Board of Governors Meeting

Via Teleconference/Webinar

July 23, 2019
12:00 PM – 1:30 PM ET

pcori
PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

Welcome and Introductions

Grayson Norquist, MD, MSPH

Chairperson, Board of Governors

Joe Selby, MD, MPH

Executive Director

Agenda

12:00 PM	**Call to Order, Roll Call, and Welcome**
12:00 – 12:05	**Consider for Approval:** Minutes of the June 18, 2019 Board Meeting
12:05 – 12:30	**Consider for Approval:** Proposed Cycle 3 2018 Slate of Large Awards for the Limited Competition Dissemination and Implementation (D&I) PFA
12:30 – 1:10	**Research Portfolio Exploration Series:** Focus on Multiple Sclerosis
1:10 PM	**Wrap Up and Adjournment**

Board Vote

Call for a Motion to:	• **Approve** the Minutes of the June 18, 2019 Board Meeting
Call for the Motion to be Seconded:	• **Second** the Motion • If further discussion, may propose an **Amendment** to the Motion or an **Alternative** Motion
Voice Vote:	• Vote to **Approve** the **Final** Motion • Ask for votes in favor, opposed, and abstentions

Proposed Funding Slate from the Limited Competition PCORI Funding Announcement (Cycle 3 2018):

Implementation of PCORI-Funded Patient-Centered Outcomes Research Results

Sharon Levine, MD
Chair, Engagement, Dissemination, and Implementation Committee (EDIC)

Joanna E. Siegel, ScD
Program Director, Dissemination & Implementation

Cycle 3 2018 – Limited Competition Dissemination & Implementation PFA
Purpose of this funding initiative

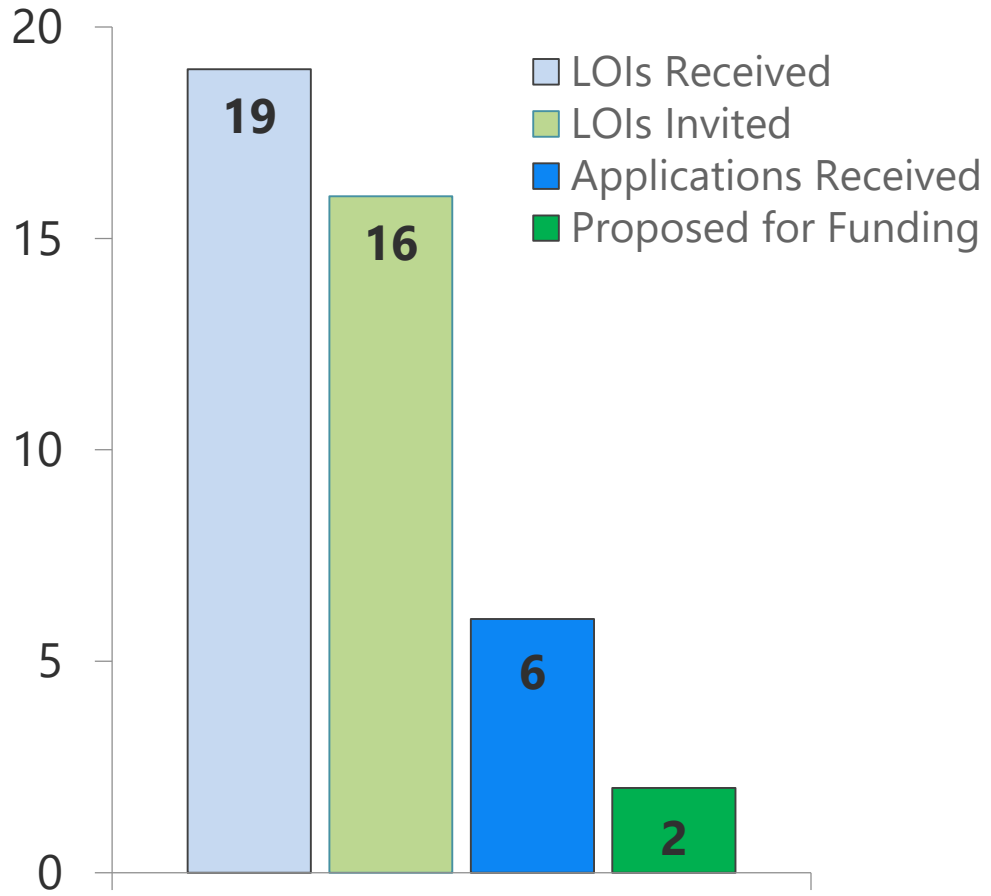
- To give PCORI awardee teams an opportunity to
  - Propose **investigator-initiated** strategies for disseminating and implementing findings from their PCORI funded studies in the context of existing evidence
  - Undertake the **next step(s)** for promoting the uptake of their findings in practice

Cycle 3 2018 – Limited Dissemination & Implementation PFA
Merit Review Criteria

1. Importance of research results in the context of the existing body of evidence
2. Readiness of the research results for implementation
3. Technical merit of the proposed implementation project
4. Project personnel and environment
5. Patient-centeredness
6. Patient and stakeholder engagement

Cycle 3 2018 – Limited Dissemination & Implementation PFA
Process Overview

- **Application overview**
  - 19 Letters of Intent (LOIs) submitted
  - 16 LOIs invited to submit a full application (84% of submitted LOIs)
  - 6 applications received (38% of invited LOIs)
- **Overall funding rate is 33 percent**
  - EDIC is proposing to fund 2 applications out of 6 received applications
- **Proposed funding slate is recommended by the Engagement, Dissemination, and Implementation Committee (EDIC)**



Cycle 3 2018 – Limited Dissemination & Implementation PFA
Slate of 2 Recommended Projects

Project Title	Budget
Implementing Patient Decision Support for Lung Cancer Screening through Tobacco Quitlines	$1.4M
Widespread Implementation of a Patient-Centered Online Therapy for Adolescent Traumatic Brain Injury	$0.9M

- All proposed projects, including requested budgets and project periods, if approved by the Board, will be subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract.

Project 1:
Implementing Patient Decision Support for Lung Cancer Screening through Tobacco Quitlines

This Dissemination and Implementation project will:

- Expand the use of a tested patient decision aid, shown in a PCORI-funded study to help patients at high-risk for lung cancer make screening decisions based on a better understanding of the tradeoffs and be more prepared to discuss screening with their provider
- Train staff at 8 state tobacco quitlines to identify and refer callers eligible for screening to the patient decision aid and other lung cancer screening resources
- Evaluate the successful implementation of the program and its impact on referred callers (e.g., effect on patients' knowledge regarding screening; preparation for decision making; scheduling a visit with their doctor to discuss screening; screening visits)

Project 2:

Widespread Implementation of a Patient-Centered Online Therapy for Adolescent Traumatic Brain Injury

This Dissemination & Implementation project will:

- Increase access to treatment for adolescents with behavior problems following traumatic brain injury, more than half of whom don't receive treatment
- Implement three ways of delivering the Family Choice Problem-Solving Therapy program (in-person, therapist-guided online, and self-guided online) at 10 children's hospitals and rehabilitation centers across 7 states
- Develop materials that will allow Spanish-speaking families to participate in the program
- Certify trainers at each site who can continue to train and support therapists
- Evaluate the continued success of the program and its impact on adolescent and family healthcare and health outcomes

Cycle 3 2018 – Limited D&I PFA
Slate of 2 Recommended Projects

PFA	Amount Budgeted per Year	Proposed Total Award*
Implementation of PCORI-Funded Patient-Centered Outcomes Research Results	$9M	$2.2M

*Note: Budgeted amount is for up to 3 cycles per year. This is the third cycle for FY-2019. If the Cycle 3 2018 slate is approved, the total 3-cycle budget will be $8.9M.

