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INFOCORNER



What is the Goal of NARCOMS?

The NARCOMS Global MS Patient Registry is a registry program that helps to facilitate research about multiple sclerosis for research centers in North America and around the world. Collaboration between MS centers of excellence throughout the world helps to increase knowledge, improve clinical care, and enhance the quality of life for persons with MS.



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Robert Fox, MD
Managing Director

Ruth Ann Marrie, MD, PhD
Scientific Director

Amber Salter, PhD
Coordinating Center Director

Gary R. Cutter, PhD
Scientific Advisor

Michele Curran
NARCOMS Project
Coordinator

Katherine Wandersee
Medical Writer

James Ticchio
Creative Director

Joseph J. D’Onofrio
Frank Marino
Delaware Media Group
Publishers



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DIRECTOR'S LETTER

Dear *NARCOMS Now* Readers:

Our feature article in this issue focuses on comorbidities—medical conditions that occur in addition to MS. These may include heart disease or diabetes, or mental health conditions like depression and anxiety. The risk for multiple health conditions grows for everyone as we age, and these conditions can increase the challenge of living with MS. Studies using NARCOMS data have shown that healthier habits are associated with a lower risk of comorbid conditions.

Findings from the NARCOMS surveys have been invaluable in studying comorbidities in MS. Over a period of many years, my colleagues and I have published multiple studies on comorbid conditions using NARCOMS data. The findings from NARCOMS studies have also prompted other researchers to work in this area. Unlike a drug trial that compares one treatment with another, to learn more about comorbid diseases we need to gather detailed information from the people affected. We are grateful to have the participation of so many in the NARCOMS surveys. Some of our recently published papers have included data drawn from as many as 7,400 people with MS. Based on NARCOMS data, the Consortium of Multiple Sclerosis Centers (CMSC) has developed a resource guide for medical professionals to help them manage comorbid conditions in people with MS.

Also in this issue is a summary of trial results for an experimental drug for progressive MS. Since there are few effective treatments for people with progressive MS, clinical trials like this one are important to meet the needs of people with progressive MS.

Again, I would like to reiterate our appreciation to you as participants in NARCOMS. We have learned a great deal and will continue to do more in an effort to serve the MS community.

Sincerely,

Ruth Ann Marrie, MD, PhD
Scientific Director, NARCOMS



Ruth Ann Marrie, MD, PhD



Coping With MS and Comorbid Health Conditions

One serious medical condition like multiple sclerosis (MS) would seem like enough of a challenge for anyone. However, multiple diseases can co-exist. Co-existing medical conditions are referred to as comorbidities. The risk of comorbidity typically increases as a person ages. NARCOMS Scientific Director Ruth Ann Marrie, MD, PhD, is an international expert on the subject of comorbidities and MS. Dr. Marrie, based at the University of Manitoba, has researched comorbidities associated with MS. She talked with *NARCOMS Now* about what is known about comorbid diseases, some of which was learned using data from the NARCOMS surveys.

MS comorbidities are separate from MS symptoms such as fatigue and numbness, or complications like urinary tract infections, Dr. Marrie explained. An example of a comorbid condition might be diabetes or heart disease. Several comorbid conditions occur more often among people with MS than in the general population. These include depression, some autoimmune diseases, and others (see Table 1).

People who are coping with MS and comorbidities are not alone. In a 2006 NARCOMS Survey involving nearly 9,000

Table 1. Health Conditions More Common in MS

(Compared with age-matched population without MS)

- Depression
- Anxiety
- High blood pressure
- Migraine headaches
- High cholesterol levels
- Chronic lung disease (such as asthma)
- Psoriasis

respondents, most (77%) said they had at least one comorbid condition and many reported having multiple conditions. Similarly, a review of studies from around the world that focused on comorbidities and MS found that depression, anxiety, and high blood pressure were the most common conditions (Figure 1).

“Now that we know how common comorbid conditions are in MS, we need to learn the answers to several other questions,” Dr. Marrie said. Among them:

- Whether an existing condition might affect a person’s risk of getting MS
- Whether having MS might heighten the risk of getting a comorbid disease and why

