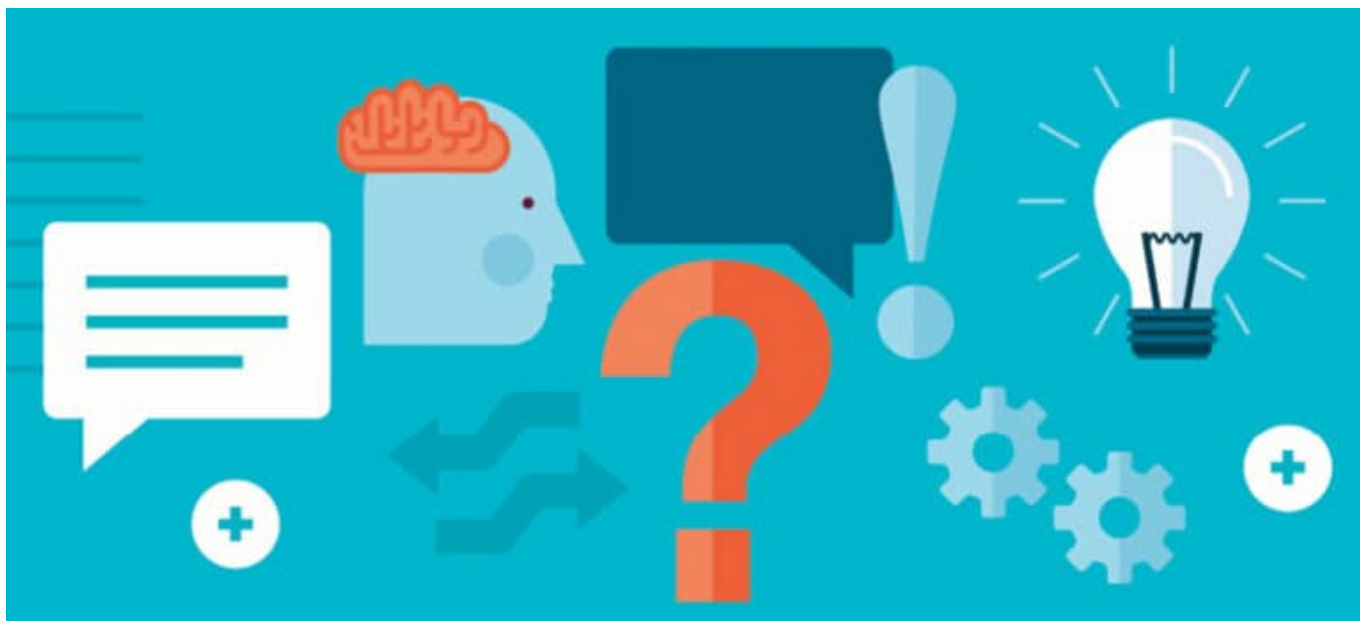


Pressing questions



People with MS can help guide research addressing the disease.

by **Mary E. King, PhD**

People who face the daily realities of multiple sclerosis and their doctors have practical questions about day-to-day issues, such as the best treatment approach, dealing with fatigue or the side effects of medications. But each person's concerns may not be addressed by traditional research. Fortunately, people with real-life experience now can help guide the thinking behind the design, implementation and funding of certain MS studies.

The Patient-Centered Outcomes Research Institute (PCORI) is an independent nonprofit organization authorized by Congress in 2010 to fund research to answer practical, patient-focused questions.

New research projects

PCORI announced five new MS research awards totaling \$38 million in September 2017. These projects address issues that people with MS, clinicians, researchers and other health care stakeholders have identified as priorities. Topics include managing fatigue, comparing outcomes of more aggressive versus less aggressive treatment in newly diagnosed relapsing-remitting MS, and using exercise to improve mobility.

Of the new grantees, three were National Multiple Sclerosis Society Sylvia Lawry Physician Fellows who received training in how to conduct clinical research in MS: **Ellen M. Mowry,**

MD, Johns Hopkins University; **Tiffany Braley, MD**, University of Michigan; and **Daniel Ontaneda, MD**, Cleveland Clinic Foundation.

One was trained through the Society's Mentor-Based Postdoctoral Rehabilitation Fellowship program: **Matthew Plow, PhD**, Case Western Reserve University.

The fifth grantee is **Deborah Backus, PhD**, Shepherd Center. With these awards, PCORI has now invested \$64 million to fund 12 comparative clinical effectiveness studies in MS.

Called comparative clinical effectiveness research (CER), the studies PCORI sponsors compare current health care options to help patients and doctors choose the right ones. PCORI funds studies in a number of conditions, including cardiovascular and kidney diseases, cancer, dementia, and pain care, and the organization is already making a real difference for MS research working in collaboration with the National Multiple Sclerosis Society.

"We focus on patient-centered outcomes—it's even in our name," emphasizes Diane E. Bild, MD, associate director in the Clinical Effectiveness and Decision Science Program at PCORI. "For example, how do different treatments for a condition such as MS affect quality of life? While other research funding organizations may emphasize basic science questions, such as identifying a new biochemical marker for a disease, we look at the impact on patients.

"Our focus is not on identifying new therapies, since others are doing that, but rather on gathering the information that will enable clinicians and individuals with a disease to choose the optimal approach from among the many options available," Dr. Bild adds. "In MS, for example, there are many different disease-modifying therapies [DMTs], but it is not always clear which ones will have the best ratio of benefits to harms for a specific individual."

