Using Real-World Evidence to Achieve High Quality Care that Improves Payer Outcomes for

MULTIPLE SCLEROSIS

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Welcome and Pre-Survey Questions

Dana McCormick, RPh, FAMCP
Director of Pharmacy
Blue Cross Blue Shield of Texas

Agenda

6:30 AM	Pre-Activity Learning Assessment and Opening Comments **Dana McCormick, RPh, FAMCP**
6:35 AM	*Clinical Overview of MS: Optimizing Treatment Selection in Diverse Patient Populations* **Mitzi Joi Williams, MD, FAAN**
7:00 AM	*Using Real-World Evidence to Inform Appropriate Access and Reimbursement* **Dana McCormick, RPh, FAMCP**
7:25 AM	*Medical and Pharmacy Management Strategies to Enhance MS Outcomes for all Patient Types: A Case-Based Discussion* **Dana McCormick, RPh, FAMCP and Mitzi Joi Williams, MD, FAAN**
7:40 AM	Audience Q&A Session
7:55 AM	Key Takeaways and Closing Comments; Post-Activity Assessment and Evaluation
8:00 AM	Adjournment

Learning Objectives

- Review the impact of health equity and the unique challenges presented by MS in diverse patient populations
- Assess how current and emerging therapies impact disease control in diverse patient populations and their fit into the MS treatment algorithm
- Interpret the value of real-world evidence to inform appropriate access and reimbursement decisions for patients with MS
- Illustrate collaborative treatment optimization approaches to balance costs with improved outcomes for the management of MS

Join us online to submit questions and respond to polls!

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- OR just point your phone's camera at the QR code to join directly

Pre-Survey

Clinical Overview of MS: Optimizing Treatment Selection in Diverse Patient Populations

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

Learning Objectives

- Review the impact of health equity and the unique challenges presented by MS in diverse patient populations
- Assess how current and emerging therapies impact disease control in diverse patient populations and their fit into the MS treatment algorithm

MS is Not Exclusively a Disease in Patients of White/European Descent

Average Annual Incidence Rates / 100,000 Person Years

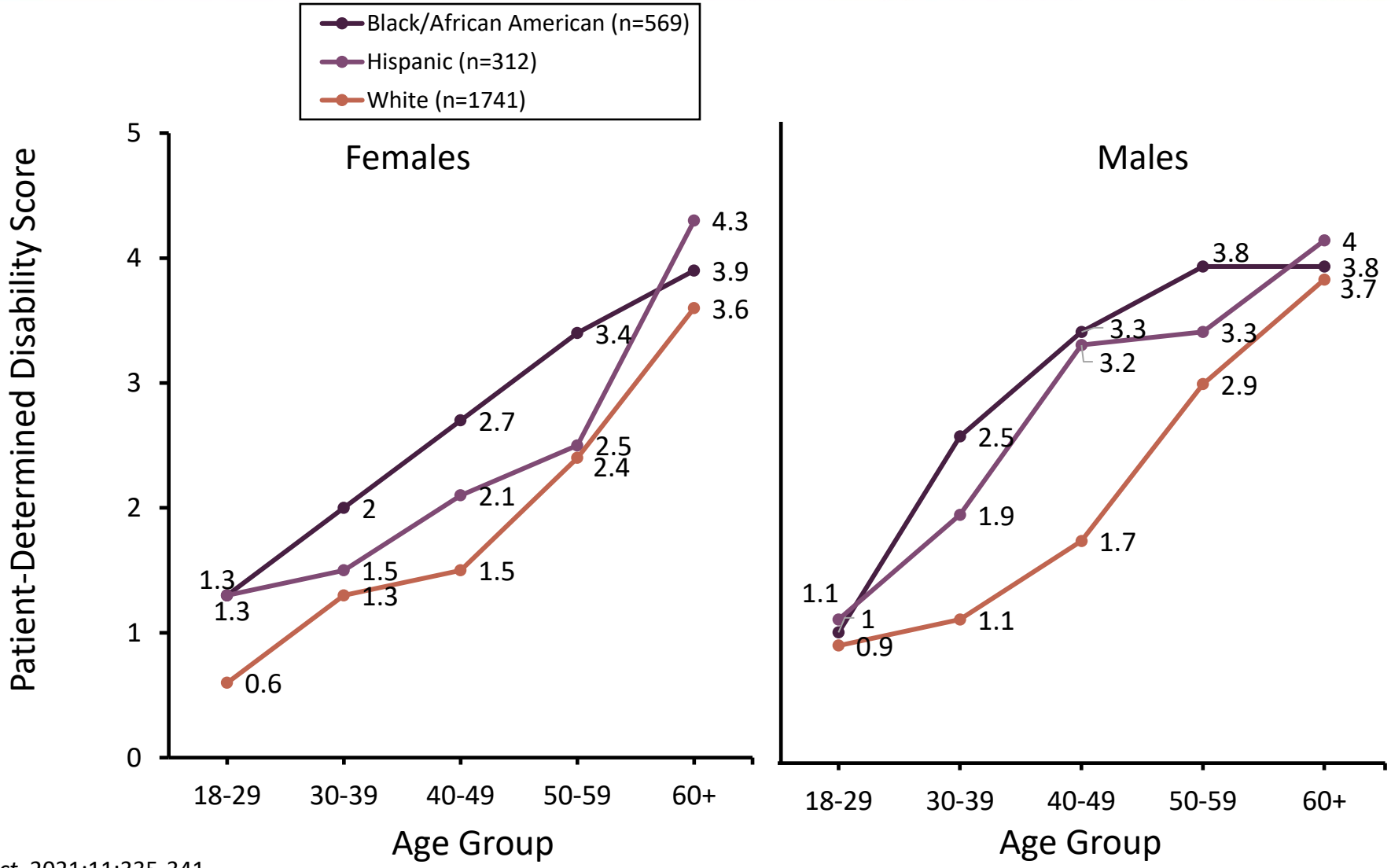
Patient Cohort	Data Collection Timeframe	White	Black / African American	Hispanic	Asian / Pacific Islander	Native American
Southern California Kaiser Health Plan	2008-2010	**6.9**	**10.2**	**2.9**	**1.4**	
US Veterans*	1990-2007	**9.3**	**12.1**			
	2000-2007			**8.2**	**3.3**	**3.1**
	2007-2016	**14.8**	**20.3**	**11.3**		

- MS incidence for Blacks / African Americans is higher than that for Whites
- Black women have a higher risk of MS (but not Black men) compared to Whites

*military personnel on active duty during the timeframe listed.

Langer-Gould A, et al. *Neurology.* 2013;80:1734-1739; Wallin MT, et al. *Brain*. 2012;135(Pt 6):1778-1785; Williams VF, et al. *MSMR*. 2017;24(8):2-11.

Minority Patients with MS Experience a More Severe Course vs. Whites



Kister I, et al. *Neurol Clin Pract*. 2021;11:335-341.

