Accelerated Cure Project for MS

April 2019

Accelerating research towards a cure for multiple sclerosis

PCORI – Enabling Patient-Centered MS Research

People living with MS are often faced with choices in the course of their disease, for example medication or therapy changes. To make the best decision, they must have access to reliable information about the potential benefits and harms of each choice. This information isn't always available. When it is available, it is often hard to understand. The Patient-Centered Outcomes Research Institute (PCORI) is an independent, nonprofit organization in Washington, D.C. that aims to fill in these information gaps. PCORI funds research that provides patients and caregivers the information they need to make important healthcare decisions. iConquerMS is an ACP initiative, funded by PCORI at its outset, created to (among other things) gather data about the effectiveness of different MS treatment strategies, the disease course, its symptoms and how all of these things affect the quality of life of those living with the disease. The first-hand experience of people with MS can help inform the decisions of others living with the disease. PCORI has funded a number of other MS studies that may also have tremendous impact on quality of care.

According to the National MS Society, 80% of people with MS experience fatigue, and over half rank it as one of their most troubling symptoms. Our March 2019 newsletter covered the complexity of MS fatigue, including several treatment options and management strategies. PCORI provided support for three studies looking at different ways to help those struggling with fatigue. The information gained from these clinical trials will fill important gaps in the current knowledge about the treatment of MS fatigue and provide useful information to help people with MS and their caregivers make better-informed decisions in their care options.

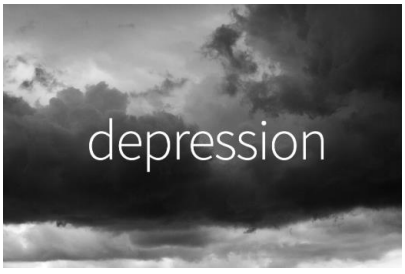
Fatigue Studies

Researchers at the University of Michigan are comparing a widely accepted behavioral treatment strategy for fatigue, cognitive behavioral therapy (CBT), and a commonly used fatigue medication, Modafinil. The research team is recruiting subjects in southeastern Michigan and Seattle, Washington who experience fatigue from MS. Participants are assigned to one of three treatment groups by chance (CBT by phone with a therapist, modafinil, or a combination of both), and receive treatment for 12 weeks. The research team is comparing subjects' levels of fatigue, how well they follow their treatment plan, and any side effects. The team is also comparing how well the therapies work for people with MS who have other conditions, such as depression or difficulty sleeping. This study is currently recruiting, with an enrollment goal of 330 subjects. Interested in helping these researchers to reach their goal? Please contact the study team directly for details.

Investigators at Case Western Reserve University are evaluating three non-drug therapies that can ease fatigue and enable individuals with MS to become more active. In many cases, barriers exist to attending a fatigue management course in person, which led the team to investigate more remote ways to administer therapy. This trial evaluates three methods of administering a fatigue management course in different groups of people: by phone, online, and in person. The research team is comparing how the three formats affect fatigue and quality of life for people with MS. Researchers are looking for participants, and hope to enroll 610 adults with MS from community organizations and outpatient clinics. Subjects are assigned, by chance, to receive a seven-week course via one of the three methods. Want more information? Ask the study team!

To date, there are no FDA-approved drugs to treat fatigue in people with MS. Three commonly used medications for MS fatigue, amantadine, modafinil, and methylphenidate, are approved to treat other health problems. Little research has been done on these mediations. To address this, researchers at Johns Hopkins University are conducting the TRIUMPHANT-MS Study. This clinical trial is evaluating whether these three medications lessen fatigue in people with MS, and if one is more effective than the other in certain groups of patients (for example, those with progressive or relapsing-remitting forms of MS and those with higher or lower levels of disability). Results of this study will provide evidence-based, personalized treatment options for people affected by MS-related fatigue. The TRIUMPHANT-MS study is active, but not enrolling new subjects at this time.

Depression and chronic pain are also common symptoms in people with MS. They frequently co-occur and negatively impact an individual's daily life, as well as their relationships. Those interested in learning more about MS-related depression may find the accompanying article in this newsletter entitled "Shedding Light on the Dark Days of MS" an interesting read. Two recent studies have received funding from



PCORI to help address these burdensome symptoms.