Dr. Bild also stressed that PCORI involves a variety of stakeholders in MS research—individuals with the disease, family members, caregivers and organizations like the Society that represent them—to identify the most pressing MS questions to fund. PCORI also seeks input from those with professional experience with MS and influence on decisions that affect patients, such as clinicians, researchers, the pharmaceutical industry, hospitals and insurers.

Three questions specific to MS are among the subjects of PCORI-funded research that exemplify its mission to increase timely, useful, trustworthy information to support health decisions: Can an older person with MS stop taking the DMT without experiencing disease activity? What is the best way to treat pain and pain-related depression? How can more minorities participate in MS research?

1. Can I ever discontinue my treatment?

"We are looking at a big picture question. While we may know an individual will likely benefit from a given therapy, we really don't yet know how long the treatment must continue. Could some individuals stop a DMT for MS at some point?" asks John Corboy, MD, professor of

neurology and co-director of the Rocky Mountain MS Center at the University of Colorado Hospital Anschutz Medical Campus in Aurora, Colorado.

“To begin to answer this, we are looking at individuals with MS who are 55 and older, but only at those who have had no relapses or brain magnetic resonance imaging [MRI] changes for at least five years while continuously taking DMTs,” Dr. Corboy explains. “We will randomly assign half of the participants to continue their current treatment and the other half to discontinue it. We will monitor all of the participants closely, including identifying any relapses, new MRI lesions, disability progression and quality-of-life issues.”

He also emphasized that it will always be up to the patient and his or her physician to decide whether to maintain or change treatment during the study.

“We want to learn whether the older individual with MS is really still deriving benefit from DMT [if they are not having] relapses or changes to brain MRI scans,” says Dr. Corboy. “While published studies show that DMTs are clearly beneficial for younger patients with MS, we don’t know if that is true for older patients, who tend to have less frequent and less severe relapses as they age or even stop having relapses. It may be safe to discontinue these medicines. We may learn they will do no worse than their peers [in the study] who continue on medication, or we could learn that the disease still recurs and continued DMT is needed.”

The trial, funded in part by the Society, is underway but still enrolling additional participants at 15 clinical sites. The enrollment goal is 300 individuals with MS who meet all enrollment criteria. Dr. Corboy hopes to have results available as early as 2020.

2. Better care for pain and depression?

“People with MS don’t always have access to pain and depression care,” explains Dawn M. Ehde, PhD, clinical psychologist and professor of rehabilitation medicine at the University of Washington Harborview Medical Center in Seattle. “It is a complex disease, so the primary focus is on disease modification, as it should be. But these individuals often have difficulty getting additional care for pain and/or depression.

And added to that, they may have problems physically getting to a site that offers this support.”

PCORI funding allowed Ehde and colleagues to create and study the impact of a novel approach to care delivery. Their program featured a special care manager, a nurse supervised by physicians, psychiatrists and psychologists who helped coordinate and provide high-quality, evidence-based treatments for depression and pain. To help those who had difficulty visiting the medical center, the study added the option to provide care by phone or in person, based on the participant’s preferences.

“Our study has wrapped up, and we are now analyzing the data and writing up the results for publication,” Ehde says. “This approach significantly improved pain and depressive

symptoms. Our preliminary numbers indicate that 57 percent of those in our program had good pain and depression control, compared with less than a third of those in usual care. Participants also described less pain severity, disability and fatigue, and greater satisfaction with pain and depression care.” They also found a very high rate of adherence to this program, she added.

Ehde also stresses that people with MS truly partnered with the research team, including helping them figure out the optimal study design.

3. How can more minorities participate in MS research?

“The number of minority participants in MS clinical trials is quite low,” says Hollie Schmidt, vice president of scientific operations for the Accelerated Cure Project for Multiple Sclerosis (ACP), a national nonprofit organization in Waltham, Massachusetts. Founded by a person with MS, the organization focuses on meeting the research needs and interests of people with MS. “We know this is true for other diseases as well, and that barriers include mistrust of the scientific establishment as well as logistical and practical considerations,” Schmidt says.

The first step in the PCORI-funded project, which has now completed its first year, was to gather more information. “We needed MS-specific data about what motivates people of different racial and ethnic groups to participate in research as well as factors that discourage participation,” Schmidt explains. Researchers also wanted to know where these individuals would go for trusted information about research if they do want to participate in a study.

ACP, working collaboratively with individuals with MS and other stakeholders, created and disseminated an online survey via email and social media for people with MS to explore these issues. Schmidt says the response was excellent, with more than 2,600 replies that included many different racial and ethnic groups. Most of the responses came from the United States, but investigators received some international feedback, too. The research is being analyzed and will soon be summarized in two ways, both as a scientific report and as a lay language report that will be posted on the ACP website, Schmidt says.

The next step will be to take what the researchers have learned from the survey and apply it to outreach efforts to minority communities. Schmidt explains that they will use the survey suggestions about where to post information, for example, social media, magazines and online, to link individuals with MS to clinical trials. “We will also reach out to researchers who wish to increase minority participation, to clinicians and to interested organizations to provide them with toolkits to help them improve outreach efforts to minorities,” she says.

Schmidt summarizes the importance of the work in this way: “If your ethnic or racial group is not included in a clinical trial, say for a new drug, as often happens for minorities, then anyone who looks at the data from that research won’t be able to tell if your group will or will not benefit as much. We are moving toward personalized medicine, including for MS, but we are still far from this goal. This research will help us move toward this important objective.”

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