Board Vote

Call for a Motion to:	• **Approve** funding for the recommended slate of awards from the Cycle 3 2018 Limited Competition Implementation of PCORI-Funded Patient-Centered Outcomes Research Results PFA
Call for the Motion to Be Seconded:	• **Second** the Motion • If further discussion, may propose an **Amendment** to the Motion or an **Alternative** Motion
Roll Call Vote:	• Vote to **Approve** the **Final** Motion • Ask for votes in favor, opposed, and abstentions

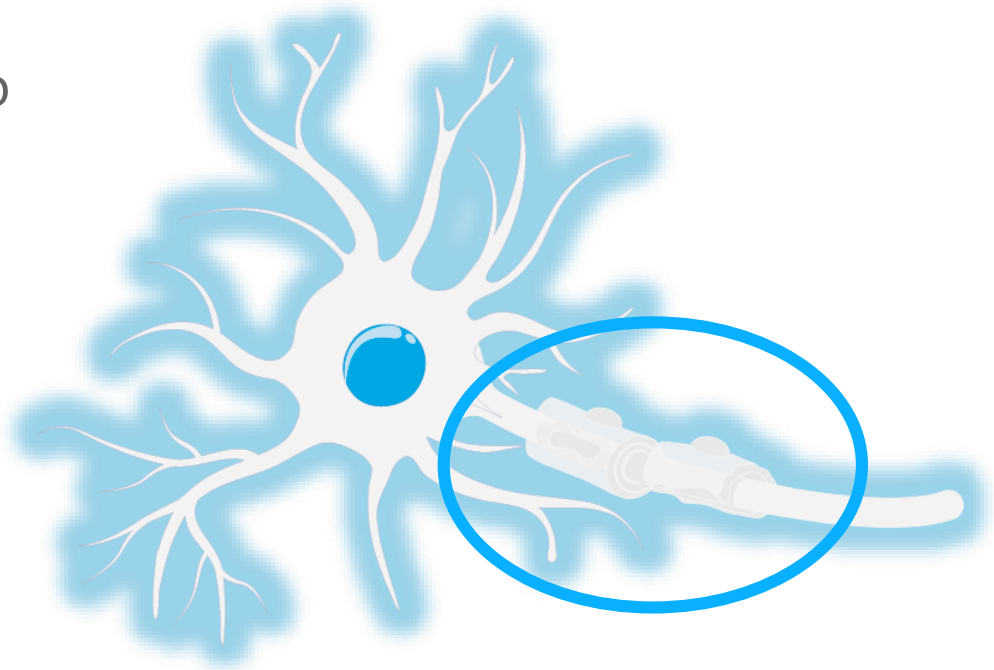
Overview of PCORI's Multiple Sclerosis (MS) Portfolio:

Filling Unmet Needs

Kimberly Bailey, MS
Senior Program Officer
Clinical Effectiveness and Decision Science

Background

- Multiple sclerosis (MS) is a chronic condition of the central nervous system characterized by damage to the myelin sheaths that cover and protect nerves
- Estimates indicate nearly 1 million Americans have MS
- Most patients are diagnosed between 20 and 50 years of age; approximately three-quarters are women
- The clinical course is highly variable, generally unfolding over decades, and symptoms range from mild to the development of severe disability

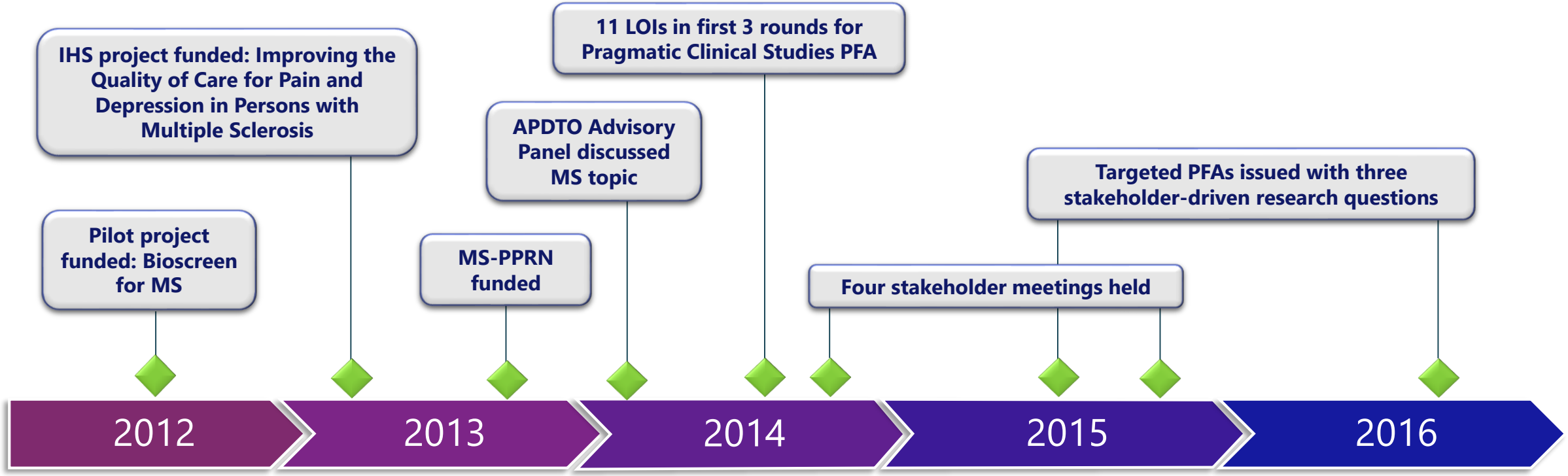


Goals of Treatments for MS

MS has no cure, but patients and clinicians have clear treatment goals

- **Address acute relapses**
  - Generally with corticosteroids
- **Modify the disease course to prevent disability**
  - Focused on altering the natural history of MS
- **Managing symptoms**
  - Fatigue
  - Difficulty walking
  - Memory or attention problems
  - Bladder problems
  - Numbness, tingling, pain

History of MS Research at PCORI



Three Key Patient and Stakeholder-Identified Areas of Need

Comparing DMTs

What are the **comparative benefits and harms** of **different disease-modifying therapies (DMTs)** or **therapeutic strategies** in patients with relapsing, remitting multiple sclerosis (RRMS)?

