

The Evolving Landscape in the Management & Treatment of MULTIPLE SCLEROSIS



Payer Considerations for Providing Support
to People with MS and Their Care Partners

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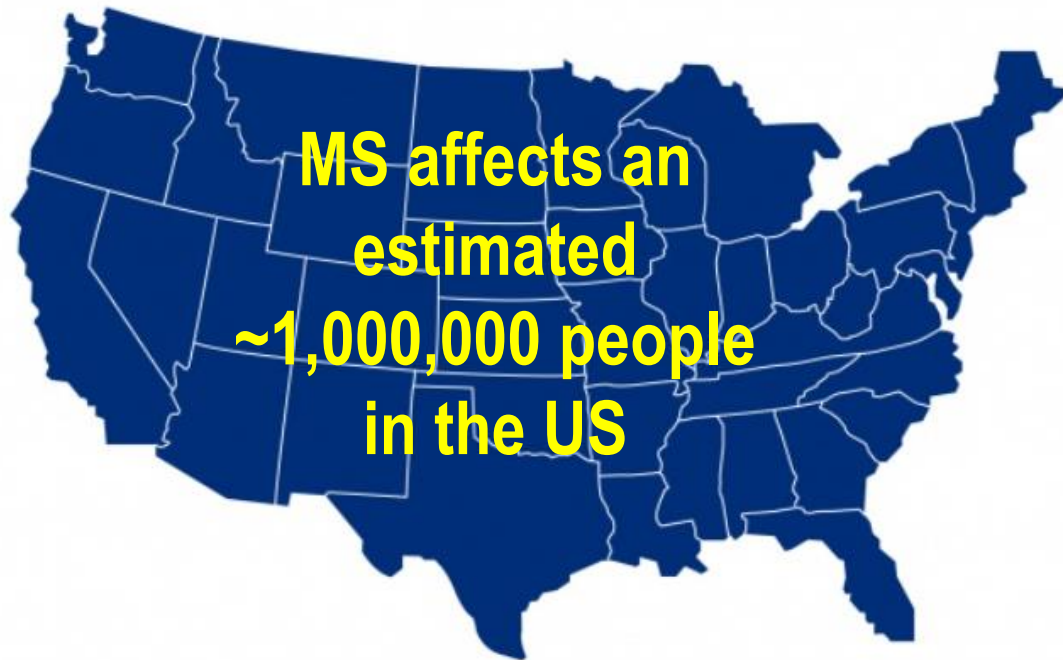


Clinical Update and Economic Impact of MS

Andrew Woo, MD, PhD

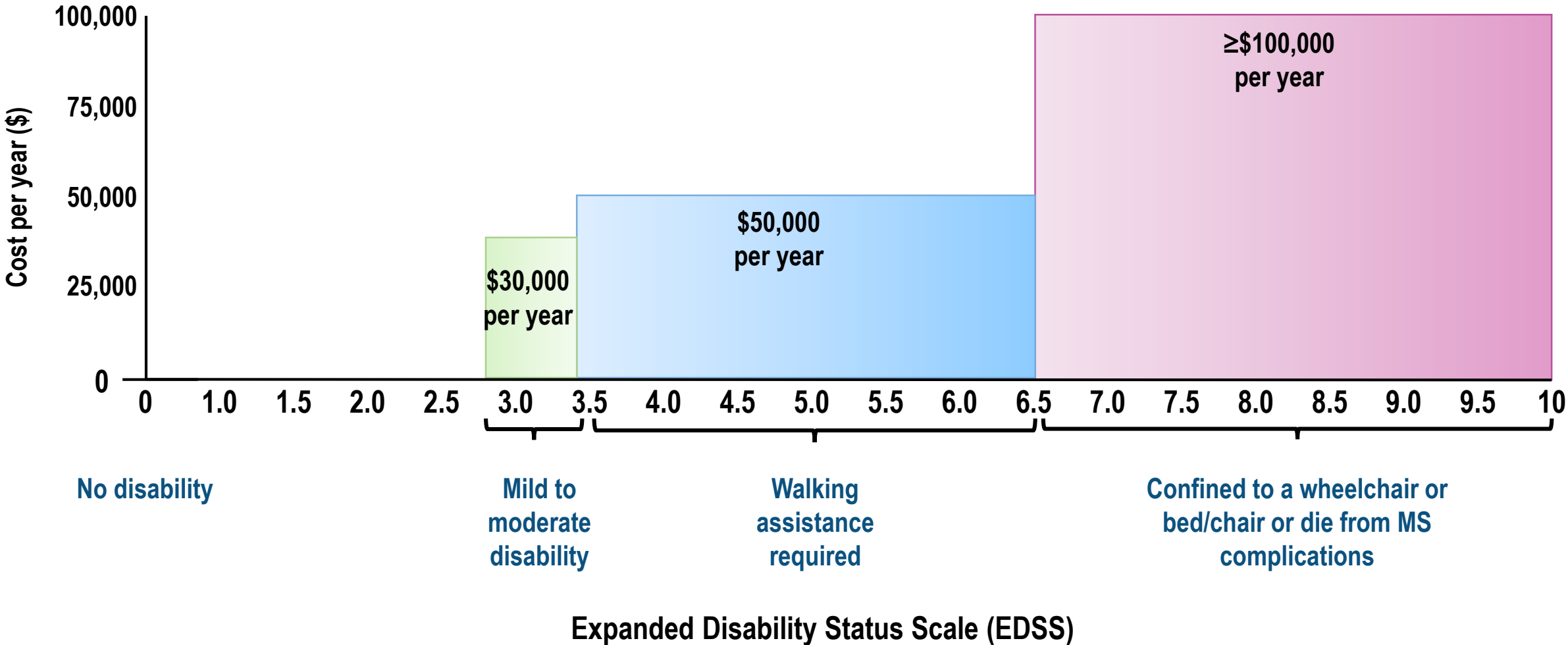
Assistant Clinical Professor of Neurology
David Geffen School of Medicine at UCLA
Santa Monica Neurological Consultants

Prevalence and Burden of MS

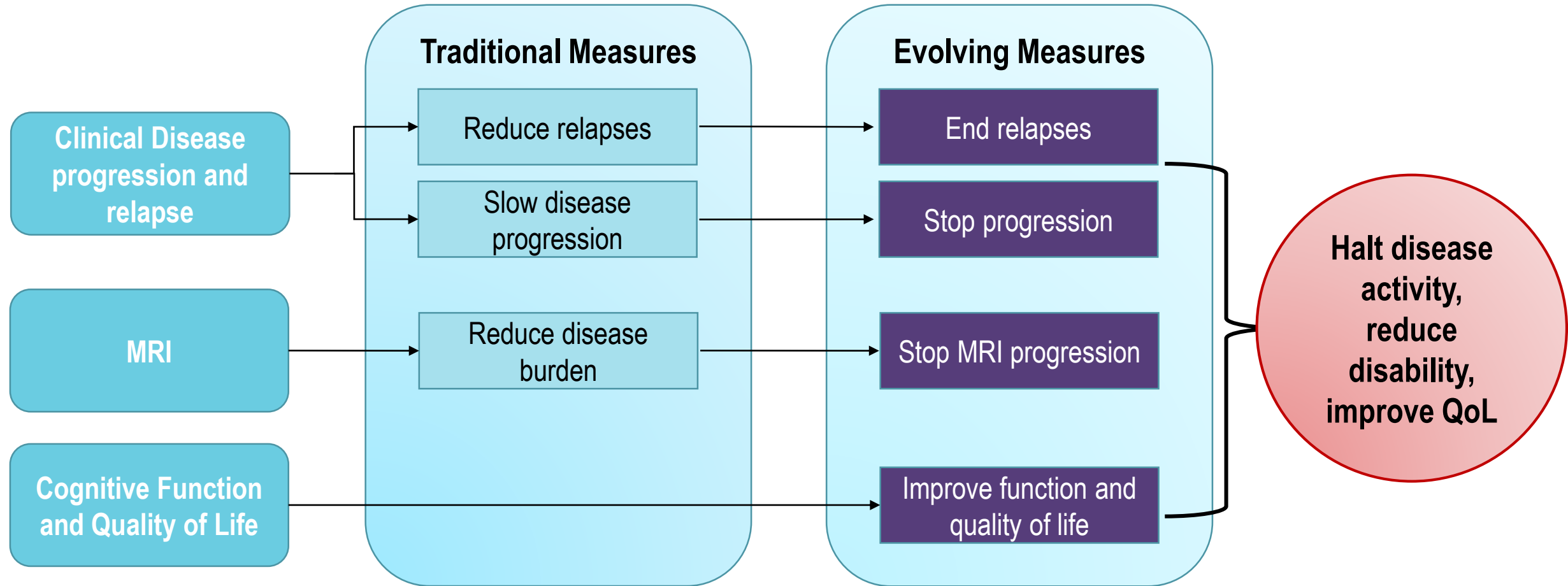


- Majority of cases diagnosed between 20 and 50 years of age
- MS can have a significant negative functional, financial, and psychosocial impact during the prime of a patient's life
- Costs associated with MS are considerable and rise with increasing disability
- There is currently no cure

