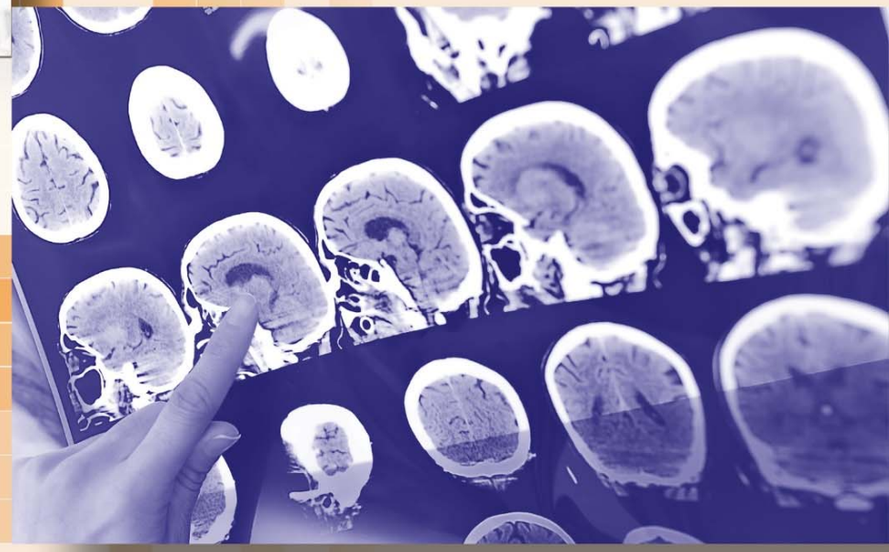

Managing Multiple Sclerosis:

Current Treatment and Care Management **Strategies** for Managed Care

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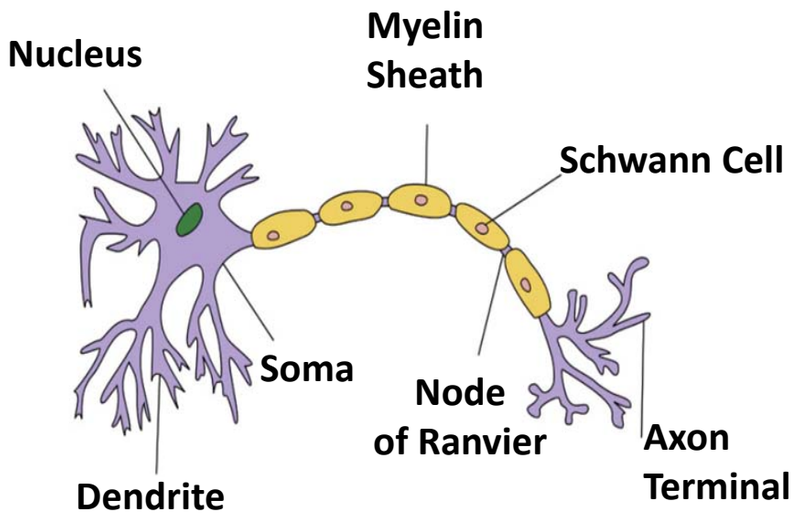
AMCP Academy of Managed Care Pharmacy®

Held in conjunction with AMCP Managed Care & Specialty Pharmacy Annual Meeting 2018

Clinical Update: Current Insights into MS Treatment

Harold Moses, Jr., MD
Associate Professor of Neurology
Neuroimmunology Division
Vanderbilt University

Defining Multiple Sclerosis

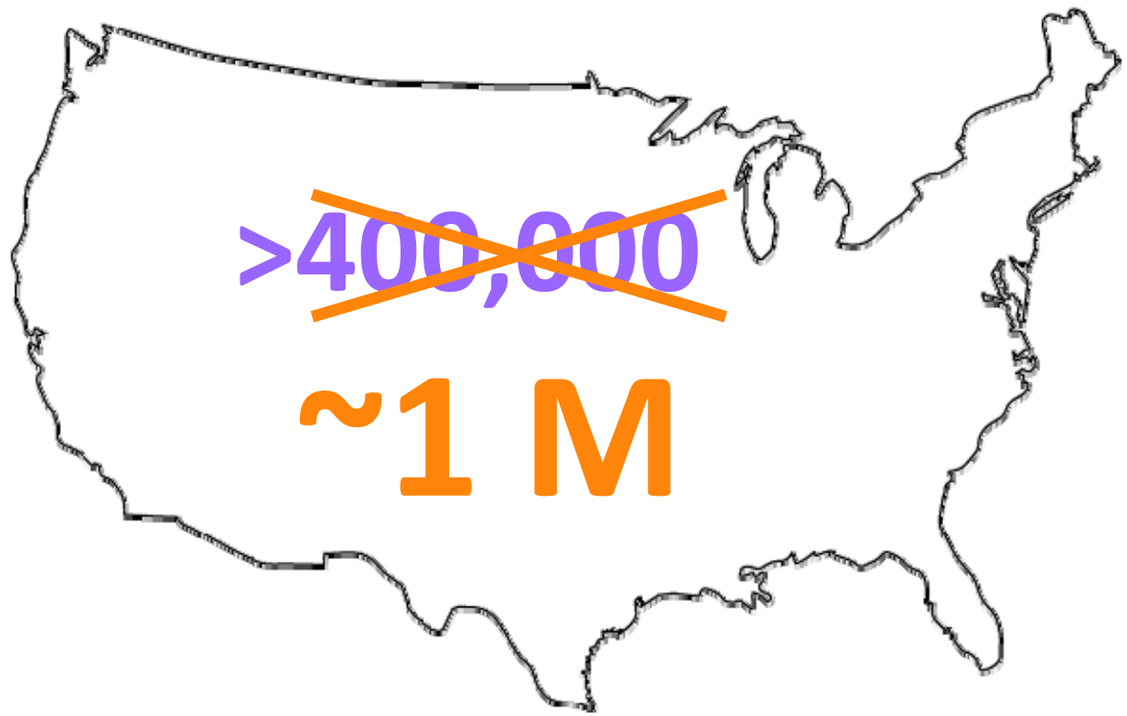


- Chronic progressive immune-mediated disease of the central nervous system (CNS)
- Associated with focal areas of inflammation, demyelination, axon transection, neurodegeneration, and subsequent scar or plaque formation
- Often leads to significant disability
  - Median survival in MS population is less than observed in the general population (~7-9 yrs less)
- Primary etiology unknown, but likely multifactorial
- Potential risk factors include genetic background, environmental exposures (infection with Epstein-Barr virus, smoking), overweight/obesity, and low vitamin D

Calabresi PA, Newsome SD. Multiple sclerosis.
In: Weiner WJ, Goetz CG, Shin RK, Lewis SL, eds. *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.

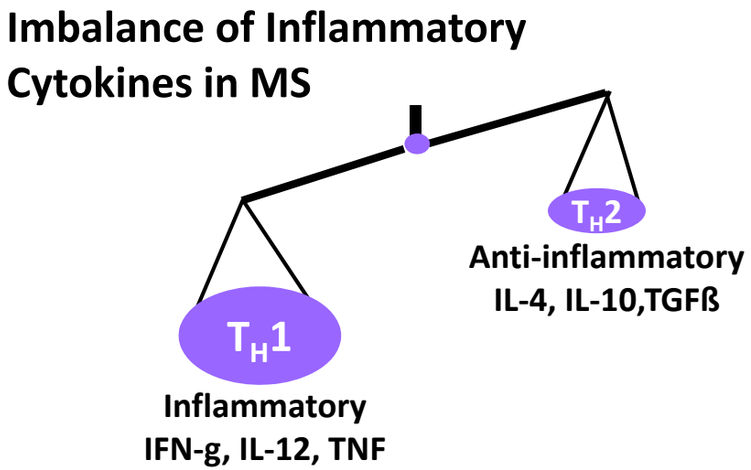
Epidemiology

- Recent reports estimate that MS affects ~1 M people in the United States, more than twice the previously estimated figure
- Most diagnosed are 20 - 50 years old
- Affects 2x-3x more women than men



MS Prevalence. National Multiple Sclerosis Society Web site. http://www.nationalmssociety.org/About-the-Society/MS-Prevalence.
Who Gets MS? National Multiple Sclerosis Society Web site. https://www.nationalmssociety.org/What-is-MS/Who-Gets-MS.
Adelman G, Rane SG, Villa KF. *J Med Econ*. 2013;16(5):639-47.

Inflammation and Neuronal Degeneration



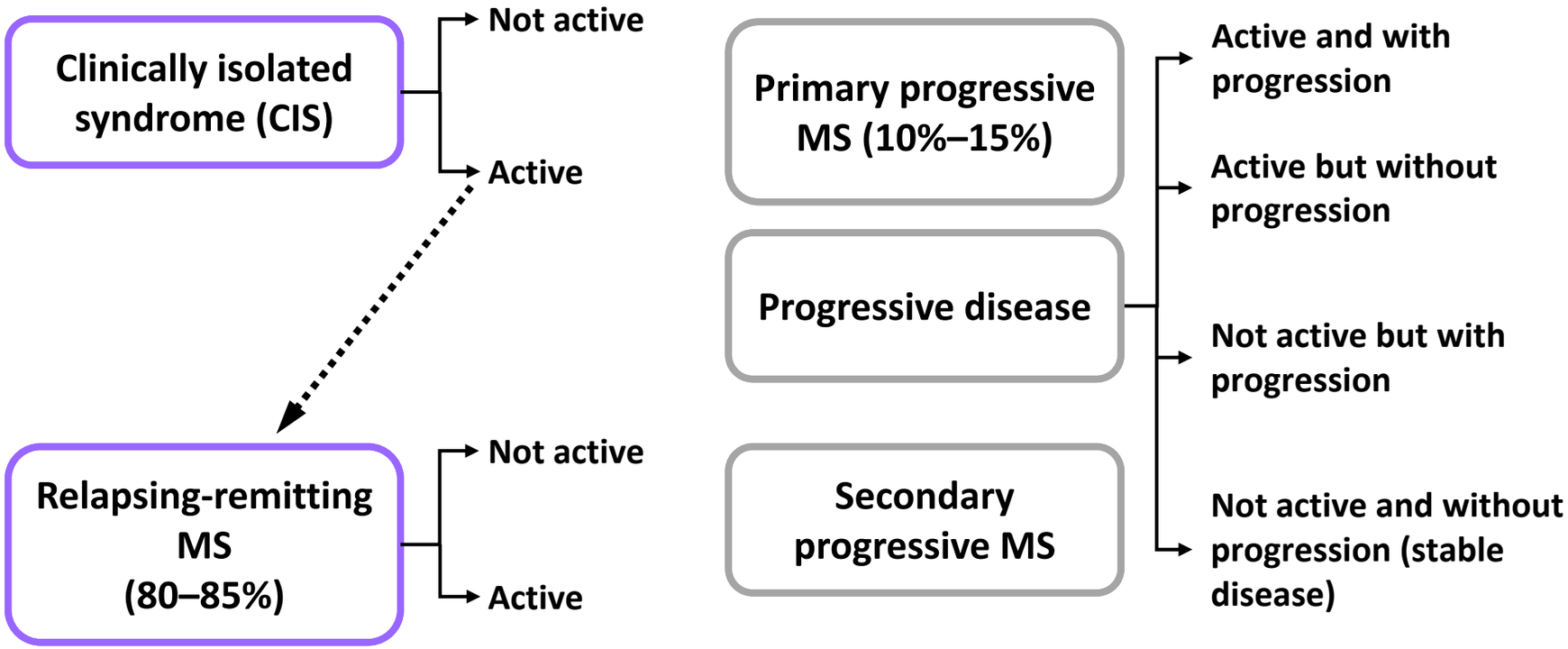
Acute Inflammation → **Relapse**

Neuronal Degeneration → **Disability**

- Loss of axons is likely the main cause of permanent disability in MS
- Axonal damage has been shown to occur in acute inflammatory plaques[1]
- Axonal damage could be the result of cumulative inflammatory damage over time or a parallel degenerative process related to loss of trophic support or an independent degenerative process[2]

1. Trapp BD, Peterson J, Ransohoff RM, Rudick R, Mörk S, Bö L. *N Engl J Med*. 1998;338(5):278-85.
2. Trapp BD, Ransohoff RM, Fisher E, Rudick RA. *The Neuroscientist.* 1999;5:48-57.

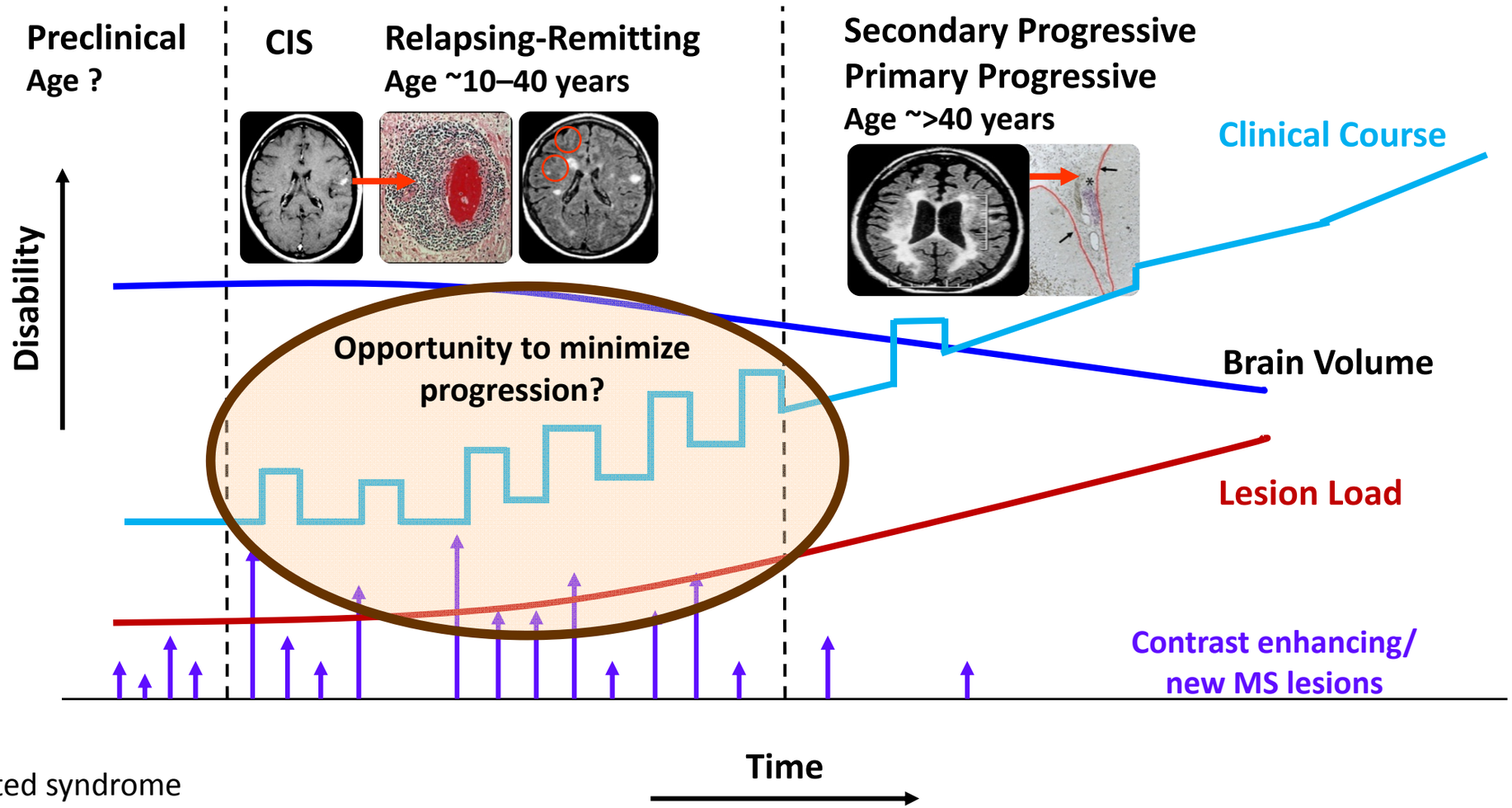
Multiple Sclerosis Disease Subtypes



- Active: Inflammatory activity measured by clinical relapses and/or MRI activity
- Progression: Measured by clinical evaluation
- Radiologically isolated syndrome not included

Lublin FD, Reingold SC, Cohen JA, et al. *Neurology*. 2014;83(3):278-86.

Multiple Sclerosis Disease Course



CIS: clinically isolated syndrome

Slide courtesy of P. Calabresi, MD.

Factors Associated With More Disabling Multiple Sclerosis

Clinical factors

- Male gender
- Older age at onset
- African American
- Motor involvement
- Cerebellar involvement
- Sphincter involvement
- Frequent relapses
- Poor recovery from relapses
- Multifocal involvement at onset

Paraclinical factors

- MRI high lesion burden at presentation
- ≥2 gadolinium-enhancing/new T2 lesions or ≥2 T1-hypointense lesions
- ≥2 spinal cord lesions
- Brain atrophy
- Low vitamin D

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

Common Multiple Sclerosis Symptoms

Primary

- Fatigue
- Weakness
- Numbness/tingling
- Dizziness/vertigo
- Gait difficulties
- Spasticity
- Diplopia (binocular)
- Visual loss
- Cognitive decline
- Mood disorder
- Pain
- Bladder and bowel problems
- Sexual dysfunction

Secondary

- Falls
- Injury
- Bladder infections from urinary retention
- Physical deconditioning

Tertiary

- Vocational changes
- Social isolation
- Change in relationships

MS Symptoms. National Multiple Sclerosis Society Web site. http://www.nationalmssociety.org/Symptoms-Diagnosis/MS-Symptoms.

Diagnosis of Multiple Sclerosis

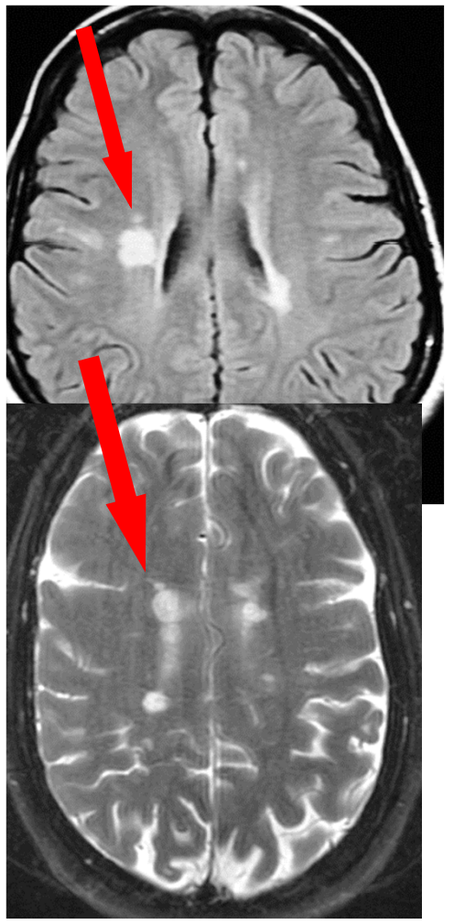
- Based on clinical history, neurologic exam, paraclinical tests (ie, MRI), and exclusion of other possible causes
- Objective evidence of CNS white matter lesions disseminated in time and space
  - Disseminated CNS lesions in time and space can be demonstrated clinically (exacerbations with objective signs on examination, eg, optic neuritis) or by MRI with/without gadolinium
  - Can diagnose MS after a single attack with 2010 McDonald criteria
- CSF in selected patients: cell count, protein level, IgG index, and oligoclonal bands
- Blood work obtained to rule out mimics

CSF: cerebrospinal fluid

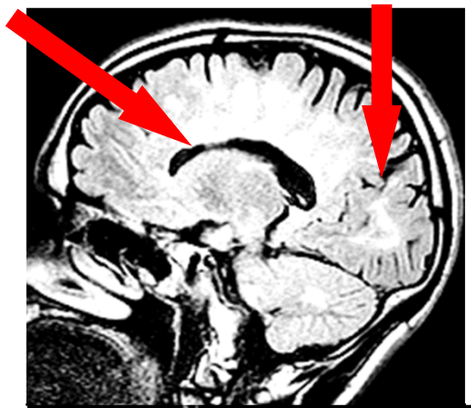
Polman CH, Reingold SC, Banwell B, et al. *Ann Neurol*. 2011;69(2):292-302.
Polman CH, Reingold SC, Edan G, et al. *Ann Neurol*. 2005;58(6):840-6.

