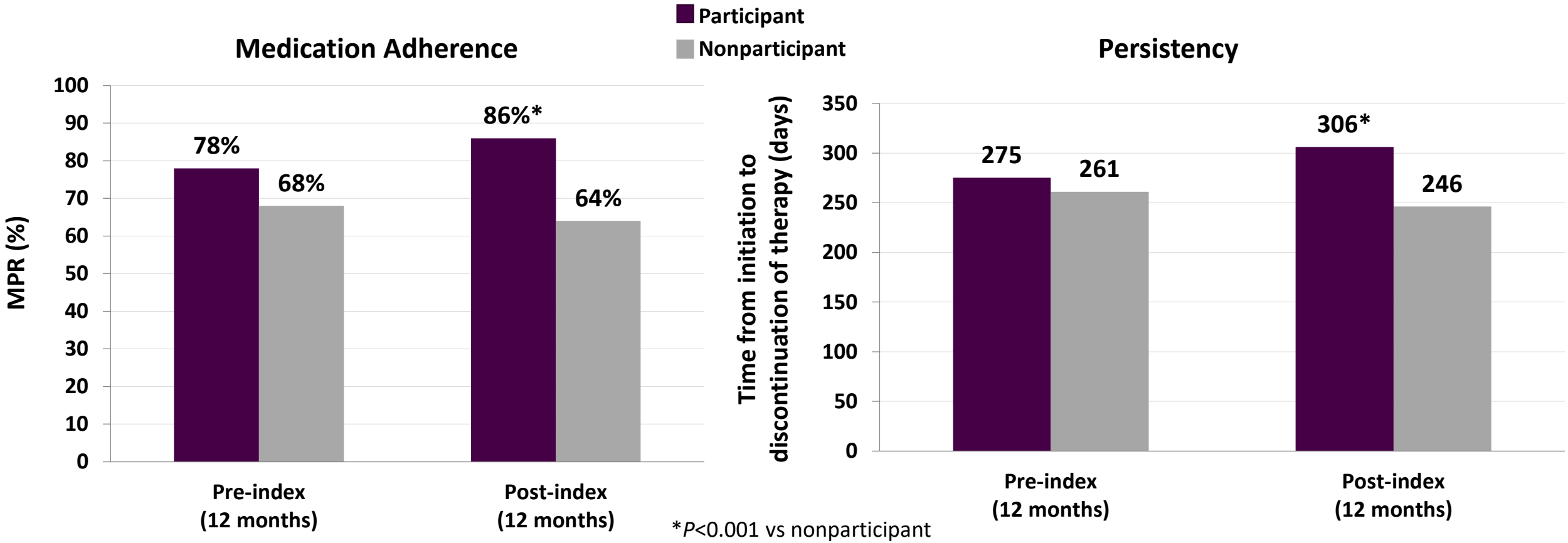
Data source: Walgreens Connected Care MS Treatment Management Program

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

Duchane J, Clark B, Staskon F, Miller R, Love K, Duncan I. *Int J MS Care*. 2015;17(2):57-64.

Care Pathways Improved Adherence and Persistency



*P<0.001 vs nonparticipant

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

Tan H, Yu J, Tabby D, Devries A, Singer J. *Mult Scler*. 2010;16(8):956-63.

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

	Before (mean)	After (mean)	Change (mean)	*P value*
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

Groeneweg M, Forrester SH, Arnold B, et al. *J Manag Care Spec Pharm*. 2018;24(5):458-463.

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)

Neter E, et al. *Mult Scler Relat Disord*. 2020 May;40:101951. Epub 2020 Jan 15

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

Gromisch ES, et al. *Arch Phys Med Rehabil*. 2019 Dec 3. [Epub ahead of print]