Total MS Costs Rise as Disability Progresses



Goals of MS Treatment: Halt Disease Activity, Reduce Disability, and Improve Quality of Life



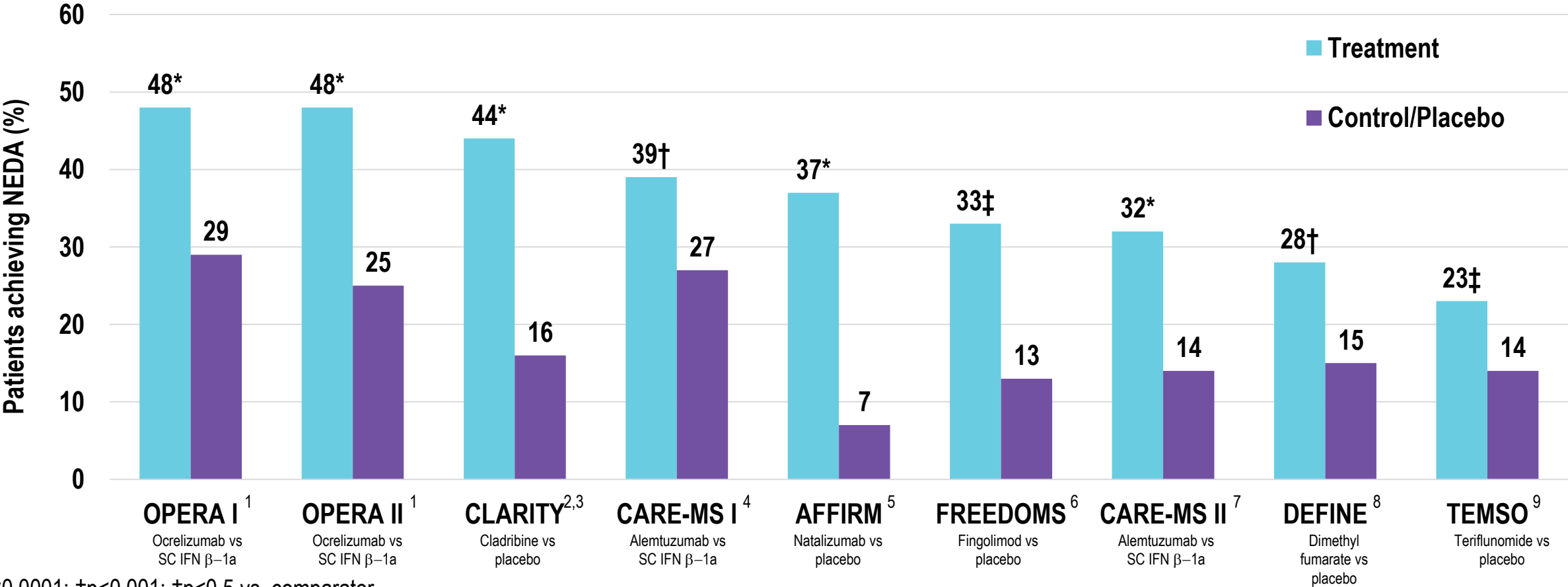
Approach to MS Treatment

- **Early treatment:** patients with MS should be advised to start treatment with a DMT as early as possible
- **Early treatment with DMTs:** may limit disability and attenuate secondary progression and in patients with active RRMS
- **Treat-to-target:** a common treatment goal is to minimize and/or stop disease activity; currently, however, there is minimal evidence that this approach improves outcomes
- AAN Guidelines Recommendation #14: Clinicians should start patients with highly active MS on alemtuzumab, natalizumab, or fingolimod
 - Ocrelizumab was not available at the time of the analysis but would qualify for this indication as well

FDA Indications for Currently Available DMTs

Agent	Approval	RRMS	PPMS	SPMS
Interferon β -1b (Betaseron; Extavia)	1993	✓		✓
Interferon β 1-a (Avonex)	1996	✓		✓
Glateramer acetate (Copaxone/Glatopa)	1996/2018	✓		✓
Interferon β -1a (Rebif)	1996	✓		✓
Mitoxantrone (Novantrone)	2000	✓		✓
Natalizumab (Tysabri)	2004	✓		✓
Fingolimod (Gilenya)	2010	✓		✓
Teriflunomide (Aubagio)	2012	✓		
Dimethyl fumarate (Tecfidera)	2013	✓		✓
Alemtuzumab (Lemtrada)	2014	✓		
Peginterferon β -1a (Plegridy)	2014	✓		✓
Ocrelizumab (Ocrevus)	2017	✓	✓	✓
Siponimod (Mayzent)	2019	✓		✓
Cladribine (Mavenclad)	2019	✓		✓

No Evidence of Disease Activity (NEDA) Rates in Phase 3 Trials



*p<0.0001; ‡p<0.001; †p<0.5 vs. comparator

NEDA defined as no relapses, no 3-month CDP, no new T1 Gd+ lesions, and no new enlarging or enlarged T2 lesions on MRI

1. Traboulsee A, et al. *Neurology*. 2016;86(suppl). Abstract PL02.004; 2. Giovanni G, et al. *Lancet Neurol*. 2011;10:329-337; 3. Papadopoulos D, Mitsikostas D. *CNS Drugs*. 2018;32:1069-10783; 4. Cohen JA, et al. *Lancet*. 2012;380:1819-1828; 5. Havrodova E, et al. *Lancet Neurol*. 2009;8:254-260; 6. Bevan CJ, et al. *JAMA Neurol*. 2014;71:269-270; 7. Coles AJ, et al. *Lancet*. 2012;380:1829-1839; 8. Giovannoni G, et al. *Neurology*. 2012;75(suppl). Abstract PD05.005; 9. Freeman MS. *Ther Adv Chronic Dis*. 2013;4:192-205.

Patient Factors Influencing Initial Choice of MS Therapy

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
 - Other

Factors Influencing a Decision to Switch the DMT

Line of Therapy	Factor Influencing a Switch
<p>First-line DMT to another first line (lateral switch)</p> <p>1st line: IFN; GA; teriflunomide; DMF</p>	<ul style="list-style-type: none"> • Tolerability/safety issues <ul style="list-style-type: none"> • Suboptimal efficacy with suboptimal response but still a low risk for imminent progression
<p>First-line to a second-line DMT (i.e., escalation)</p> <p>2nd line: fingolimod; natalizumab; alemtuzumab; ocrelizumab; cladribine; siponimod</p>	<ul style="list-style-type: none"> • Suboptimal response to first-line DMT with a moderate-higher risk for progression (as opposed to low risk) • RRMS patients transitioning to the secondary progressive phase with evidence of relapses or MRI activity
<p>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)</p> <p>3rd line/higher: mitoxantrone; cyclophosphamide; experimental therapy (eg, cladribine)</p>	<ul style="list-style-type: none"> • RRMS patients continuing to experience relapses on a second-line therapy • Progressive forms of MS with relapses and/or active MRI despite treatment • Safety issues (e.g., patients on natalizumab at high risk of developing progressive multifocal leukoencephalopathy)
<p>Second-line to a first-line DMT</p>	<ul style="list-style-type: none"> • Tolerability/safety issues should the patient maintain the second-line agent AND the perception that the disease is under good control and the patient's risk for imminent progression has been reduced