Typical MRI Features in MS

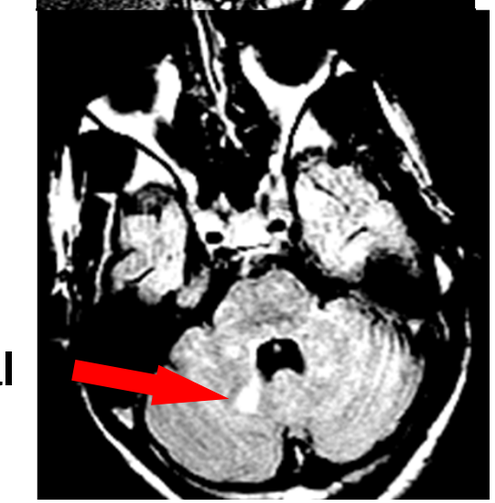
Periventricular



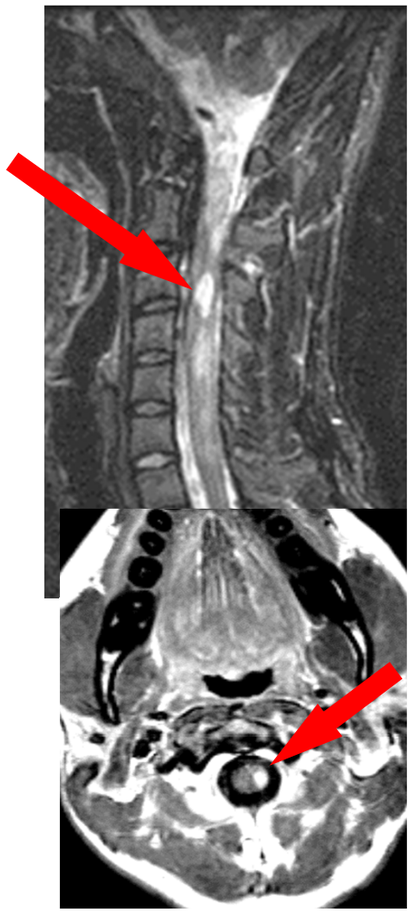
Corpus callosum and juxtacortical



Infratentorial



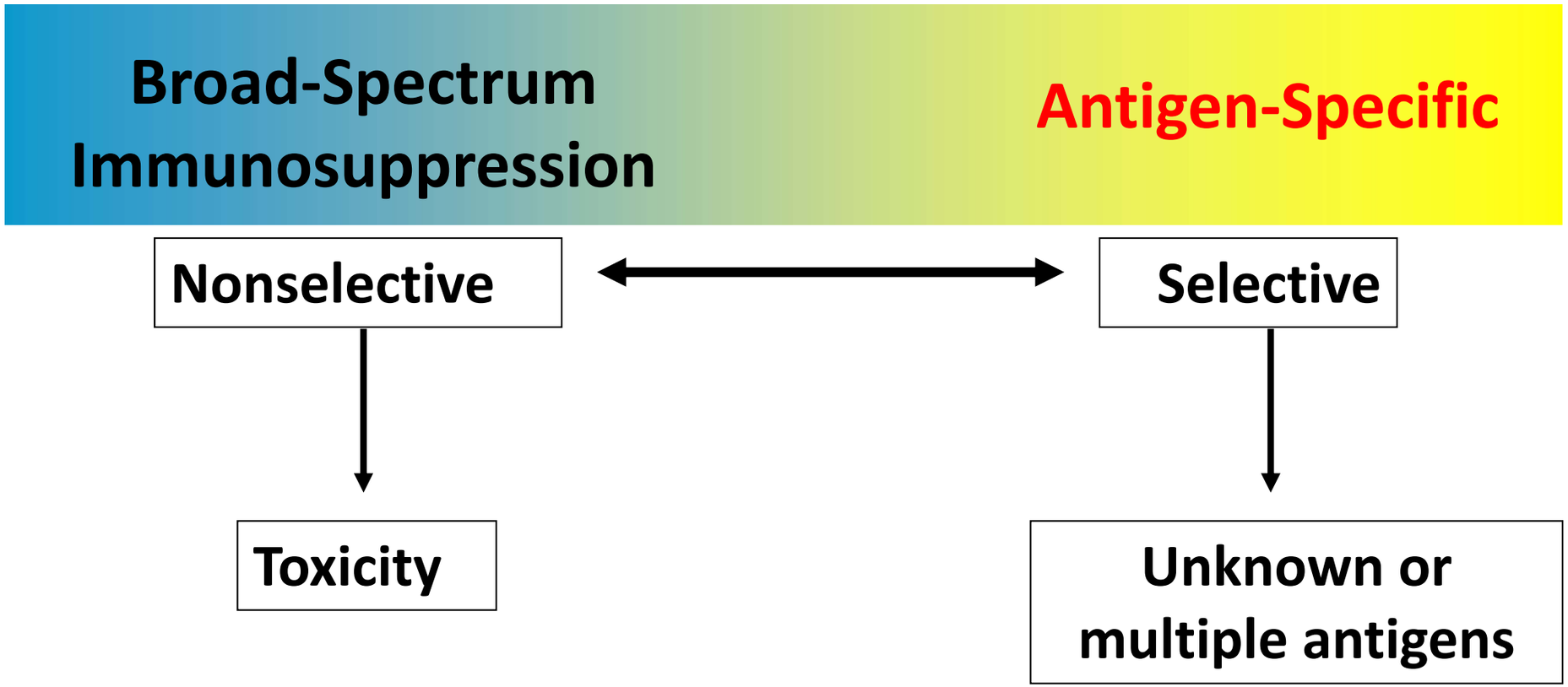
Spine lesions



Therapeutic Goals in Multiple Sclerosis

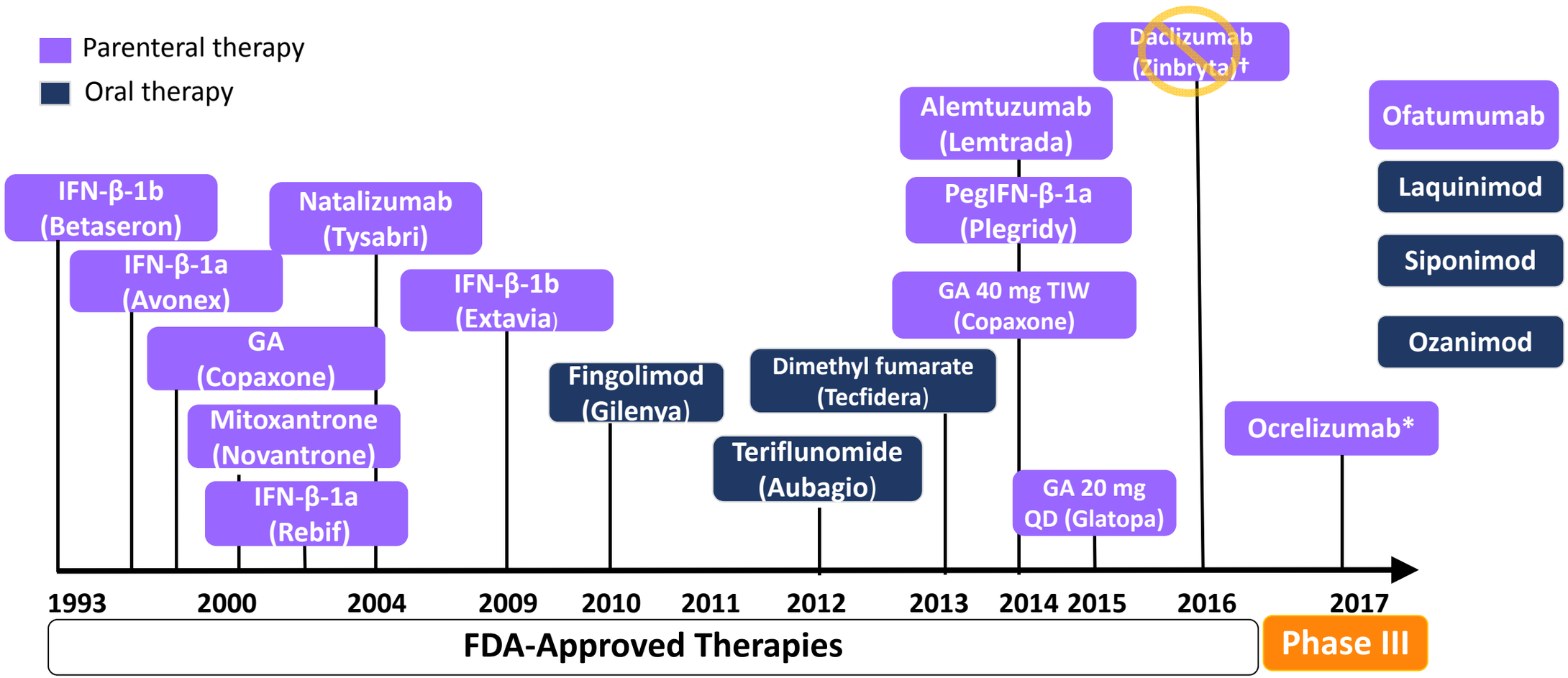
- In the absence of a cure for MS, current goals of disease-modifying therapy are to
  - Prevent relapses
  - Prevent development of new or enhancing lesions on MRI
  - Prevent disability
- Additional goals in the management of MS are to
  - Relieve symptoms
  - Maintain well-being
  - Optimize quality of life

Strategies to Attenuate an Immunologically-Mediated Attack



Slide courtesy of P. Calabresi, MD.

The Evolving Multiple Sclerosis Treatment Landscape: Relapsing-Remitting Disease*



*Ocrelizumab is approved for both RRMS and primary progressive MS.
†Daclizumab is being voluntarily withdrawn from the market in 2018.

Timeline of approved compounds in MS. Multiple Sclerosis Discovery Forum Web site. http://www.msdiscovery.org/MSLine.

Oral DMTs: Efficacy

Pivotal Clinical Trials	Agent	Relapses	MRI Activity	12-Week Disability Progression-EDSS
FREEDOMS[1]	**Fingolimod**	ARR: ↓ 54%	Gd+ lesions: ↓82% T2 lesions: ↓74%	↓ 32%
TEMSO[2]	**Teriflunomide** (14 mg)	ARR: ↓ 32%	Gd+ lesions: ↓80% Lesion volume: ↓67%	↓ 30%
DEFINE[3]	**Dimethyl fumarate**	ARR: ↓ 53%	Gd+ lesions: ↓90% T2 lesions: ↓85%	↓ 38%

FREEDOMS: Efficacy and Safety of Fingolimod in Patients with RRMS; TEMSO: Study of Teriflunomide in Reducing the Frequency of Relapses and Accumulation of Disability in Patients with MS; DEFINE: Efficacy and Safety of Oral BG00012 in RRMS.

1. Kappos L, Radue EW, O'connor P, et al. *N Engl J Med*. 2010;362(5):387-401.
2. O'connor P, Wolinsky JS, Confavreux C, et al. *N Engl J Med*. 2011;365(14):1293-303.
3. Gold R, Kappos L, Arnold DL, et al. *N Engl J Med*. 2012;367(12):1098-107.

Injectable DMTs: Efficacy

Pivotal Clinical Trials	Agent	Relapses	MRI Activity	12-Week Disability Progression – EDSS
Multiple Sclerosis Collaborative Research Group[1-3]	**IFN β-1a** (Low dose)	ARR: ↓ 18%	Gd+ lesions: ↓50% T2 lesions: no effect	↓ 37%
PRISMS[4,5]	**IFN β-1a** (High dose)	ARR: ↓ 33%	Gd+ lesions: ↓84% T2 lesions: ↓78%	↓ 30%
ADVANCE[6,7]	**Peg IFN β-1a**	ARR: ↓ 36%	Gd+ lesions: ↓86% T2 lesions: ↓67%	↓ 38%
IFNB Multiple Sclerosis Study Group[2,8,9]	**IFN β-1b**	ARR: ↓ 34%	Gd+ lesions: ↓83% T2 lesions: ↓75%	↓ 29% (insignificant Δ from baseline)
Copolymer 1 MS Study Group[10]	**Glatiramer acetate**	ARR: ↓ 29%	Not adequately assessed	Not significant

ADVANCE: Efficacy and Safety Study of Peg IFN β-1a in Participants with RMS; ARR: annual relapse rate; DMTs: disease-modifying therapies; EDSS: Expanded Disability Status Scale; Gd: gadolinium; PRISMS: Prevention of Relapses and Disability by IFN β-1a Subcutaneously in MS

1. Jacobs LD, Cookfair DL, Rudick RA, et al. *Ann Neurol*. 1996;39(3):285-94. 2. Klawiter EC, Cross AH, Naismith RT. *Neurology*. 2009;73:984-90. 3. Simon JH, Jacobs LD, Campion M, et al. *Ann Neurol*. 1998;43(1):79-87. 4. PRISMS (Prevention of Relapses and Disability by Interferon beta-1a Subcutaneously in Multiple Sclerosis) Study Group. *Lancet*. 1998;352(9139):1498-504. 5. 3 ways Rebif was proven effective. EMD Serono Web site. http://www.rebif.com/why-rebif/rebif-efficacy. 6. Calabresi PA, Kieseier BC, Arnold DL, et al. *Lancet Neurol*. 2014;13(7):657-65. 7. Plegridy [prescribing information]. Cambridge, MA: Biogen Idec Inc; 2015.8. The IFNB Multiple Sclerosis Study Group. *Neurology*. 1993;43(4):655-61. 9. Paty DW, Li DK. *Neurology*. 1993;43(4):662-7. 10. Johnson KP, Brooks BR, Cohen JA, et al. *Neurology*. 1995;45(7):1268-76.

IV DMTs: Efficacy

Pivotal Clinical Trials	Agent	Relapses	MRI Activity	12-Week Disability Progression- EDSS
AFFIRM[1]	**Natalizumab**	ARR: ↓ 68%	Gd+ lesions: ↓92% T2 lesions: ↓83%	↓ 42%
CARE-MS I[2]	**Alemtuzumab vs IFNβ-1a**	ARR: ↓ 55%	Gd+ lesions: 7% vs 19% T2 lesions: 48% vs 58%	Not significant
CARE-MS II[3]	**Alemtuzumab vs IFNβ-1a**	ARR: ↓ 49%	Gd+ lesions: 9% vs 23% T2 lesions: 46% vs 68%	↓ 42%
OPERA I & OPERA II[4]	**Ocrelizumab vs IFNβ-1a**	ARR: ↓ 46% ARR: ↓ 47%	Gd+ lesions: 2% vs 29%; 2% vs 42%	↓ 60%

AFFIRM: Safety and Efficacy of Natalizumab in the Treatment of MS; CARE-MS I and II: Safety and Efficacy of Alemtuzumab vs. IFNβ-1a in RRMS; ARR: annualized rate of relapse.

1. Polman CH, O'connor PW, Havrdova E, et al. *N Engl J Med*. 2006;354(9):899-910.
2. Cohen JA, Coles AJ, Arnold DL, et al. *Lancet*. 2012;380(9856):1819-28.
3. Coles AJ, Twyman CL, Arnold DL, et al. *Lancet*. 2012;380(9856):1829-39. 4. Ocrelizumab [package insert]. San Francisco, CA: Genentech, Inc; 2017.

Injectable DMTs: Safety and Monitoring

Agent	Minor Side Effects	Major Side Effects	Pregnancy Category	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	C	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	C	Same as above
Peg IFNβ-1a[3]	Same as above	Same as above	C	Same as above
IFNβ-1b[4,5]	Same as above	Same as above	C	Same as above
Glatiramer acetate[6]	Injection-site reactions; post-injection vasodilatory reaction	Lipoatrophy, skin necrosis, anaphylaxis	B	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; 2016. 2. IFNβ-1a [prescribing information]. Rockland, MA: EMD Serono, Inc; November 2015. 3. Pegylated IFNβ-1a [prescribing information]. Cambridge, MA: Biogen Idec Inc; October 2015. 4. IFNβ-1b [prescribing information]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; 2016. 5. IFNβ-1b [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; March 2015. 6. Glatiramer acetate [prescribing information]. Overland Park, KS: TEVA Neuroscience, Inc; 2015. O'Connor PW, et al. *Handb Clin Neurol*. 2014;122:465-501.

Oral DMTs: Safety and Monitoring

Agent	Minor Side Effects	Major Side Effects	Pregnancy Category	Monitoring
Fingolimod[1]	Lymphopenia (absolute lymphocyte count >200), transaminitis	Bradycardia, heart block, hypertension, risk of infections (herpetic), lymphopenia (absolute lymphocyte count <200), transaminitis, macular edema, skin cancer, reactive airway, PRES, PML	C	First-dose cardiac monitoring, eye and skin examinations, CBC with differential, LFTs, varicella-zoster virus IgG prior to starting medication, PFTs (if clinically indicated)
Teriflunomide[2]	Diarrhea, headache, nausea, hair thinning	Transaminitis, neutropenia, teratogenic (men and women), latent tuberculosis, neuropathy, hypertension, hypersensitivity	X	CBC with differential, LFTs (monthly for first 6 months), PPD prior to starting, wash out (if needed)
Dimethyl fumarate[3]	Flushing, gastrointestinal distress	Transaminitis, lymphopenia, PML	C	CBC with differential, LFTs

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]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; February 2016. 2. Teriflunomide [package insert]. Cambridge, MA: Genzyme Corporation; June 2016. 3. Dimethyl fumarate [prescribing information]. Cambridge, MA: Biogen Idec Inc; February 2016.

IV DMTs: Safety and Monitoring

Agent	Minor Side Effects	Major Side Effects	Pregnancy Category	Monitoring
Natalizumab[1]	Infusion reactions, headache, joint pain, fatigue, wearing-off phenomenon	Progressive multifocal leukoencephalopathy, infusion, herpes zoster, other infections, liver failure	C	CBC with differential, LFTs, serum JCV antibody (every 6 months), MRI, natalizumab antibodies (if clinically warranted)
Alemtuzumab[2]	Infusion reactions	Autoimmune thyroid disease, ITP, Goodpasture syndrome, infections (HSV, VZV)	C	Monthly CBC with differential, LFTs, urinalysis with urine cell counts, TFTs every 3 months
Ocrelizumab[3]	Infusion reactions	Infections, malignancies	Not Assigned	

ITP: immune thrombocytopenic purpura

1. Natalizumab [prescribing information]. Cambridge, MA: Biogen Idec Inc; May 2016. 2. Alemtuzumab [package insert]. Cambridge, MA: Genzyme Corporation; May 2016. 3. Ocrelizumab [prescribing information]. San Francisco, CA: Genentech, Inc. 2017.

Current Guidelines Address the Clinically Appropriate Use of Imaging and DMTs

Imaging

- Consortium of Multiple Sclerosis Centers (CMSC)
- MAGNIMS (Magnetic Resonance Imaging in MS) Network
- European Academy of Neurology (EAN)

DMTs

- Multiple Sclerosis Coalition
- European Committee for Research and Treatment of Multiple Sclerosis (ECTRIMS) and the European Academy of Neurology (EAN)

Imaging Guideline: CMSC, 2015

Brain MRI protocol with gadolinium at baseline

- Spinal cord MRI if transverse myelitis, inconclusive brain MRI, or age older than 40 with non-specific brain MRI findings
- Cervical cord MRI performed simultaneously with brain MRI is advantageous in patients with or without transverse myelitis
- Orbital MRI if severe optic neuritis with poor recovery

Recommended schedules for follow-up brain MRI in patients with a CIS or suspected MS are as follows:

- 6–12 months for high-risk CIS (≥2 ovoid lesions on first MRI)
- 12–24 months for low-risk CIS (normal brain MRI findings) and/or uncertain clinical syndrome with suspicious brain MRI features (eg, radiologically isolated syndrome [RIS])

Traboulsee A, Simon JH, Stone L, et al. *AJNR Am J Neuroradiol*. 2016;37(3):394-401.