Black/African Americans with MS Exhibit Faster Progression and Greater Disability

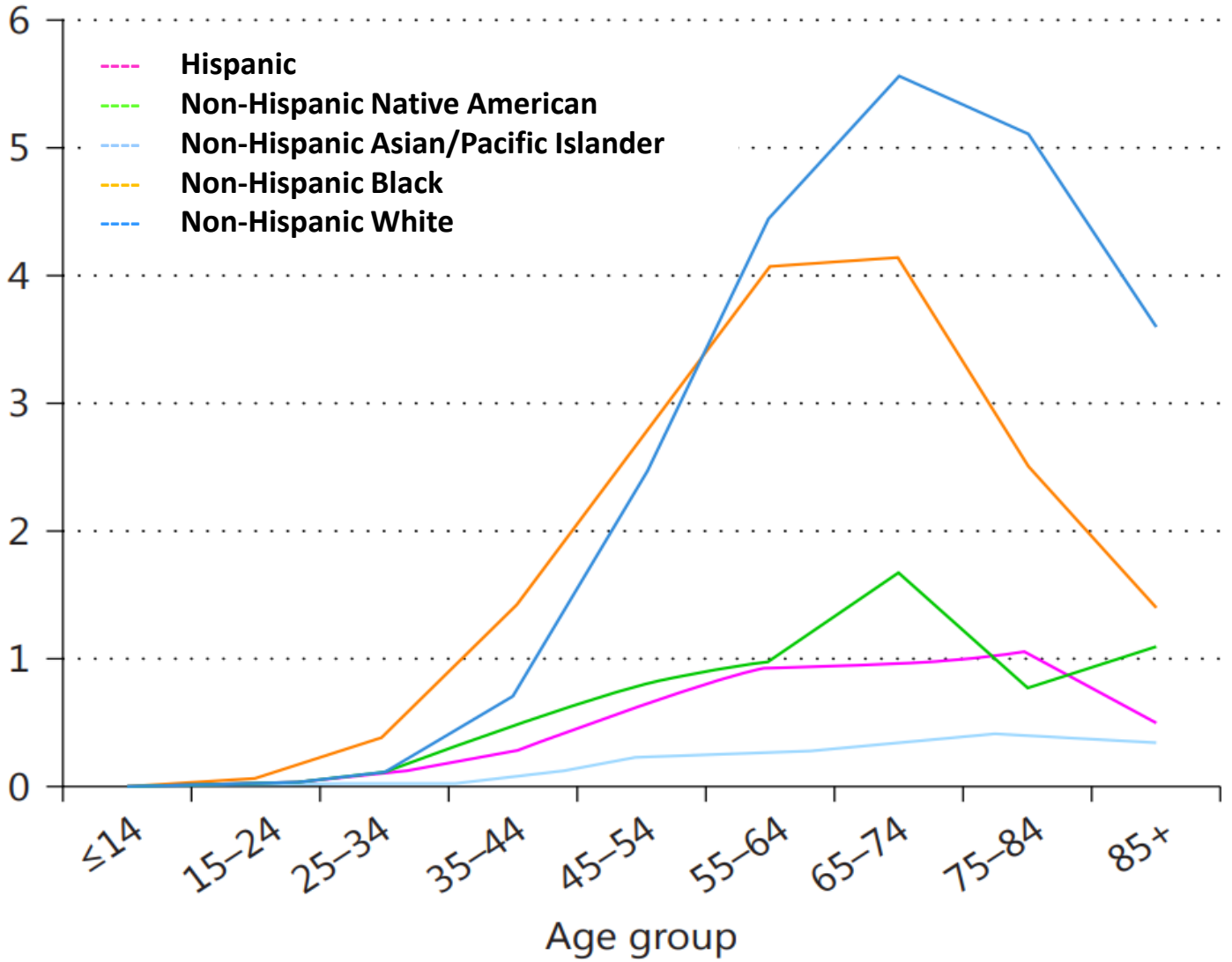
Non-White persons with MS have greater disease severity, faster disease progression, and greater disability vs. White patients

- Relapses and poorer recovery
- Cognitive deficits
- Visual impairments
- Balance and coordination problems
- Walking problems
- Earlier onset of disability
- Faster disease progression

Amezcua L, et al. *Neuroepidemiology*. 2018;50:35-40; Amezcua L, McCauley JL. *Mult Scler*. 2020;26:561-567; Cree BA, et al. *Neurology*. 2004;63:2039-2045; Wallin MT, et al. *Neurology*. 2019;92:E1029-E1040; Kister I, et al. *Neurology*. 2010;75:217-223; Langer-Gould A, et al. *Neurology*. 2013;80:1734-1739; Naismith RT, et al. *Mult Scler*. 2006;12:775-781; National Multiple Sclerosis Society. Accessed February 2023. https://www.nationalmssociety.org/What-is-MS/Who-Gets-MS/How-Many-People; National Multiple Sclerosis Society. Accessed February 2023. https://www.nationalmssociety.org/What-is-MS/Who-Gets-MS/MS-in-the-Black-Community. Perez C, et al. *Mult Scler Relat Dis*. 2021;56:103248; Dykes E, et al. AAN 2022. Abstract P17.001.

Black/African Americans Experience the Highest MS Mortality for Individuals <55 Years

Age-specific MS mortality by Race / Ethnicity in US females: 1999-2015* (rate per 100,000)



*MS confirmed as the cause of death using the Compressed Mortality File in the Data for Epidemiological Research system developed by the Center for Disease Control and Prevention.

Amezcua L, et al. *Neuroepidemiology*. 2018;50:35-40.

Racial/Ethnic Disparities in Health Care Delivery Limit Timely Access to Appropriate MS Care

Annual Health Care Utilization for Neurologic Conditions by Race/Ethnicity			
Health Care Encounter	**Non-Hispanic White**	**Non-Hispanic Black**	**Hispanic**
Office-based neurologist visits			
Persons with an encounter (%)	**17.21**	14.38	10.79
Number of encounters/100 persons with a neurologic condition	**43.16**	34.77	27.01
Emergency Department visits for a neurologic diagnosis			
Number of encounters for a neurologic diagnosis/100 persons with a neurologic condition	7.70	**12.55**	7.66
Hospital inpatient discharges			
Number of encounters for a neurologic diagnosis/100 persons with a neurologic condition	4.50	**9.39**	4.69

- **Black and Hispanic patients are less likely to see an outpatient neurologist**
- **Use of ED services and hospitalization are higher among Black patients**

Saadi A, et al. *Neurology.* 2017;88:2268-2275.

FDA-Approved Disease-Modifying Therapy for the Treatment of MS*

Injectable	Intravenous	Oral
Interferon β-1b (1993)	Mitoxantrone (2000)	Fingolimod (2010)
Interferon β-1a (1996)	Natalizumab (2006)	Teriflunomide (2012)
Glatiramer acetate (1996)	Alemtuzumab (2014)	Monomethyl fumarate (2013; 2020)
Pegylated interferon β-1a (2014)	Ocrelizumab (2017)	Dimethyl fumarate (2013)
Ofatumumab (2020)	Ublituximab (2022)	Diroximel fumarate (2019)
	Rituximab/Rituximab biosimilar†	Siponimod (2019)
		Cladribine (2019)
		Ozanimod (2020)
		Ponesimod (2021)

*current as of February 2023; †not FDA approved

Indications of the Disease-Modifying Agents

- DMTs are indicated for treatment of relapsing forms of MS including CIS, RRMS, and active SPMS in adults
- Exceptions:
  - Ocrelizumab also indicated for PPMS in adults
  - Fingolimod also indicated in patients ≥10 years
  - Cladribine not indicated for CIS; use for patients with an inadequate response to, or poor tolerance of, an alternate DMT
  - Alemtuzumab not indicated for CIS; use for patients with an inadequate response to ≥ 2 DMTs

Emerging Therapy for MS: Bruton's Tyrosine Kinase (BTK) Inhibitors

- BTK activity can affect autoimmune diseases involving B cells in autoimmune disorders, including MS
- BTK inhibitors are likely CNS penetrant, decrease B cell activation, and may limit myeloid pro-inflammatory responses
- Several BTK inhibitors are in late-phase development

Investigational BTK inhibitor	Phase	Manufacturer
Evobrutinib	3	Merck/KGaA
Tolebrutinib	3	Sanofi
Fenebrutinib	3	Genentech
Remibrutinib	3	Novartis
Orelabrutinib	2	InnoCare
BIIB091	1	Biogen

Contentti EC, et al. *Drug Design Dev Ther.* 2022;16:3473-3490.