Treating Symptoms

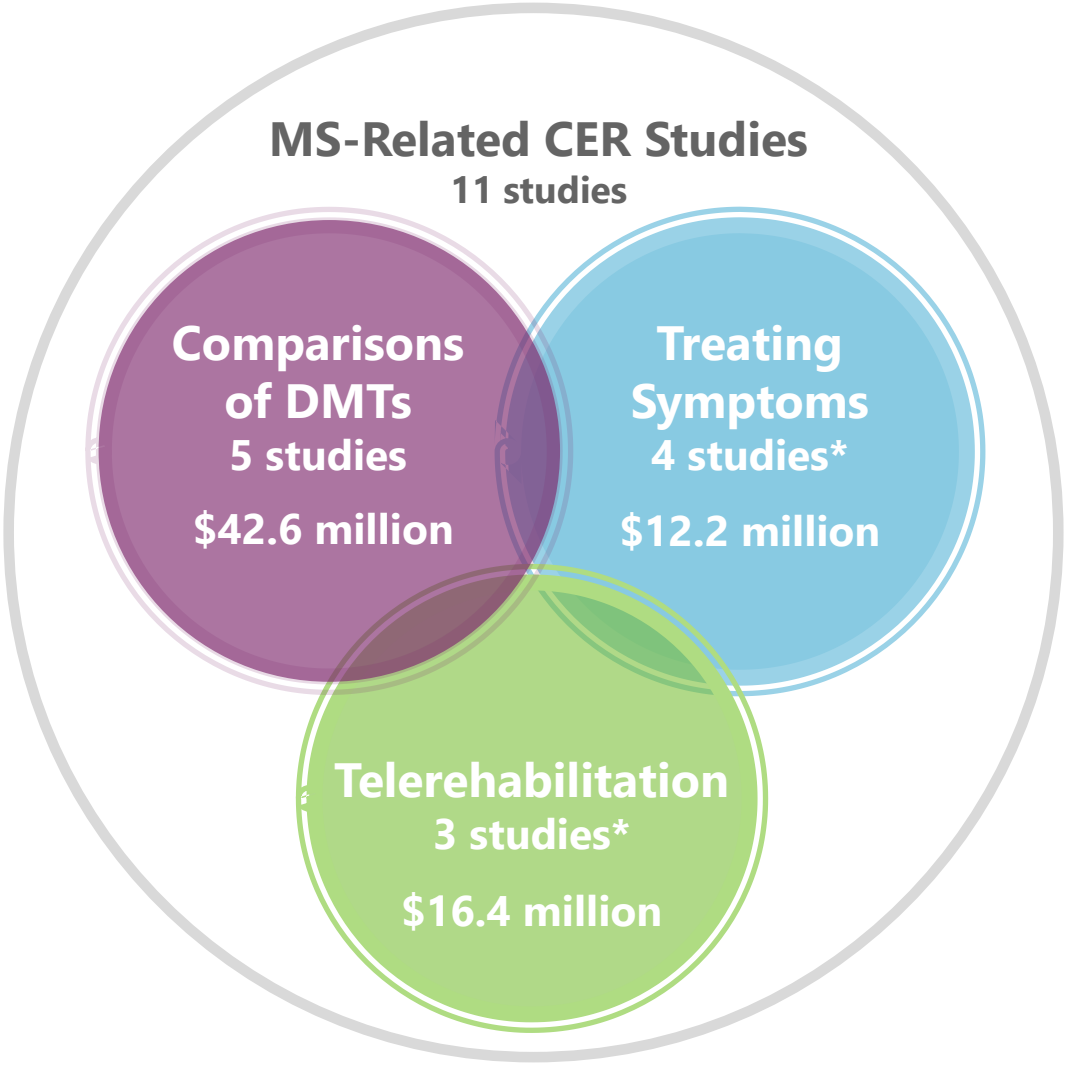
What are the **comparative benefits and harms** of different approaches, other than DMTs, **for ameliorating important symptoms** in people with MS?

Telerehabilitation

What is the **comparative effectiveness of telerehabilitation vs. conventional direct care** interventions for improving outcomes in people with MS?

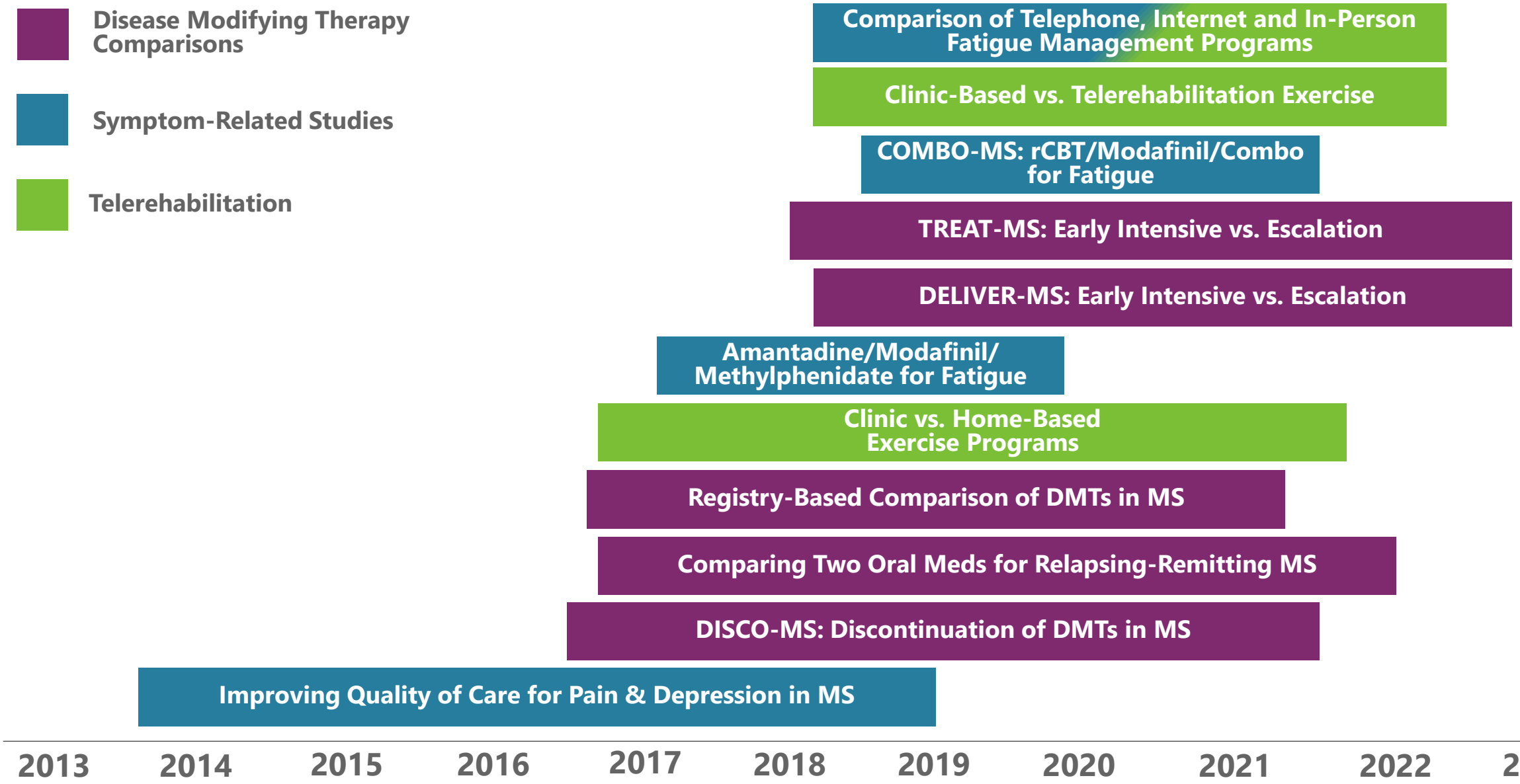
PCORI's CER Studies on MS

- Total investment of **$66.2 million**
- **10** out of **11** are RCTs
- **4** are large, multi-site trials **enrolling >500 patients**