Imaging Guideline: CMSC, 2015 (cont.)

Follow-up brain MRI with gadolinium is recommended for patients with an established diagnosis of MS in the following circumstances:

- No recent prior imaging available (eg, patient with MS transferring to a new clinic)
- Postpartum, to establish a new baseline
- Prior to starting or switching disease-modifying therapy
- Approximately 6 months after switching disease-modifying therapy, to establish a new baseline on the new therapy
- Every 1–2 years while on disease-modifying therapy, to assess subclinical disease activity
- In the event of unexpected clinical deterioration or reassessment of original diagnosis

In addition, brain MRI is recommended to monitor for progressive multifocal leukoencephalopathy (PML) at the following intervals:

- Every 12 months for patients negative for serum JC virus antibody
- Every 3–6 months for patients positive for serum JC virus antibody treatment and treatment duration with natalizumab ≥18 months

Traboulsee A, Simon JH, Stone L, et al. *AJNR Am J Neuroradiol*. 2016;37(3):394-401.

Imaging Guideline: MAGNIMS, 2015

Diagnosis

- Spinal cord MRI should be performed in patients with spinal cord symptoms at disease onset
- Spinal cord MRI should be considered when brain MRI results are inconclusive, and for all patients with brain MRI suggestive for RIS
- 3-6 months after baseline brain scan for patients with RIS or CIS and abnormal MRI
- If the second brain scan is inconclusive, a third can be done 6-12 months later
- Follow-up spinal cord MRI in patients with CIS, to demonstrate dissemination in space (DIS) and dissemination in time (DIT), has limited value and should not be done routinely

Rovira À, Wattjes MP, Tintoré M, et al. *Nat Rev Neurol*. 2015;11(8):471-82.

Imaging Guideline: MAGNIMS, 2015 (cont.)

Monitoring

- T2-weighted and contrast-enhanced T1-weighted brain MRI are the modalities of choice for monitoring
- The use of spinal cord MRI in addition to brain MRI is not recommended for routine monitoring and should be limited to certain clinical situations (eg, unexplained and/or unexpected spinal cord symptoms)
- Although assessment of brain volume does not have a role in the diagnosis of MS, it can be a good predictor of long-term disability
- Rates of change in brain volume are not recommended as a marker of disease progression in patients
- MRI should be included in drug monitoring to screen for opportunistic infections, unexpected disease activity (including paradoxical reactions), and comorbidities
- In patients at high risk of developing opportunistic infections who are switching DMTs, brain MRI should be performed at the time the current treatment is discontinued and after the new treatment is started
- Enhanced pharmacovigilance, including brain MRI every 3–4 months for up to 12 months, is required in patients who switch from natalizumab to other therapeutics

Wattjes MP, Rovira À, Miller D, et al. *Nat Rev Neurol*. 2015;11(10):597-606.

DMT Guideline: MSC, 2014

Treat with an FDA-approved disease-modifying agent as soon as possible after any of the following events:

- Diagnosis of relapsing MS
- First episode of neurologic symptoms with MRI findings consistent with MS, and other possible causes have been ruled out

Treatment with any disease-modifying medication should be continued indefinitely, unless any of the following occur:

- The patient or healthcare provider determines that the treatment is failing to adequately control the disease
- The side effects are intolerable
- The patient is unable to follow the recommended treatment regimen
- A more appropriate treatment becomes available

The Use of Disease-Modifying Therapies in Multiple Sclerosis. Multiple Sclerosis Coalition. National MS Society Web site. http://www.nationalmssociety.org/getmedia/5ca284d3-fc7c-4ba5-b005-ab537d495c3c/DMT_Consensus_MS_Coalition_color Published July 2014. Updated March 2017.

DMT Guideline: MSC, 2014 (cont.)

Additional recommendations:

- Switch from one disease-modifying treatment to another should only occur for medically appropriate reasons
- When a medication is not providing adequate benefit, another agent with a different mechanism of action should be considered
- Factors affecting choice of treatment are complex and should be addressed collaboratively by the patient and healthcare provider
- Access to treatment should not be limited by frequency of relapses, level of disability, or personal characteristics such as age, gender, or ethnicity
- Absence of relapses may indicate that the treatment is working and should not be considered a justification for discontinuing the treatment

The Use of Disease-Modifying Therapies in Multiple Sclerosis. Multiple Sclerosis Coalition. National MS Society Web site. http://www.nationalmssociety.org/getmedia/5ca284d3-fc7c-4ba5-b005-ab537d495c3c/DMT_Consensus_MS_Coalition_color Published July 2014. Updated March 2017.

DMT Guideline: ECTRIMS/EAN, 2018

Recommendations with strong supporting evidence

- Offer interferon or glatiramer acetate to patients with CIS and abnormal MRI findings with lesions suggesting MS who do not fulfill full criteria for MS
- Offer early treatment with disease-modifying drugs in patients with active relapsing-remitting MS (RRMS), as defined by clinical relapses and/or MRI activity (active lesions: contrast-enhancing lesions; new or unequivocally enlarging T2 lesions assessed at least annually)
- Offer a more efficacious drug to patients treated with interferon or glatiramer acetate who show evidence of disease activity

Montalban X, Gold R, Thompson AJ, et al. *Mult Scler.* 2018;24(2):96-120.

Investigational Therapies for MS

Agent	Target/ Mechanism of Action	Possible Indication	Route of Administration	Status
Ofatumumab	Anti-CD20 MAb	RRMS	IV/SC	Phase 3
Ponesimod	Sphingosine-1-phosphate receptor 1 (S1P1) modulator	RRMS	Oral	Phase 3
Ozanimod	S1P modulator for receptor subtypes 1 and 5	Relapsing MS	Oral	Phase 3
Siponimod	S1P modulator for receptor subtypes 1 and 5	SPMS	Oral	Phase 3
Masitinib	Tyrosine kinase inhibitor	PPMS SPMS	Oral	Phase 3

Krieger S, Fabian M. MS Research Update. Multiple Sclerosis Association of America Web site. https://mymsaa.org/publications/msresearch-update-2017/. Published 2017.

Results from Selected Trials of Investigational Therapies for MS

Agent	Study Population	Results
Ofatumumab	232 patients with RRMS	• 65% contrast lesion reduction during Week 0-12; ≥90% contrast lesion reduction during Week 4-12 for cumulative doses ≥30 mg
Siponimod	1,651 patients with SPMS	• 21% reduction in risk that disability would progress one EDSS step at 3 months • 26% reduction in risk that disability would progress one EDSS step at 6 months
Ozanimod	1,320 patients with RRMS	• 48% reduction in new or enlarging T2 lesions over one year for 1 mg ($p<0.0001$) and 25% reduction for 0.5 mg ($p=0.0032$) compared with IFN • 63% reduction in gadolinium-enhanced MRI lesions at 1 year was also demonstrated for ozanimod 1 mg ($p<0.0001$) and ozanimod 0.5 mg (34 percent, $p=0.0182$) compared with IFN

Kappos L, Bar-Or A, Cree B, et al. Efficacy and safety of siponimod in secondary progressive multiple sclerosis - Results of the placebo controlled, double-blind, Phase III EXPAND study. Presented at: American Academy of Neurology 2017 Annual Meeting; April 22-28, 2017; Boston, Massachusetts. Abstract 250
Sorensen PS, Lisby S, Grove R, et al. *Neurology*. 2014;82(7):573-81.
MS: Ozanimod successful in clinical trials. Scripps Research Institute. ScienceDaily Web site. https://www.sciencedaily.com/releases/2017/11/171109224027.htm. Published November 9 2017.

Summary

- Multiple sclerosis is a chronic, progressive demyelinating disease of the central nervous system that is more common than previously estimated
- Ability to treat MS is evolving rapidly and becoming more complicated as additional agents are introduced, particularly for relapsing-remitting disease
- Despite the availability of clinical guidelines for the use of imaging and DMTs, a “one-size-fits-all” approach is not warranted
- Goal of treatment is to balance efficacy, safety, and tolerability of therapeutic interventions for each patient
- Effective treatment for progressive subtypes of MS remains a significant unmet need, with only one therapy currently approved
  - A number of agents are in clinical development for various subtypes

MS Care Pathways and Algorithms to Improve Clinical and Economic Outcomes

Edmund Pezalla, MD, MPH
CEO
Enlightenment Bioconsult, LLC

MS Disease Characteristics Have a Profound Impact on Economic Outcomes

Chronic, progressive autoimmune disease	Lifetime disability considerations	Worsening morbidity and corresponding health care service utilization over time
Leads to severe neurologic and motor/sensory symptoms	Symptoms affect a myriad of activities of daily living	Health care service utilization related to ambulatory and inpatient care as well as monitoring/testing
Age of onset most often between 20 and 50 years	Directly impacts adults of working age	Implications for health care purchasers in terms of absenteeism and lost productivity

The Economic Burden of MS is Virtually Unsurpassed Among Chronic Conditions

- Patients with MS utilize health care services considerably more than those without chronic illnesses
- Compared with healthy individuals, patients with MS…
  - …will visit their physician an average of 3 times more often
  - …are 3.5 times more likely to be hospitalized
  - …are 2 times more likely to have ≥1 ER visits
  - …are 2.4 times more likely to have ≥1 visit for physical, speech, or occupational therapy
- The total lifetime cost per patient with MS is estimated to be $4.1 million (in 2010 dollars)
- For patients using DMTs to manage their MS, approximately 75% of total MS-related health care costs in 2011 was for DMT monotherapy

DIRECTLY AND INDIRECTLY, MS COSTS

$8,528 - $54,244

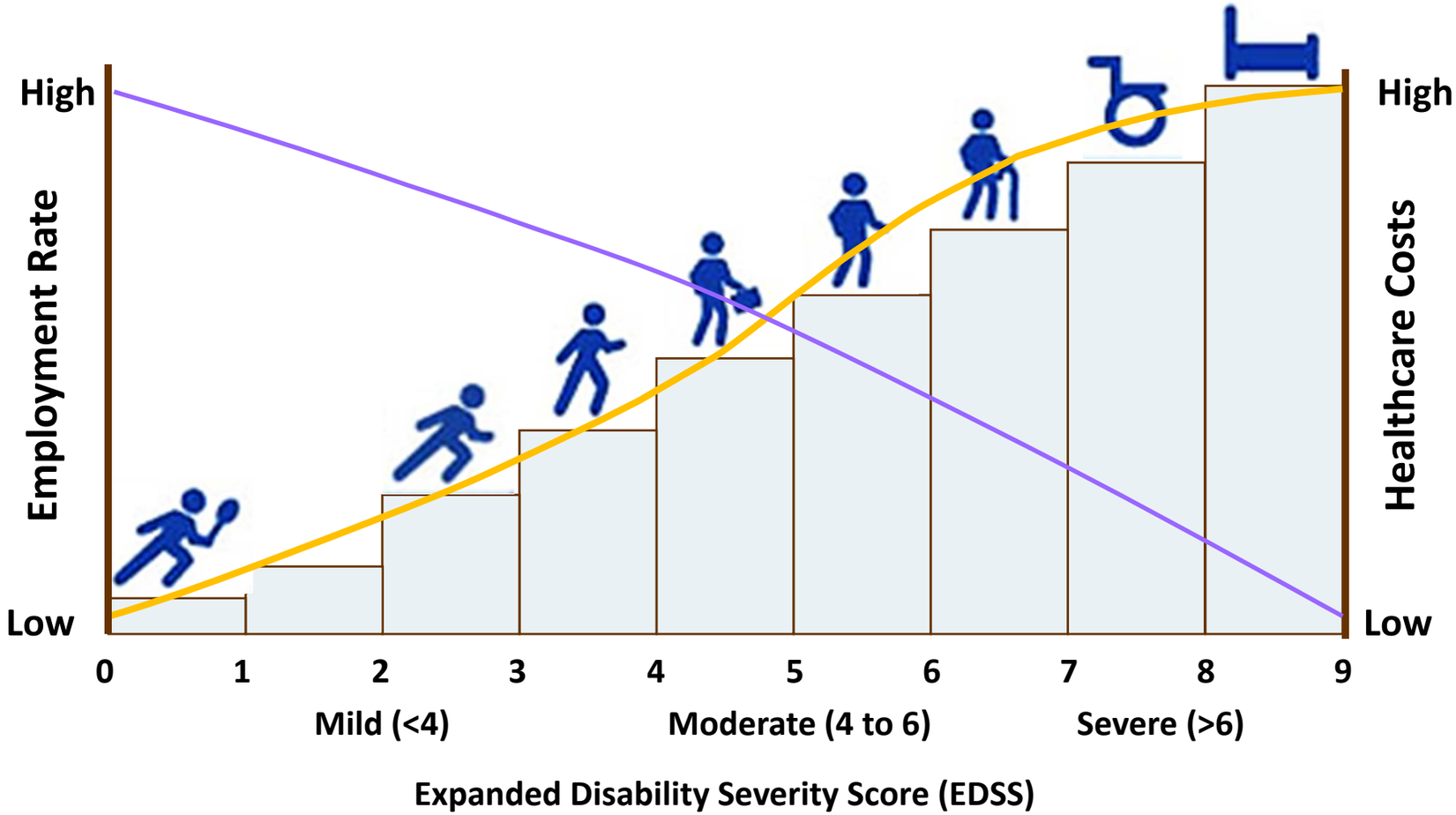
PER PATIENT PER YEAR IN THE U.S.

Compared with other chronic conditions, MS ranks second only to congestive heart failure in terms of costliness.

Pozniak A, Hadden L, Rhodes W, Minden S. *Int J MS Care*. 2014;16(3):132-9. Asche CV, Singer ME, Jhaveri M, Chung H, Miller A. *J Manag Care Pharm*. 2010;16(9):703-12.
Anderson SS, Philbrick AM. *J Manag Care Pharm*. 2014;20(3):254-61. Adelman G, Rane SG, Villa KF. *J Med Econ*. 2013;16(5):639-47.
Owens GM, Olvey EL, Skrepnek GH, Pill MW. *J Manag Care Pharm*. 2013;19(suppl 1A):S41-S53.

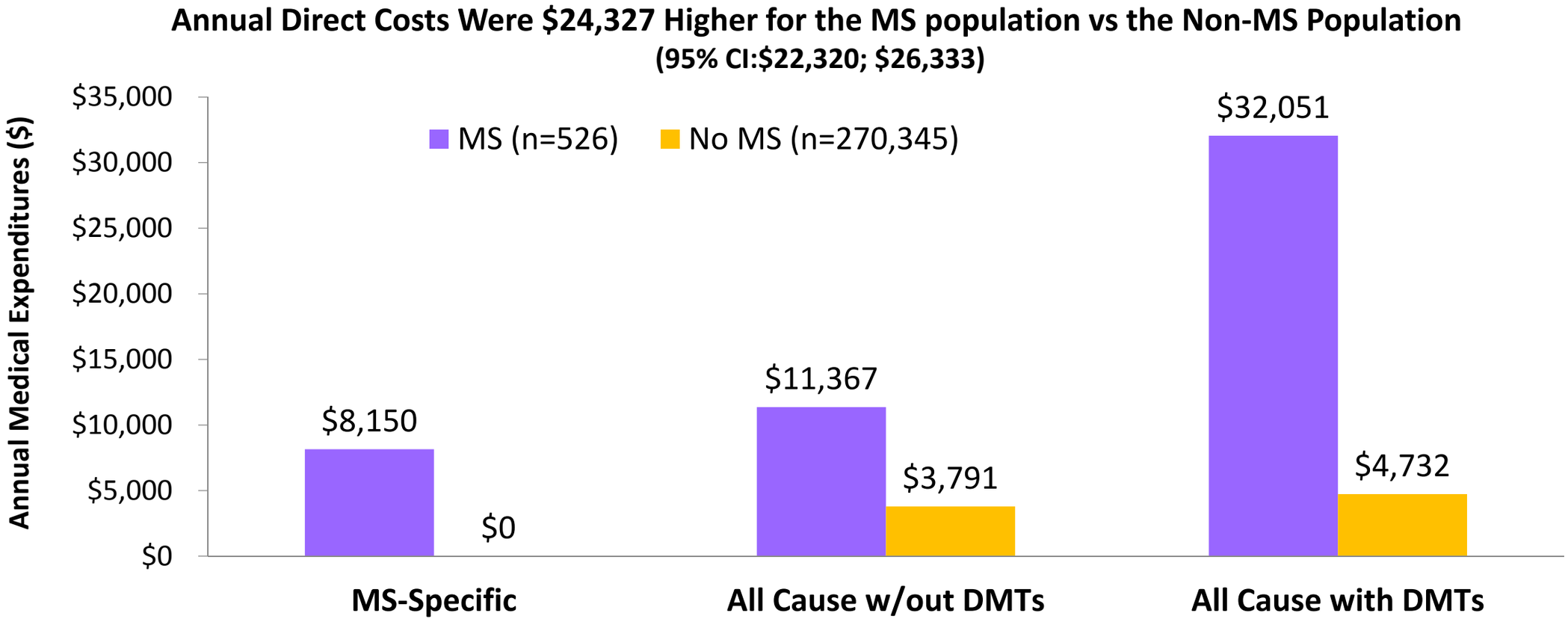
DMT=disease modifying therapy

Costs Increase and Productivity Decreases as MS Progresses in Severity



Burks J. *J Manag Care Med*. 2009;12:26-31. http://jmcmpub.org/pdf/12-1/?pdf_page=26. Comi G. *Neurol Sci*. 2006;27(suppl 1):S8-S12. Kobelt G, Berg J, Atherly D, Hadjimichael O. *Neurology*. 2006;66(11):1696-702. Campbell JD, Ghushchyan V, Brett mcqueen R, et al. *Mult Scler Relat Disord*. 2014;3(2):227-36.

MS-specific and All Cause Annual Medical Expenditures

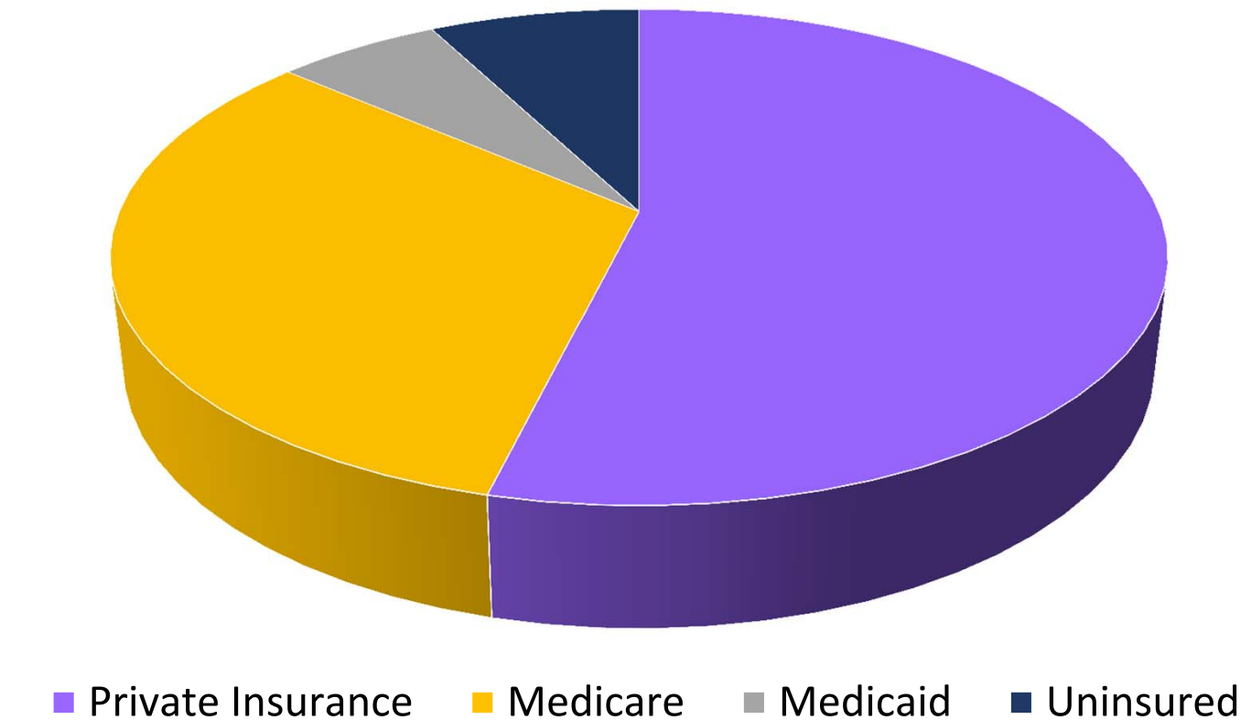


Data from the Medical Expenditure Panel Survey of non-institutionalized MS patients (≥18); 1998 to 2009

DMT=disease modifying therapy

Campbell JD, Ghushchyan V, Brett Mcqueen R, et al. *Mult Scler Relat Disord*. 2014;3(2):227-36.

