According to Oprah Winfrey, “On the road of life, you can’t get off the exit ramp without some bumps and roadblocks – and a few detours.” For many, the ups and downs of living with MS abound – making sacrifices, negotiating unforeseen challenges, accepting new realities, to name a few. This emotional rollercoaster takes a toll, causing some to feel discouraged or depressed. In fact, studies show approximately half of people with MS struggle with depression, which often has a ripple effect in their lives. Such feelings of unhappiness can affect how an individual thinks and feels, how they relate to other people, as well as their ability to participate in daily activities. While depression is common in people with MS, it is not universal and shouldn’t be considered normal or expected. It is one of the most treatable of all MS symptoms, and there are a number of strategies that can help an individual cope with such feelings. Our first article sheds light on the dark days of MS.

The practice of mindfulness has become increasingly popular in recent years. This philosophy is most commonly defined as “paying attention in a particular way: on purpose, in the present moment and non-judgmentally.” This can be achieved through meditation or simply by observing one’s surroundings without opinion. Those practicing mindfulness learn to think about their thoughts and emotions as passing events, rather than attributing importance to them. There is ample scientific evidence supporting the widespread benefits of this mental discipline, including for those living with MS. Learn more about putting your mind over MS and how this practice may benefit you.

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 and when it is, 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 aimed at providing patients and caregivers the information they need to make important healthcare decisions. This organization’s support enabled ACP to launch the iConquerMS initiative in 2015. PCORI has funded a number of other MS studies that may also have tremendous impact on quality of care, many of which are currently underway and looking for participants. For
details, read more about the groundbreaking MS research, made possible by this patient-focused organization.

ACP is dedicated to facilitating research to improve diagnosis, to optimize treatment and to cure MS. Real-life patient data plays a pivotal role in our work. Our Repository Spotlight focuses on ACP’s strategies for collecting, growing and curating this vital information, including exciting plans for the future!

Our iConquerMS Spotlight describes the MS Minority Research Engagement Partnership Network, which was featured on the PCORI website earlier this month. The Network is one of the many ways the ACP/iConquerMS team is working to improve the health and quality of life of people living with MS.

We hope you enjoy this newsletter and encourage you to share it with anyone you think may be interested in learning more about ACP.

Jan and Lindsey, on behalf of the Accelerated Cure Project Team

**Shedding Light on the Dark Days of MS**

According to the Canadian poet, Atticus, “Depression is being colorblind and constantly told how colorful the world is.” Depression is one of the most common symptoms of MS. Studies show approximately half of people with MS struggle with this condition. Depression can affect how an individual thinks and feels, as well as their ability to participate in daily activities. It can occur in any person with MS at any point in the course of the disease. When depression occurs, it requires the same careful assessment and treatment as any other symptom of MS. Left untreated, depression has the potential to reduce quality of life, make other MS symptoms, such as fatigue, pain, or cognitive changes, feel worse, and may be life threatening.

There are several different types of depression. Major depression is an overall state of sadness and loss of interest in activities, even ones that are usually enjoyable. The Diagnostic and Statistical Manual of Mental Disorders (DSM) is the reference used by physicians to diagnose mental disorders, like depression. According to the DSM, individuals with major depression experience at least five of the following symptoms in a two-week period: 1) Sadness or depressed mood; 2) Lack of pleasure or interest in activities; 3) Trouble sleeping, or sleeping all the time; 4) Fatigue or lack of energy; 5) Feelings of worthlessness or guilt; 6) Lack of concentration or focus; 7) Changes in appetite; 8) Agitation, or moving in slow motion; or, 9) Recurrent thoughts of death or suicide. It’s important to note that the symptoms of depression are complex and can vary widely from person to person. Several are also symptoms of MS, such as fatigue, insomnia and cognitive difficulties. These similarities make diagnosing depression challenging in people with MS. A trained health professional who is familiar with both conditions is needed to make an accurate diagnosis of depression for an individual with MS.
Persistent depressive disorder (also called dysthymia) shares many symptoms with major depression, however the symptoms are more insidious and tend to be less severe. These symptoms are typically present for at least two years, rather than two weeks. This form of depression tends to slowly become a part of everyday life and may eventually be perceived as a person’s normal, unhappy mood. Bipolar disorder (sometimes referred to as manic-depressive disorder) is characterized by extreme mood swings. Individuals with this type of depression experience episodes of low spirits, but they also go through periods of unusually high energy or activity. Manic symptoms (for example, unrealistically high self-esteem or a decreased need for sleep) are typically short-lived and followed by a period of depression. In some cases of bipolar disorder, the depressive phase can lead to self-destructive behavior. Seasonal affective disorder is a type of depression that is related to the change in seasons. It usually occurs in the fall and winter, when days are shorter.