*Categories are not mutually exclusive

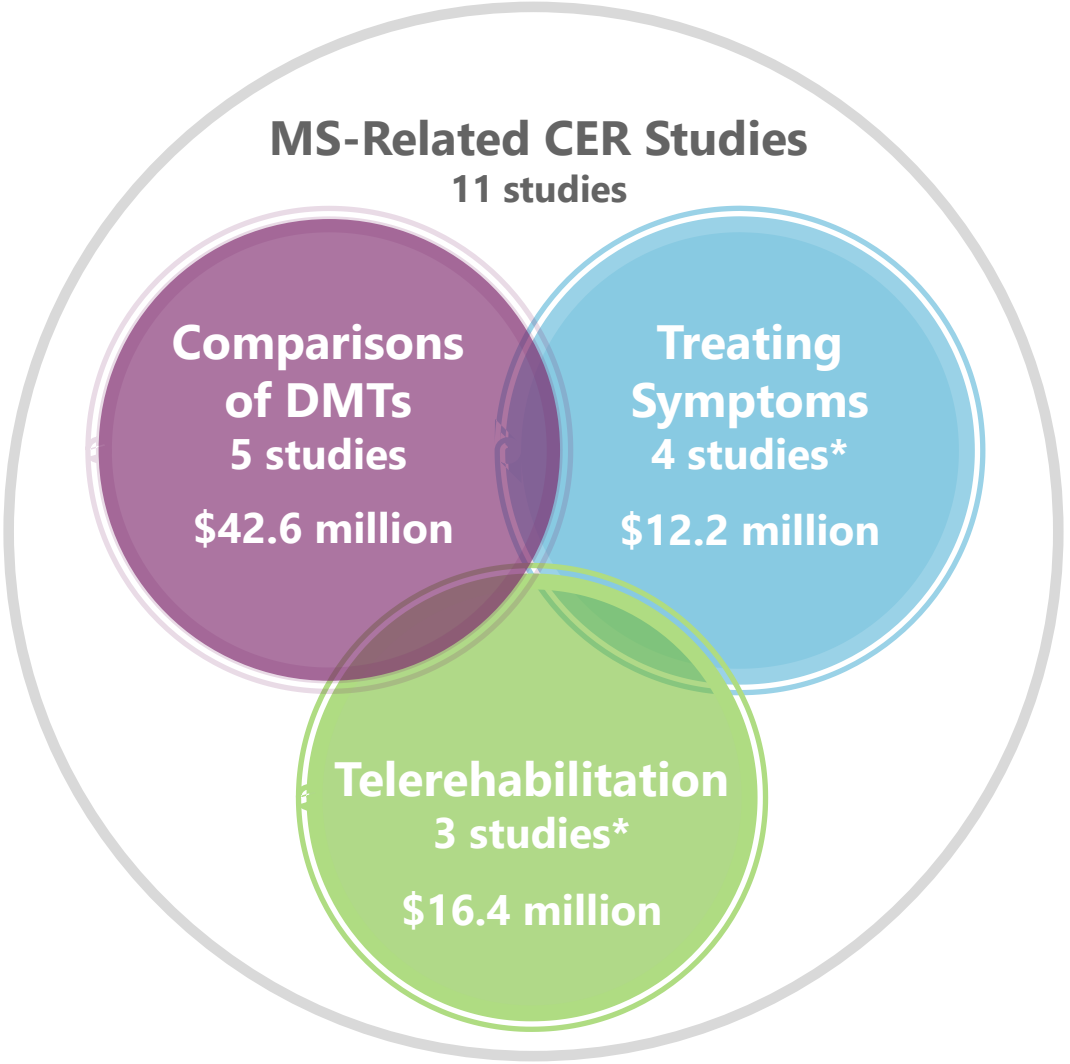
Timeline of Ongoing MS CER Studies



Focus on Patient-Centered Outcomes

- Endpoints included in PCORI studies were identified as high priority by patients, including:
  - Cognition
  - Mobility
  - Fatigue
  - Disability
  - Disease progression
- PCORI staff worked with awardees to harmonize outcomes across studies, which will facilitate joint analyses and shared dissemination

Comparisons of Disease Modifying Therapies



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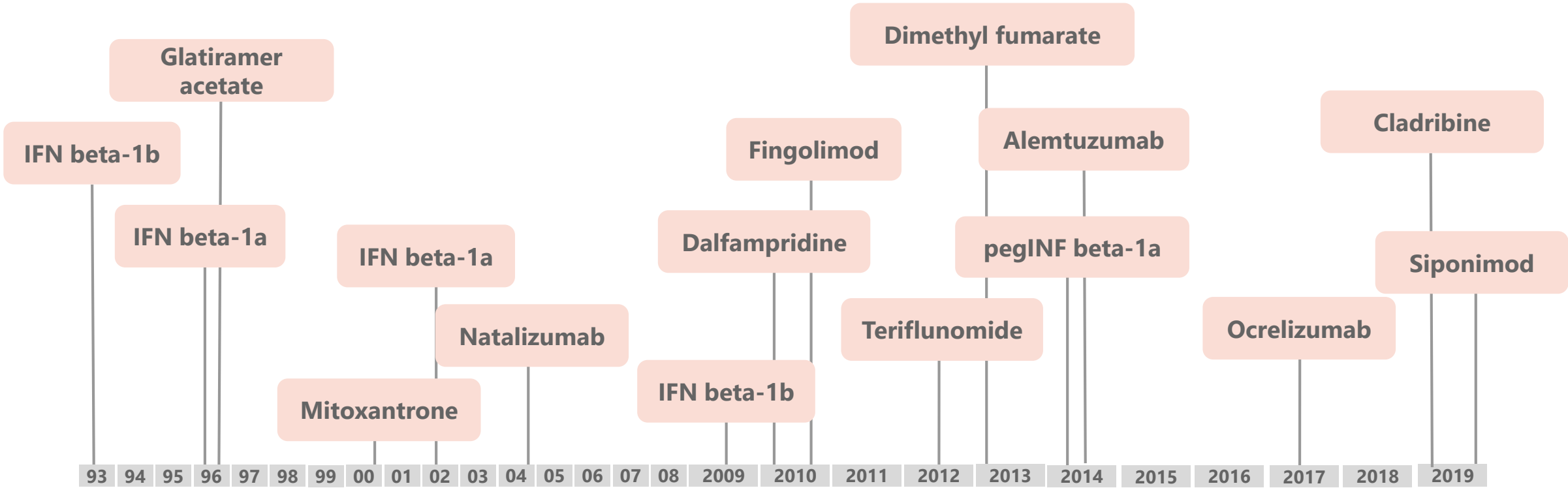
Timeline of FDA Approval of DMTs for MS Treatment