People with MS Need Access to a Range of DMTs in Order to Personalize Treatment

Disease Factors

- Disease activity
- Duration of disease
- Prognostic factors

Patient Factors

- Treatment history
- Adherence
- Comorbidities
- Personal preferences

Treatment Factors

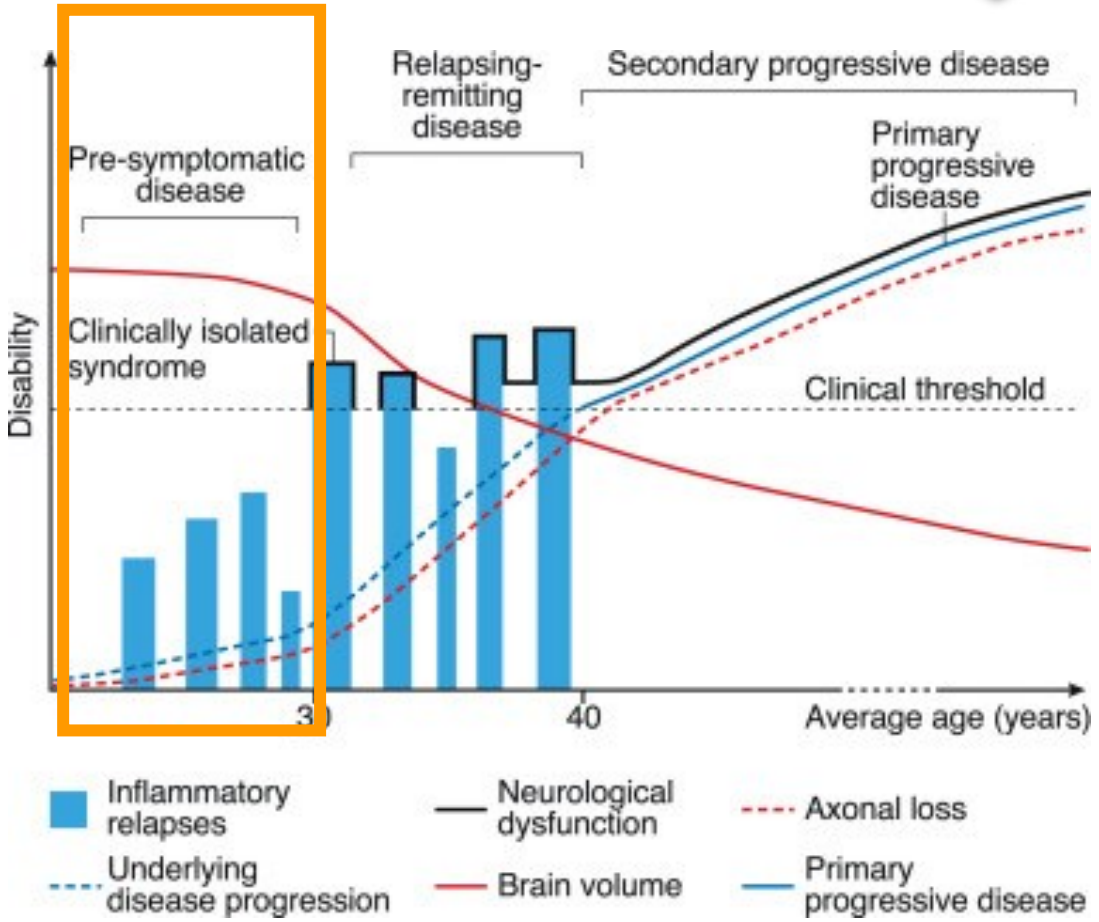
- Mechanism of action
- Efficacy
- Drug safety/tolerability
- Route of administration
- Monitoring frequency

Align factors with patient goals to optimize treatment outcome

Rae-Grant A, et al. *Neurology.* 2018;90:789-800.

Earlier Treatment May Optimize Outcomes

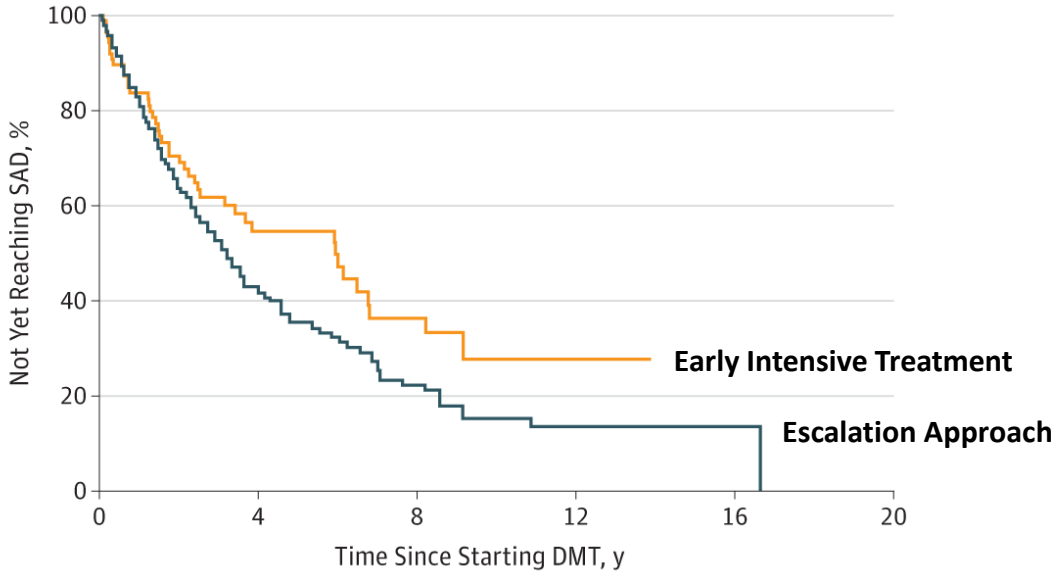
- Optimal treatment window may be earlier than previously thought
  - Tissue damage and atrophy start early and lead to loss of function
  - Irreversible damage occurs before clinical signs/symptoms
  - DMT efficacy is maximal in early, inflammatory stage of MS



Fernandez O. *Mult Scler Relat Dis*. 2017:17:75-83; Dendrou CA, et al. *Nat Rev Immunol*. 2015;15:545-558.

Early, Intensive Disease-Modifying Treatment Delays MS-Related Disability

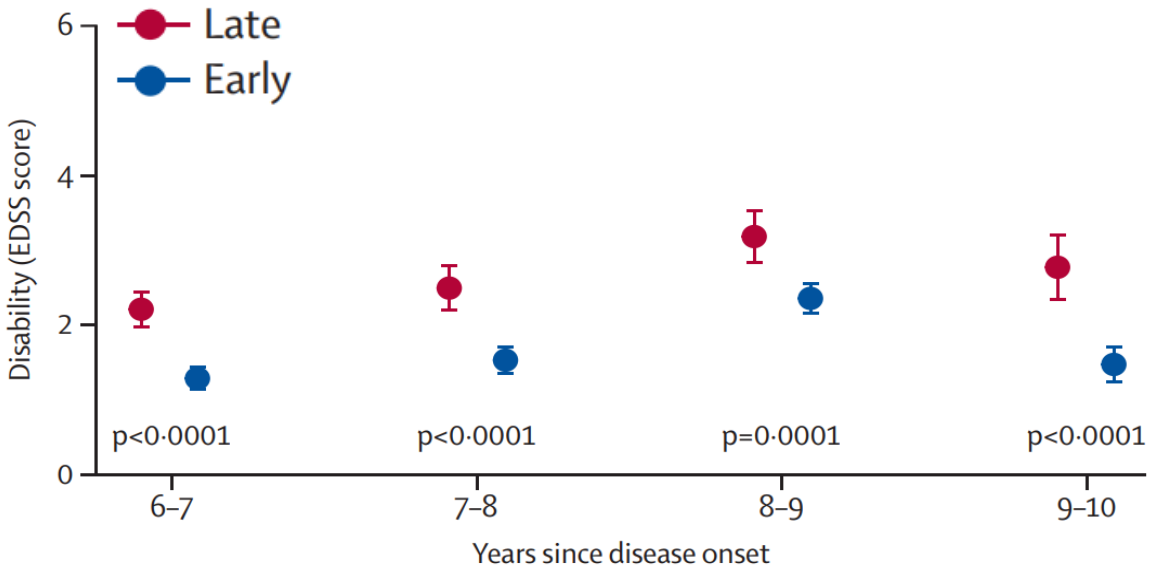
Time to Sustained Accumulation of Disability by Initial Treatment Strategy