Generic DMTs: Glatiramer Acetate

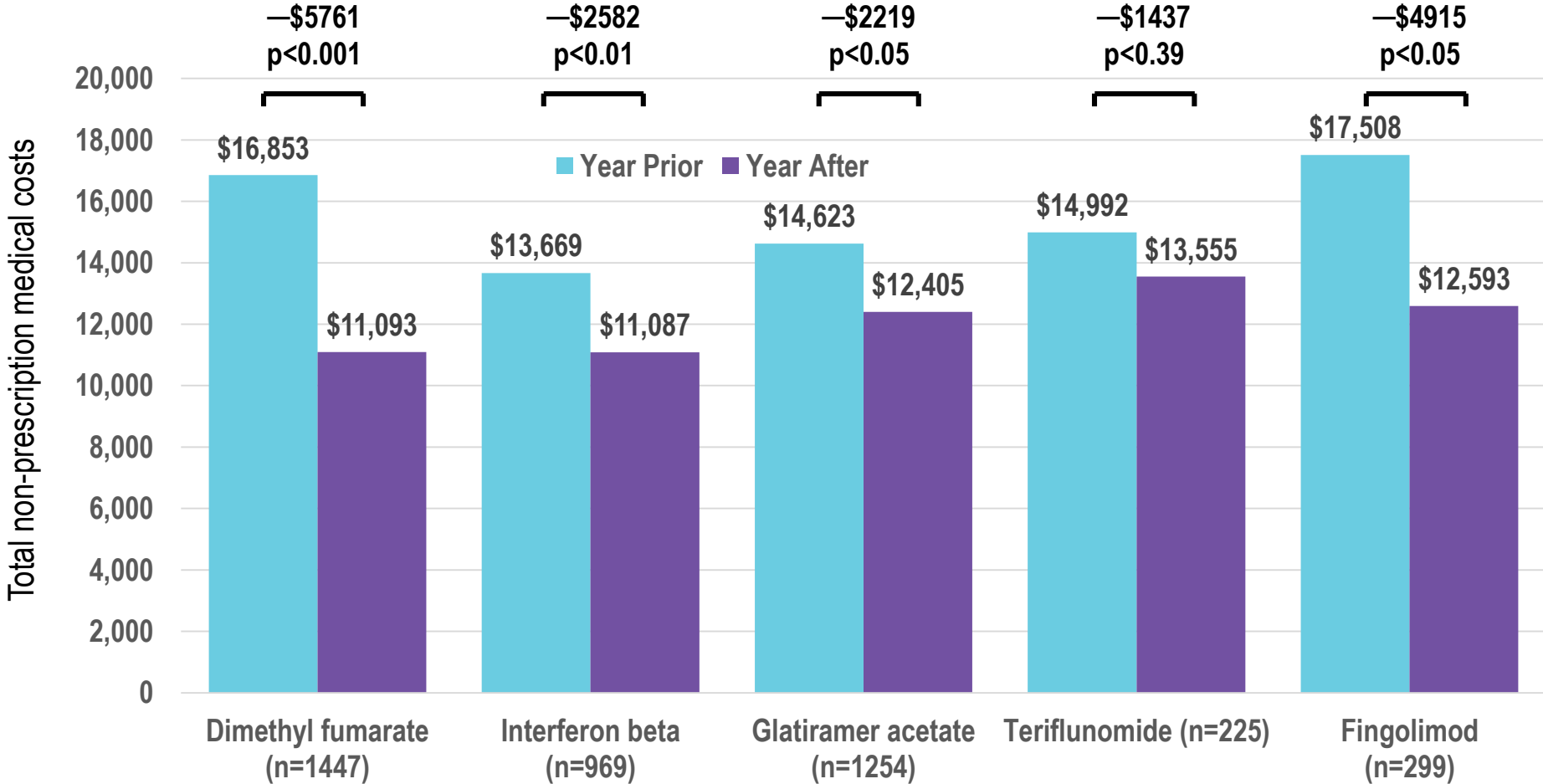
- Generic glatiramer acetate (GA) is available in 2 dosage forms¹
 - 20 mg administered daily
 - 40 mg administered 3x/week
- Three-times-weekly dosing elicited a 50% reduction in mean annualized rate of injection-related adverse events compared to the daily 20 mg dose version²
- In addition to potential cost advantage, patient preference for three-times-weekly dosing may reduce reluctance to initiate a generic DMT

1. National MS Society. <https://www.nationalmssociety.org/About-the-Society/News/FDA-Approves-Another-New-Generic-Form-of-40mg-Copa>. Accessed April 2019.

2. Wolinsky JS, et al. *Mult Scler Relat Disord*. 2015;4:370-376.

DMT Initiation Was Associated with Reductions in Health Care Resource Utilization

- Analysis of 4194 claims in the 2012-2015 Truven MarketScan Commercial Database
- Hospitalization, ER or urgent care visits in the year after initiating DMT for patients who did not receive a DMT in the previous year

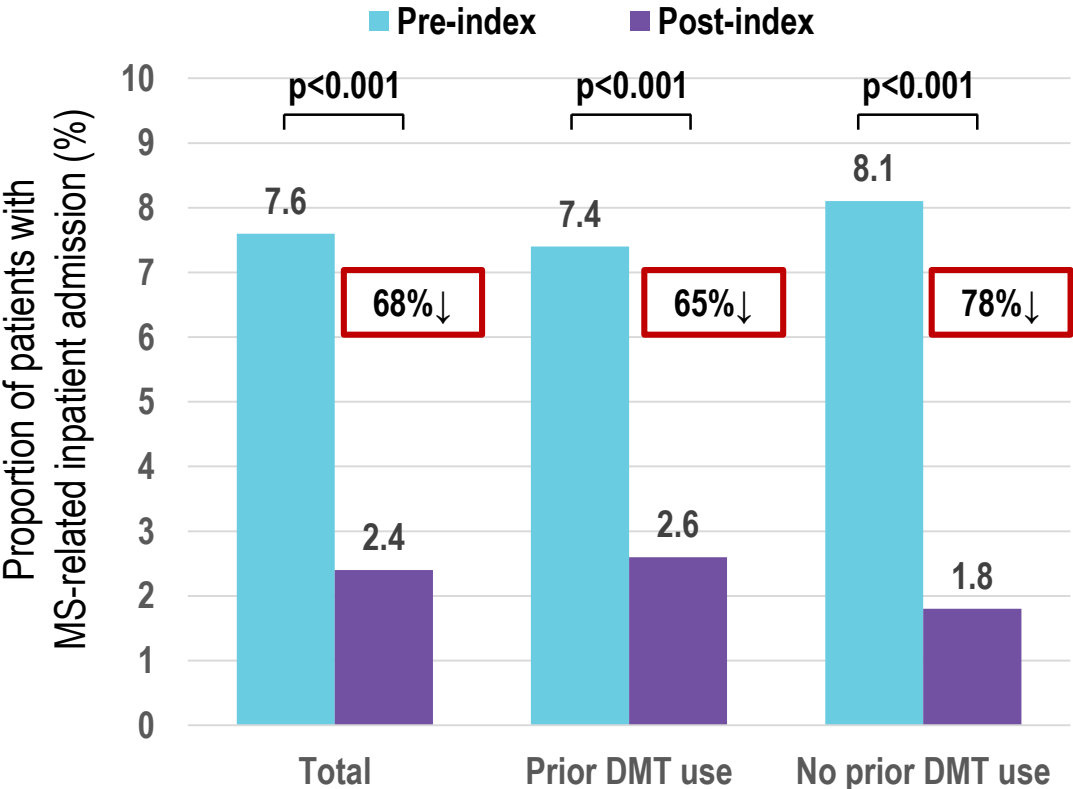


Cost reductions predominantly driven by decreased use of outpatient services and decreased inpatient hospital stays