The options for, and efficacy of, disease-modifying therapies for MS have increased over the past two decades



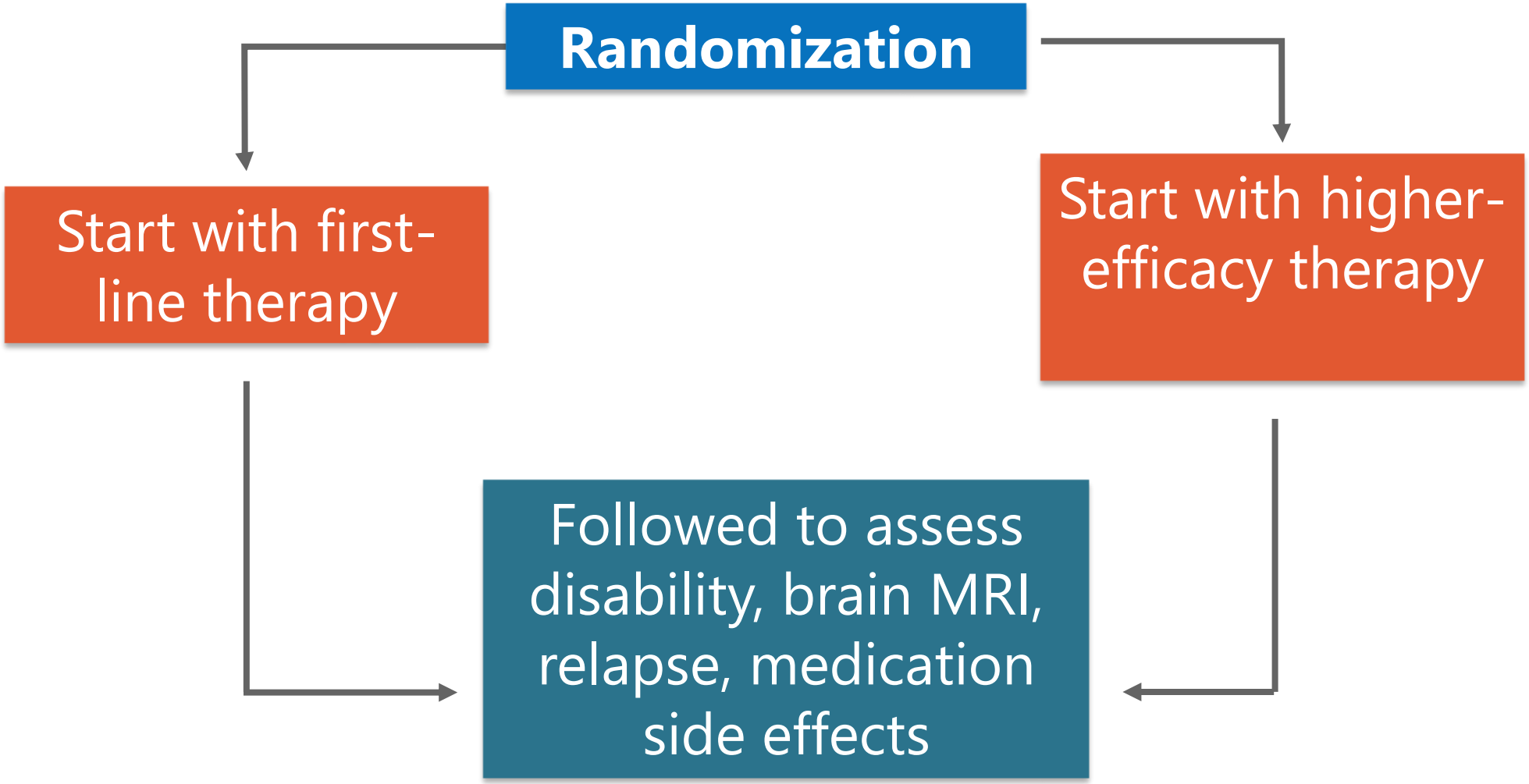
Tradeoffs Associated with the Selection of DMTs

- Mode of administration: Injectable, Oral, Transfusion
- Monitoring, vaccination, and premedication required
- Side effects/safety profile
  - Risk tolerance/preferences of individual patient
  - Contraindications
- Financial burden to patients
  - Variability of patient-facing costs across treatments
  - Mean monthly out-of-pocket drug expenses for patients with MS increased from $15 in 2004 to $309 in 2016 (Callaghan, et al, Neurology, 28 May 2019)

A Key Decisional Dilemma for Newly-Diagnosed Patients with MS

- In the early stages of MS, should patients take a **standard, first-line agent** or should they start with a **higher-efficacy medication** to reduce relapses, and prevent disease progression and disability?
- It is not known if **starting** with standard, first-line medicine and then **escalating** to other therapy as needed is better for preventing long-term MS disability than starting with aggressive medicines

Two PCORI trials addressing this key Question



Early Intensive versus Escalation Approaches in Newly Diagnosed RRMS

- Two complementary trials
  - Harmonized endpoints
    - Total brain volume
    - Disability
    - Fatigue, quality of life
- Examining heterogeneity of treatment effects (what works best for whom)
  - Demographic characteristics
  - Level of baseline disease activity
  - Risk for disability
- Strong engagement, National Multiple Sclerosis Society involvement including collection of biospecimens
- Both projected to conclude in early 2023

TREAT-MS
Ellen Mowry, MD
Scott Newsome, DO
Johns Hopkins University

DELIVER-MS
Daniel Ontaneda, MD
Nikolaos Evangelou, MD, Dphil
Cleveland Clinic Foundation

Discontinuation: Another Key DMT-related Question

April 2015

- Reviewed long-term observational studies and concluded that MS patients and providers have little information to guide decision regarding whether to discontinue DMT

STUDY PROFILE

Can People in Later Stages of MS Stop Taking Disease-Modifying Therapies? (The DISCO-MS Trial)