Two types of depression are influenced by reproductive hormones and may occur in women. Perinatal depression occurs during pregnancy or within one year after birth (also known as postpartum depression). This type of depression may include both major and minor depressive episodes. While it is most common in women, postpartum depression can also occur in men after the birth of a child. Premenstrual dysphoric disorder (PMDD) is a severe form of premenstrual syndrome. PMDD typically causes extreme, disruptive mood swings. These symptoms usually begin shortly after ovulation and end once menstruation starts.

While depression can potentially occur in any person with MS at any point in the course of the disease, a number of factors increase its likelihood. Chronic illness in and of itself is a known risk factor for depression. Depression is nearly twice as likely to occur in women than men. For some, difficult life situations or stresses may lead to discouragement or despair. People living with MS may experience such emotions following diagnosis, or during an exacerbation. Those with a susceptibility to depression prior to their MS diagnosis may be at an even higher risk afterward. Factors such as a lack of support, and drug dependence may also contribute to the onset of depression. As mentioned in our March 2019 newsletter, researchers at Case Western Reserve University recently identified several risk factors for depression in MS, including obesity, hypertension, mononucleosis, and obstructive pulmonary disease. This groundbreaking research also identified genetic influences on the condition. For example, the major alleles for the APOE gene are called E2, E3 and E4. Data from this study show that the E4 genotype is a risk factor for depression and the E2 genotype appears to have an opposite, protective effect. The research team also concluded that a family history of depression (specifically when an individual’s mother is affected) is a causative factor. Researchers in Greece have confirmed this finding. Other illnesses can contribute to depression as well, such as hormone or thyroid problems, changes in blood sugar levels, and urinary tract or other infections. Therefore, it is of
primary importance for those struggling with depression to have a physical examination and laboratory testing to rule out any underlying (and treatable) physical cause.

Many aspects of living with MS, and the disease itself, have the potential to cause depression. It may be the result of neurological damage to the central nervous system. One imaging study suggests that people living with MS and depression have more lesions in the left anterior temporal/parietal regions of the brain. Researchers at UCSF suggest the cytokines involved in the abnormal immune response that occurs in MS may, in fact, cause depressive symptoms. Subsequent studies have confirmed these findings. Some of the medications used to treat MS may be linked to depression. Steroids are often prescribed during exacerbations, a time when people with MS are already vulnerable to depressive symptoms. Steroids often cause a short term “high” when first given followed by an emotional plunge once the medication is stopped. Depression is a suspected side effect of interferon beta treatments for MS (Avonex, Betaseron and Rebif), although the evidence to support this is mixed. Two MS clinical trials (the SPECTRIMS trial and the PRISMS trial) show no association between depression and interferon beta-1a treatment. Other studies suggest interferons decrease the amount of serotonin formed in the brain, which may, in turn, be linked to depression. Medications used to manage MS symptoms may also cause depression. For example, despondency is a side effect of baclofen (for spasticity), benzodiazepines (for dizziness, vertigo or spasticity), and other sedating drugs.