No. at risk					
ESC	316	75	21	6	1
EIT	89	29	12	1	0

SAD=sustained accumulation of disability; EIT=early intensive treatment (alemtuzumab, natalizumab); ESC=escalation approach (IFN, GA, DMF, fingolimod, teriflunomide)

Disability Trajectory 6–10 Years After Disease Onset: Early vs. Late Treatment with High-Efficacy DMT

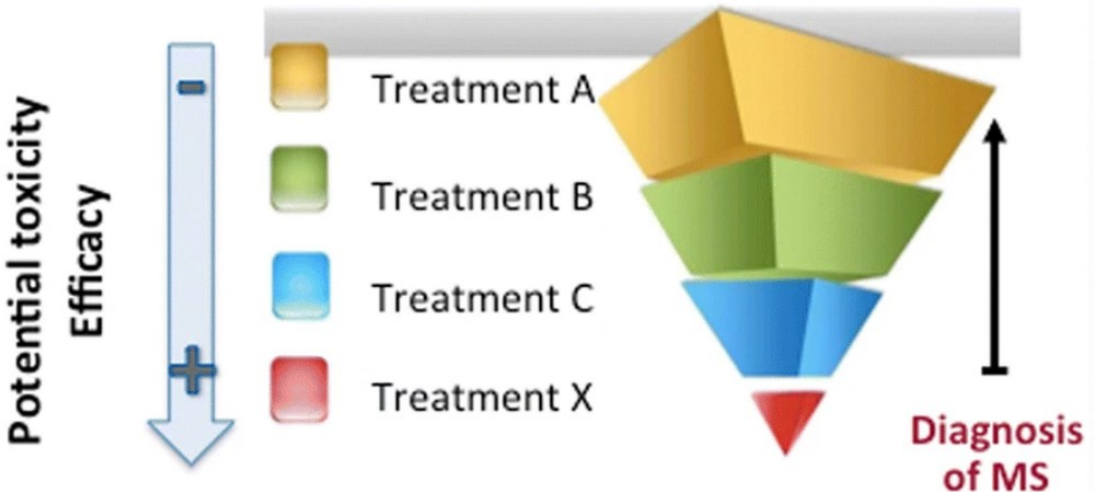


Number of patients				
Late	233	192	168	135
Early	189	140	126	89
Proportion of patients above EDSS 6 score				
Late	14 (6·0%)	16 (8·2%)	17 (9·9%)	15 (11·0%)
Early	5 (2·6%)	3 (2·1%)	4 (3·2%)	3 (3·4%)

Harding K, et al. *JAMA Neurol*. 2019:76:536-541; He A, et al. *Lancet Neurol*. 2020;19:307-316.

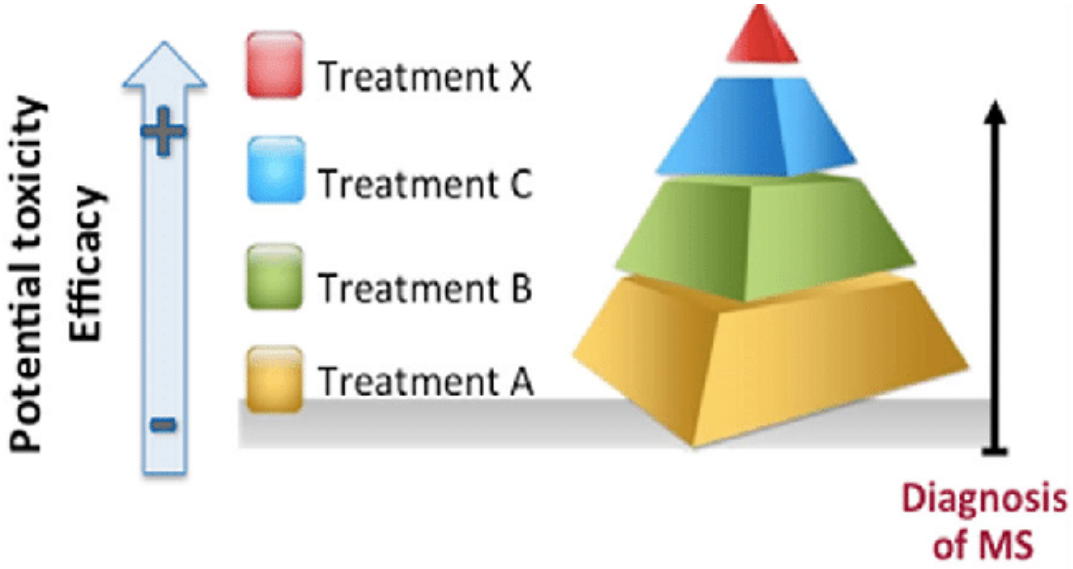
Drug Characteristics Can Influence the MS Treatment Strategy

High Efficacy Early
Induction Strategy



Early use of immunosuppressive drugs followed by long-term maintenance treatment

Escalation Strategy



Start with 1st line DMTs; Switch to 2nd line DMTs if ineffective or partially effective

Ruggieri S, et al. *Mult Scler Demyelinating Disord*. 2018;3:5.

“Higher Efficacy” MS DMTs

Efficacy

Monoclonal antibodies

- Natalizumab
- Alemtuzumab
- Anti-CD20’s

Cladribine

S1P receptor modulators

- Fingolimod
- Siponimod
- Ozanimod
- Ponesimod

Spelman T, et al. *JAMA Neurol.* 2021;78:1197-1204.

Application of an Early High-Efficacy Treatment Strategy

High Efficacy Therapies	
Continuous Modulation	**Induction Therapy**
• **Ublituximab** (2022) Anti-CD20 mAb • **Ofatumumab** (2020) Anti-CD20 mAb • **Ocrelizumab** (2017) Anti-CD20 mAb • **Natalizumab** (2004) Integrin receptor antagonist	• **Cladribine (2019)** Purine antimetabolite • **Alemtuzumab (2014)** CD52-directed cytolytic mAb • **Mitoxantrone (2000)** Synthetic antineoplastic anthracenedione

Giovannoni G. *Curr Opin Neurol*. 2018;31:233-243; Steinman L, et al. *N Engl J Med*. 2022; 387:704-714.

POLL

White patients are put on DMT's ____% more often relative to Black patients.

1) 5%
2) 10%
3) 15%
4) 20%
5) 25%
6) 30%
7) Other

Disparities in the Treatment of MS Across Patient Subgroups

Choosing DMTs

Only 30% of Black/African American and 20% of Hispanic patients initiated high-efficacy DMT vs. 39% for White patients

With patients at risk for faster progression, monitoring for signs to switch to high-efficacy DMTs is critical

Treatment Response

- **45% of patients with suboptimal response to treatment are Black**
- Black patients had the **highest rate of non-response and poor tolerability to 1st line treatment with interferons**

Greater social vulnerability index score predicts greater MS disability

Comorbidities

- Black patients **>2x likely to be diagnosed with diabetes or hypertension vs. White patients**

Assessing for cardiometabolic comorbidities allows for early intervention and can help optimize MS treatment outcomes

Geiger C, et al. American Academy of Neurology; April 7, 2022; Seattle, WA; Chase C, et al. *Arch Phys Med Rehab*. 2022;103:331-335; Orlando C, et al. American Academy of Neurology; 2022 Seattle, WA. https://index.mirasmart.com/aan2022/PDFfiles/AAN2022-000413.html; Perez CA, et al. *Mult Scler Relat Dis.* 2021; 56:103248.

Access to and Reimbursement for DMTs Can Be Impacted by Health Disparities

- Racial and ethnic minority groups may experience coverage barriers in accessing the DMTs they need for optimal outcomes
- Coverage criteria varies by insurance provider
  - Patients receiving drug coverage from different providers may experience different levels of access and coverage for DMTs[1]
  - High copays and lack of coverage for certain therapies limit treatment options for most patients[2]

1. Chambers JD, et al. *Am J Pharm Benefits*. 2017;9;155-159; 2. Bourdette DN, et al. *Neurol Clin Pract.* 2016;6:177-182.