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

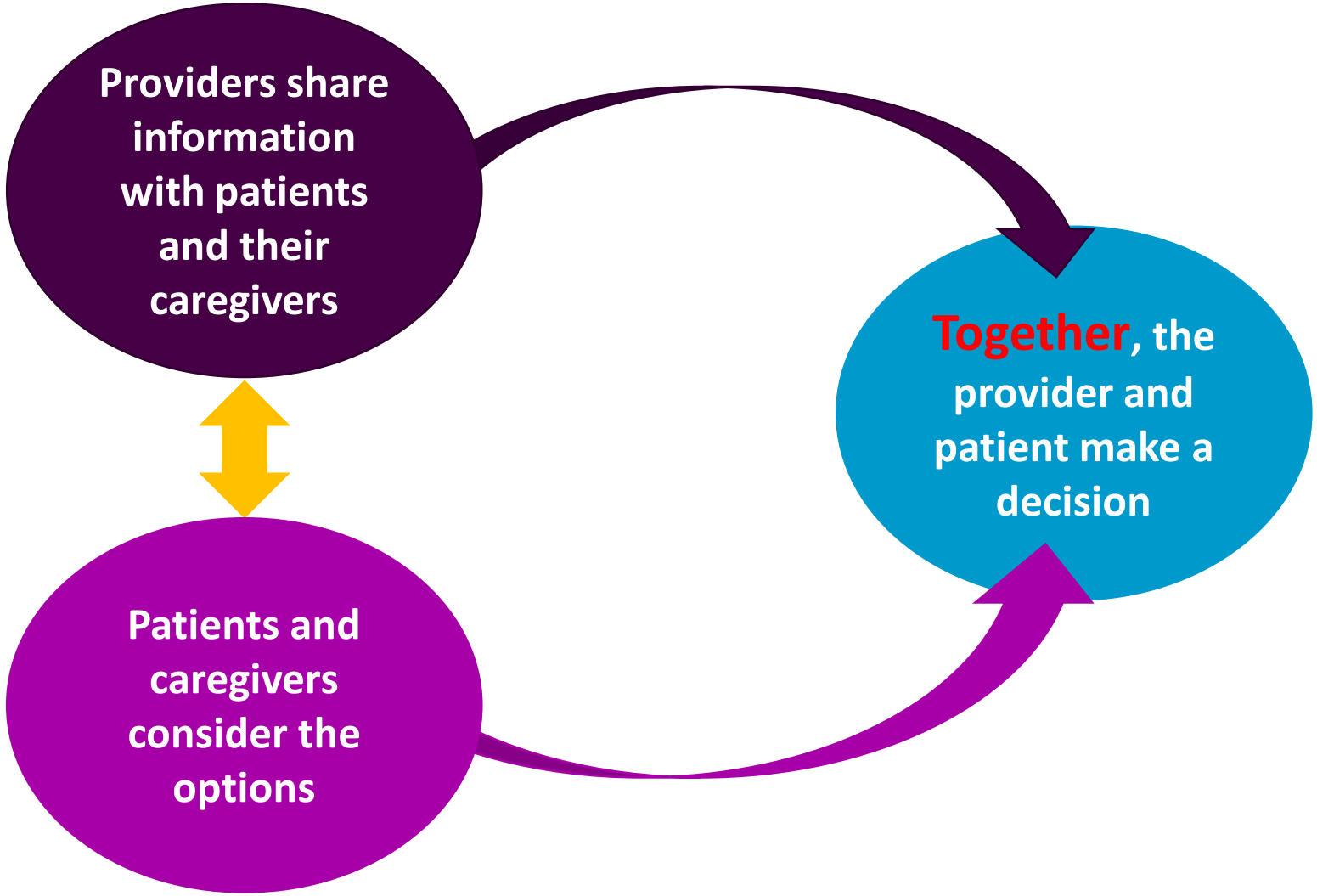
Providers

- 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

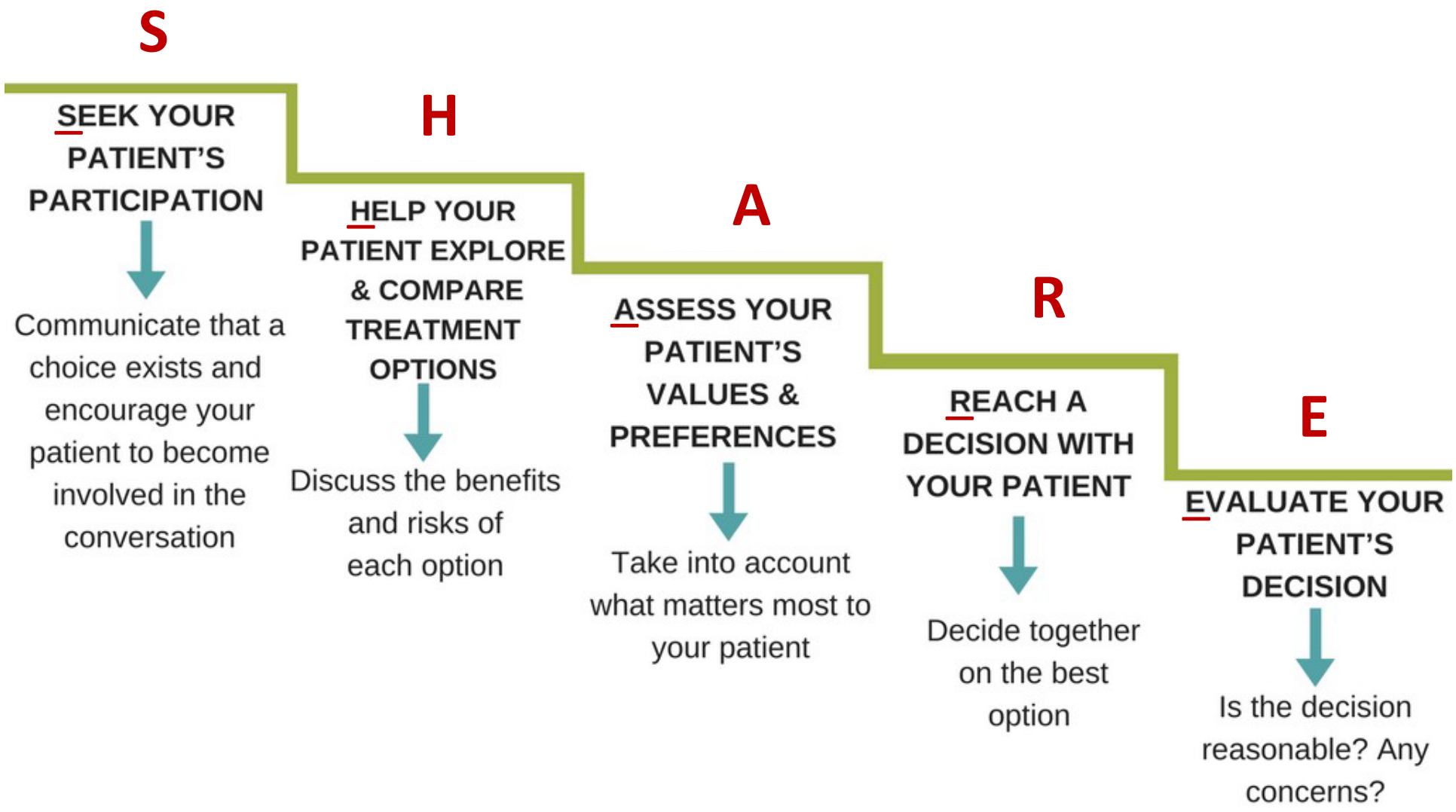
Patients

- 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

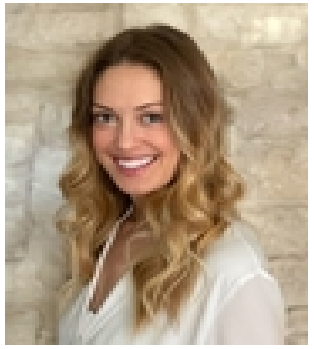
To identify and accommodate patient preference

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



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Joi Life Wellness Group, LLC

Michael Zeglinski, RPh
SVP & CEO
Optum Specialty &
Infusion Pharmacies

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Please go to www.impactedu.net/cpe
Enter code: **5520**

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, **May 5, 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.**

Option 2: Print the 'Fax Evaluation Form' in the *Handouts* section and turn in the completed version via fax or email to the number or email address located at the top of the form. A certificate will be emailed to you within 3-4 weeks.
For Pharmacists: upon receipt of the completed evaluation form, you will receive an email within 3 weeks with a link and directions to submit your credit to the NABP CPE Monitor Service. **Pharmacists have up to 30 days to complete the evaluation and claim credit for participation so that information can be submitted to CPE Monitor as required.**

Multiple Sclerosis Update

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

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SPECIALTY PHARMACY 2020 summit