A number of instruments are used in the clinical and research settings to evaluate depression. One of the most commonly used tools is the Beck Depression Inventory (BDI), which is a questionnaire containing 21 multiple-choice questions aimed at assessing the mood, symptoms and behaviors of people who are depressed. Each answer is assigned a score, from one to three (based on severity). These numbers are added together to determine a total score, which is used to evaluate an individual’s level of depression. Dr. Max Hamilton, a psychiatrist at Leeds University, developed the Hamilton Depression Rating Scale (HAM-D) in the late 1950’s. This questionnaire is used to determine the severity of depression in people who have already been diagnosed with the condition. The HAM-D consists of 21 multiple-choice questions, each relating to a particular sign or symptom of depression. Scoring is based on the first 17 items. The remaining four questions measure factors that are related to depression, but are not thought to be measures of severity, such as paranoia or obsessive and compulsive symptoms. Individual answers are scored (zero through four), added together and higher total scores indicate more severe depression. The Zung Scale is another instrument, designed by Duke University psychiatrist Dr. William Zung, to assess the level of depression in individuals with existing depression. It contains 20 questions that are framed in terms of positive and negative statements. Scores for individual questions are added to obtain an overall score, ranging from 20 to 80, with scores above 50 indicating depression.
The effects of depression can be devastating. Those struggling with it may find even simple activities, like getting out of bed in the morning, challenging. Bigger tasks (i.e. getting to a doctor’s appointment) may feel impossible. An individual living with both MS and depression may not be inclined or able to follow his or her treatment plan, which could have detrimental effects in the long run. Depression may erode relationships. Many of its symptoms are invisible, which often leads to misunderstandings. Those struggling with depression frequently turn inward, withdraw from family and friends, and stop participating in social activities. Support systems tend to crumble when they are needed the most. Loss of libido is a chief complaint among individuals experiencing depression, which may also damage relationships. Depression may impact a person’s ability to work. A 2012 study looking at its impact on work productivity in people with RRMS suggests depression negatively impacts both the ability to work, and one’s productivity while there. For the depressed individual with MS, a loss of employment and insurance benefits can have a devastating impact.

Depression is one of the most treatable of all MS symptoms. One type of medication frequently used is a selective serotonin reuptake inhibitor (SSRI). These drugs inhibit the reuptake of serotonin (a chemical produced within the body which is know to elevate mood), allowing it to remain in the body’s system longer. Some commonly prescribed SSRIs include Celexa, Lexapro, Paxil, Prozac and Zoloft. Another class of antidepressants is a serotonin and norepinephrine reuptake inhibitor (SNRI), such as Cymbalta and Effexor, which work by increasing the amounts of serotonin and norepinephrine in the brain. These medications have similar side effects to SSRIs. Numerous other drugs are also FDA-approved for the treatment of depression, such as Desyrel, Remeron, Serzone and Wellbutrin. There is wide variability in response to antidepressant drugs and it may be necessary to try different medications and doses before an effective medication, or combination of medications is found. In addition, many of the drugs used to treat depression can take up to six weeks before reaching maximum effectiveness. Many need to be continued for at least four to nine months to prevent depression from quickly returning. For those with severe depression, medication may need to be continued indefinitely. As mentioned in our February 2019 newsletter, dietary supplements such as St. John’s wort and ginkgo biloba are thought to help with symptoms of depression. Recent research suggests that fish oil supplementation can also be beneficial in this regard. It’s important to note that anyone considering dietary supplements should first consult his or her physician as these can cause serious side effects and/or interactions with other medications.

Studies show the most successful treatment plan for depression is to seek counseling in conjunction with a prescribed drug therapy. The National MS Society’s MS Navigator program provides people living with MS with the information, resources and support they need to combat depression and other challenges in MS. A number of professionals are specifically trained to provide objective insight and coping skills to
help manage the symptoms of depression, including a psychiatrist, psychologist, social worker, or a counselor. A variety of therapeutic approaches may be used during the counseling process, such as talk therapy and behavioral therapy. Counseling sessions may be conducted individually, with couples, families, or larger groups. Some less traditional therapy options also include phone therapy and online therapy. These options may be attractive to those who are home bound or otherwise unable to attend a counseling session. In rare instances, a number of procedures may be used to treat significant depression that does not respond to more traditional forms of therapy and medication. These include transcranial magnetic stimulation, vagus nerve stimulation and electroconvulsive therapy (also known as electroshock treatment).