The Majority of Americans with MS Receive Health Care Services via Commercial Insurance



Financial wellness among individuals living with multiple sclerosis. National Disability Institute Web site. www.realeconomicimpact.org/data/files/reports/financial%20wellness%20survey%20report%20-%2009.04.12.pdf. Published September 2012. Accessed March 2018.

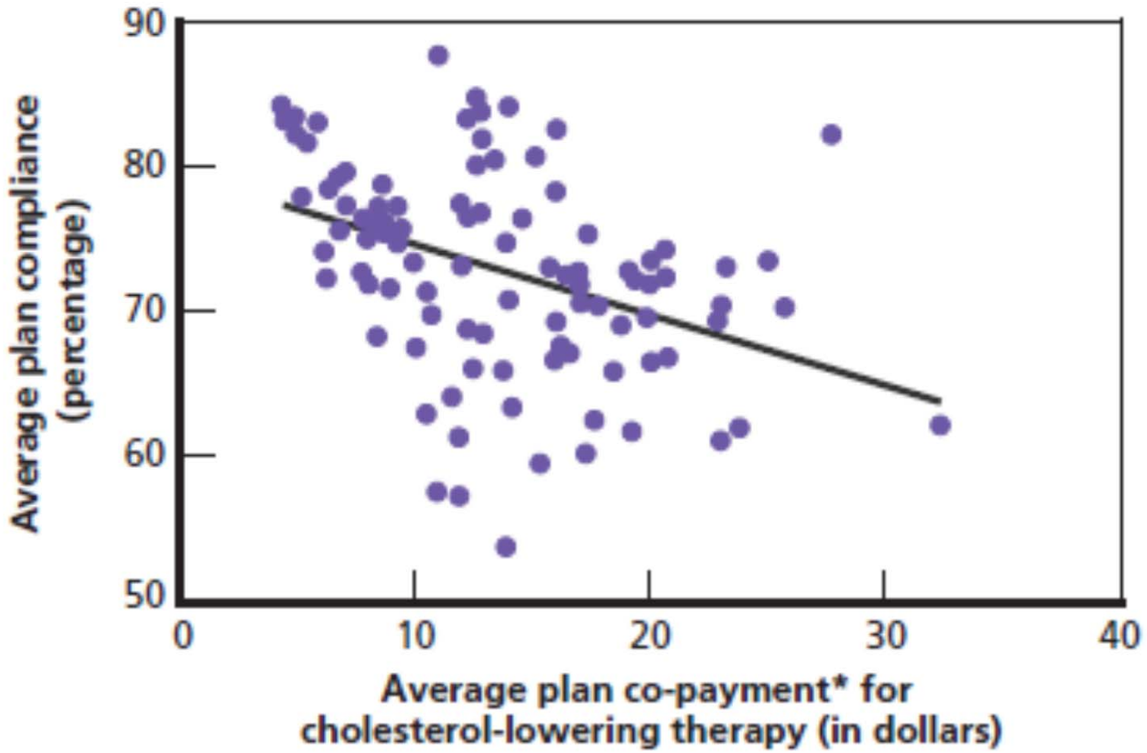
Out-of-Pocket Costs May Be Significant for Patients with MS Regardless of Insurance Type

- Data from 2016 show that patient out-of-pocket (OOP) costs for 3 sample MS agents ranged from $5,979 to $6,448 annually
  - By comparison, OOP costs for patients with cancer may reach as high as $11,538 for a single current drug
- For the 3 MS drugs studied, an average of 34.7% of OOP costs were incurred by Part D enrollees after their spending reached the catastrophic coverage phase of the Part D benefit
  - The data demonstrated that a substantial share of the OOP costs for these specialty-tier drugs can be incurred even after enrollees' drug spending reaches the drug benefit's catastrophic threshold

Hoadley J, Cubanski J, Neuman T. It pays to shop: Variation in Out-of-Pocket Costs for Medicare Part D Enrollees in 2016. Kaiser Family Foundation Web site. http://www.nasuad.org/sites/nasuad/files/issue-brief-it-pays-to-shop.pdf. Published December 2015. Accessed March 2018.

Effectively Managing Rising Drug Expenditures with Member Cost-Share Remains Challenging

- Over the next 3-5 years, it is estimated that medical pharmacy costs will continue to increase
  - Particularly troubling for specialty where breakthrough therapies for rare diseases will contribute significantly
- Payers seeking risk mitigation strategies look to low-hanging fruit such as increased copays and coinsurance
  - Such cost shifting strategies may show early onset savings for payers, but could actually increase future total cost of care



*30-day supply

Historical trends that have increased co-payments in lockstep with rising prices do many patients a disservice, and in some cases they increase overall health care costs

Magellan Rx Management Medical Pharmacy Trend Report, 8th ed. 2017. Magellan Rx Management Web site. https://www1.magellanrx.com/media/722153/tr2017_final_for-website-use.pdf. Published 2018. Rand Health. Research Highlights. 2009. Accessed March 2018.

Despite Being Related to Reduced Drug Utilization, Nonadherence Results in Billions of Dollars in Health Care Service Utilization

Nearly half of all Americans live with at least one chronic disease

Patients who adhere to their medication regimens have better health outcomes and use less urgent care and inpatient hospital services

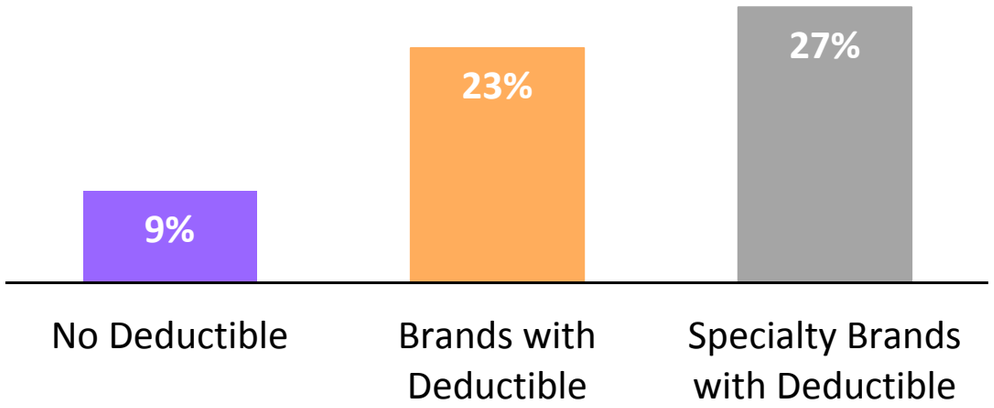
Despite evidence of improved outcomes, average rates remain at ~50%

Between $100 and $300 billion of avoidable health care costs have been attributed to nonadherence in the US annually, representing 3%-10% of total US health care costs

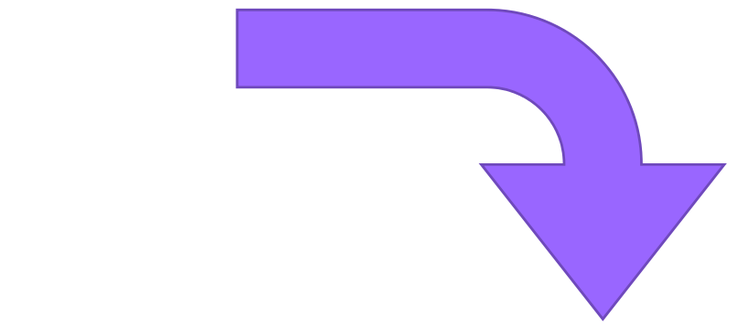
Roebuck MC, Liberman JN, Gemmill-toyama M, Brennan TA. *Health Aff*. 2011;30(1):91-99.

High Levels of Cost-Share are Often Responsible for Specialty Prescription Abandonment, Giving Rise to Copay Assistance

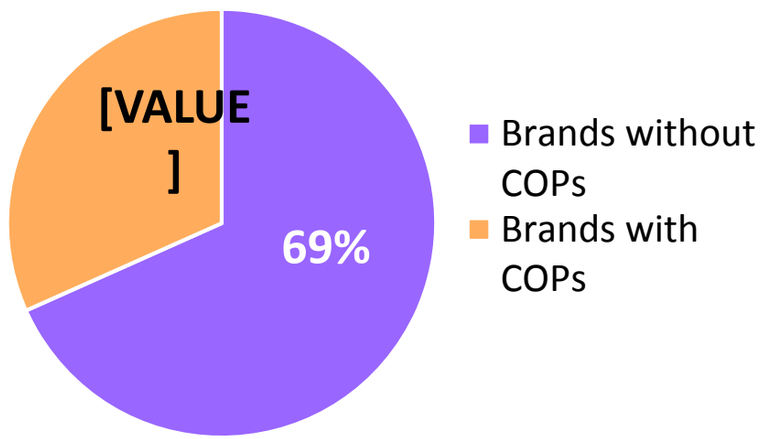
Chart 19: Abandonment Rates for Brand Medicines in Commercial Plans



Source: Amundsen Consulting (a division of QuintilesMS) analysis for PhARMA; IMS FIA; Rx Benefit Design; Dec. 2017

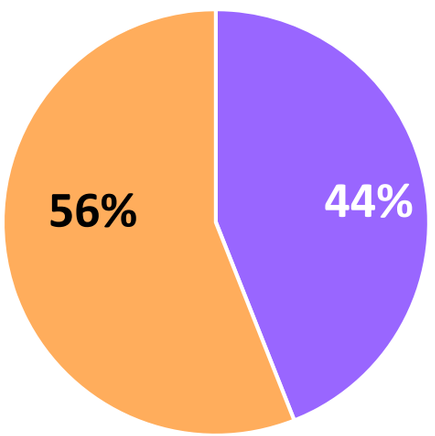


Biologics Brand Universe



Percentage of Biologics Brands
n = 101 biologics brands

Non-Biologic Brand Universe



Percentage of non-Biologics Brands
n = 976 non-biologic brands

Medicines Use and Spending in the US: A Review of 2016 and Outlook to 2021. IMS Health Web site. https://www.iqvia.com/institute/reports/medicines-use-and-spending-in-the-us-a-review-of-2016. Published May 4, 2017. Accessed March 2018.
Optimizing Your Co-Pay Offset Program Strategy: Metrics to Measure for Success. The Zitter Group. Published August 2012.

Current Environment of Copay Assistance

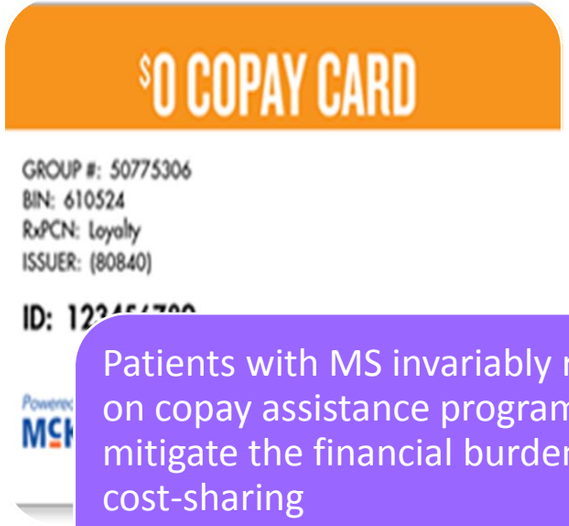
- While copay cards have some positive benefits for patients (improves access, affordability, and compliance), some plan sponsors believe they increase costs via the following:
  - Assisting beneficiaries to expend their accumulators more quickly can remove barriers to unnecessary testing/procedures by limiting the patients' stake
  - Potentially incentivizing patients to utilize non-preferred drugs that are less cost-effective
- In response to these issues and as a way to drive greater savings for plan sponsors, two new specialty copay card programs were introduced in 2017: accumulator adjustment and copay allowance maximization
  - However, when applied to high-cost/high-value drugs, these programs may create a barrier to patients' utilization of necessary and potentially life-saving therapies

Cleveland Research Company, 2017.

Copay Assistance Mitigates Patient Cost Burden in MS, but Accumulator Adjustment Programs Reintroduce Financial Barriers to Access

For patients with complex, chronic conditions like MS, finding the right DMT can be a long and difficult journey

- DMT adherence can result in improved QoL and decreased health care service utilization



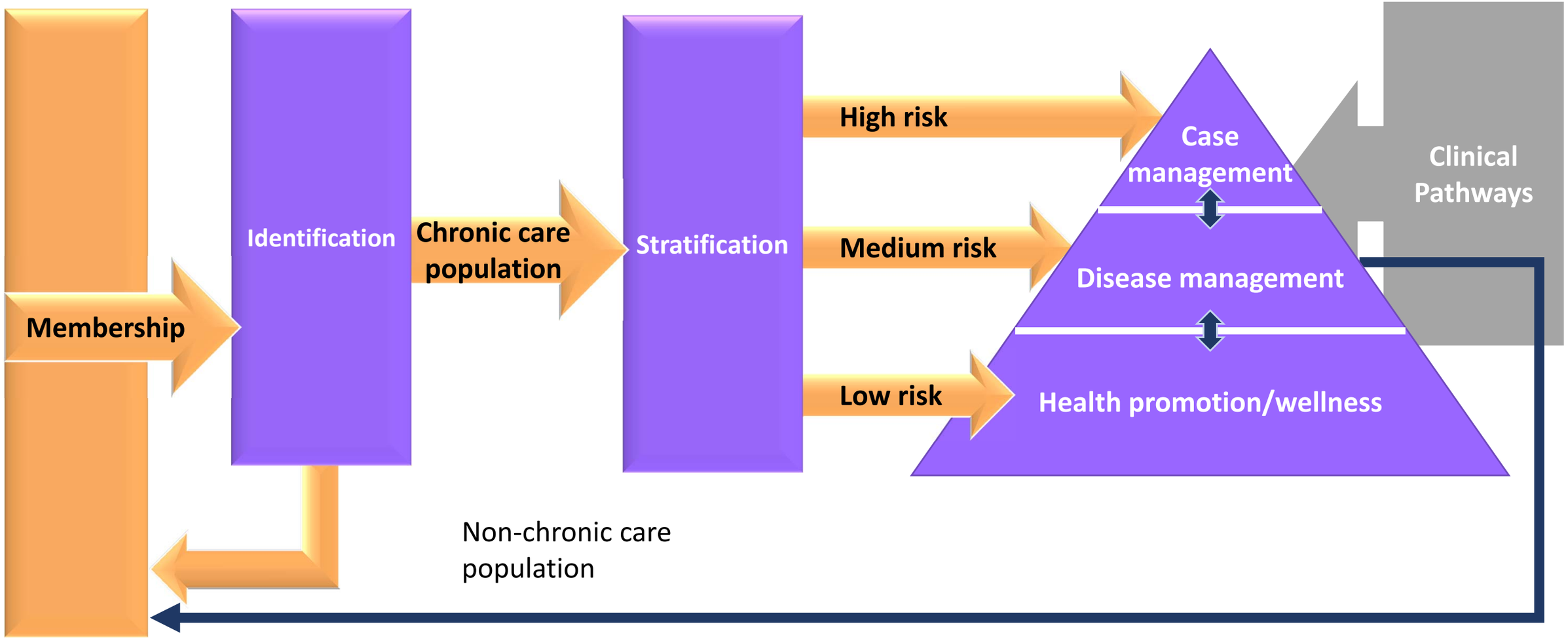
Patients with MS invariably rely on copay assistance programs to mitigate the financial burden of cost-sharing

- A significant proportion of patients now only have high-deductible plan options
- Copay assistance programs are offered by all manufactuers of specialty drug products

Copay Accumulator Programs interfere with a vital lifeline for patients with chronic conditions necessitating specialty drugs

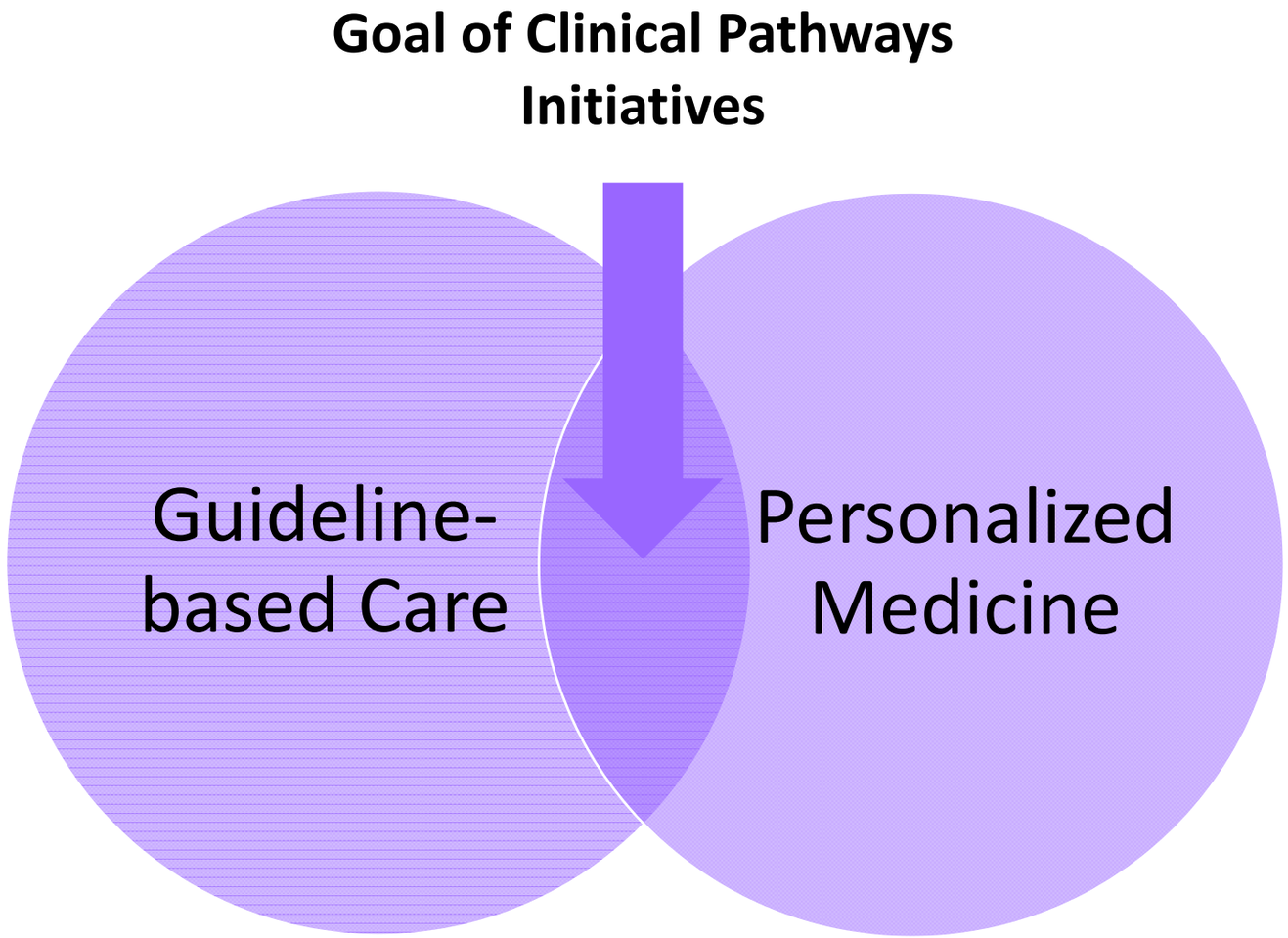
- Accumulator adjustment and copay allowance maximization negate the benefits of copay assistance programs and reintroduce financial barriers to care

In Addition to Chronic Care Management Programs, Clinical Pathways Initiatives Provide an Evidence-based Means of Managing Costs Beyond Increased Member Share



Mattke S, Higgins A, Brook R. *Am J Manag Care*. 2015;21(5):370-6.