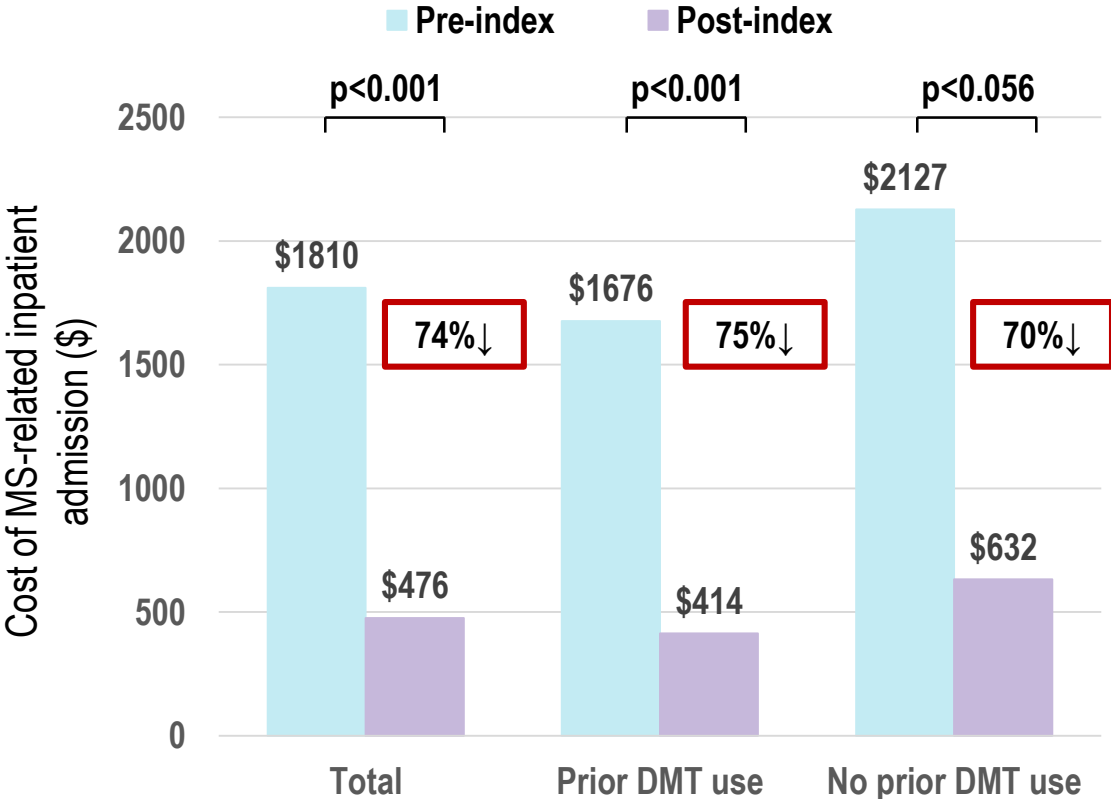
Health Care Use and Costs Were Decreased After Initiation of Treatment with a DMT

Claims Analysis* of Patients with MS (n=1458) Initiated on Natalizumab and Followed for 12 Months

MS-Related Inpatient Utilization



MS-Related Inpatient Costs



*Truven MarketScan commercial database

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



*Evolving Advocacy and Policy Landscape Impacting
Health Plan Patients with MS*

Edmund Pezalla, MD, MPH
CEO
Enlightenment Bioconsult, LLC

Healthcare Policy

- **Definition:**

- Decisions, plans, and actions undertaken to achieve specific health care goals

- **Goals:**

- Define a vision
- Establish targets for the short and medium term
- Outline priorities
- Build consensus
- Educate stakeholders and constituents



Healthcare Advocacy

- **Definition:**

- Efforts to change policies associated with access to care, navigation of the healthcare system, mobilization of resources, addressing health inequities, and influencing health policy

- **Goals:**

- Improve access
- Enhance affordability
- Create minimum standards
- Eliminate disparities



Payers Are Well-Positioned to Participate in Policy Discussions That Impact MS Outcomes

- Payers have the data, the incentives, and the role in the healthcare value chain to make a significant contribution to policy discussions
 - For example, payers can facilitate optimal treatment decisions and minimize perverse incentives that erode quality and value



Several Policy Priorities Are Shared By MS Patients and Payers

Policy Priorities	NMSS ¹	Payers ²
• Access to comprehensive, quality healthcare	✓	✓
• Healthcare affordability	✓	✓
• Standardization of medication coverage	✓	✓
• Access to long-term care	✓	✓
• Disability rights	✓	✓
• Home modification policies	✓	✓
• Transparency of coverage and care	✓	✓
• Medicare Advantage/Medicaid coverage		✓
• Funding for MS research	✓	
• Increase awareness of MS	✓	
• Industry and market issues		✓

NMSS=National Multiple Sclerosis Society; Payers=represented by America's Health Insurance Plans (AHIP)

1. National Multiple Sclerosis Society. <https://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Brochure-Health-Care-Reform-Principles.pdf>. Accessed April 2019.
2. America's Health Insurance Plans. <https://www.ahip.org/issues/>. Accessed April 2019.

Using Policy Advocacy to Promote Solutions that Advance Healthcare Value, Expanded Access, and Patient Well-Being

Payer Policy Goal	Advocacy Goal
Access	<ul style="list-style-type: none">• Expand access, help control costs, and preserve flexibility
Delivery system and payment reform	<ul style="list-style-type: none">• Ensure the right medical care gets to the right person at the right time and at the right price
Disability insurance	<ul style="list-style-type: none">• Protect disabled patients from taking on additional debt or losing their assets due to their disease-related disability
Drug costs	<ul style="list-style-type: none">• Promote policies that preserve innovation and competition• Encourage greater transparency to improve the value of prescription drugs
Health care affordability	<ul style="list-style-type: none">• Create pricing transparency• Ensure a competitive marketplace• Promote value-based payment• Provide flexibility for health plans to offer all products

Using Policy Advocacy to Promote Solutions that Advance Healthcare Value, Expanded Access, and Patient Well-Being (cont'd)

Payer Policy Goal	Advocacy Goal
Healthcare quality	<ul style="list-style-type: none">• Develop quality measures for consumers and employers• Encourage a system where high-quality healthcare is rewarded
Long-term care	<ul style="list-style-type: none">• Promote policies that provide benefits to help manage the potentially significant costs of LTC
Industry and market issues	<ul style="list-style-type: none">• Improve coordination across the healthcare system (e.g., patients, providers, hospital, payers, manufacturers, and data analytics)
Medicare Advantage	<ul style="list-style-type: none">• Continued access to disease and care management services that reduce hospitalizations and improve care
Medicaid coverage through private plans	<ul style="list-style-type: none">• Increase access to programs that coordinate care for people with multiple chronic conditions• Improve outreach and education initiatives to promote prevention and healthy living

Summary



- Payers are uniquely positioned to influence healthcare policies that impact treatment outcomes in individuals with MS
- Payers and MS patients share many policy priorities
- Payers continue to advocate for healthcare policies that promote
 - Expanded access to appropriate care
 - Improved healthcare affordability
 - Delivery of high-quality care
 - Enhanced patient experience