MS Care and Outcomes in Diverse Patient Populations

MS Characteristics in Black vs. White Patients

- Greater MS severity
- Worse manual dexterity, cognitive performance
- Higher rates of uncontrolled hypertension

MS Characteristics by Race

- Black patients had higher rates of EDSS score ≥4 vs. Whites
- Hispanics used DMTs at a lower rate than non-Hispanics
- Black patients least likely to use DMTs

Characteristics in Black Patients

86%
Seeing an MS specialist

4 Years
Delay in Diagnosis

19%
Not Receiving DMTs

Treatment Outcomes by Race

- Siponimod had similar efficacy in Hispanic MS patients as in the general cohort in a *post hoc* analysis of the EXPAND trial
- Ofatumumab had similar efficacy across races in a *post hoc* analysis of the ASCLEPIOS trials

Okai AF, et al. *Neurology.* 2022;98:1015-1020; North American Registry for Care and Research in Multiple Sclerosis. Accessed February 2023. https://www.narcrms.org; National African Americans with MS Registry. Accessed February 2023. . https://www.naamsr.org/registrant/consent; Cree BA, et al. *Mult Scler*. 2022;28:1591-1605; Gartner J, et al. *Mult Scler*. 2022;28:1562-157

POLL

Race/Ethnicity Can Influence Response to MS DMT.

1) Strongly disagree
2) Disagree
3) Somewhat disagree
4) Neither agree or disagree
5) Somewhat agree
6) Agree
7) Strongly agree

Race/Ethnicity Can Influence Response to MS DMT

- Faster B-cell repopulation following anti-CD20 in Black/African American patients
- Interferons may be less effective in Black/African American patients with MS

Saidenberg L, et al. *Mult Scler Relat Disord*. 2022;63:103830; Cree BAC, et al. *Arch Neurol.* 2005;62:1681-1683.

Non-White People with MS are Underrepresented in the Literature and Clinical Trials

Less than 1% of all literature

- 136 of 60,000 articles on MS are focused on Black/African American or Hispanic patients

Systematic review of clinical trials reported the average enrollment of Black and African American patients was <3%

Nearly 40% of clinical trials

Fail to report the race/ethnicity of enrolled patients

Khan O, et al. *Neurol Clin Pract*. 2015;5:132-142; Telesford KM, et al. *Neurol Neuroimmunol Neuroinflamm*. 2020; 7(1); Onuorah HM, et al. *Neurology*. 2022;98:e880-e892.

Real-World Data Can Guide Treatment in Patients Underrepresented in Clinical Trials

Clinical
Demographics, HER Date, Lab Test Results, Diagnoses, Procedures, Pathology/Histology Data, Radiology Images, Microbiology Data, Provider Notes, Admission/Discharge and Progress Reports, Performance Status

Medication
Medical Orders, Administration (Dose, Route, NDC/RxNorm codes), Concomitant Therapies, Point-of-Sale Data, (Prescription & OTC) Prescription Refill, Allergies

Claims
Medical Claims, Prescription Drug Claims, Other Drug and Treatment Use Data

Molecular Profiling
Genomic and Genetic Testing Data (SNPs/Panels), Multi-Omics Data (Proteomics, Transcriptomics, Metabonomics, Lipidomics), Other Biomarker Status

Family History
Historical Data on Health Conditions and Allergies Relating to Patient and Extended Family, Smoking Status, Alcohol Use

Mobile Health
Fitness Trackers, Wearable Devices, Other Health Apps Measuring Activity and Body Function

Environmental
Climate Factors, Pollutants, Infections, Lifestyle Factors (Diets, Stress), Other Environmental and Occupational Sources

Patient Reported
Patient Reported Outcomes, Surveys, Diaries (Diets, Habits), Personal Health Records, Adverse Event Reporting, Quality-of-Life Measures

Social Media
Patient Communities, Twitter, Facebook, Blogs

Literature
Disease Burden, Clinical Characteristics, Prevalence/Incidence, Rates of Treatment, Resource Use and Costs, Disease Control, Quality-of-Life Measures

Swift B, et al. *Clin Transl Sci.* 2018;11:450-460.

National African Americans with MS Registry (NAAMSR)

Launched in September 2020

Primary Objectives

- Expand evidence-based knowledge of MS and its management in African Americans
- Education AAwMS and increase opportunities for clinical trial participation
- Engage in research beneficial to AAwMS

Registry Design

- Target enrollment: 20,000-30,000 participants in urban, suburban and rural settings
- Broad recruitment and outreach to self-identifying AAwMS
- All recruits complete an extensive questionnaire; topics include demographic and socioeconomic status; timing of symptom onset and diagnosis; MS pattern; use of DMTs; quality of life; disability status; access to care

Outcome Measures

- Impact of social determinants of health on access to care, timeliness of diagnosis, DMT initiation, and long-term outcomes
- Potential effect of racial identity on disease pattern and severity
- Relationship between disease severity and medication efficacy

National African Americans with MS (NAAMS) Registry. Accessed February 2023. https://www.naamsr.org/registrant/consent; Okai AF, et al. *Neurology.* 2022;98:1015-1020.

Summary

- MS is not exclusively a disease in patients of European/Caucasian descent
- Minority patients with MS experience a more severe course, including faster progression and greater disability than Whites
- Disease-modifying MS therapies are indicated for treatment of relapsing forms of MS including CIS, RRMS, and active SPMS in adults
- Earlier treatment may optimize MS outcomes; early, intensive disease-modifying treatment can delay MS-related disability
- Data suggests MS treatment disparities exist
- Real-world evidence may provide insights when selecting treatments for patients underrepresented in the clinical trial literature

Using Real-World Evidence to Inform Appropriate Access and Reimbursement

Dana McCormick, RPh, FAMCP
Director of Pharmacy
Blue Cross Blue Shield of Texas

Learning Objective

- Interpret the value of real-world evidence to inform appropriate access and reimbursement decisions for patients with MS

Using Real-World Evidence in MS Treatment Decision-Making

- Randomized clinical trials (RCTs) provide evidence in carefully selected patients treated under controlled conditions
- In the real world, patients are more heterogeneous, and their behaviors are more varied
- Payers and providers can look to real-world evidence (RWE) for answers not found in the RCT data
- High-quality real-world studies can provide insight on clinical questions such as drug sequencing and switching

Cohen JA, et al. *Mult Scler*. 2020;26:23-37.

RCTs Are Not Always Available or Appropriate

RCTs are not always ethical, feasible, or practical

- No established comparators
- A placebo arm is unethical in life-threatening disorders
- When low patient enrollment limits statistical comparisons between groups

Uncontrolled studies are acceptable

- Natural history studies
- Time-to-event studies

Noncomparative studies may provide the "best available evidence"

- Dose-ranging studies, single-arm trials, case series, case reports
- Registry studies, claims data

Modeling

- Comparison of single-arm trial with artificial comparator built out of real-world data

Real-World Data vs. Real-World Evidence

- Real-world data (RWD) is data collected **outside traditional clinical trial settings**
- RWE is derived from RWD and allows for insight in the **actual setting of use**

Anbil PS. PharmExec.com. March 14, 2019. Accessed February 2023. https://www.pharmexec.com/view/there-evidence-real-world-evidence.