Clinical Pathways Initiatives Aim to Reduce Treatment Variability While Allowing Individualized Care

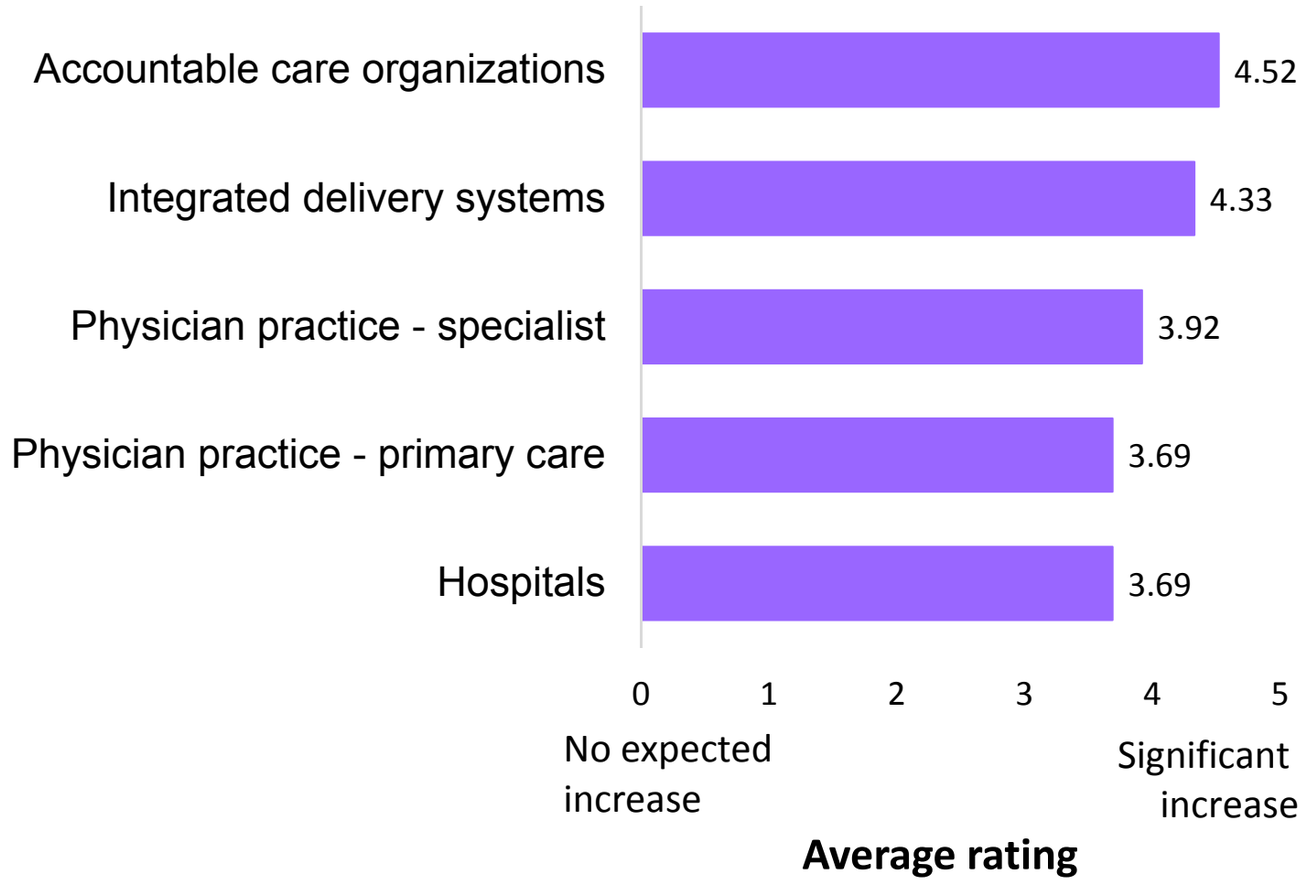


Anticipated Increase in Pathway Use by Setting

Question:

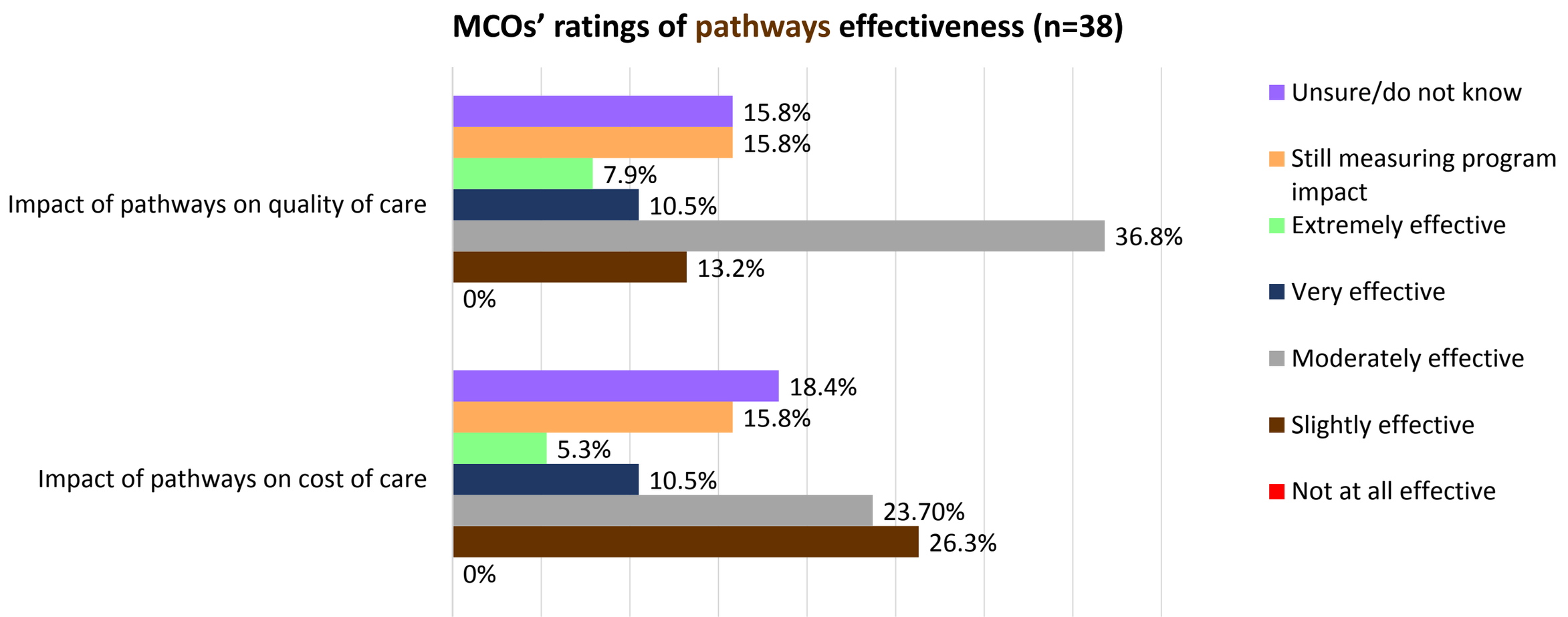
"Do you expect the use of care pathways (oncology- and/or non–oncology-related) to increase in any of the settings listed below?"

Source: Online survey of 26 payers, providers, vendors



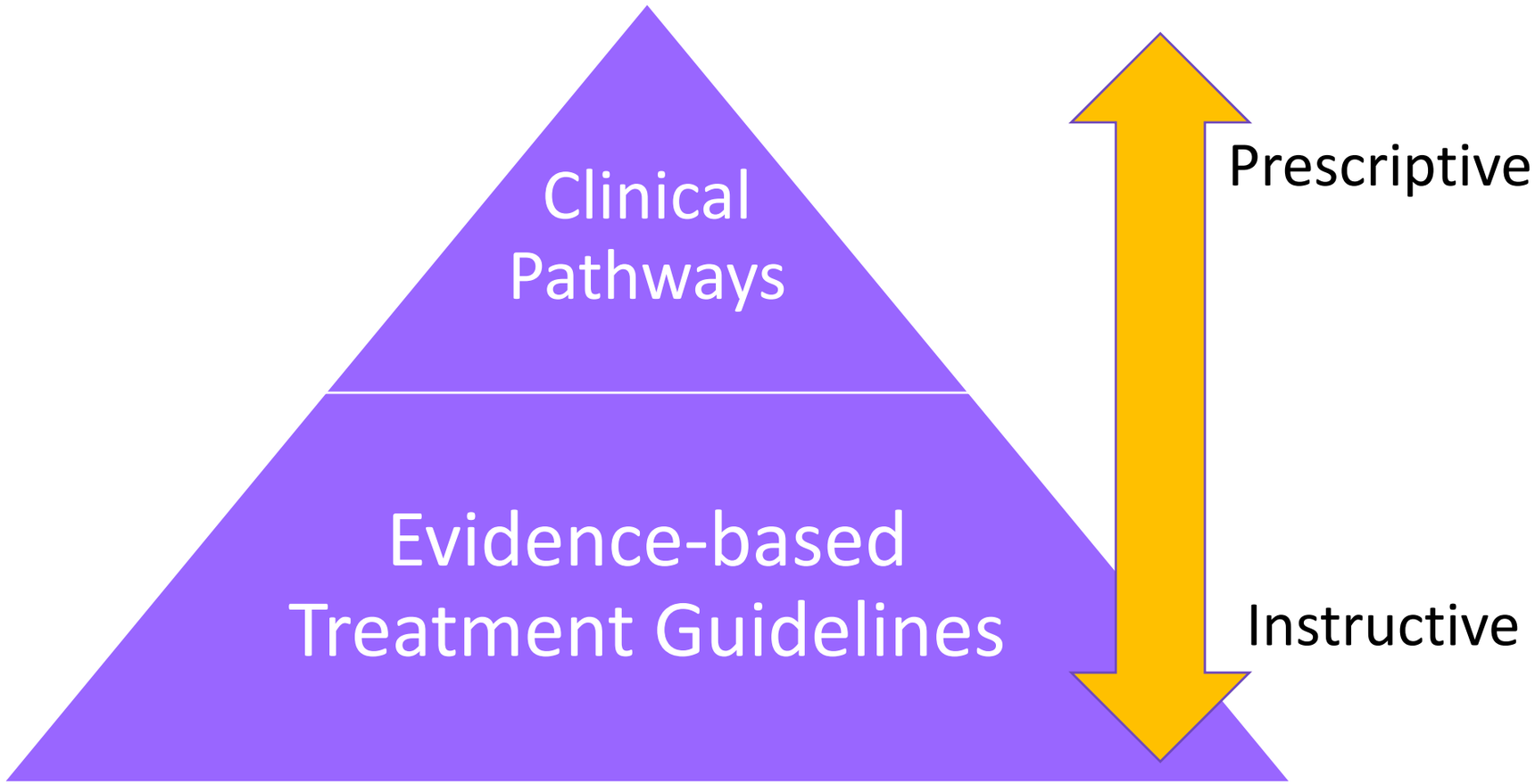
Chawla A, Westrich K, Matter S, Kaltenboeck A, Dubois R. *Am J Manag Care*. 2016;22(1):53-62.

Most MCOs Perceive Pathways Programs to be Moderately or at Least Slightly Effective in Impacting Care Quality and Cost



The 2016 Genentech Oncology Trend Report: Perspectives From Managed Care, Specialty Pharmacies, Oncologists, Practice Managers, and Employers. 8th ed. South San Francisco, CA: Genentech; 2016. https://www.gpbch.org/docs/2016_genentech_oncology_trend_report.pdf. Accessed March 2018.

Existing Evidence-based Treatment Guidelines Serve as the Foundation for Clinical Pathways Initiatives

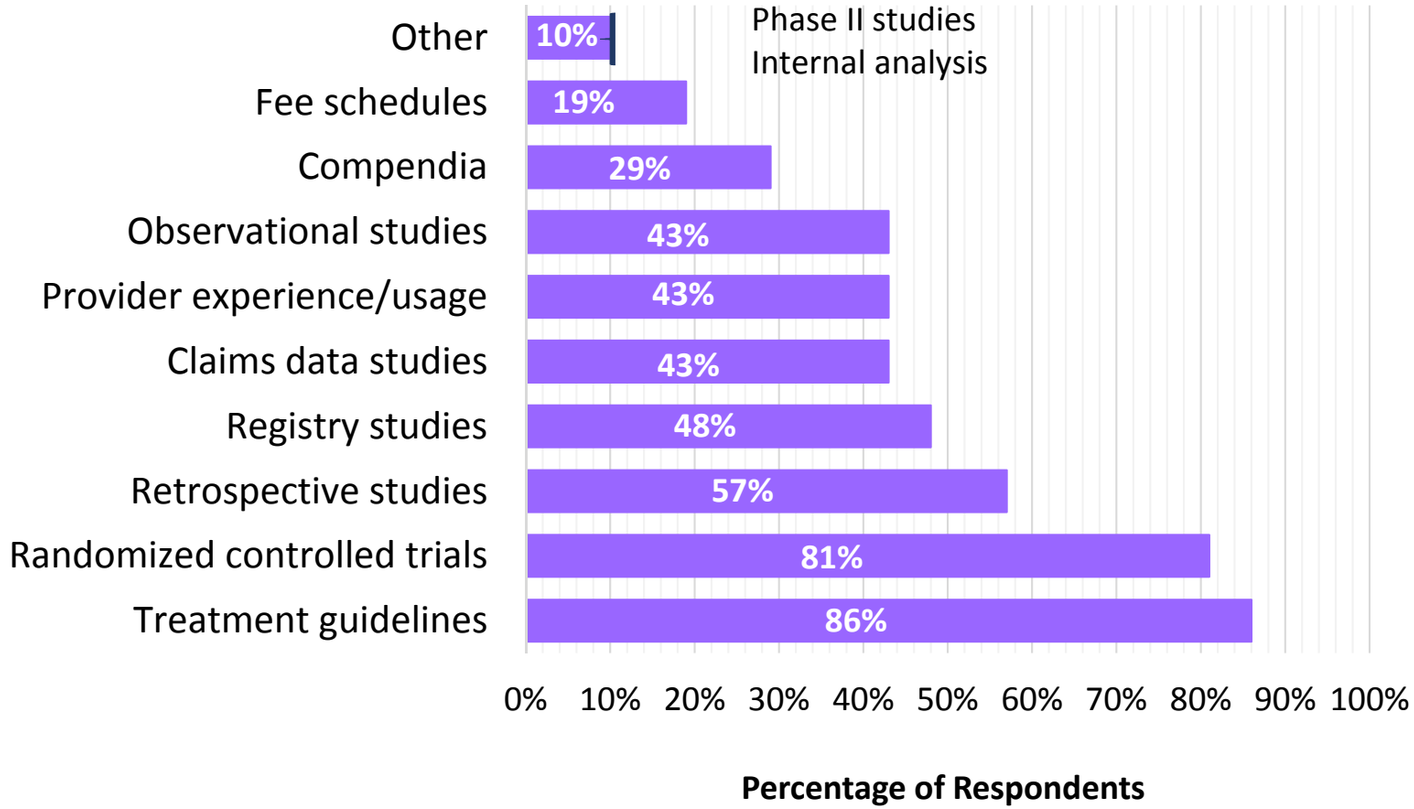


Key Sources of Information for Pathway Development

Question:

"In developing a care pathway, different types of evidence or information may be used to develop the clinical algorithm. Please indicate which of the following types of evidence or information are typically used to develop the clinical algorithm."

Source: Online survey of 21 stakeholders (payers, providers, and vendors)



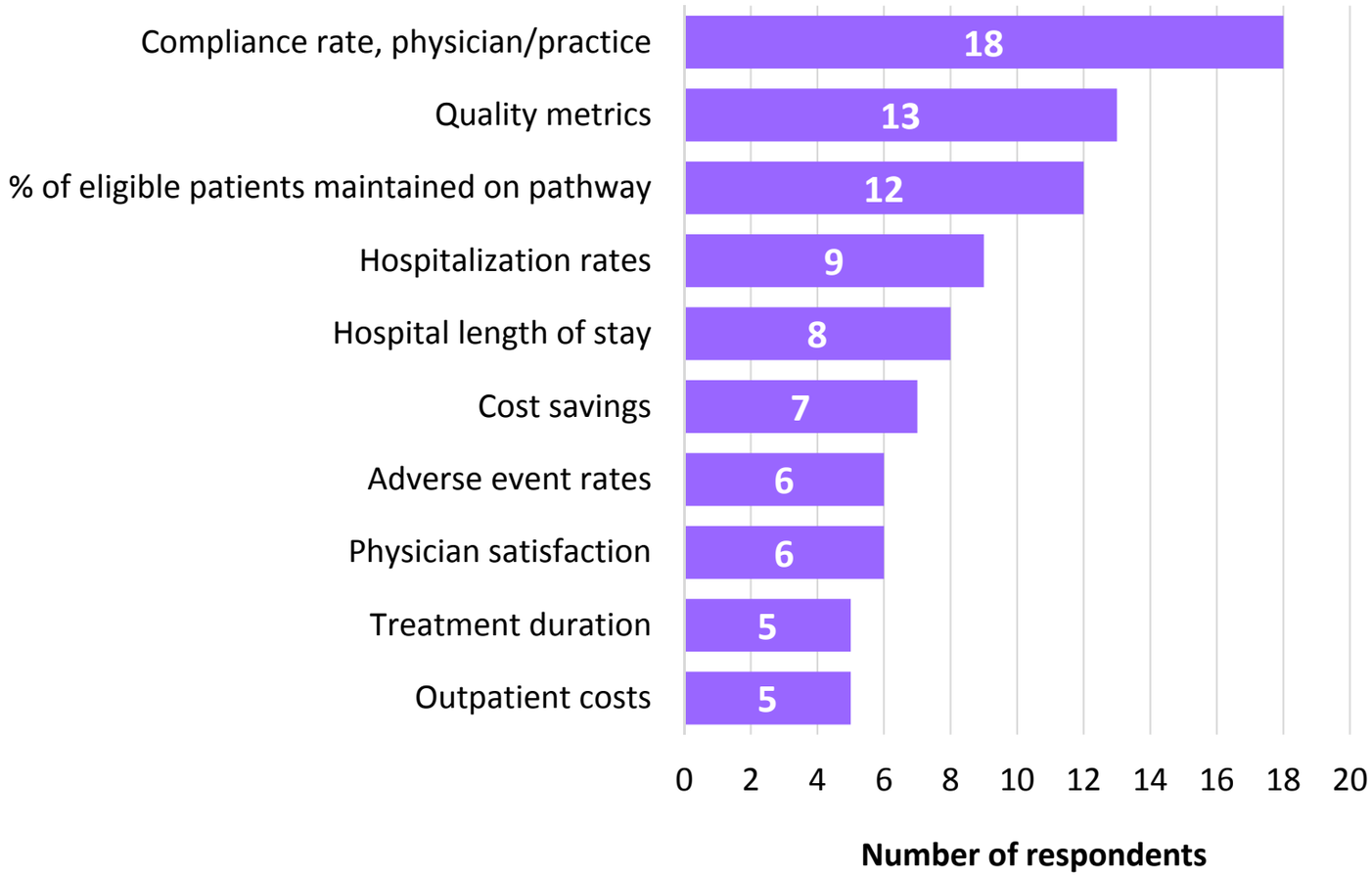
Chawla A, Westrich K, Matter S, Kaltenboeck A, Dubois R. *Am J Manag Care*. 2016;22(1):53-62.