Overall wellness strategies can be very helpful in coping with depression. Such strategies include exercising daily, reducing stress, maintaining social networks, and abstaining from addictive substances like alcohol. Many people find that helping others, for example by volunteering, is a great way to lift their mood. In fact, research shows that giving support to others can sometimes be more beneficial than receiving help. Such a boost after doing a good deed, or an act of kindness is often referred to as a “helper’s high.” To help with depression, some find it helpful to journal their feelings. Such an activity may not only help individuals feel better, but can be an effective way of documenting changes in mood, which can be very helpful information for healthcare providers. Some people find great comfort in sticking to a routine. These individuals may find doing whatever is possible to maintain a normal schedule when forced to make a change often helps them adjust. Other helpful strategies include adopting a pet, developing a spiritual interest (prayer, meditation, or some other spiritual practice) and, above all else, maintaining a sense of humor when possible.

Despite all of the devastating implications of depression, it is often ignored, and as a result, under-treated. While depression is common in people with MS, it is not universal and shouldn’t be considered normal or expected. A common misconception is that depression can be overcome by willpower or religious belief alone, when, in fact, it is an illness that requires time, attention and treatment. Individuals with MS and their families should pay attention to symptoms of depression and notify their health care provider should any arise. There are effective therapies that can help dispel the gloom and return one to a happier, more peaceful life.
Mindfulness – Put Your Mind Over MS

The practice of mindfulness has become increasingly popular in recent years and its benefits are well documented. This age-old philosophy can be traced as far back as the fifth century BC, when it appeared in the Buddha’s most essential teachings. According to Dr. Jon Kabat-Zinn, mindfulness is “paying attention in a particular way: on purpose, in the present moment and non-judgmentally.” This can be achieved through meditation or simply by observing your surroundings without opinion. People practicing this philosophy learn to think about their thoughts and emotions as passing events, rather than attributing importance to them.

Dr. Kabat-Zinn is internationally known for his work as a scientist, writer, and meditation teacher. He developed the mindfulness-based stress reduction (MBSR) program at the University of Massachusetts Medical School (UMMS), and is recognized for bringing this philosophy into the mainstream of medicine and society. In 1979, he recruited chronically ill patients not responding well to traditional treatments to participate in an eight-week stress-reduction program (now known as MBSR). Each week, participants took part in a two and a half hour session learning mindfulness meditation, body awareness, yoga and other techniques that support stress reduction, self-awareness and relaxation. This was the beginning of the Mindfulness-Based Stress Reduction Clinic at UMMS. Dr. Kabat-Zinn founded the Center for Mindfulness at UMMS in 1995. These programs are now offered in over 720 medical centers, hospitals, and clinics around the world.