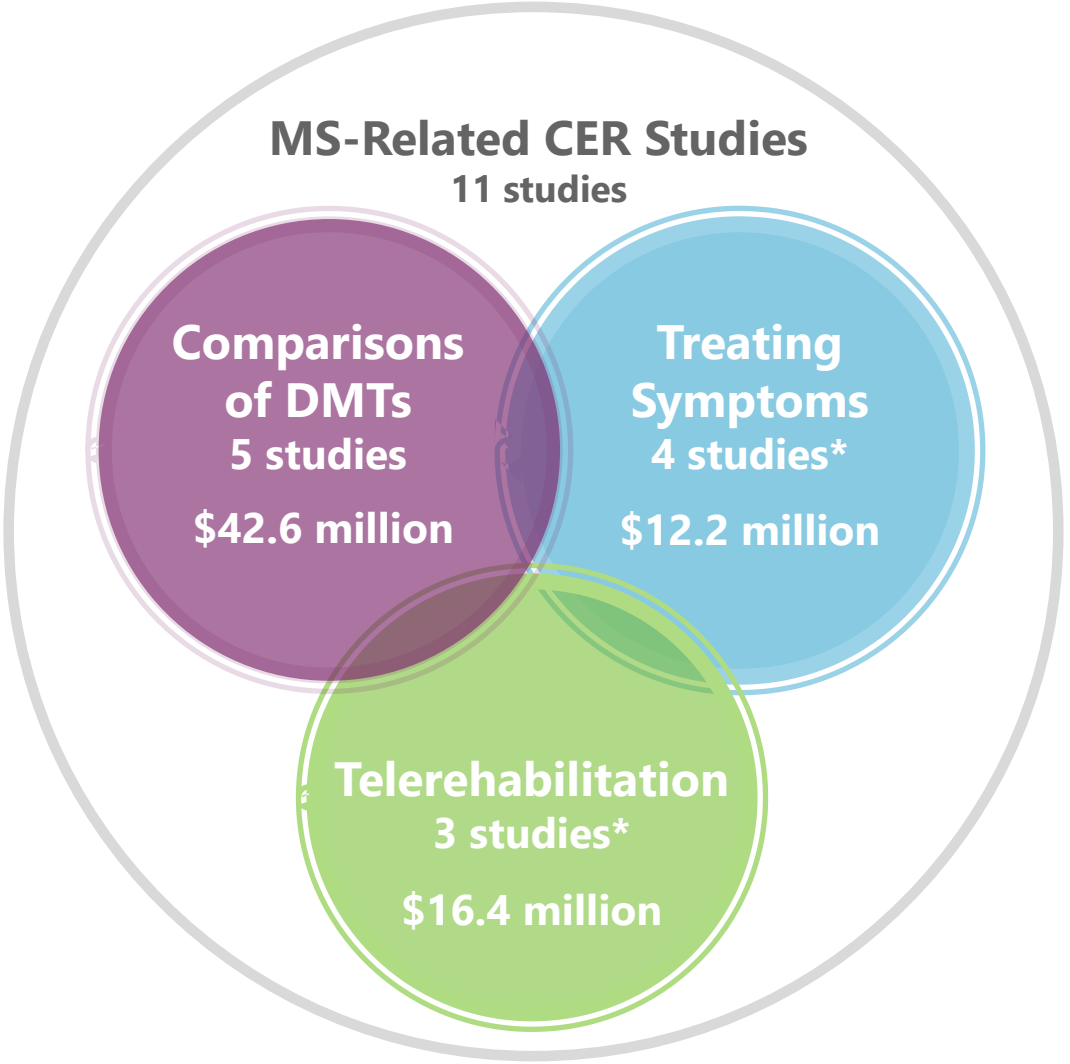
- **Patient Population:** Adults aged 55 years or older with MS who have not had a relapse for 5 years or longer or a change in brain MRI scan in 3 years or longer
- **Design:** RCT randomizing 300 patients to:
  - –Discontinue DMT
  - –Continue DMT
- **Follow-up:** 6, 12, 18, 24 months
- **Primary outcomes:** Relapse and/or new disease activity observed on brain MRI
- **Secondary outcomes:** Disability progression, quality of life, patient-reported change in disability

Potential Impact: Findings will generate much-needed information for clinicians, patients, and families members of patients with MS regarding the safety of stopping DMTs among older patients with MS who have stable disease

PI: John Corboy, MD, MA
University of Colorado Denver

Study projected to conclude: Mid-2021

Treating MS-related Symptoms



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Patient Experience of Fatigue in MS

"MS fatigue is like hitting a wall or having a door slam shut on you … My entire focus is on how tired I am and what I cannot do."

Patient Partner, PCORI-funded COMBO-MS Study

"I often tell myself, 'How can one human being be this tired and continue to live?' "

Patient with MS

"I really, really just feel fatigued. Just mentally, you're tired. Physically, you're tired. Emotionally, you're tired, and you just don't wanna do anything, and even sitting there and just being an empty vessel, you're still tired."

Patient with MS

STUDY PROFILE

Comparing Three Medicines to Treat Fatigue in Patients with MS – The TRIUMPHANT-MS Study

- **Patient Population:** People aged 18 years and older with MS and fatigue
- **Design:** Randomized, double-blinded, placebo-controlled crossover trial. 140 patients randomized to:
  - –Amantadine
  - –Modafinil
  - –Methylphenidate
  - –Placebo
- **Outcome assessment:** Week five of each six-week treatment period
- **Primary outcome:** Patient-reported fatigue severity
- **Secondary outcomes:** Quality of life, sleepiness

Potential Impact: Will provide MS-specific evidence on the comparative effectiveness of three agents commonly used to treat fatigue in patients with MS, helping patients and clinicians decide whether to treat MS-related fatigue with a drug