Common Evaluation Metrics for Pathways Programs

Question:

"Which of the following metrics (if any) are typically used to evaluate care pathway performance? For the metrics that you selected, please indicate the 3 most important metrics when it comes to evaluating care pathway performance."

Source: Online survey of 19 payers, providers, and vendors



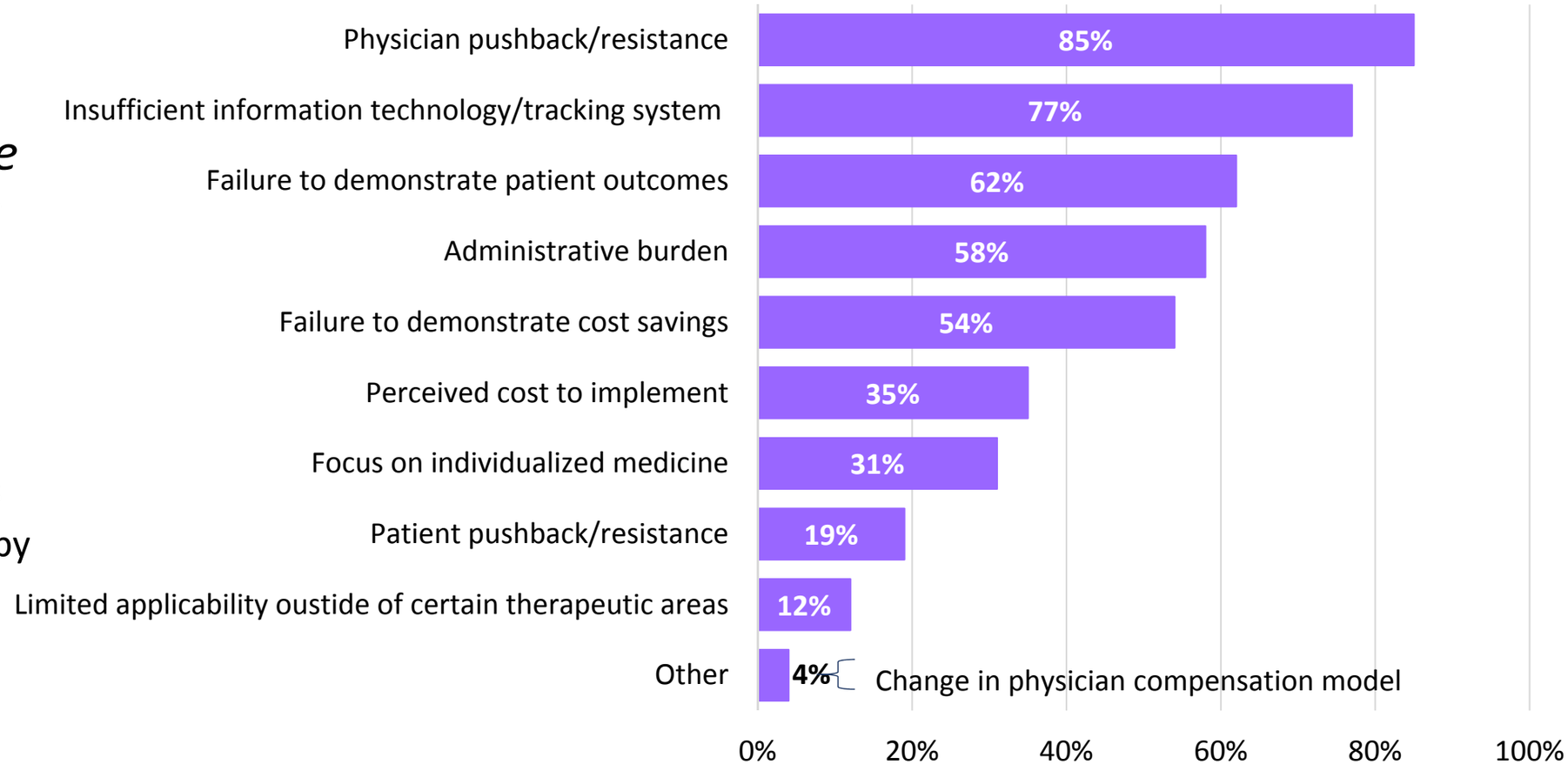
Chawla A, Westrich K, Matter S, Kaltenboeck A, Dubois R. *Am J Manag Care*. 2016;22(1):53-62.

Potential Barriers to Pathway Expansion

Question:

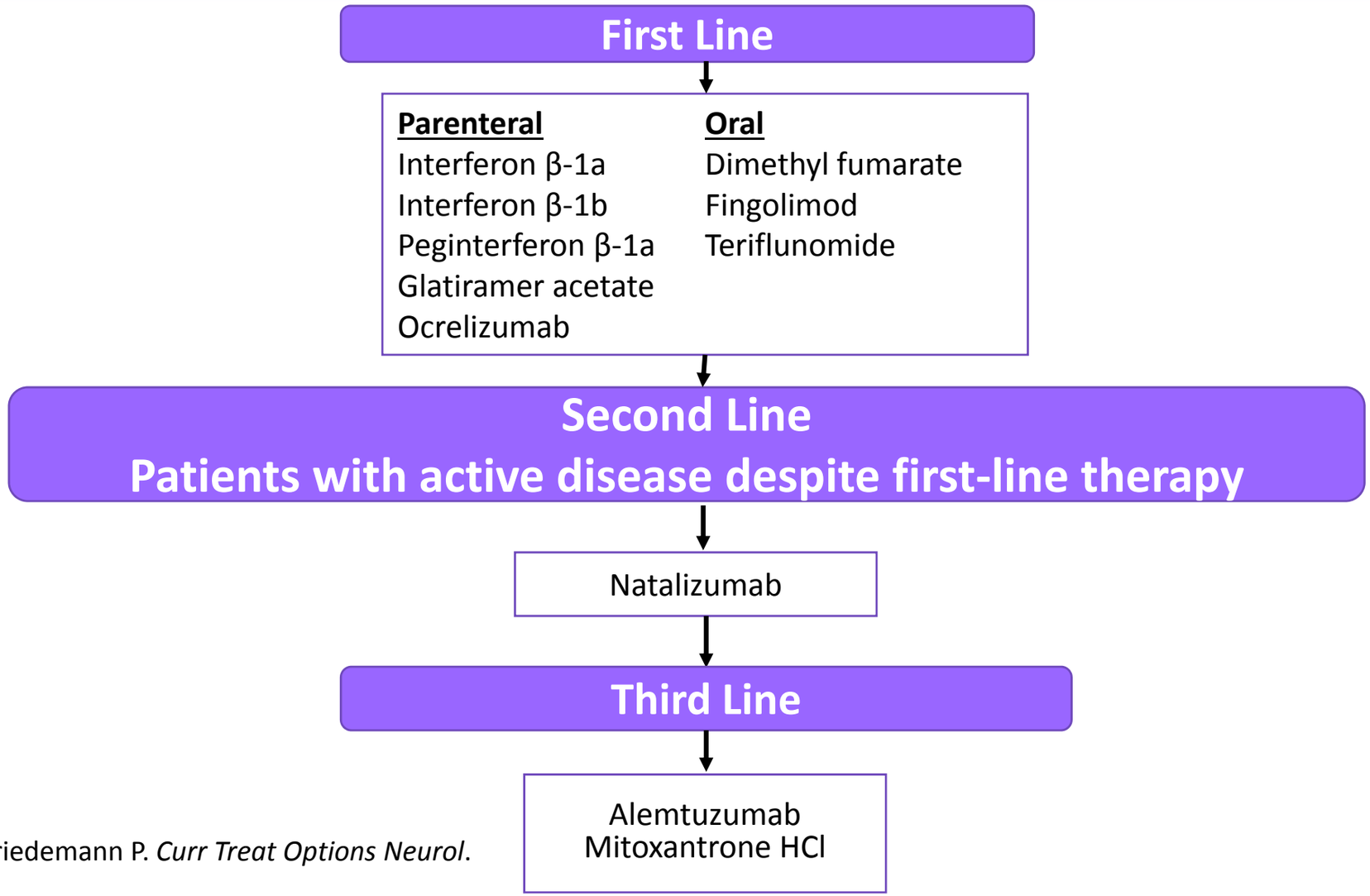
"What do you see as potential barriers to the expansion or uptake of care pathways?"

Source: Online survey of 26 payers, providers, and vendors who influence or are affected by care pathways



Chawla A, Westrich K, Matter S, Kaltenboeck A, Dubois R. *Am J Manag Care*. 2016;22(1):53-62.

Potential Relapsing-Remitting MS Treatment Pathway/Algorithm



Adapted from Dörr J, Friedemann P. *Curr Treat Options Neurol*. 2015;17:25.

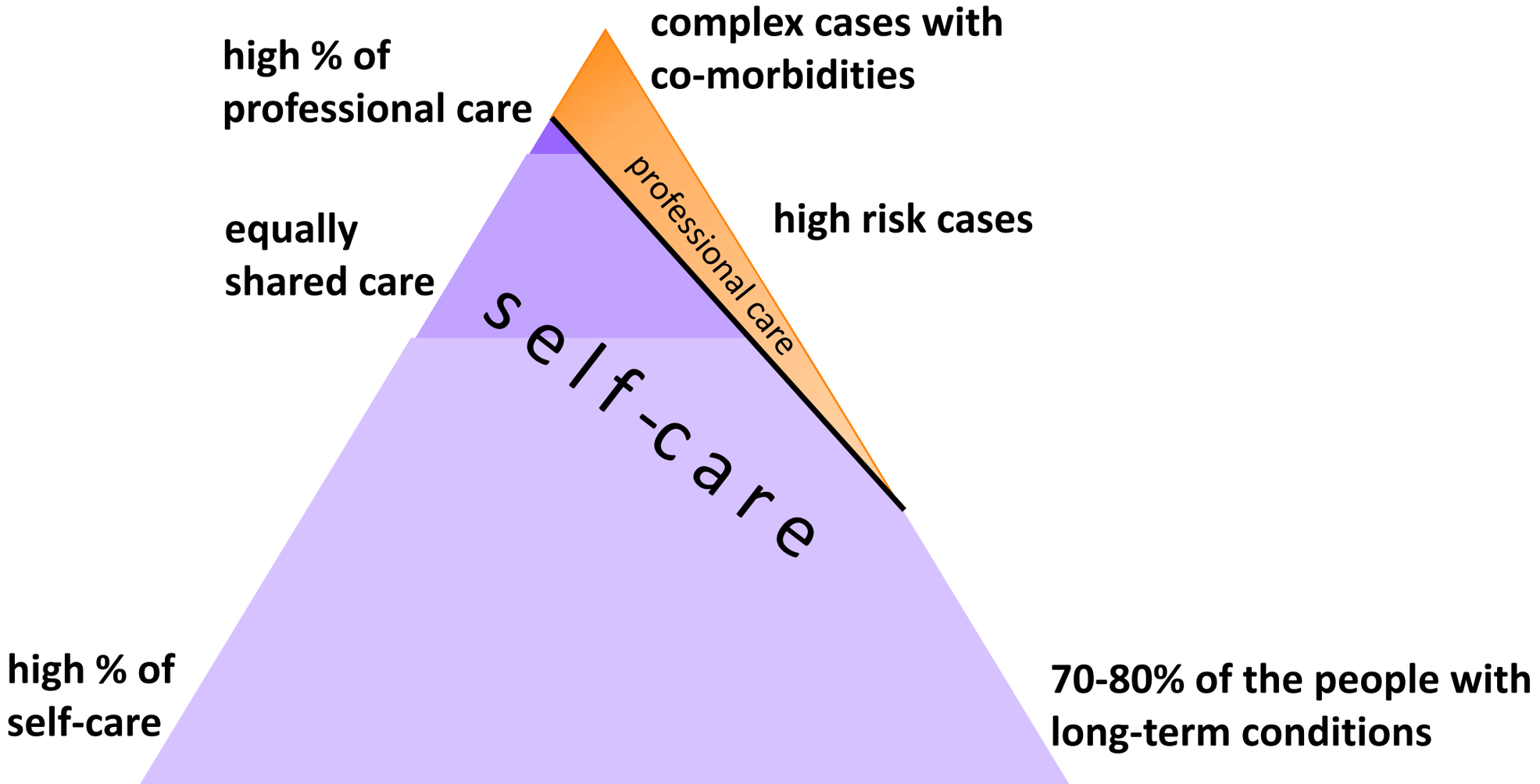
Summary

- MS is characterized by progressive disability and markedly increasing health care service utilization and total cost of care compared with healthy individuals
- In an effort to manage the economic burden across all disease states, managed care stakeholders have resorted to increased member cost-share in the form of deductibles, copays, and coinsurance
- Such payer interventions may result in decreased therapeutic adherence and further increased health care service utilization
- Clinical pathways initiatives represent an evidence-based means of decreasing treatment variability and managing costs of care

Health Coaching Strategies for Optimal Multiple Sclerosis(MS) Management

James T. Kenney, RPh, MBA
Manager, Specialty and Pharmacy Contracts
Harvard Pilgrim Health Care

Self-Care Comprises the Largest Share of Chronic Disease Management



Kennedy A, Rogers A, Bower P. *BMJ*. 2007;335(7627):968-70.

Patient Engagement Has Been Termed "The Blockbuster Drug of the Century"

- Patients can play an integral role in improving the quality, safety, and cost of health care interventions.
- Furthermore, the importance of patient engagement as an essential component of high-quality health care has been recognized worldwide
- The list of parameters shown to be influenced by patient engagement includes:
  - Improved clinical outcomes
  - Reduced health care resource utilization
  - Improved service quality
- Improved clinical outcomes that facilitate patient engagement include improved treatment adherence, faster recovery, and reduced mortality rates

Rieckmann P, Boyko A, Centonze D, et al. *Mult Scler Relat Disord*. 2015;4(3):202-18.
Chase D. "Patient engagement is the blockbuster drug of the century." Forbes. 2012. https://www.forbes.com/sites/davechase/2012/09/09/patient-engagement-is-the-blockbuster-drug-of-the-century/#5b5dea325638. Accessed March 2018.

Lifelong Therapy and an Evolving Treatment Paradigm Underscore the Importance of Patient Engagement in Multiple Sclerosis

Patients face decisions relating to treatment, available interventions and services, and Quality of Life(QoL)

Previously, interferon beta or glatiramer acetate therapy were the mainstays of treatment for Multiple Sclerosis, and the side effects were known, reversible, predictable, and treatable

Over the past decade, new treatments have emerged with improved efficacy and ease of administration; however, they have the potential to cause serious side effects

It is imperative that the risks and their relationship to clinical benefit are taken into account by the health plan, provider, and patient

Patient engagement and health coaching are necessary to help patients navigate treatment decisions and lifestyle decisions

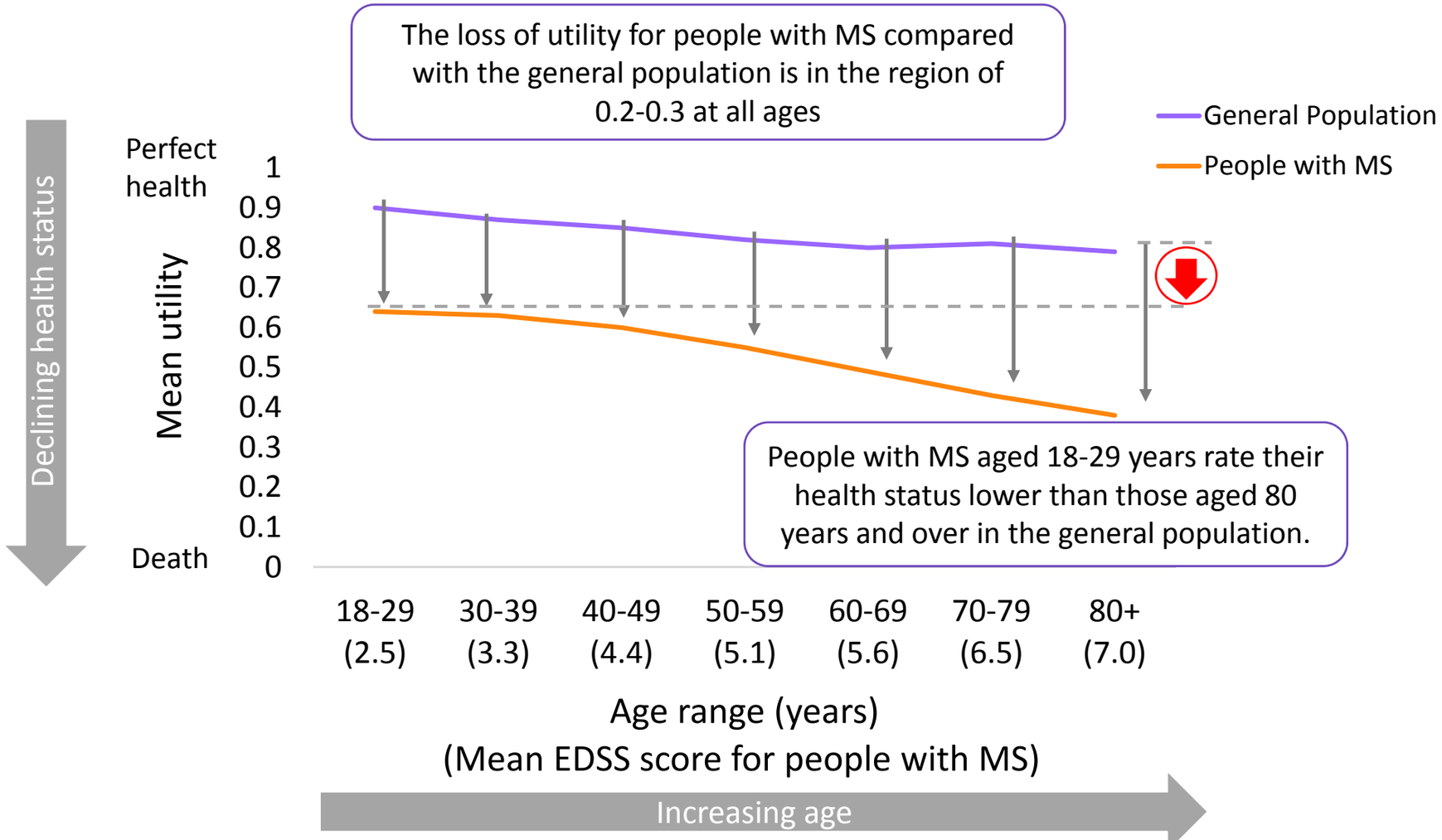
Rieckmann P, Boyko A, Centonze D, et al. *Mult Scler Relat Disord*. 2015;4(3):202-18.