Medical and Pharmacy Management Strategies to Enhance MS Patient Outcomes

James T. Kenney, Jr., RPh, MBA

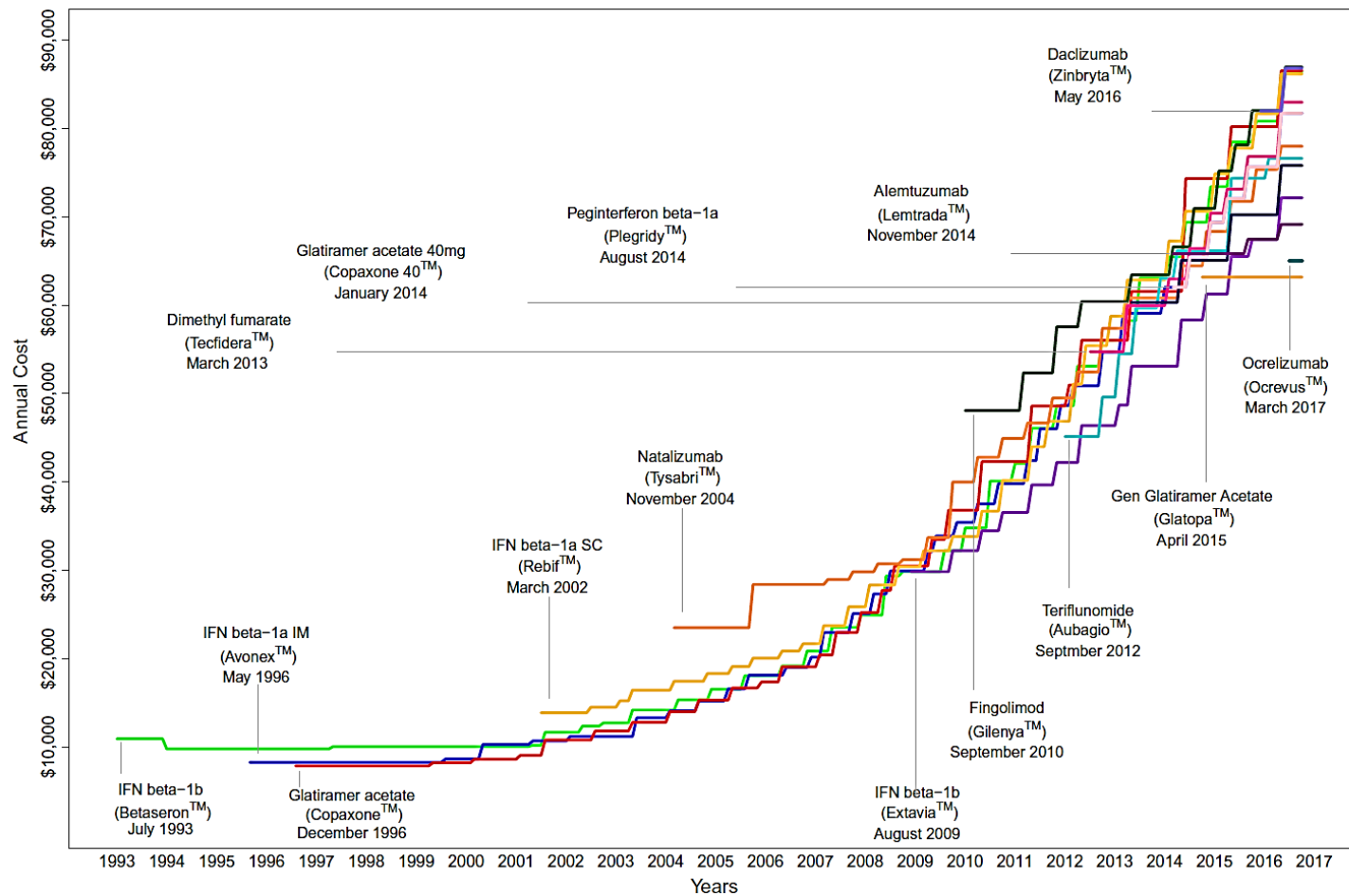
Founder and President

JTKenney, LLC

MS Drug Spend Ranks Among the Highest in Commercial Plans

Therapy Class	Type	PMPY Spend	Trend	
			Utilization	Total
Inflammatory conditions	Specialty	\$157.49	3.9%	15.3%
Diabetes	Traditional	\$116.23	4.2%	2.1%
Oncology	Specialty	\$70.66	4.3%	17.4%
Multiple Sclerosis	Specialty	\$60.20	-3.4%	3.0%
HIV	Specialty	\$26.82	2.5%	13.7%
Pain/Inflammation	Traditional	\$44.06	-2.1%	-15.0%
Attention disorders	Traditional	\$36.12	2.9%	-0.3%
Asthma	Traditional/Specialty	\$33.40	2.6%	0.7%
Hypertension/heart disease	Traditional	\$31.41	0.6%	-7.1%
High cholesterol	Traditional	\$26.82	0.3%	-30.6%

Cost of Existing DMTs Have Risen, Matching Prices Set by the Most Recent Competitor*



*Pricing estimated from WAC for year of therapy.

Clinical Trial Evidence Supports Initiating DMT Therapy Promptly After Diagnosis

“The goal of disease-modifying treatment is to reduce the early clinical and sub-clinical disease activity that is thought to contribute to long-term disability.”

DMT Selection is Patient Specific

- MS treatment guidelines in the United States do not endorse a specific treatment algorithm due to the heterogeneity of the patient population¹
- The efficacy of DMTs may vary from one individual to another and for any given individual at different points in time²
- Treatment decisions take into account patient attitudes about their disease, how the disease affects their life (eg, considerations with pregnancy), and risk-benefit profile of the therapy^{1,3}