Useful Data is Derived From Multiple Sources

Real-World Data Sources

- Claims data
- EHRs
- Observational data
- Patient pathways
- Surveillance
- Mortality data
- Primary & secondary care data
- Administrative data
- Disease registries
- Pharmacy data
- Cost studies
- Wearables & mobile devices
- Consumer data
- Social media

Real-World Evidence
Identifying Unmet Needs

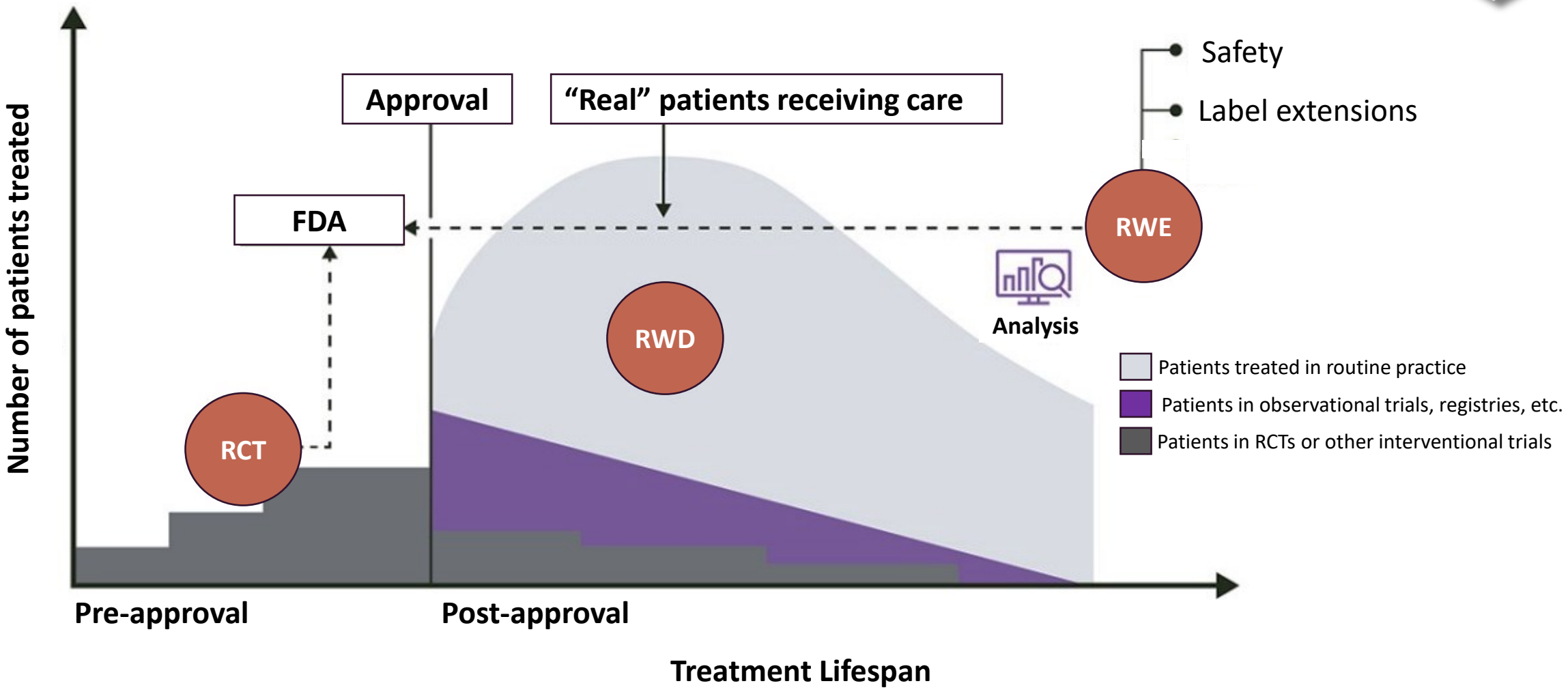
- Natural history
- Comorbidities
- Burden of illness
- Incidence & prevalence
- Disease mechanisms
- Clinical practice patterns

Real-World Evidence
Informing Clinical & Policy Decisions

- Utilization patterns
- Outcomes predictors
- Benefit/risk in subgroups
- Pharmacovigilance
- Population-level impact
- Benefit design & formulary position

Galson S, Simon G. National Academy of Medicine. Accessed February 2023. https://nam.edu/real-world-evidence-to-guide-the-approval-and-use-of-new-treatments/

The Experience of Most Patients Receiving Care is Reflected in RWD



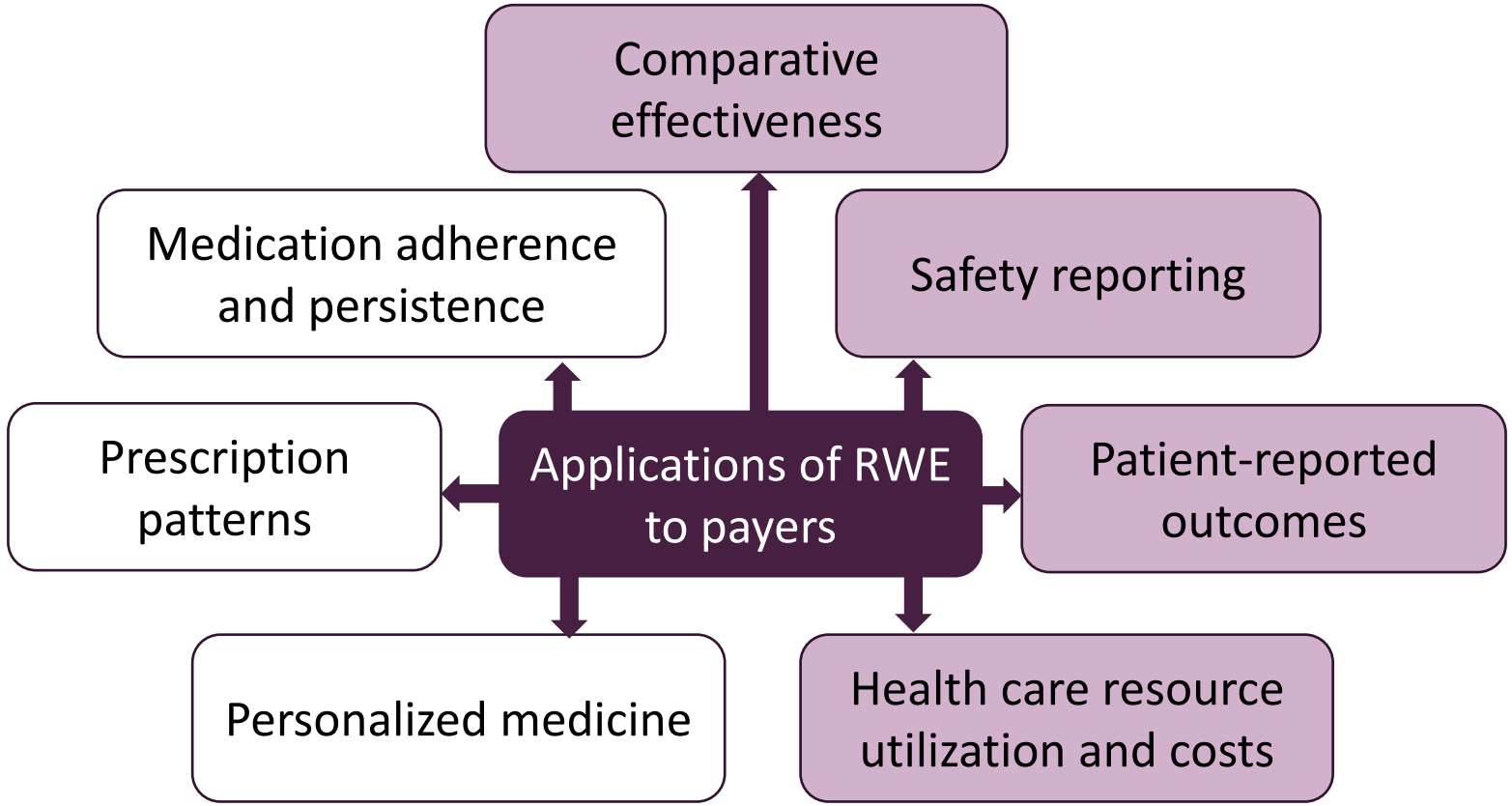
DXC Technology. Accessed March 2023. https://dxc.com/us/en/insights/perspectives/paper/how-real-world-evidence-transforms-the-entire-healthcare-ecosystem.

POLL

Based on your perspective, what is the best way payers can use RWE?

1) Address health inequities
2) Comparative effectiveness
3) Healthcare resource utilization and costs
4) Medication adherence and persistence
5) Patient reported outcomes
6) Prescription patterns
7) Personalized medicine
8) Safety reporting

Payers Use RWE in Many Ways



Areas of concern to payers where RWE can provide valuable evidence to aid decision-making

RWE can generate additional information depending on the sources of RWE

Roberts MH, Ferguson GT. *Pharmacoecon Open*. 2021;5:3-11.