There is ample scientific evidence supporting the widespread benefits of practicing mindfulness. To name a few, a recent study reported significant, long-lasting improvements in anxiety, depression, and perceived wellness in subjects who completed an 8-week MBSR program. Other research suggests that mindfulness meditation also helps with symptoms of social anxiety. Researchers at the University of California Santa Barbara found that just a few days of mindfulness training may improve both concentration and attention. There is evidence that this philosophy can be very effective in helping people recover from various types of addiction. One study compared mindfulness training to the American Lung Association's freedom from smoking (FFS) program, and found that people who learned mindfulness were more likely to have quit smoking by the end of the training and at 17 weeks follow-up, than those in the conventional treatment. Other research has found that this practice can be helpful in treating other forms of addiction, such as drug and alcohol abuse. In addition, there is evidence that people who are more mindful tend to have less pain. The benefits of mindfulness are not limited to adults. A 2014 study evaluated the effect of a 5-week mindfulness-based curriculum on student classroom behavior. Investigators concluded that mindfulness meditation has both cognitive and emotional benefit in children.
One might wonder how a mental discipline, like mindfulness, can have such a broad and powerful effect. The human brain changes throughout a person’s lifetime. Changes in neural connections may occur when an individual learns new things or memorizes new information. This ability to change is often referred to as neuroplasticity. These new nerve networks are reinforced and strengthened through behavior. Mindfulness, when approached as a form of mental exercise, can lead to changes in the brain. Researchers at Harvard Medical School found subjects who incorporate meditation into their daily routine had increased cortical thickness in the areas of the brain that govern learning and memory, as well as emotion regulation and other cognitive processes. MRI results from these subjects showed decreases in brain cell volume in areas of the brain responsible for fear, anxiety, and stress. These results were confirmed in a subsequent study. Researchers at UCLA found less grey matter atrophy in subjects practicing long-term meditation as they aged. MRI results from a 2011 study at Yale University showed mindfulness meditation decreases activity in the default mode network (the area of the brain responsible for daydreaming or mind wandering). Data from this study showed new neural connections, formed as a result of meditation, allowed subjects to refocus more easily when their minds did wander.

MS is a stressful condition. Its chronic, unpredictable nature and unpleasant symptoms can wreak havoc in the lives of those living with the disease. The resulting increased stress is often associated with more severe MS symptoms, which sets up a vicious cycle. Although medications can impact the disease course and help improve some symptoms, they are not as effective in relieving the stress caused by the nature of the disease and many have unpleasant side effects. One of the key ways mindfulness may help people with MS is by reducing stress. Numerous studies show mindfulness practices have other mental and physical benefits for people living with the disease, as well. For example, a recent study confirms that people with MS practicing mindfulness also experience less pain. A review of three studies on mindfulness training for people with MS concludes this training is especially helpful for improving mental health and quality of life. None of the studies showed any adverse effects from this practice. Researchers in Scotland conducted a clinical trial evaluating whether a standard, eight-week MBSR program was feasible and effective for people with MS. Results showed most participants were able to complete the program, and those that did reported less anxiety and felt more positive emotions than the control group (who received usual care). Mindfulness practice appears to be a safe, drug-free approach to coping with stress and anxiety, which in turn may help reduce MS symptoms and help individuals living with the disease feel their best.
Healthy Mind Healthy You

Most mindfulness programs are taught in weekly sessions over the course of 8 weeks. Researchers at Massachusetts General Hospital (MGH) will be conducting a nationwide clinical study entitled “Healthy Mind Healthy You” to determine if this length of training is necessary, or if the same benefit can be derived from a shorter program.

Healthy Mind Healthy You is funded by PCORI (the Patient Centered Outcome Research Institute), which means patients have played an integral role in designing the study since its inception. PCORI established PCORnet (the National Patient-Centered Clinical Research Network) as a national resource that could harness multiple sources of health data to make research more effective, efficient, and patient-centered. Healthy Mind Healthy You will involve all patient-powered research networks (PPRNs) including ACP’s iConquerMS and, potentially, clinical data research networks (CDRNs), in PCORnet to recruit and enroll subjects. As a result, investigators will be able to evaluate the effects of mindfulness on a wide variety of populations and conditions, including MS.

The MGH study team hopes to recruit more than 2,000 adult subjects nationwide, including patients, caregivers and family members, who are members of one of PCORI’s PPRNs. Participants will be randomly assigned to a “standard” eight-week mindfulness-training program or a “light” mindfulness training consisting of three sessions. Participants will fill out standard well-being assessments every other week throughout the study and after they have completed all sessions to see how they are doing. All sessions and assessments will be done online. The knowledge gained will help clinicians, patients and caregivers know the best dose of mindfulness to manage stress and increase wellness, with a substantial impact on care. It may also reveal what groups of people do better with one or the other program.

We will soon be inviting iConquerMS members to join the Healthy Mind Healthy You study. Are you already a member of the iConquerMS network and are interested in learning more? Email us! If you are not a member of iConquerMS, please consider joining to add your voice to those already helping to steer the direction of MS research, and to contribute valuable data that may one day lead to better MS treatments and a cure!
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 medications. 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.