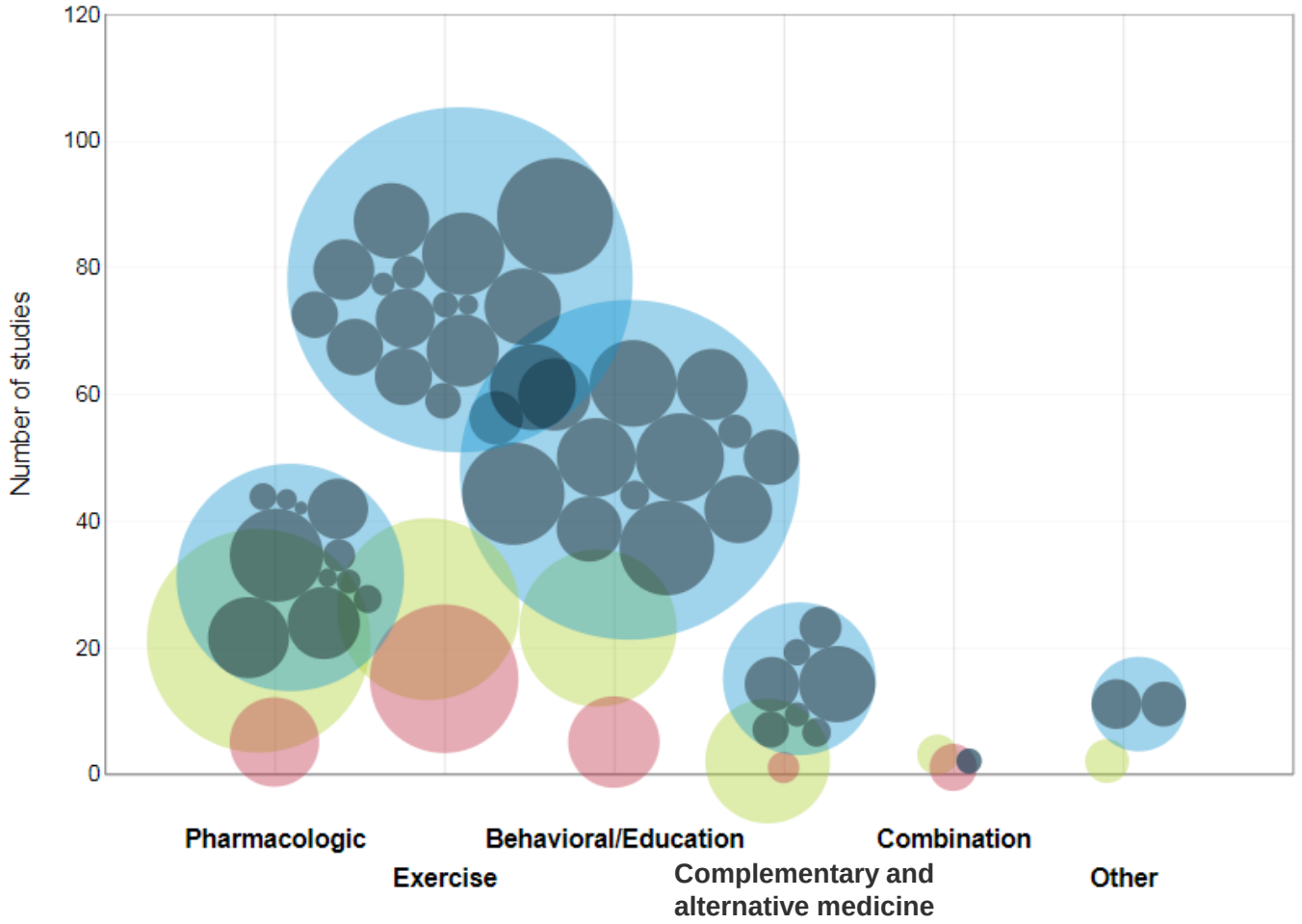
PI: Bardia Nourbakhsh, MD
Johns Hopkins University

Study projected to conclude: Early 2020

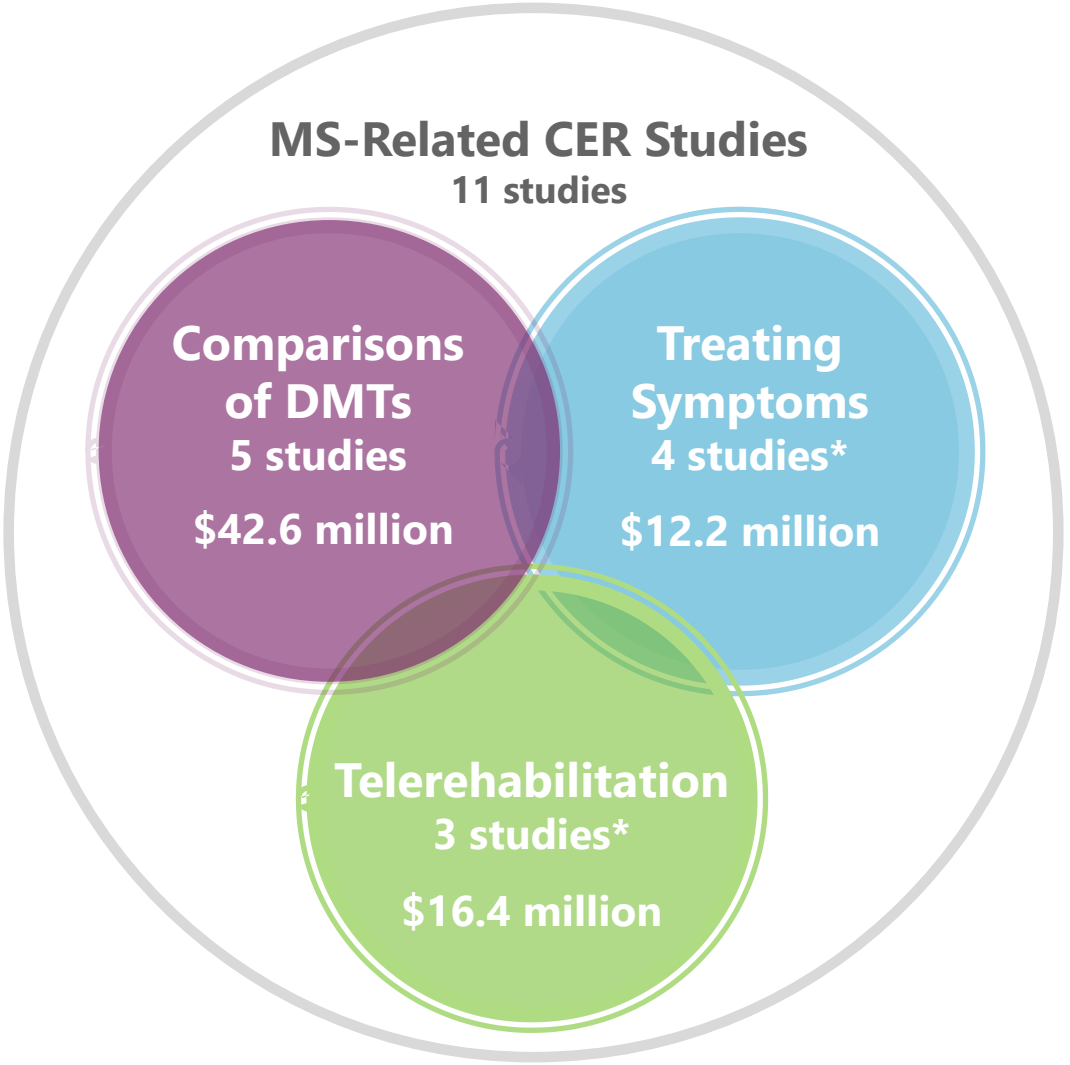
Evidence Map on Treatment of Fatigue in MS

Overview of All Study Designs for Multiple Sclerosis Fatigue Interventions

- Randomized trial
- Observational study
- Case series



Telerehabilitation



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Telerehabilitation Comparisons for Patients with MS

Expanding Reach

Increasing provider access to the expertise of specialists

Increasing Access

Making it easier for patients to get the care they need

Improving Patient-Centered Outcomes

Focusing on quality of life and other outcomes of interest to patients

STUDY PROFILE

Comparing Clinic- and Home-Based Exercise Programs to Help Adults with MS – The TEAMS Study

- **Patient Population:** People with MS aged 18-70 with mild to moderate disability and use of arms and legs for exercise
- **Design:** Cluster randomized controlled trial of 820 patients. Clinic randomized to:
  - Clinic-based rehabilitation/exercise program (DirectCAM)
  - Home-based rehabilitation/exercise program (TeleCAM)
- **Follow-up:** 3, 6, and 12 months
- **Primary outcomes:** Pain, fatigue, quality of life, physical activity
- **Secondary outcomes:** Balance, endurance, gait, strength

Potential Impact: Could reduce barriers for patients with MS to receiving exercise treatment as well as increase the convenience and appeal of such programs through the use of technology

James Rimmer, PhD, MA
University of Alabama at Birmingham

Study projected to conclude: Early 2021

Engagement in Action – The TEAMS Study Stakeholder Panel

The TEAMS Stakeholder Panel is made up of people living with MS, caregivers, and stakeholders from industry, policy, clinical practice, and advocacy organizations. Members have decision-making power.