Depression and Pain Studies

Researchers at the University of Washington conducted the MS-Care Trial, which evaluated the effectiveness of a collaborative care approach in treating depression and pain. In a collaborative care approach, a care manager helps coordinate therapy and provides strategies for better managing these symptoms. The study team enrolled 195 subjects with MS, half of which received collaborative care for 16 weeks. The other half received usual care in an outpatient MS specialty center for the same time period. The objective of this research was to test whether collaborative care improves quality of life, patient satisfaction, adherence to other treatments and quality of care. Investigators anticipate that those in the collaborative care approach will have better-controlled pain and depression compared to those in the usual care approach. Publication of these results is pending.

With PCORI's support, another research team at the University of Washington developed and tested new instruments to evaluate chronic pain and its effects. Investigators created long and short versions of two sets of questions, called item banks, to assess pain and pain-related self-efficacy (how confident a person is that they can live well with pain). The team tested these instruments in a large group of subjects living with different types of pain from MS. Testing showed that subjects understood the questions and they accurately measured pain and pain-related self-efficacy. Results also showed shorter versions provided similar information to the full versions. In the future, researchers can use these item banks in studies about treating and managing chronic pain and clinicians can use them to help patients better manage pain.

PCORI has also played an instrumental role in the development of new technology to help people with MS understand and manage the disease. They funded a study at the University of California, San Francisco that created and tested an app, called MS Bioscreen. MS Bioscreen is a platform that gathers and stores an individual's MS data, including clinical, imaging and biomarker information, and allows them to compare their information against a database of more than 2,500 people with MS and predict how their disease might change over time. A pilot study of this new technology showed physicians found it useful to see each individual's information in a single place, and having the information helped them teach patients about MS. Both patients and clinicians found the app helped them talk about treatment decisions. The research team recently published their results, and plans to do further testing in patients at the UCSF Multiple Sclerosis Center.

In addition to being essential to general health and wellbeing, exercise is helpful in managing many MS symptoms. However, some people with MS may not be able to get to a gym or may not have access to exercise equipment. PCORI is sponsoring two studies currently looking at different ways to provide access to

exercise therapy to those who cannot make it to a gym. The knowledge gained from this research will provide people living with MS information to guide their choice of exercise options.

Exercise Studies

Researchers at the Shepherd Center are conducting the STEP for MS study (Supervised versus Telerehab Exercise Program for People with Multiple Sclerosis) to see if an at-home exercise program can help improve mobility and quality of life for people with MS. The team is comparing a home-based exercise program to one that takes place in a facility like a gym. A trained instructor teaches participants how to exercise and provides encouragement throughout the program, regardless of where they exercise. The iConquerMS portal is being used for data collection, and to communicate with participants. In addition, the team is looking at whether people have better mobility and quality of life when they get to choose where they exercise, compared with when the research team assigns them by chance to exercise at home or in a facility. The research team hopes to enroll 500 subjects across seven sites in the United States. Interested in joining the study? Contact information for each site, as well as criteria for participation, can be found on the STEP for MS website.

The TEAMS Study (Tele-Exercise and Multiple Sclerosis) at the University of Alabama Birmingham is also studying alternate ways to provide exercise services to those that cannot make it to a gym. This study evaluates the benefits people with MS get from an exercise rehabilitation program delivered over the Internet or telephone, as compared to the same exercise program in a clinic. Researchers are also measuring whether the home-based and clinic-based exercise programs work differently for patients of different ages and levels of disability. This study is currently recruiting subjects in Alabama, Mississippi and Tennessee, with an enrollment goal of 820 participants. Anyone interested in participating should email study staff for more information at teamsstudy@uab.edu.

Well over a dozen medications are used in MS to modify the disease course, treat relapses and manage symptoms, none of which are one hundred percent effective. PCORI is providing support for a number of studies investigating better ways to treat MS.

MS Treatment Studies

Gilenya and Tecfidera are two oral medications used to treat relapsing remitting MS (RRMS). Researchers and clinicians don't know how these two medications compare at preventing relapses, brain damage, and long-term disability and improving quality of life. With PCORI's support, Italian researchers are examining the benefits and risks of these two medications from the patient's point of view. The results of this study will help people with MS and their healthcare providers decide which oral medication to use for RRMS. Recruitment for this study is ongoing in the United States, Israel and Europe. For details, please contact the study team.