The MS Drug Benefit Should 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

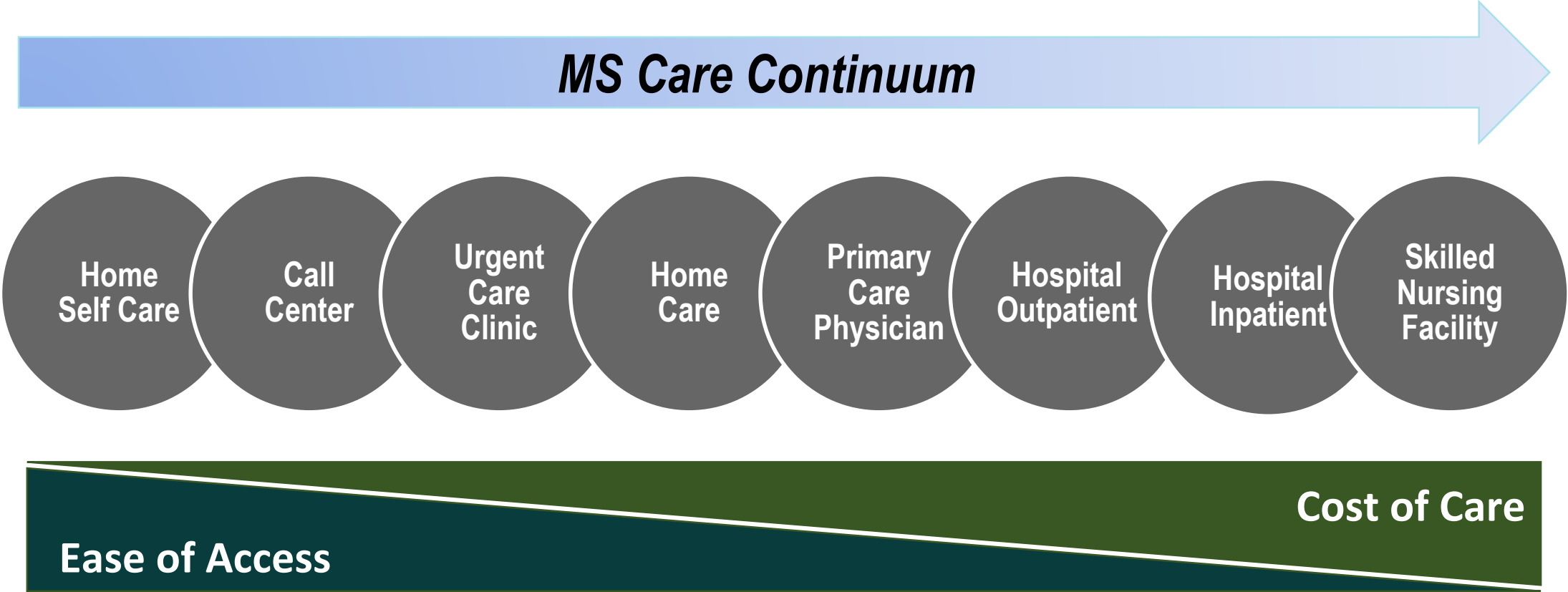
Right Cost

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

Selecting the “Right” MS Drug

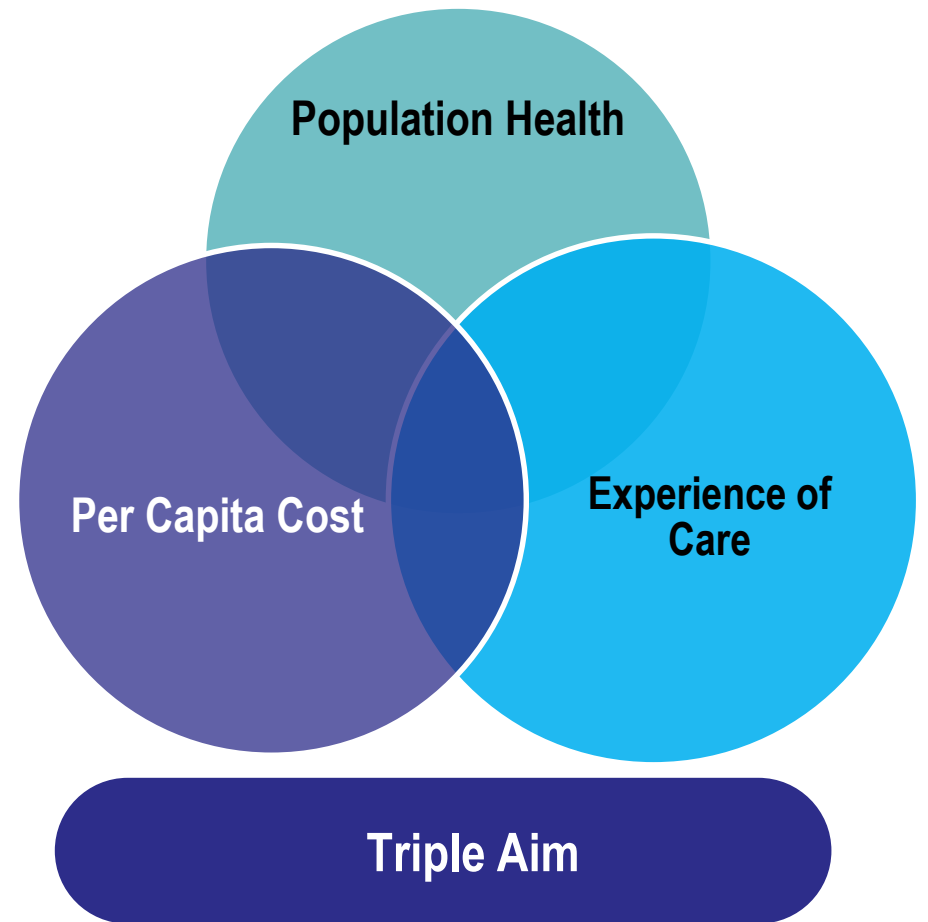
- Treatment should be individualized using shared decision making between the provider and patient
- None of the approved MS therapies is curative
- Clinicians and patients vary in their tolerance for risk and preference of route-of-administration
 - Multiple mechanisms of action
 - Oral, IV, SC, and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

Site of Care Delivery Can Influence Cost and Access



Contracting with Pharmaceutical Manufacturers Must Consider Overall Health Care Outcomes

- Contracting cannot be focused entirely upon
 - Clinical efficacy/safety
 - Adherence
- Must also consider
 - Affordability to the patient and payer
 - Overall clinical outcomes
 - Member access to care and experience with the health care system



Value-Based Contracting

- Value-based contracts:
 - Designed to demonstrate the value of selected drugs when used appropriately
 - Aligns payers, members and providers to achieve desired health outcomes
 - Requires the ability to accurately assess outcomes
- Value-based contracting for MS is often based on relapse rates
- However, measurement of relapses remains challenging
 - ER visits/hospitalizations?
 - Steroid use?
 - Risk reduction in relapses for patients on drug?
 - Adherence?

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/care management

Cost-sharing

Cost-effectiveness analysis

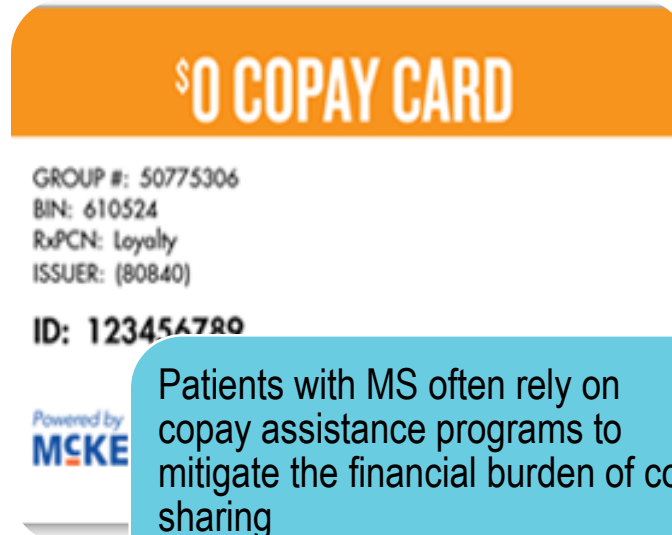


Copay Assistance Mitigates Patient Cost Burden, but Accumulator Adjustment Programs Can Reintroduce Financial Barriers to Access



Finding the right sequence of therapies in a complex chronic disease such as MS can be a challenge

- Treatment adherence can result in improved Quality of Life and decreased health care utilization



Patients with MS often 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 manufacturers of specialty drug products




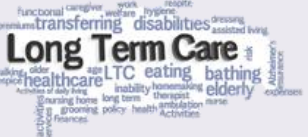


Copay Accumulator Programs interfere with a vital lifeline for patients with chronic conditions necessitating specialty drugs

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

MS Management Requires Coordinated Multidisciplinary Care



Components of MS Care		
<p>Medical intervention</p>	<ul style="list-style-type: none"> • Modifying disease course • Treating exacerbations • Managing symptoms • Addressing comorbidities 	
<p>Rehabilitative services</p>	<ul style="list-style-type: none"> • Cognitive and vocational rehabilitation • Physical and occupational therapy • Speech therapy 	
<p>Mental health support</p>	<ul style="list-style-type: none"> • Treatment/management of anxiety, depression, and other mood changes 	
<p>Long-term care</p>	<ul style="list-style-type: none"> • Home care • Day care • Assisted living • Nursing home 	

What is Care Management?

- **Care management:** A set of activities intended to improve patient care and reduce the need for medical services by enhancing *coordination of care*
- **Goal:** Improve coordination of care, reducing the rate of functional decline and improving health in the most cost-effective manner
- **Components of successful care management**
 - Communication
 - Coordinated care
 - In-person encounters
 - Physician involvement
 - Coaching
 - Informal caregivers

Effective Symptom Management is Critical in MS

Primary Symptoms

- **Brainstem:** Diplopia; nystagmus; vertigo
- **Cerebellum:** Ataxia; tremor
- **Cerebrum:** Cognitive impairment; depression
- **Optic nerve:** Optic neuritis; vision loss
- **Spinal cord:** Bladder and bowel dysfunction; weakness; spasticity
- **Other:** Fatigue; pain; temperature sensitivity