Study Design

- Contributed to development and formation of research topic and study questions
- Actively participated in selecting and refining intervention structure
- Guided protocol development, making suggestions that resulted in improved access to study materials in the telerehabilitation arm and tailoring of exercise options to patient mobility level both study arms

Study Conduct & Dissemination

- Suggested that the study provide transportation reimbursement for testing visits to increase study participation and retention
- Stakeholders identified potential sites in Tennessee, the third state participating in the study, and facilitated the expansion of the study into the state
- Panel members to lead study dissemination activities

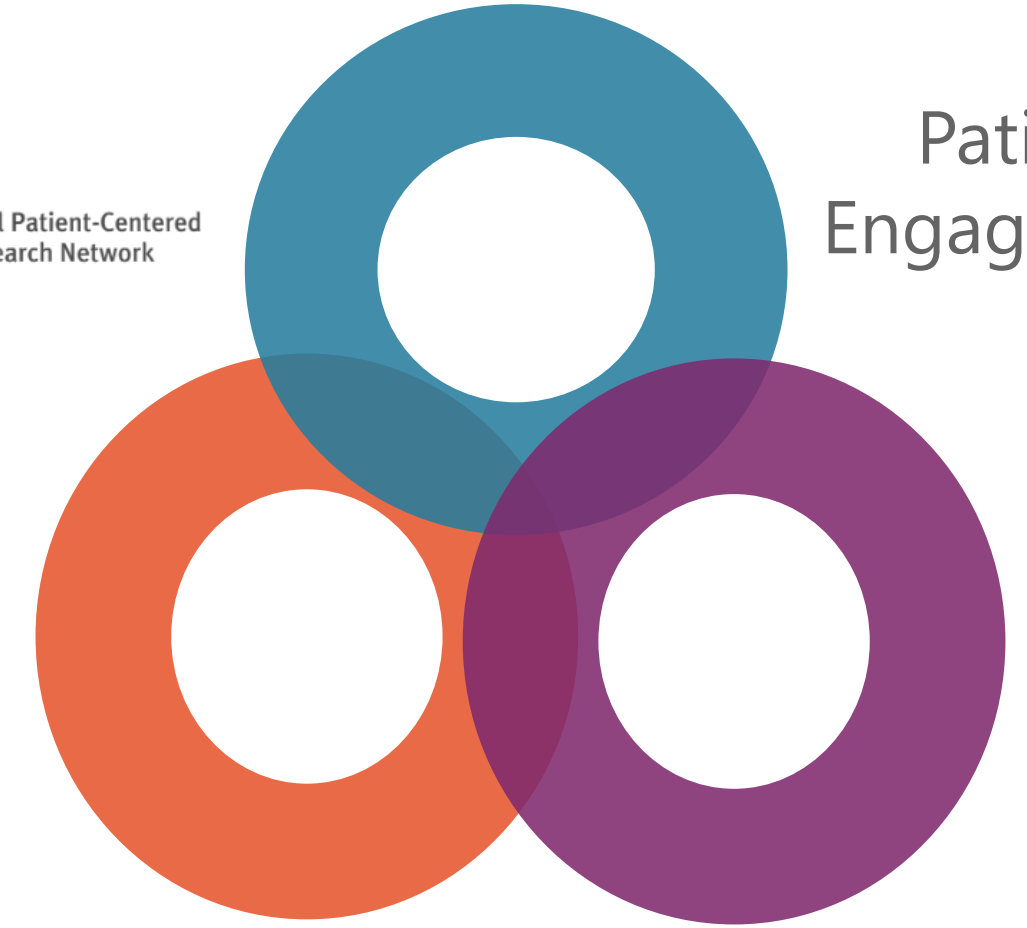
Additional Efforts to Support PCOR in MS

PCORI has supported a range of efforts to support patient-centered research

pcornet® The National Patient-Centered Clinical Research Network

iConquerMS

Infrastructure



Patient Engagement

TEAMS Tele-Exercise And Multiple Sclerosis

Research

Engagement & Infrastructure Complements to Our CER Portfolio

- PCORI has funded 5 research support projects totaling **$3.5 million**

Study Title	Funding
PCORnet PPRN The Multiple Sclerosis Patient-Powered Research Network, iConquerMS (Phase I & 2)	**$2.3 M**
Engagement Award Engaging Patients and Their Families in Patient-Centered Multiple Sclerosis Research	**$246 K**
Engagement Award The MS Minority Research Engagement Partnership Network	**$250 K**
Pipeline to Proposal Awards – Tier 1, 2, and 3 awards Developing a Patient-Led Multiple Sclerosis Research Community (Tier I, II, and III awards)	**$90 K**
Pilot Project Creating an App to Help Patients Understand and Manage Their Multiple Sclerosis	**$580 K**

ENGAGEMENT AWARD PROJECT PROFILE

The MS Minority Research Engagement Partnership Network

Objectives

- Document barriers that prevent engagement of minorities in MS research
- Implement strategies to overcome these barriers through direct outreach
- Long-term objective is to improve MS research through greater inclusion of all communities

Hollie Schmidt, MS, BS
Accelerated Cure Project

Awarded: $250,000
Project Period: Sept 2016- Aug 2018

Outcomes

- Establishment of the multi-stakeholder partnership
- Report on barriers affecting minority engagement in MS research and needs to be addressed
- Outreach materials and messages
- Metrics regarding effectiveness of the methods
- Dissemination of the project's results and materials

iConquerMS ™ Patient-Powered Research Network

pcornet® The National Patient-Centered Clinical Research Network

- iConquer MS is a PPRN comprised of people affected by MS. Led by the Accelerated Cure Project for MS, the network connects people with MS, advocates, caregivers, clinicians, and researchers to encourage and conduct research that reflects the priorities and concerns of people with MS
- Accomplishments
  - Enrolled nearly 5,000 members who contributed data, prioritized research goals, and participated in clinical studies
  - Established leadership and governance structure led by MS patients
  - Developed and launched a multi-faceted web-based platform to collect data and support the engagement of people affected by MS in research
  - Participated in 10 research studies funded by PCORI, NIH, and industry

What's Next?
Future Directions for MS Research at PCORI

- The PCORI research portfolio in MS is in its early stages, with key results expected in the coming years, which we will bring to your attention
- Given the number of DMTs available and being introduced, other emerging treatments, and the multiplicity of symptoms and needs experienced by MS patients, the need for CER will continue
- Staff continue to monitor developments in the field through efforts including our horizon scanning work, and will continue to work with the research and stakeholder communities to identify important gaps

Questions?

Wrap Up and Adjournment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