There are two different approaches to treating RRMS, **escalation** and **early treatment** with highly effective medicine. Escalation starts with a medication thought to be safe, but not one hundred percent effective (it may not prevent all relapses or new brain lesions). Physicians prescribe stronger medications should relapses or new lesions occur. Early treatment with highly effective medicine starts with one of the strong medications. Researchers and clinicians don't know which approach is most beneficial to people with MS in the long run. The DELIVER-MS Study is ongoing at the Cleveland Clinic Foundation to determine whether starting treatment with a highly effective disease modifying therapy improves the prognosis (delays worsening of the disease) for people with MS. The team is also examining whether one approach is safer and easier for patients. The results of this study will help physicians know how aggressively to treat people newly diagnosed with RRMS. The DELIVER-MS study team is working with treatment centers in the United States and the United Kingdom to recruit 800 subjects with RRMS who have not yet had treatment for the disease. Subjects will receive either escalation or early highly effective treatment. Those interested in participating can find the contact information for participating sites here.

Most people who are diagnosed with RRMS will eventually transition to a secondary progressive course (SPMS) in which there is typically a progressive worsening of neurologic function (accumulation of disability) over time. Doctors don't know whether early aggressive MS therapy versus a less aggressive approach is better for preventing long-term MS disability. In addition, it is unclear when people with RRMS experiencing flares should switch therapies and, if they do switch, whether they should consider a different first-line therapy or escalate immediately to a stronger therapy. The TREAT-MS Study, at Johns Hopkins University, is examining which of these treatment choices would benefit people with MS most, that is, which can prevent, delay or reduce disability in people with MS. This study will lead to a better understanding of the risks and benefits of using stronger medications to prevent or delay disability in MS, and also help identify if there is a specific patient population or biomarker(s) that may predict long-term disability. Investigators are looking for a total of 900 subjects with MS at approximately 45 sites across the United States, half will receive standard medications, and half will receive more aggressive medications. Anyone interested in more information should email the research team at Johns Hopkins University.

Previous studies have shown that rituximab, a drug approved to treat some cancers and other diseases, is also effective in treating RRMS. However, it is not FDA-approved for the treatment of MS. Physicians and researchers don't know how the safety and efficacy of rituximab and other disease modifying therapies (DMTs) compare over a long period of time (many years), or if these medications work differently in people who are newly diagnosed versus those with more advanced MS. With PCORI's support, the COMBAT-MS study will shed light on these questions. The research team is studying information from a Swedish database of people with MS and expects to include information from about 3,700 subjects by the end of the study. The primary goal of this research is to determine whether rituximab is more effective, and safer, than other commonly used DMTs. Investigators are also looking at how well DMTs prevent MS symptoms and maintain quality of life, as well as whether safety issues like dangerous side effects cause patients to stop taking them. This research can help guide decisions regarding

the best medications to try first when treating RRMS, as well as treatment choices in cases where a medication proves ineffective.

Research suggests that the number of new MS lesions in people living with the disease decreases over time. Researchers at the University of Colorado, Denver are conducting the DISCO-MS trial to determine whether people with MS who have had no relapses or changes on brain MRIs for five years can stop taking DMTs without disease progression. The study team is also looking at whether there is a difference in symptom progression and quality of life in subjects who keep taking DMTs compared with those who stop them. Findings from this study can help older people with MS and their physicians decide whether to stop treatment with DMTs. This study is actively enrolling subjects. The research team hopes to recruit 300 subjects with MS, ages 55 and older, from 15 MS centers across the country. Anyone interested in participating can click here for contact information at participating sites.

According to Marston Bates, "Research is the process of going up alleys to see if they are blind." PCORI's mission is to enable research that is informed by the people who are most affected by the results – patients, caregivers and others in the broader healthcare community. These stakeholders are involved in the design and conduct of all PCORI-funded studies. The high-quality, evidence-based information generated from their MS studies will help people living with the disease make informed healthcare decisions, improve their quality of care, and health outcomes.