Repository Spotlight – The Power of Data

ACP is dedicated to facilitating research to improve diagnosis, to optimize treatment and to cure MS. Real-life patient data plays a pivotal role in our work. Collecting this vital information has been key to achieving ACP’s mission since its inception. The organization’s first large project was the collection of blood samples from people with MS, their relatives and unrelated controls, along with detailed clinical and other phenotypic data (the ACP Repository). These samples have been made available to over 100 investigators with the stipulation that their research data must be returned to ACP. Some of these studies have been highlighted in previous newsletters. We now have a growing collection of returned research data that is also available to investigators for further research and analysis. This large amount of returned data is an important resource for the discovery of MS drug targets and disease biomarkers, however it presents a logistical challenge with regard to storage and access. In the fall of 2017, we signed an agreement with BC Platforms to store and curate the patient clinical phenotype data as well as the returned research data. This will allow ACP and its research partners to more easily access this valuable information resource.
iConquerMS has expanded our data focus from the clinical sites used for the collection of Repository samples into the patients' living rooms. This initiative has added an important data category – patient reported outcomes (PROs). As ACP moves forward, we will continue to make these anonymized data available to investigators. In addition, we are planning a new, updated Repository collection that will allow us to collect new data, along with blood samples, and to integrate a broad range of important data categories. Stay tuned!

iConquerMS™ Spotlight – Expanding the MS Research Toolbox

The MS Minority Research Engagement Partnership Network (MREPN) was featured on the PCORI website earlier this month. MS is a neurological disease that impacts the lives of people of all backgrounds, but such diversity is not reflected in those participating in MS research. Participation in research by people of all races and ethnicities is key to ensuring that discoveries, treatments, and prevention strategies are relevant to those populations. As discussed in our February 2018 newsletter, the MREPN is a collaboration designed to identify and address disparities and increase participation by underrepresented communities in MS medical research. In October 2016, a team led by Hollie Schmidt at ACP was awarded a Eugene Washington PCORI Engagement Award that supported the building of the MREPN. These awards support projects that encourage active integration of patients, caregivers, clinicians, and other healthcare stakeholders as essential participants in patient-centered, comparative effectiveness research (CER). The MREPN team has made great strides toward this goal. In Hollie’s words, “Our engagement award is aimed at understanding why there is a lack of diversity in MS research participation when it comes to racial and ethnic minorities. We’ve been doing a lot of learning about what the barriers are to participation and also what the facilitators of participation are. We’re trying to disseminate that information to researchers and clinicians, as well as to the populations themselves. We are conducting a number of outreach activities. We’re also disseminating the results of a survey we conducted among people with MS and are trying to publish that in a medical journal to reach the medical and research communities. We’ve also published a couple of toolkits, one for researchers and one for clinicians that help to educate them about the topic of underrepresentation in research and how they can help to promote diversity in research.” When asked how a Eugene Washington PCORI Engagement Award made the team’s work possible, Hollie states, “We knew that ACP, being a small, independent nonprofit organization, could only do so much on our own. So, PCORI and its award enabled us to bring together stakeholders from different organizations, different advocacy groups, researchers, clinicians, industry representatives, communication specialists and, most importantly, people with MS belonging to minority groups, so we could all tackle this challenge together. I think it made for a much more impactful project and we were able to accomplish much more than any one of us could have done on our own.” In September, the iConquerMS governance and other stakeholders in the MS community gathered at our Leadership Summit to discuss the future direction of the initiative. A key focus of this meeting was
collaborations, such as MREPN, in which partners come together as equals, take fullest advantage of differing ideas to approach the problem at hand and achieve the desired outcome (in this case, diversity in MS research). To keep the momentum going, a Next Steps Committee is working to bring this important work to fruition. This is one of the many ways the ACP/iConquerMS team is working to improve the health and quality of life of people living with MS.