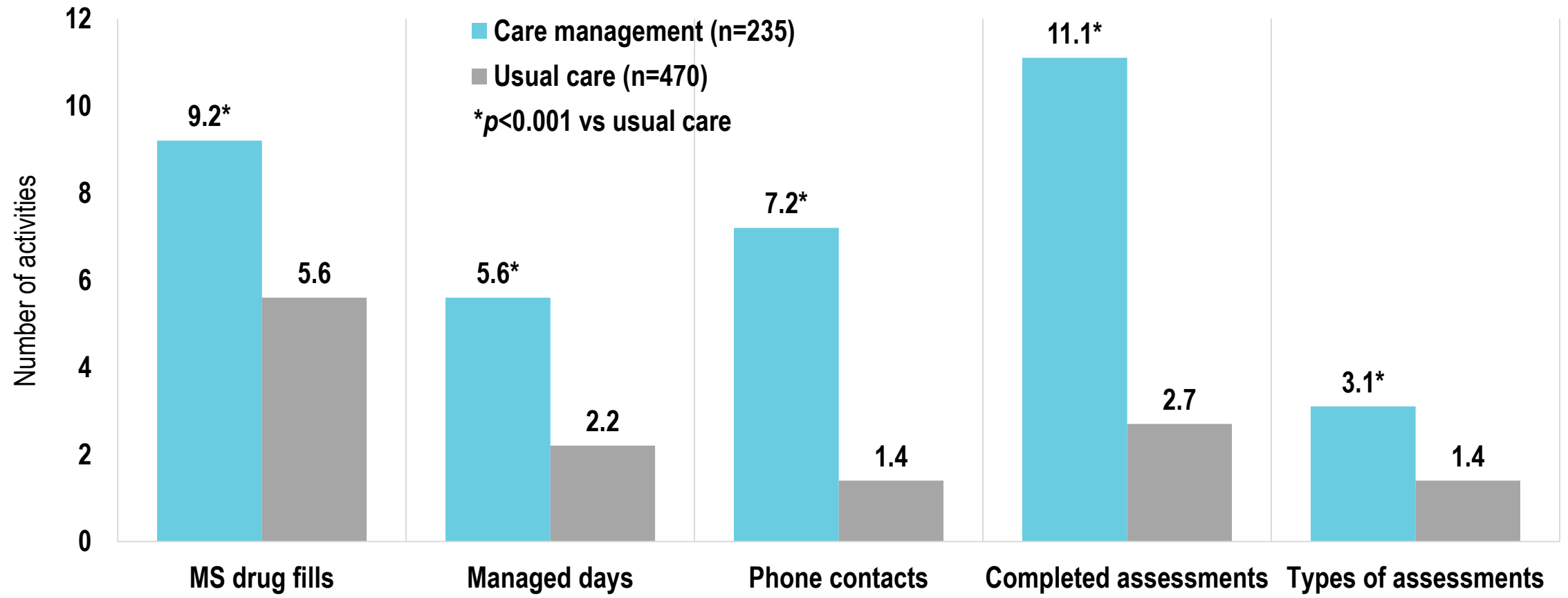
Secondary Symptoms

- **Neurogenic bladder:** Urinary tract infection
- **Inactivity:** Loss of muscle tone; poor posture; decreased bone density
- **Immobility:** Pressure sores

Tertiary Symptoms

- **Social isolation**
- **Depression**
- **Lost work/personal productivity**

Comprehensive Care Management Increased Delivery of Appropriate MS Care

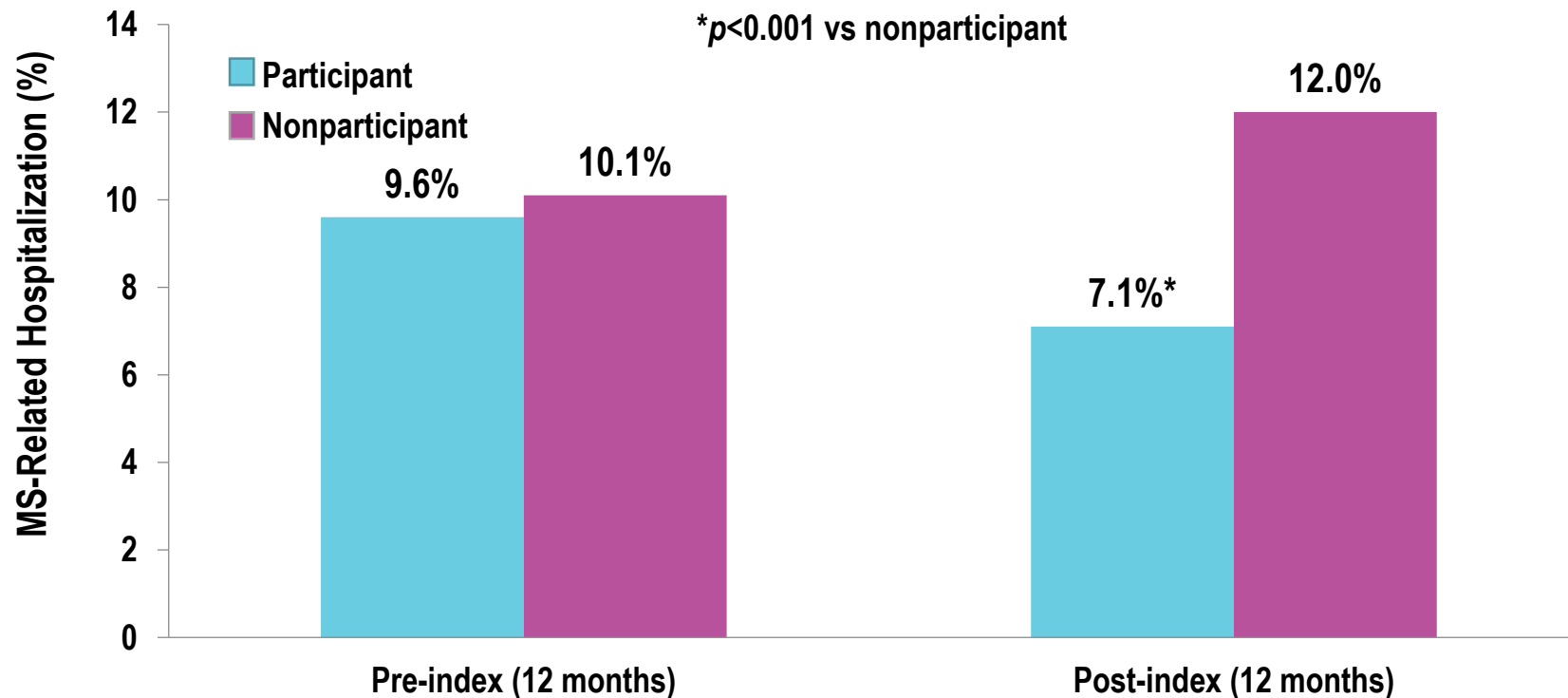


Data source: Walgreens Connected Care MS Treatment Management Program

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

Outcomes assessed: Clinical services received and adherence at 12 months

Care Management Reduced Hospitalizations

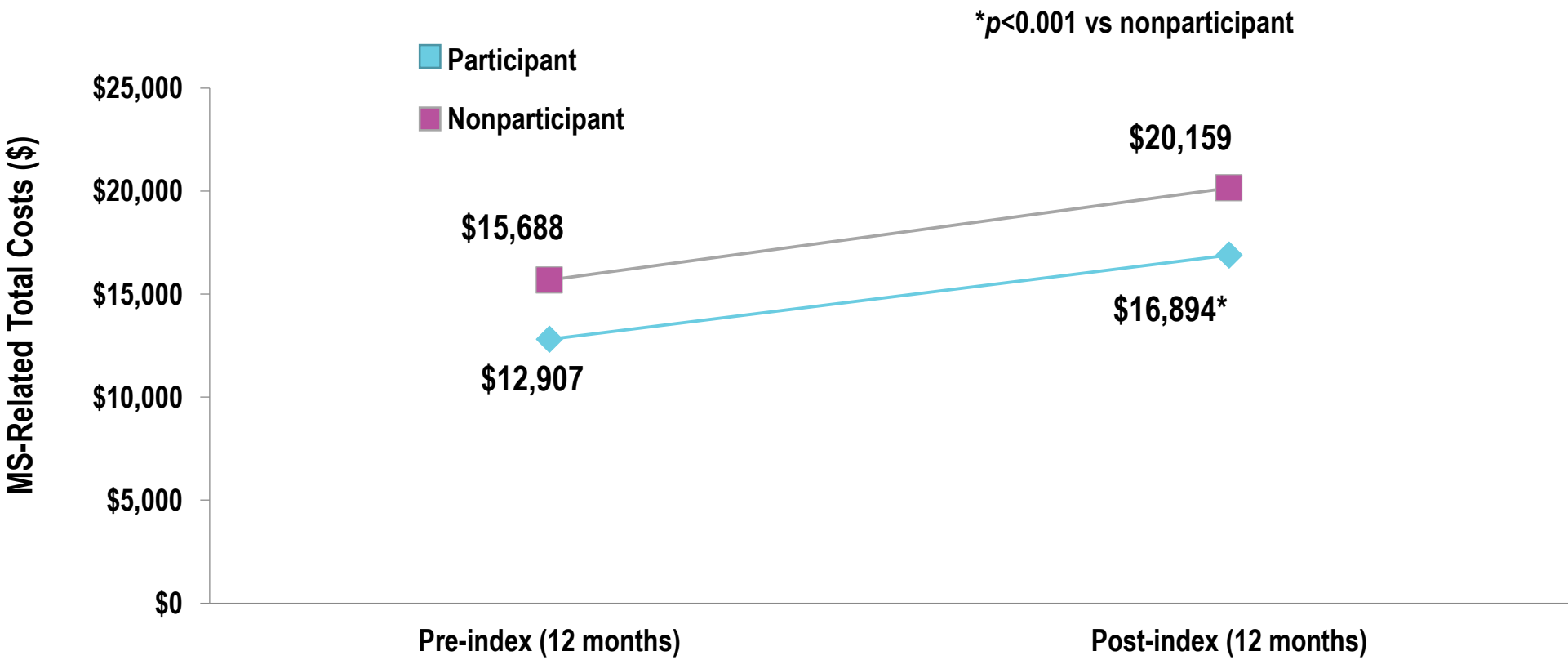


Data source: Retrospective claims analysis of MS patients ≥ 18 years (n=3993) from the HealthCore Integrated Research Database (January 2004-April 2008)