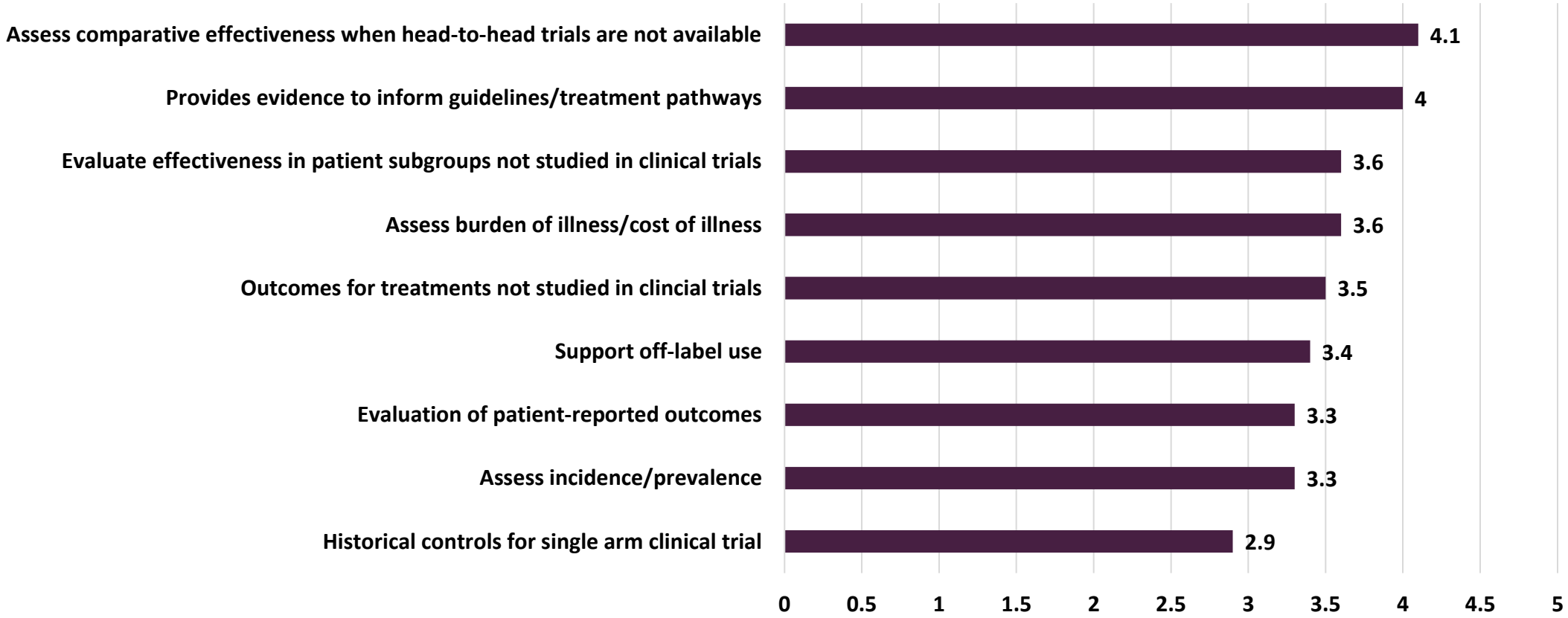
RWE and Reimbursement Opportunities

- RCTs remain the gold standard for making coverage and reimbursement decisions
- However, payers are increasingly recognizing the role high-quality RWE can play
- RWE has been used by payers to support decisions related to
  - Identifying the patient population(s) that may be eligible for a drug
  - Determining preliminary cost estimates
  - Coverage, discounts, and formulary tiering
  - Product utilization decisions

Roberts MH, Ferguson GT. *Pharmacoecon Open*. 2021;5:3-11; Hampson G, et al. *J Comp Eff Res*. 2018;7:1133-1143.

Payer Perception of RWE

Usefulness of RWE When Making Formulary Decisions



Survey distributed to 221 US payers through the AMCP Market Insights program; February 2020 (n=99 respondents)

Brixner D, et al. *J Manag Care Spec Pharm*. 2021;27:1096-1105.

Types of RWE Used by Payers

Payers value RWE to fill evidence gaps not addressed by RCTs, including

- Long-term effectiveness and safety data
- Head-to-head drug comparisons
- Cost analyses for tiering formulary placement
- Medication use patterns, including adherence
- Identification of relevant responder and non-responder patient subpopulations
- Patient-reported outcome (PRO) data

Roberts MH, Ferguson GT. *Pharmacoecon Open*. 2021;5:3-11; Leung MY, et al. *J Manag Care Pharm*. 2012;18:256–264; Malone DC, et al. *Value Health*. 2018;21:326–333; Moloney R, et al. *Int J Technol Assess Health Care*. 2015;31:90–98; Wang A, et al. *Am J Manag Care*. 2012;18:Sp71–76; Brogan AP, et al. *J Manag Care Spec Pharm*. 2017;23:125–134.

Using RWE to Understand the Value of Care

Effectiveness

- How effective is this treatment outside of a clinical trial?
- Which patient subgroups will benefit? (e.g., age, disease stage, comorbidities)
- How does early intervention impact disease course?
- How do different HCP and patient behaviors impact treatment effectiveness?

Safety

- What adverse events have been observed in real-world patients taking this drug?
- How might safety results observed in RCTs translate to the wider patient population seen in clinical practice?

Prescribing behaviors

- In which patients do HCPs choose a certain treatment?
- How is dosing adjusted in clinical practice?
- When do HCPs switch patients to new treatments?

Patient health

- How is this disease impacting patients' health-related quality of life?
- Does this treatment improve outcomes that matter most to patients?
- How long do patients typically stay on therapy and how adherent are they to therapy?

Offering value

- What is the impact of this treatment on health care resource utilization?
- Are there societal benefits to this treatment?
- How cost-effective is this treatment versus suitable comparators?
- Does this treatment offer improved value versus current treatments?

Medical Affairs Professional Society. Accessed February 2023. https://medicalaffairs.org/essentials-real-world-evidence

Using RWE to Support MS Decision-Making

- Identification of treatment patterns
- Comparative effectiveness of treatments in disease sub-types (e.g., RRMS, SPMS)
- Comparative effectiveness of treatment strategies (e.g., treat-to-target, escalation vs. early high-efficacy treatment)
- Safety and risk/benefit assessments (e.g., less common AEs, delayed AEs, and cumulative risk of AEs)
- Identification of factors that determine or predict safety and tolerability (e.g., comorbidities, health behaviors, concomitant medications, genetics, race and ethnicity, and therapy adherence and persistence)

Cohen JA, et al. *Mult Scler*. 2020;26:23-37.