Multiple Sclerosis in the 21st Century Steering Group: Themes that Require Action for Patient Engagement in MS

- Setting and facilitating engagement by education and confidence building
- Increasing the importance placed on Quality of Life and patient concerns through patient-reported outcomes (PROs)
- Providing credible sources of accurate information
- Encouraging treatment adherence through engagement
- Empowering through a sense of responsibility

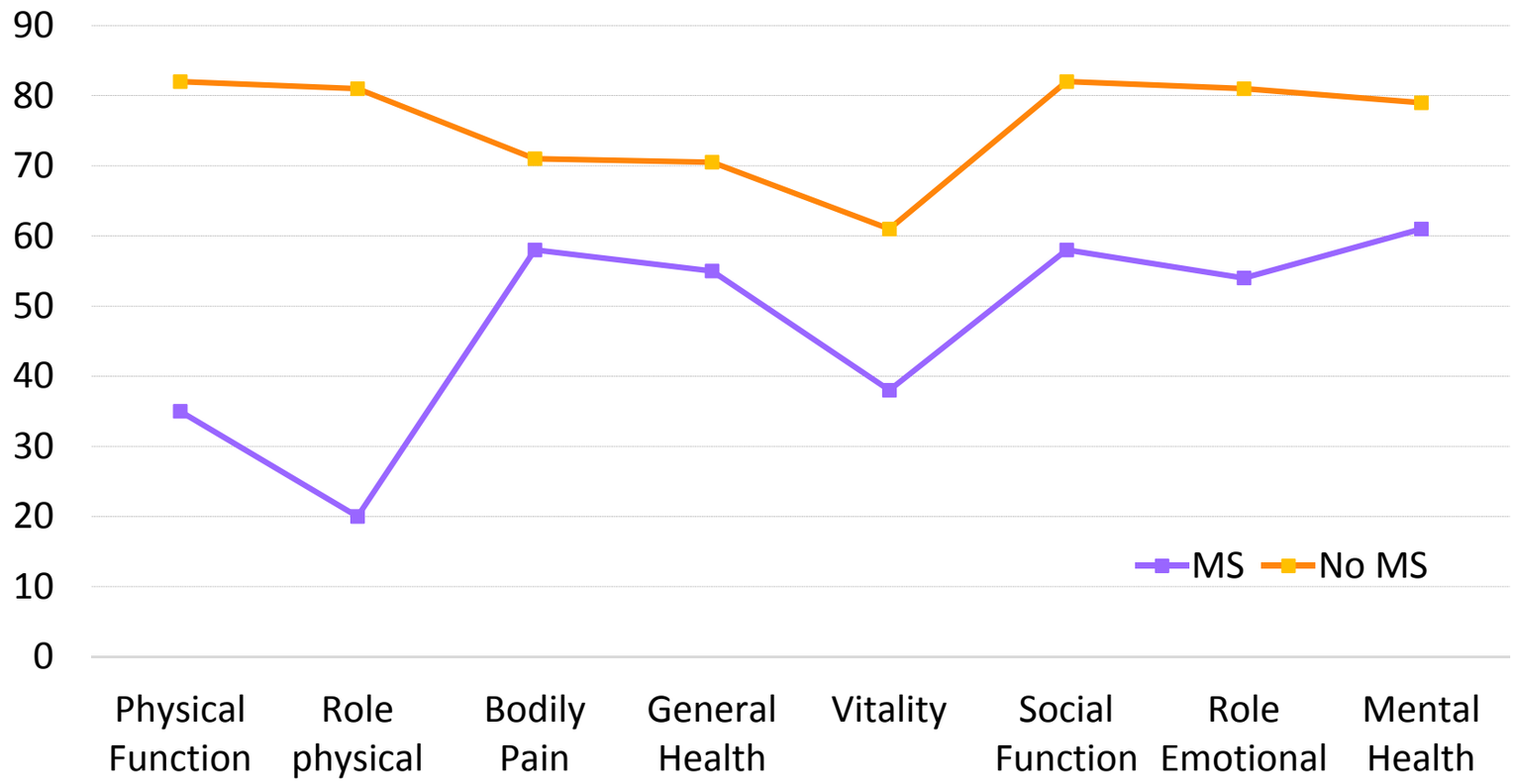
Rieckmann P, Boyko A, Centonze D, et al. *Mult Scler Relat Disord*. 2015;4(3):202-18.

MS Has a Progressive Negative Affect on Health Status



Kobelt G, Kasteng F. Access to innovative treatments in multiple sclerosis in Europe. The European Federation of Pharmaceutical Industry Associations (EFPIA) 2009. http://www.comparatorreports.se/Access%20to%20MS%20 treatments%20-%20October%202009.pdf. Accessed March 2018.

Health-Related Quality of Life* is Considerably Lower Among Patients with MS



*Measured with the SF-36.

Kobelt G, Kasteng F. Access to innovative treatments in multiple sclerosis in Europe. The European Federation of Pharmaceutical Industry Associations (EFPIA) 2009. http://www.comparatorreports.se/Access%20to%20MS%20 treatments%20-%20October%202009.pdf. Accessed March 2018.

Quality of Life and Patient-Reported Outcomes in Multiple Sclerosis Patient Engagement can be Important

- Clinical focus in MS has relied heavily on the Expanded Disability Status Scale(EDSS)
- More recently, the importance of MS outcome assessment from the patient's perspective has been recognized
- Patient-reported outcomes (PROs) include information provided by the patient that reflects their functioning health and well-being, including the impact of the disease and medical interventions on their QoL
- PROs introduce a more holistic approach to disease management by incorporating outcomes affecting the patient across many aspects of their QoL
- Patients report symptoms earlier and more frequently than clinicians do, and patients' reports are more highly concordant with overall health status than clinicians' reports
- Integrating PROs into clinical practice has the potential to capture those benefits and enrich the clinical encounter

Rieckmann P, Boyko A, Centonze D, et al. *Mult Scler Relat Disord*. 2015;4(3):202-18.

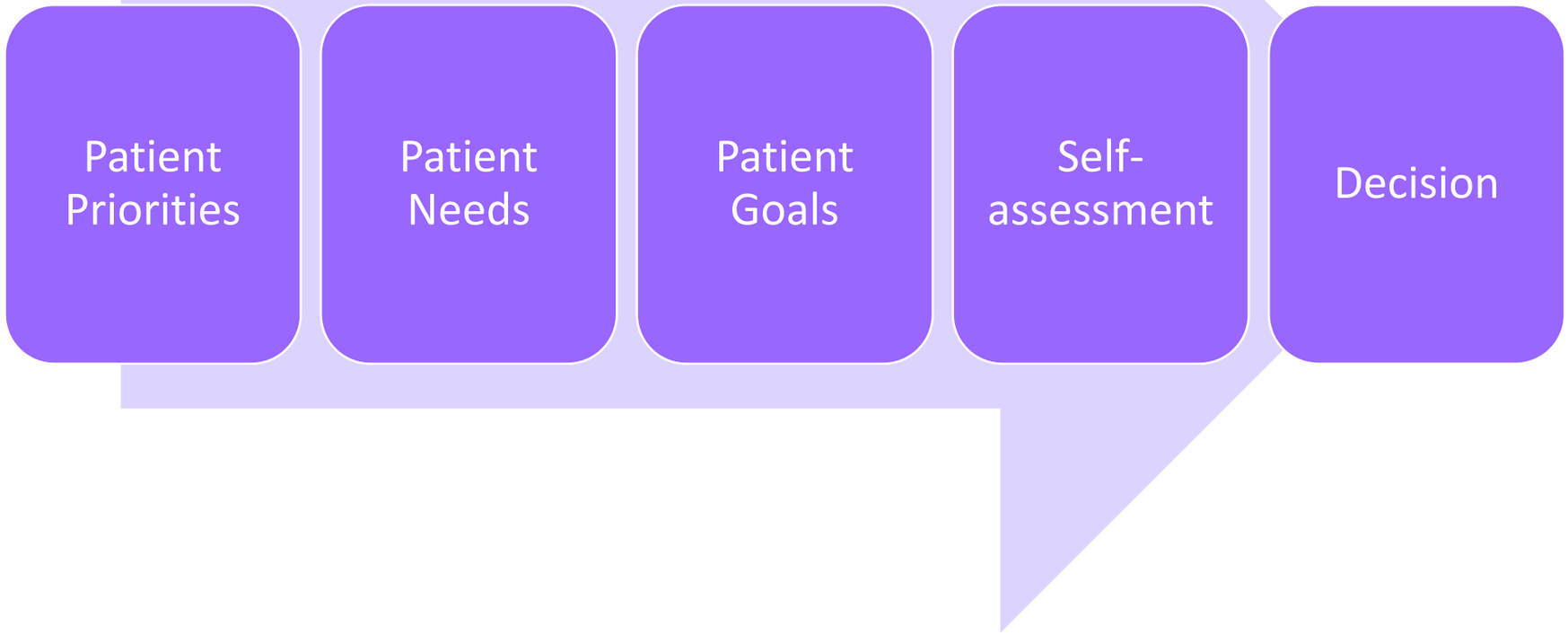
Patient Engagement Techniques

Using specific methods promotes empathy and empowers patients to be stewards of their own care

- Shared Decision Making
  - An approach de-emphasizes “adherence” as the primary goal
  - Focuses on a treatment and lifestyle plan that is customized by the clinicians in conjunction with the patients and aligned with patient priorities
- Motivational Interviewing (MI)
  - Collaborative, patient-centered form of information exchange to facilitate constructive patient communications and address a patient’s motivation for change
  - Important when working with patients who are non-adherent with their treatment regimen or have fears about having to inject themselves

Shared Decision Making

Fosters an Approach that Meets Patients Where They Are and Encourages Introspection



Gue D, Squire S, Mcintosh K, et al. *J Multidiscip Healthc*. 2015;8:527-34.

Motivational Interviewing Techniques and the Practical Application in Multiple Sclerosis

Scenario	Technique	Example
Physical Inactivity/ Exercise Avoidance	Elicit-Provide-Elicit	"Can you tell me what you know about how exercise is beneficial for your disease?" [Patient response] "Yes, that's true. It also alleviates fatigue, so if you're feeling too tired to exercise, getting out there and walking will actually help. In addition, it will improve your mood and self esteem."
	Decisional Balance	"Would you mind listing the benefits of exercise for your disease and overall health, as well as what's inconvenient about it? [Patient obliges] "It looks like the benefits outweigh the disadvantages in the long run, wouldn't you agree?"
Medication Nonadherence Related to Perceived Ineffectiveness	Reflective Listening	"It sounds like you're a little annoyed that you have to regularly take your medication and don't see any concrete benefit from it. Unfortunately, you won't necessarily get the 'proof' that your DMT is working until you *don't* take it and experience symptoms related to your MS."
	Validation	"I can totally understand your frustration. You have to take time out of your busy life to inject or receive infusions and your life goes on with no noticeable difference. The fact is, this treatment provides long-term benefits in terms of delaying or minimizing disability."
Medication Nonadherence Related to Adverse Events	Open Questions	"Tell me about what side effects are bothering you the most… And how are the injection site reactions effecting your daily activities?" [Patient responds] "Well unfortunately, that's a completely normal reaction you're having. Have you considered alternating arms? They may become less burdensome if you're not regularly injecting in the same arm."

Miller WR, Rollnick S. *Motivational Interviewing: Helping People Change*. Third Edition. New York City: Guildford Press; 2012.

Overview of Health Coaching Goals

- ✓Improve adherence to therapeutic interventions
- ✓Improve health status of patients
- ✓Reduce unnecessary and inappropriate use of health services
- ✓Reduce or “slow the rise” of health care costs
- ✓Increase productivity and decrease presenteeism
- ✓Reduce illness-related lifestyle disturbance
- ✓Improve Quality of Life

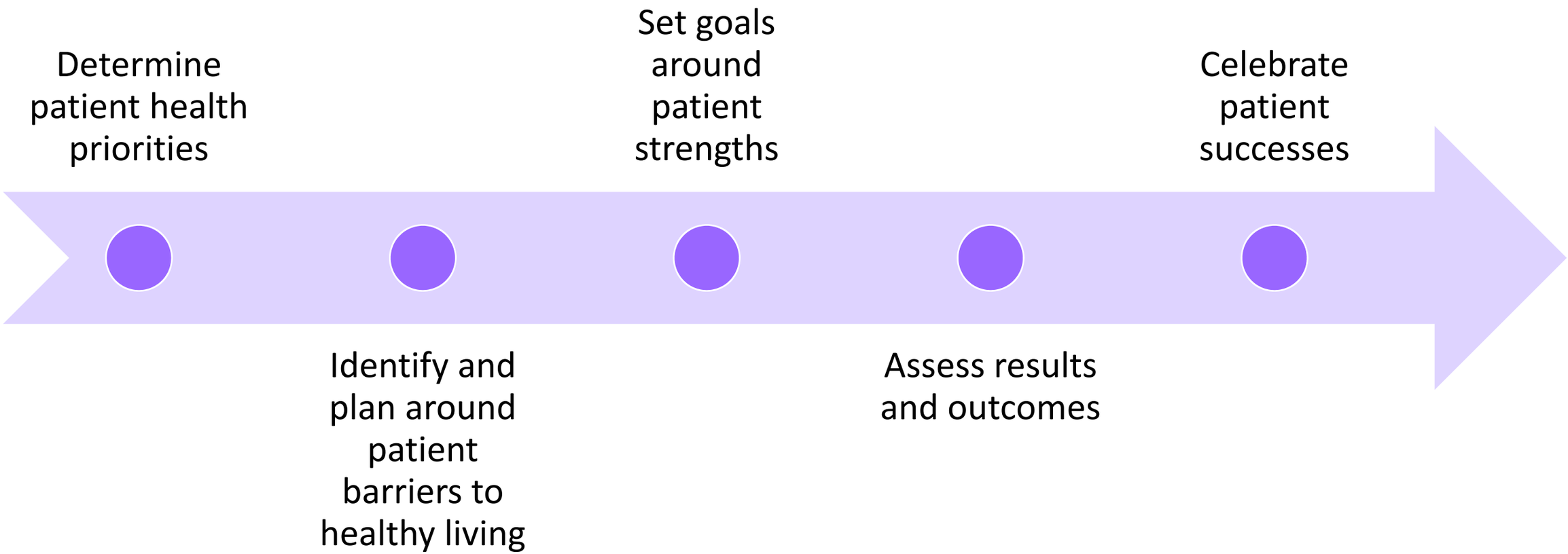
Newman P, Varnam R, McDowell A. *Practice Nursing.* 2013;24(7):344-6.

Patient-Directed Goals

- ✓Create a vision of a healthy life
- ✓Take stock of goals
- ✓Acknowledge challenges
- ✓Enlist the necessary support
- ✓Keep track of current status and potential progress
- ✓Celebrate large and small successes

Newman P, Varnam R, McDowell A. *Practice Nursing.* 2013;24(7):344-6.

Health Coaching Process



Newman P, Varnam R, McDowell A. *Practice Nursing.* 2013;24(7):344-6.

A Wide Variety of Health Coaching Models and Tactics are Available for Use

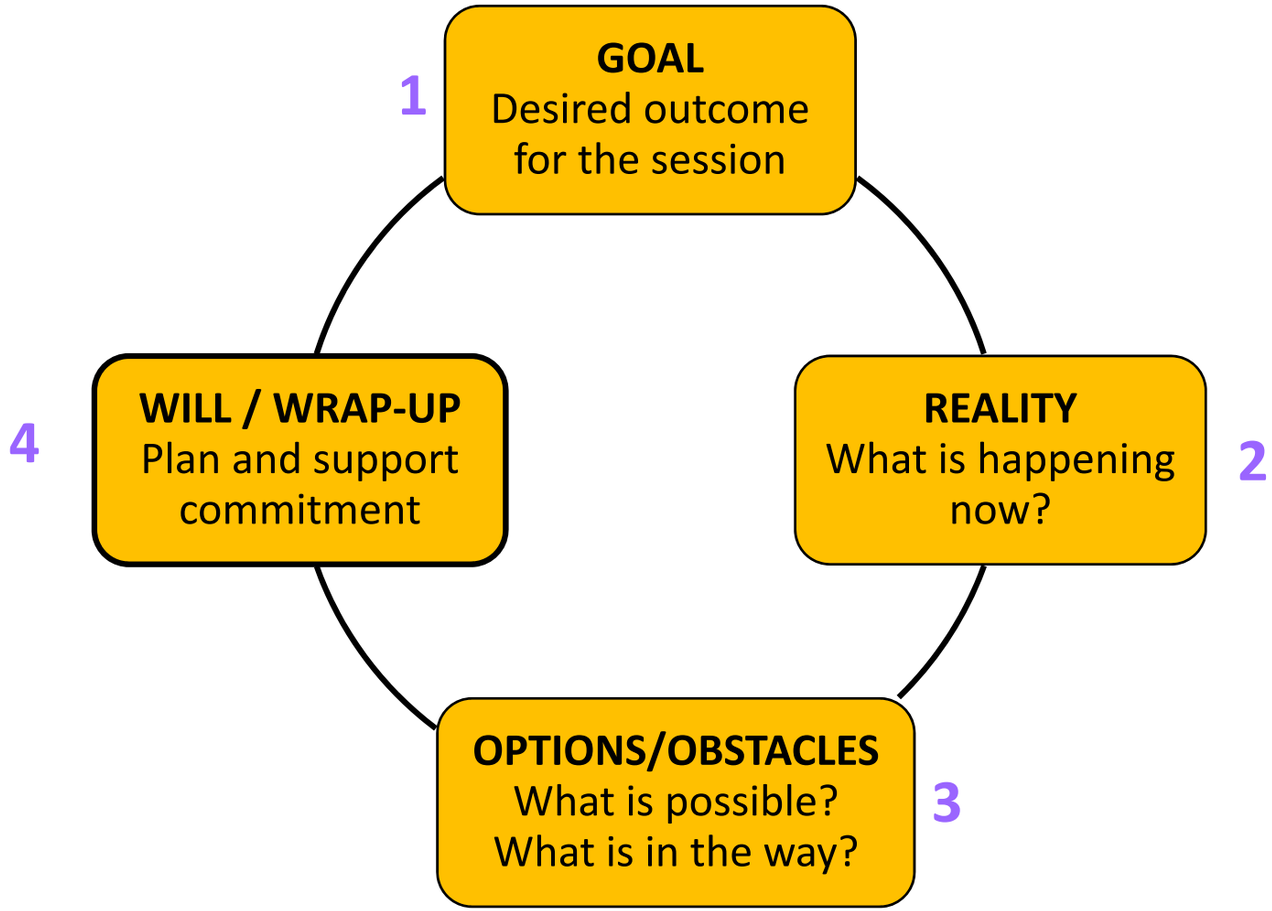
The GROW Model

The Diamond Model

The ABC Health Coaching Model

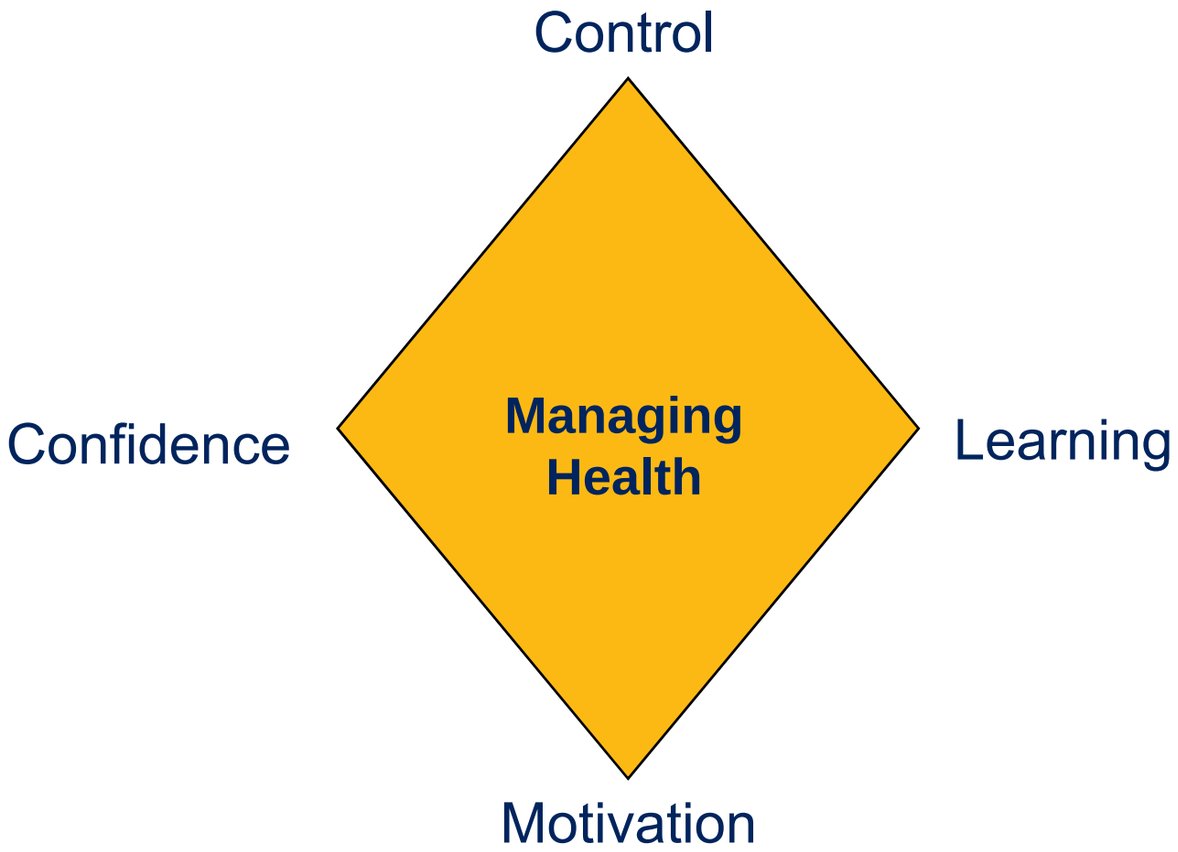
The Inner Game Method

The GROW Model



Whitmore J. *Coaching for Performance: GROWing Human Potential and Purpose*. 4th ed. Boston: Nicholas Brealey; 1992.