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

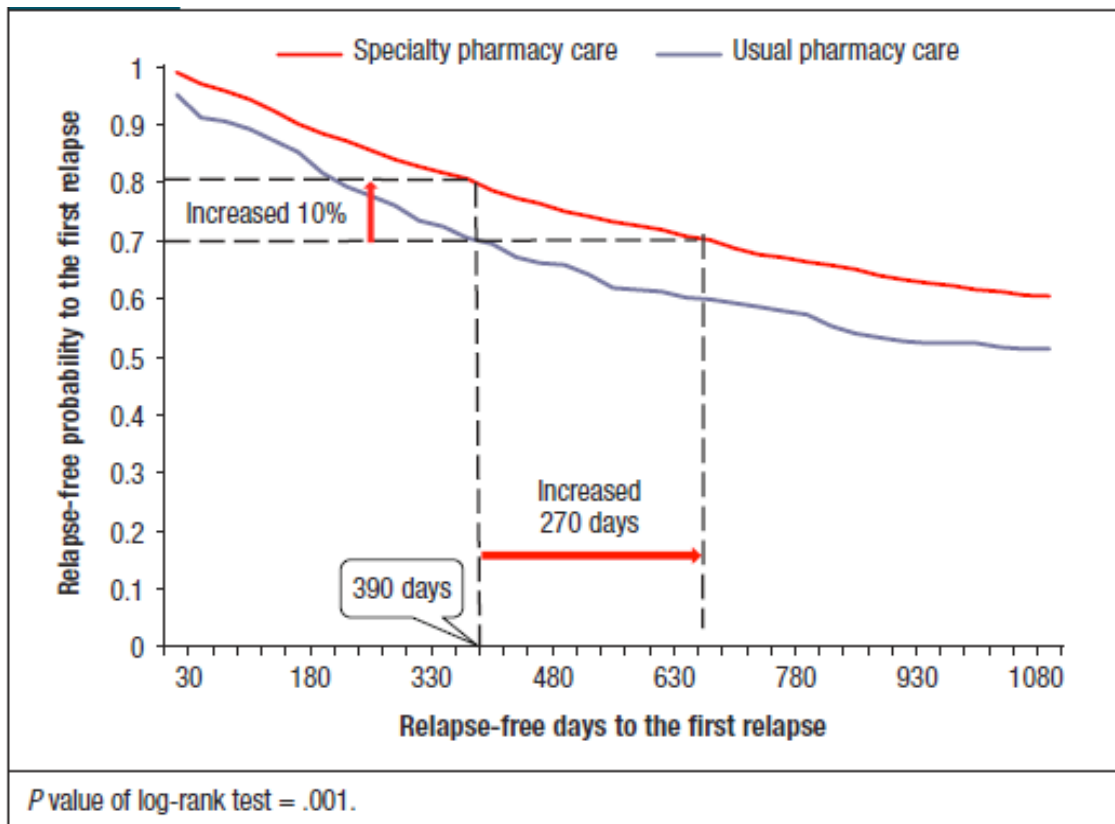
Care Management Reduced Total MS-Related Cost of Care



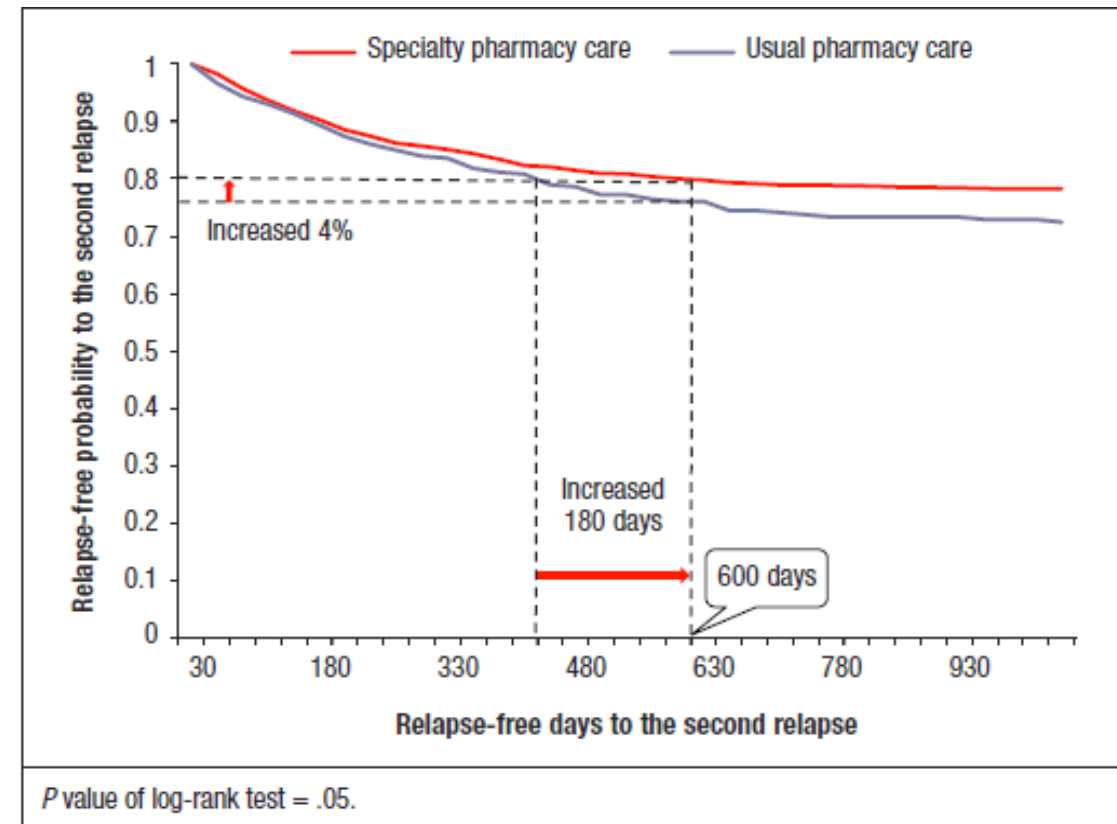
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Care Management Implemented Through Specialty Pharmacy Lowered the Risk for Disease Relapse

Time to First MS-Relapse



Time to Second MS Relapse



Data source: Retrospective claims analysis of MS patients ≥ 18 years ($n=1731$) from an integrated national PBM pharmacy and medical database (2006 - 2009)

Intervention: Specialty pharmacy vs. community pharmacy care

Outcomes assessed: Time to first and second relapse and total number of relapses

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 is associated with greater adherence, decreased risk for disease relapse, and lower cost of care



Collaborating to Improve Access to Quality Care for MS

Kyle Pinion

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

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: Services

The Core of MSAA's mission is "Improving Lives Today", as an organization we provide direct services to help achieve that goal, including the following:

- Toll-Free Telephone Helpline
- Equipment Program (Daily Living Aids and Cooling Equipment)
- MRI Access Fund
- Nationwide Educational Series (both in-person and online)
- Publications
- Other

Overview of MSAA: Advocacy

MSAA works to ensure that all MS patients have access to the appropriate therapies, treatment and comprehensive healthcare 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
- Co-Pay Accumulators
- Geographic location (i.e. distance from MS Centers/access to appropriate comprehensive healthcare team)

The Impact of MS on Patients & 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 (i.e. scooters, handicap-accessible vehicles)
- Respite care and nursing home services

Healthcare Plans & Multiple Sclerosis

- MS patients also need access to a healthcare 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 created unexpected costs such as hospitalization and costs associated with recurrent and worsening disease activity.



Multiple Sclerosis Association of America

375 Kings Highway North

Cherry Hill, NJ 08034

(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!

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Payer Considerations for Providing Support
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