Using RWE to Address Health Inequities

Certain groups continue to be underrepresented in clinical trials

Underrepresentation in trials limits the available data to guide treatment selection

RWE has the potential to fill the knowledge gaps and provide representative data

Socioeconomically disadvantaged patients

Racial and ethnic minorities: Black/African American, Hispanics, Asian, non-White people of color

Elderly

Real-World Data and Real-World Evidence. 2021. Accessed February 2023. https://www.ispor.org/docs/default-source/strategic-initiatives/pfizer-bms-ispor-infographic_final.pdf?sfvrsn=a7413b04_0

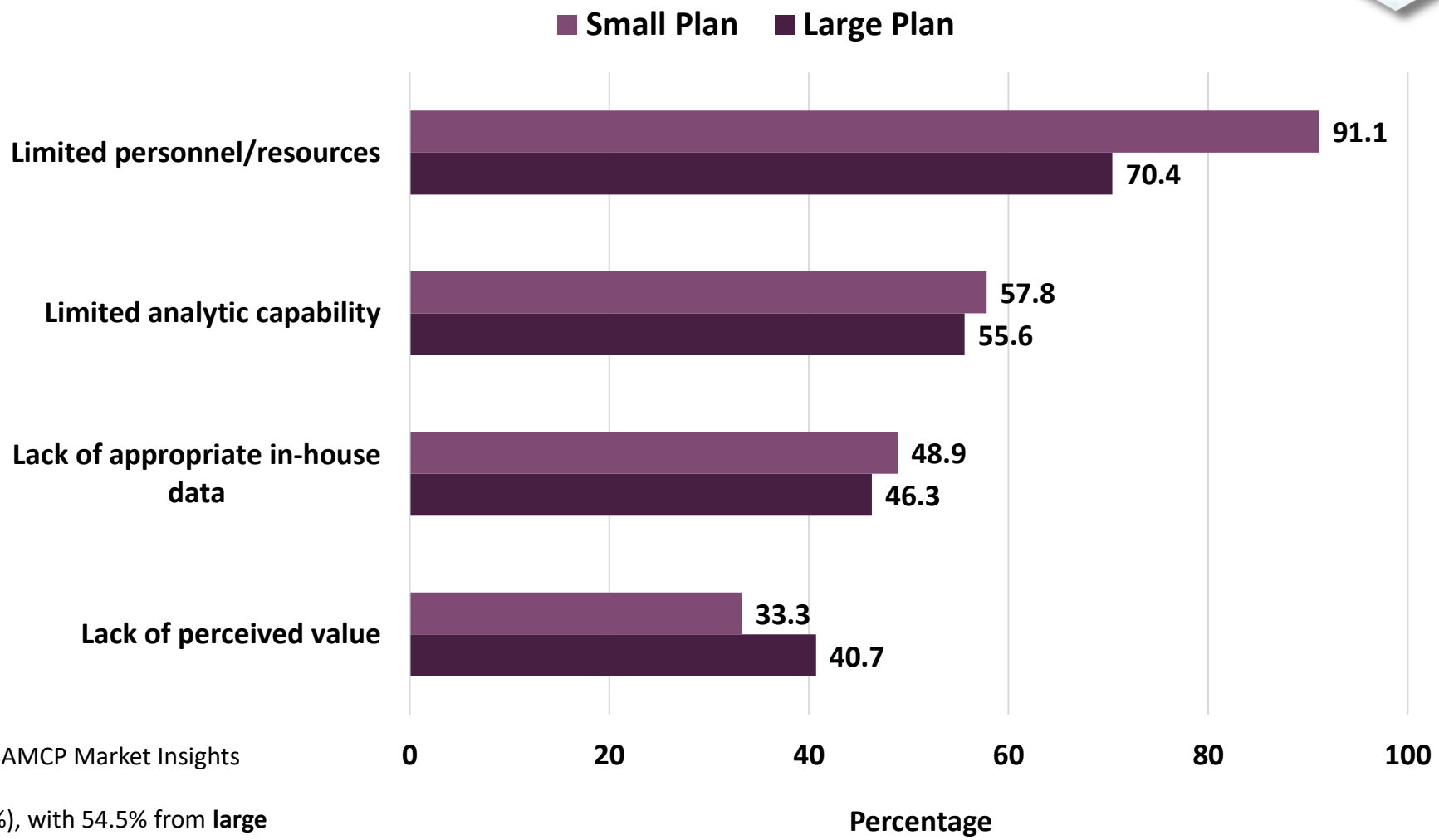
RWE and Reimbursement Challenges

Payer concerns limit the use of RWE

- Study design limitations
- Lack of transparency in research methods and analyses used
- Timeliness of results for pharmacy and therapeutic committee decisions
- Potential bias
- Lack of standardized guidance on how to interpret the entire body of evidence (RCTs and RWE)
- Lack of budget and staff training to evaluate observational studies

Roberts MH, Ferguson GT. *Pharmacoecon Open*. 2021;5:3-11; Berger ML, et al. *Value Health*. 2014;17:143–156; Dreyer NA, et al. *J Manag Care Spec Pharm*. 2016;22:1107–1113; Pearson SD, et al. *J Comp Eff Res*. 2018;7:1145–1152.

What to Consider When Conducting an In-House Analysis



Survey distributed to 221 US payers through the AMCP Market Insights program; February 2020 (n=99 respondents)
Most were from MCOs (47.5%) and PBMs (37.4%), with 54.5% from **large plans (≥1 million lives)** and 45.5% from **small plans (<1 million lives)**.

Brixner D, et al. *J Manag Care Spec Pharm*. 2021;27:1096-1105.

What to Consider When Using RWE to Support Reimbursement Decisions

Barriers to Robust Real-World Evidence to Inform Pricing and Reimbursement Decisions

Data: Availability, Governance and Quality

1. Poor quality RWD
2. Data standardization
3. Timeliness of data
4. Inadequate and disparate data infrastructure, access processes and governance

Methodology: Design and Analytic

1. RWE does not replace RCTs
2. Selection bias
3. Methodologies not well understood by HTA/payers
4. Limit capacity to critically review RWD analyses in HTA

Trust: Transparency and Reproducibility

1. Lack of trust in data and strategy
2. Lack of transparency
3. Lack of trust between stakeholders

Policy and Partnerships:

1. Lack of harmonization
2. Lack of coordination between payers/HTAs for RWD collection, context of acceptance, etc.
3. Governance issues

Capkun G, et al. *Int J Technol Assess Health Care*. 2022;38:e79.

Summary

- An increasing number of payers use RWD when making decisions about product utilization and reimbursement
- RWE can fill the evidence gap created when RCT data is limited
- RWE is increasing in importance for differentiating therapies or treatment pathways as well as coverage decisions
- RWE valued by payers includes total cost of care, burden of illness, treatment patterns, subpopulations, adverse event profiles, off-label usage, and economic data
- Payer concerns regarding data quality, study design flaws, potential bias, and lack of meaningful endpoints should be considered when using RWE
- RWE can be used to address health inequities and inform treatment decision in underrepresented patient populations

Medical and Pharmacy Management Strategies to Enhance MS Outcomes for all Patient Types: A Case-Based Discussion

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

Dana McCormick, RPh, FAMCP
Director of Pharmacy
Blue Cross Blue Shield of Texas

Learning Objective

- Illustrate collaborative treatment optimization approaches to balance costs with improved outcomes for the management of MS

Patient Case

- **Patient**: 40-year-old African American female
- **Current complaint:** numbness and tingling in the lower extremities leading to poor balance
- **Current examination**: clinical presentation suggests aggressive/active disease; MRI shows active lesions in the cervical spine
- **Diagnosis:** Multiple sclerosis
- **Prescribed treatment:** Ocrelizumab

Case Challenge

- The patient is newly diagnosed with active, aggressive disease
- Her neurologist would like to initiate treatment with ocrelizumab
- Payer denies the claim indicating the patient must first trial platform therapies prior to initiating a high-efficacy agent

Discussion

- What evidence is commonly requested by payers prior to approving access to a high-efficacy MS therapy?
- As a neurologist how would you recommend payers develop coverage criteria for MS treatments?
- How can RWE be used to support the use of high-efficacy agents as first line of MS therapy?

Faculty Discussion and Q&A Session

Dana McCormick, RPh, FAMCP
Director of Pharmacy
Blue Cross Blue Shield of Texas

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

Post-Survey

How to Claim Credit

- **Option 1:** Complete the paper-based evaluation and turn it in at the end of the meeting.
  - A certificate will be emailed to you within 3 weeks

- **Option 2:** OR, complete the evaluation online. **Please do NOT do both.**
  - Go to www.impactedu.net/evaluation to access the survey and evaluation
  - You will be instructed on how to claim your credit on the webpage immediately after clicking 'Submit' on your evaluation. Please be sure to follow these instructions or your credit will not be processed.

Pharmacist 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.

Key Takeaways and Closing Comments

Using Real-World Evidence to Achieve High Quality Care that Improves Payer Outcomes for

MULTIPLE SCLEROSIS

Jointly provided by

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This activity is supported by independent educational grants from Sanofi and Novartis Pharmaceuticals Corporation.