Components of Managing Health – The Diamond Model



Questions:

1. Where are you now and what has contributed to that?
2. Where would you like to be and what are the reasons for that?
3. What can you do that is within your control to move this forward?

Newman P, Varnam R, McDowell A. *Practice Nursing.* 2013;24(7):344-6.

ABC Health Coaching Model

1. Define the behavior
2. Antecedents
3. Consequences
4. Eliciting personal meaning
5. Eliciting goals
6. Eliciting resources
7. Way forward

Raise Awareness

Increase Responsibility

Newman P, Varnam R, McDowell A. *Practice Nursing.* 2013;24(7):344-6.

Antecedents & Consequences of the ABC Model

Newman P, Varnam R, McDowell A. *Practice Nursing.* 2013;24(7):344-6.

The Inner Game Coaching Conversation

Managing Interference to Achieve Desired Behavior

Performance = *Potential* – *Interference*

Desired Behavior = *Could do it* – *What's in the way*

Last 3 Questions

- What gets in the way MOST?
- What gets in the way LEAST?
- Where would you like to START?

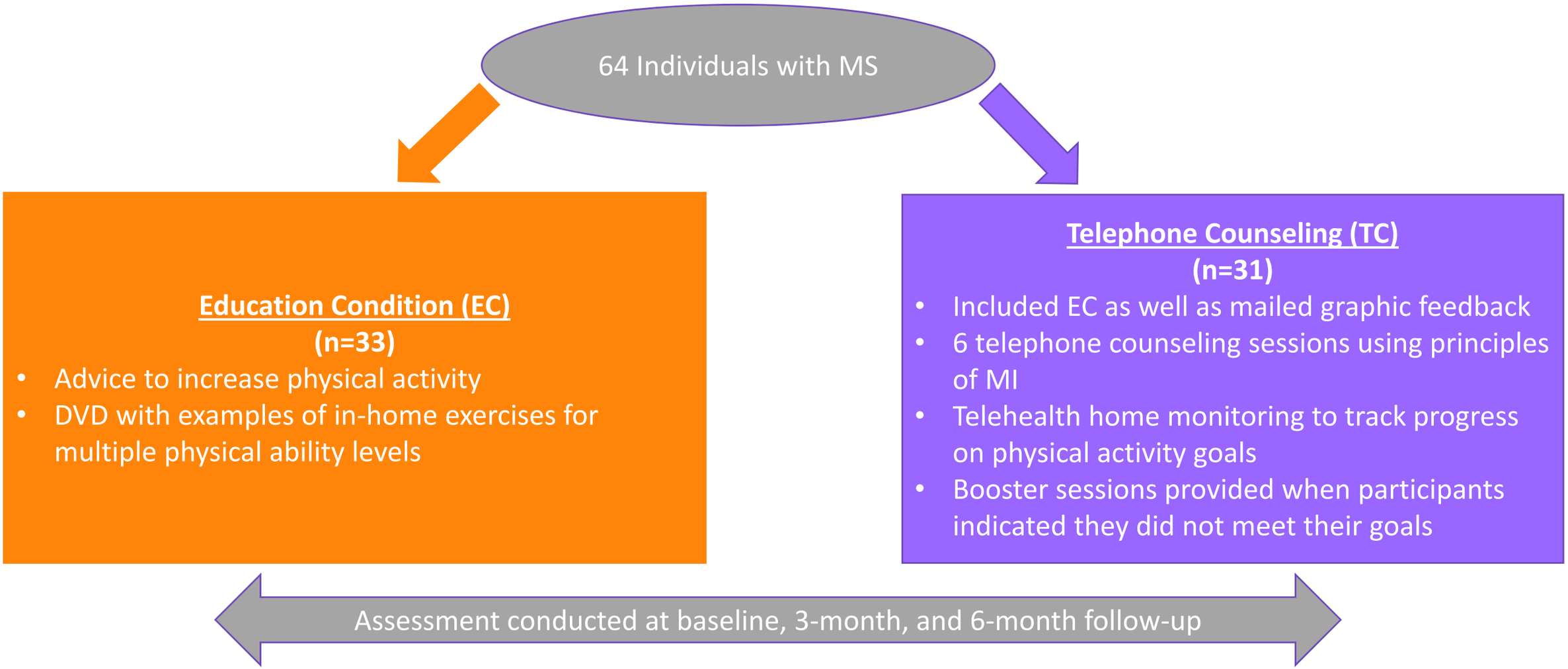
Newman P, Varnam R, McDowell A. *Practice Nursing.* 2013;24(7):344-6.

Solution-focused Coaching Questions

- What do you feel and are you ready to change?
- What is currently happening regarding this behavior?
- What would you like to achieve?
- What's helped you to achieve this in the past?
- What are your options now?
- What else could you do?
- Which do you think might work for you now?
- What specific goal could you set?
- What would support you to achieve this goal?
- What would you need to do to achieve this?
- What ELSE would you need to do?
- What do you need to do to remember this?

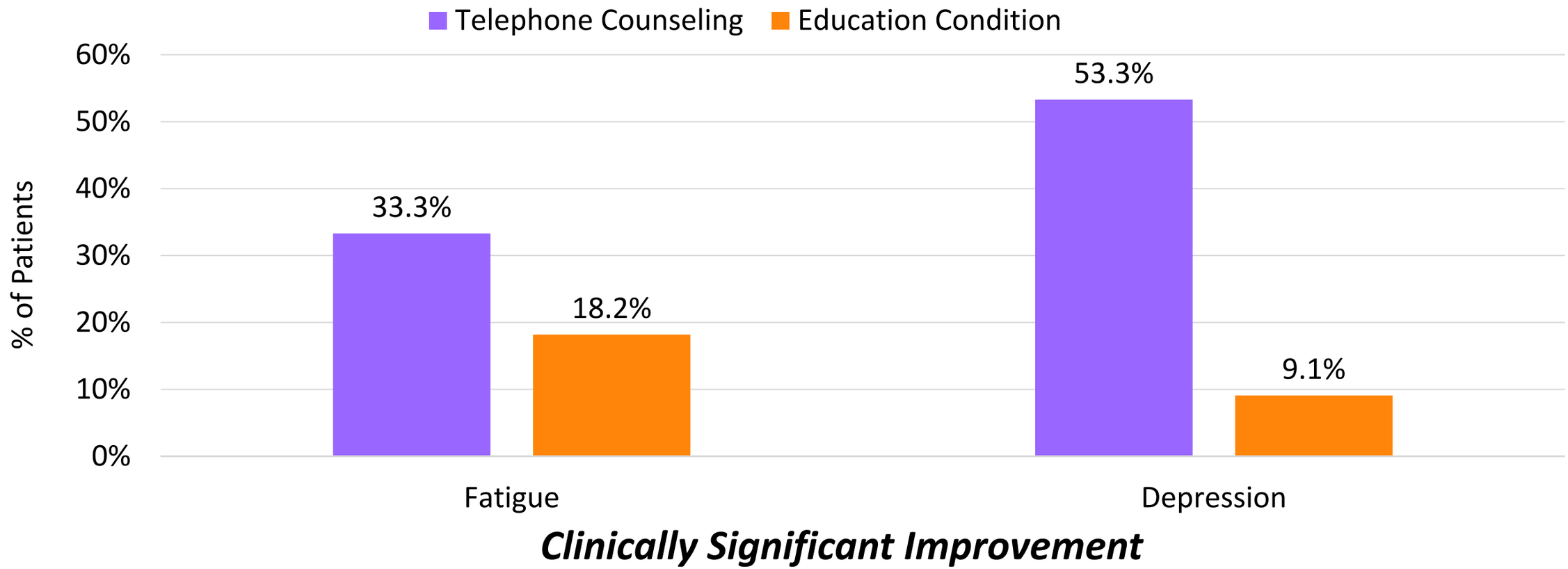
Newman P, Varnam R, McDowell A. *Practice Nursing.* 2013;24(7):344-6.

Organization-Level Health Coaching and Motivational Interviewing Interventions Have Been Applied in the Management of Multiple Sclerosis with Notable Success



Turner AP, Hartoonian N, Sloan AP, et al. *J Consult Clin Psychol*. 2016;84(4):297-309.

Multiple Sclerosis Patients Receiving Telephone Counseling with Education and Motivational Interviewing Experienced Greater Improvements in Fatigue and Depression



Turner AP, Hartoonian N, Sloan AP, et al. *J Consult Clin Psychol*. 2016;84(4):297-309.

Summary

- Self-care and therapeutic adherence represent key components of management for the vast majority of patients with chronic diseases, such as Multiple Sclerosis
- Patient engagement is a crucial tactic to promote appropriate self-care and therapeutic adherence, both of which can improve outcomes and minimize health care service utilization
- Quality of Life and Patient Reported Outcomes are vital elements of patient engagement in Multiple Sclerosis
- Health coaching takes patient engagement a step further by setting goals, addressing barriers, assessing outcomes, and celebrating successes
- Payer-led initiatives incorporating these interventions may prove beneficial for the optimal management of members with Multiple Sclerosis

Patient Perspective – MSAA Overview

Kyle Pinion
Senior Director of Education, Healthcare Relations & Advocacy
Multiple Sclerosis Association of America

MSAA Presentation Overview

- Overview of MSAA
- Barriers to Care in MS
- Key Advocacy priorities for MSAA
- Economic and Financial impact of MS on patients and family members

Overview of MSAA

The Multiple Sclerosis Association of America is a leading resource for the entire MS community, improving lives today through vital services and support.

- National organization serving over 100,000 clients
- Provides a wide array of free direct services and programs to people with MS and their families throughout the country
- Promotes greater understanding of multiple sclerosis and the diverse needs and challenges of people with MS

Overview of MSAA: Helpline

MSAA's Helpline allows clients to speak directly with one of our experienced consultants on a wide variety of issues, including:

- Resources and referrals for services, programs and medical providers
- The management of their overall health care, including reminders of regular tests and checkups needed for health issues unrelated to MS
- Information about MS symptoms, how they are managed, and medications for the treatment of MS
- Reassurance, encouragement and emotional support

Overview of MSAA: Equipment Program

MSAA offers clients an extensive inventory of products designed to improve safety, dignity, mobility and independence. MSAA provides these products at no charge and ships directly to the client. Some examples of products available to clients are:

DAILY LIVING AIDS

- Wheelchairs, walkers, grab bars, hand rails, canes, shower chairs and transfer benches

COOLING EQUIPMENT

- Vests, neck and wrist wraps

Overview of MSAA: MRI Access Fund

Assists with the payment of cranial (brain) and c-spine MRI scans for qualified individuals who have no medical insurance or cannot afford their insurance costs and require the exam to help determine a diagnosis of MS or evaluate current MS disease progression.

MSAA can provide assistance with:

- New MRIs – through referral to imaging centers MSAA work with (for those without insurance or cannot afford their insurance costs) or via covering the cost of a medical insurance co-pay or co-insurance balance up to $600. MSAA pays billing facilities directly.

- Reimbursement MRIs – From July 2017 to the present, reimbursed up to $600 to the billing facility directly.

Overview of MSAA: Educational Programs

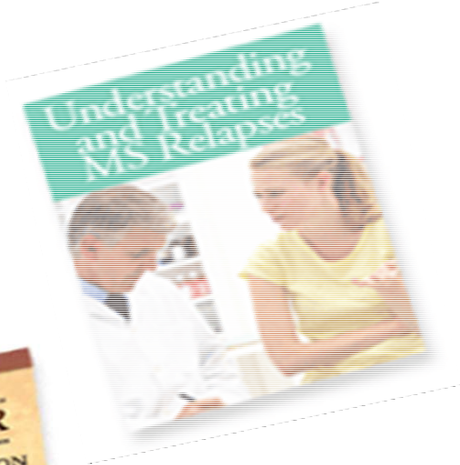
MSAA organizes and sponsors a wide array of public education and awareness events throughout the country. These events often feature expert MS neurologists and health care professionals who bring clients the latest information on the advances in MS research, available treatment options, and new techniques to meet the physical, emotional, and social challenges which arise from living with a chronic illness. Some recent topics include:

- Understanding Progression in Multiple Sclerosis
- The Latest Technologies to Help You in Managing Your MS
- Employment & MS
- The Importance of Adherence
- Taking Care of Yourself While Taking Care of Others: A Care Partners Series
- The Role of the MRI
- Nutrition and MS
- Women's Health and MS
- Brain Preservation and Cognition in MS
- Best Practices in the Management and Treatment of Primary Progressive MS

Overview of MSAA: Publications

MSAA's award-winning publications provide much needed information to the MS community on a variety of topics, including:

- MS Research Updates
- About MS
- How to S.E.A.R.C.H. for the Right MS Therapy for You!
- MS Relapse Toolkit
- Understanding Progression in MS
- Understanding and Treating MS Relapses
- Medicare Planning and Multiple Sclerosis
- The Affordable Care Act and Multiple Sclerosis
- Aquatic Exercise and Multiple Sclerosis
- Mommy's/Daddy's Story
- Understanding and Treating Depression in Multiple Sclerosis

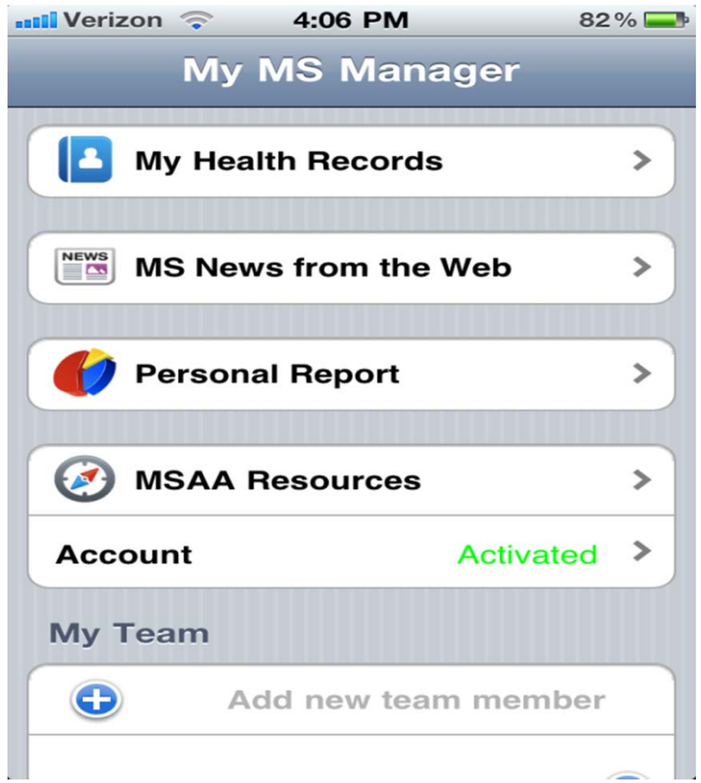


Overview of MSAA: My MS Manager

This **first-of-its kind-app for MS** offers individuals a convenient and effective tool to manage the ever-changing course of the disease.

My MS Manager allows you to input and store:

- Comprehensive medical records
- Contact information of your healthcare team
- Descriptions of MS flare-ups, tracking their duration, frequency and intensity
- Information about side effects and effective treatment strategies
- Important details essential to staying one step ahead of your MS



Overview of MSAA: Advocacy

MSAA works to ensure that all MS patients have access to the appropriate therapies, treatment and comprehensive health care support to ensure the most optimal health outcomes. As part of this work, MSAA is actively involved with several coalitions to ensure patients have access to appropriate care and treatment throughout their MS journey.

Potential access barriers for those living with MS include:

- High cost of MS therapies
- Specialty tiers within formularies
- Step-therapy requirements
- Copay Accumulators
- Geographic location (ie distance from MS Centers/access to appropriate comprehensive health care team)

Advocacy (continued)

MSAA, as a part of the MS Coalition and other symptomatic coalitions, is firmly committed to advocating on behalf of all lives impacted by the MS experience.

Some of our priorities include:

- Enhanced MS research funding at NIH, the MSRP (DoD), and the Neurological Conditions Surveillance System at the CDC
- Reformation of step-therapy protocols within the Restoring the Patient's Voice Act (HR 2077)
- Greater transparency through the FAIR Drug pricing act (S.1131/ HR 2439) and the C-THRU Act (S.637)

Advocacy (continued)

Our Federal Advocacy Priorities also include:

- The stabilization of the health care marketplace/exchanges through reinsurance and increased outreach funding
- Resident Physician Shortage Reduction Act (HR 2267/S1301)

The Impact of MS on Patients and Their Family Members

- MS is highly unpredictable, making it very challenging for MS patients and their family members to plan for the future.
- MS is a heterogeneous disease: each MS patient's experience and journey is unique.
- MS poses a number of financial and relationship challenges for both patients, care partners and their family members.

The Economic Impact of Multiple Sclerosis

MS can have a significant impact on an individual's quality of life and is associated with high costs for MS patients, their families and society as a whole. Specific economic issues facing MS patients and their families:

- Cost of disease-modifying and symptom management therapies
- Health insurance costs
- Earning potential (age of disability and retirement considerations)
- Transportation costs for medical appointments
- Home modifications and adaptive equipment (ie scooters, handicap-accessible vehicles)
- Respite care and nursing home services

Healthcare Plans and Multiple Sclerosis

- MS patients also need access to a health care plan that enables them access to the disease-modifying therapy that their doctor has prescribed
  - While there are now 15 MS disease-modifying therapies on the market, they have different mechanisms of action and not all therapies work for all patients.
- Lack of access or unaffordable access to MS therapies can create unexpected costs such as hospitalization and costs associated with recurrent and worsening disease activity

Multiple Sclerosis Association of America

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(800) 532-7667

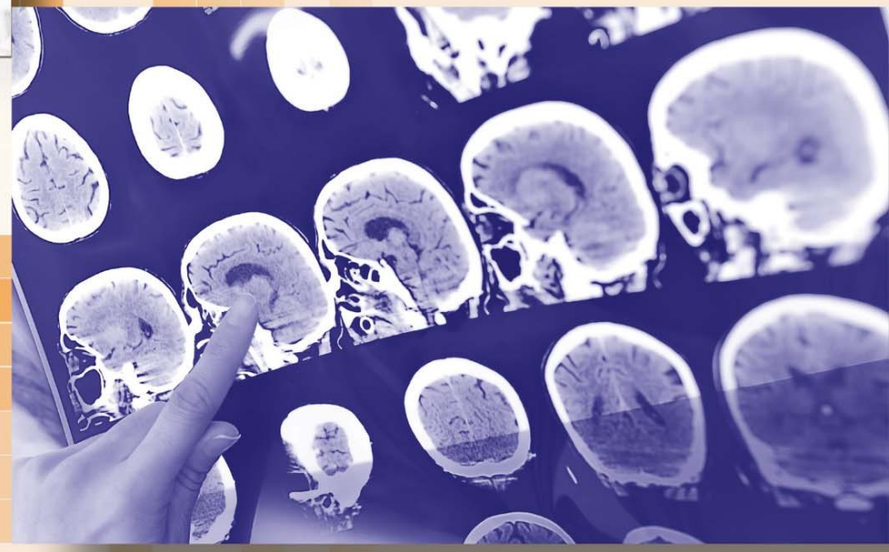
www.mymsaa.org

Thank you and looking forward to partnering with you to improve the lives of all who have been impacted by MS!

MSAA

MULTIPLE SCLEROSIS ASSOCIATION OF AMERICA

Improving Lives Today!®



Managing Multiple Sclerosis:

Current Treatment and Care Management **Strategies** for Managed Care

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AMCP Academy of Managed Care Pharmacy®

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