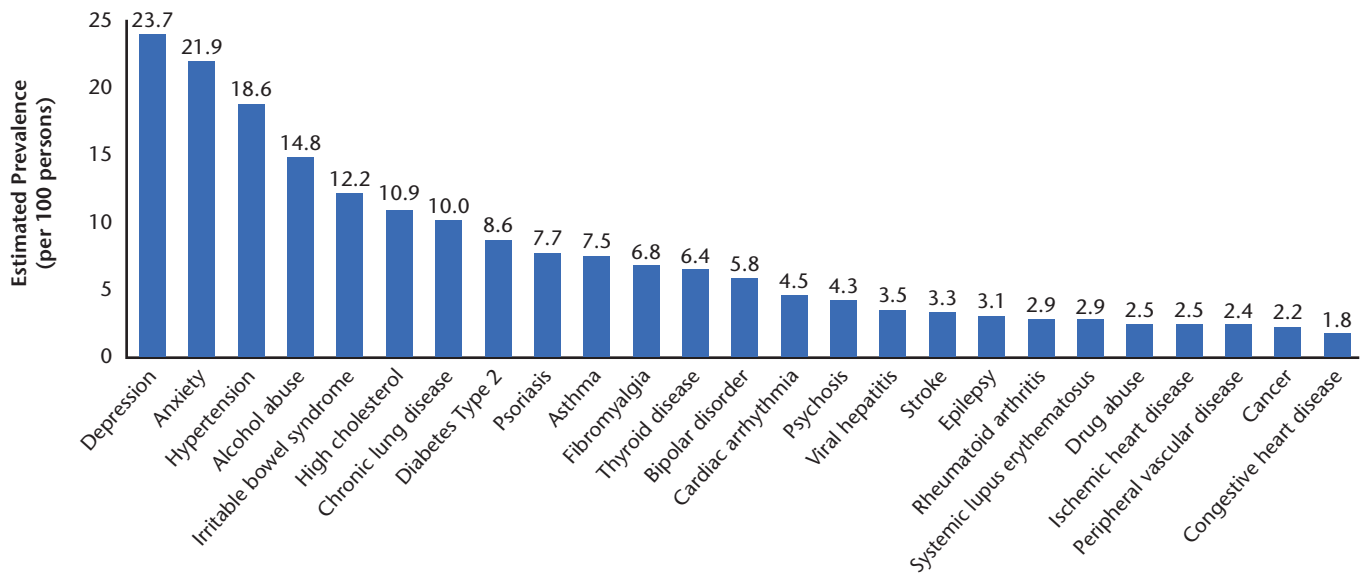


Figure 1. Comorbid Conditions in People with MS

The prevalence of a condition is the percentage of people affected at given time. The chart above shows the prevalence of various comorbid conditions among people with MS, based on a review of 249 studies.

Source: Marrie RA, et al. A systematic review of the incidence and prevalence of comorbidity in multiple sclerosis: overview. *Mult Scler.* 2015;21;263-281.

- What impact the comorbid condition has on the person with MS
- How having MS might affect the severity or treatment of the comorbid condition

MS and Mood Disorders

Depression and anxiety are mental health conditions that occur much more commonly in people with MS. Rates of depression are almost 80% higher, and anxiety rates almost 60% higher, compared with people who do not have MS. In studies by Dr. Marrie and colleagues based on NARCOMS survey data from 8,983 participants, nearly half reported at least one mental health condition and 46% said they had been diagnosed with depression. Certain MS symptoms also overlap with depression, which may make depression more difficult to diagnose in people with MS (Figure 2).

A 2017 study using NARCOMS data from over 7,400 respondents showed that certain lifestyle habits may be associated with a higher risk of depression in people with MS. In particular, being overweight and not exercising made it more likely that a person would suffer from

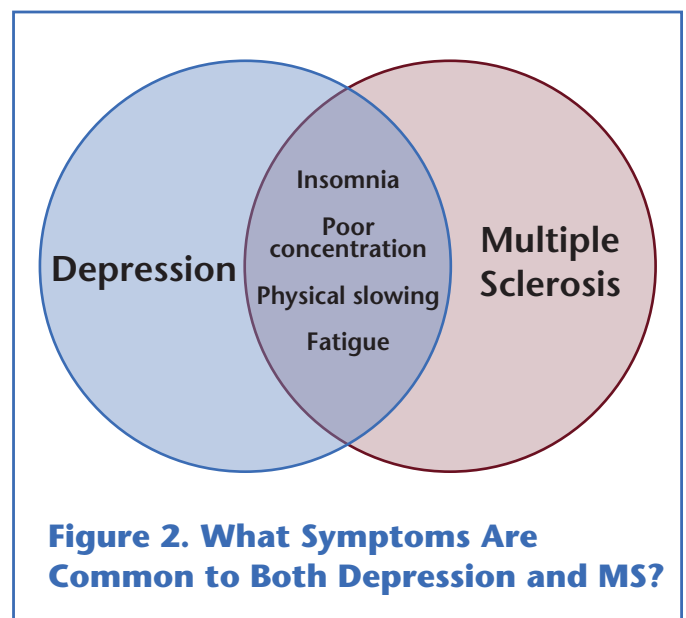


Figure 2. What Symptoms Are Common to Both Depression and MS?

depression. Other lifestyle habits associated with mood disorders included smoking and poor diet. Depression leads to impaired motivation and interest, making it difficult for a person to make the effort to exercise or to eat properly. However, this research suggests that making positive changes may improve overall health and reduce depression risk.

Heart Disease, Diabetes, and Other Vascular Conditions

Heart disease, diabetes, and other chronic health conditions occur commonly in the population as a whole. So it is not surprising that these are common among people with MS as well. In the 2017 NARCOMS survey mentioned earlier, about 53% said they had at least one vascular condition, including:

- High or imbalanced cholesterol levels 37%
- High blood pressure 30%
- Heart disease 7%
- Diabetes 6%
- Vascular disease involving arms or legs 2%

Vascular and metabolic comorbidities like heart disease and diabetes have been shown to have a substantial impact on a person with MS. Studies have shown that people with these conditions are more likely to have disability earlier in the course of their disease—including walking difficulties—compared with people with MS who do not have vascular or metabolic conditions.

Many aspects of heart disease and diabetes risk can be modified or controlled with lifestyle changes. Maintaining a healthy weight, quitting or refraining from smoking, regular

exercise, and improved diet add up to lower risk and may even reverse some vascular and metabolic problems.

Other Autoimmune Conditions

Some chronic conditions like MS involve abnormal behavior of the immune system. These immune-mediated conditions may co-occur. The immune-mediated diseases that co-occur most frequently people with MS include thyroid disease and psoriasis. A common question is, why do these conditions co-occur? Many people with MS have noticed a “family connection” when it comes to autoimmune diseases. This concept has been studied using NARCOMS data and other sources. In a survey (not related to NARCOMS) of 176 families, 64% reported an immune disorder, other than MS, in a first-degree relative (parent, sibling, or child). Some studies have shown that certain genetic factors increase the risk of a person developing MS, as well as other immune conditions like inflammatory bowel disease.

Some aspects of thyroid disease are worth highlighting. Thyroid hormone imbalance is a common cause of fatigue and should be considered when a person with MS develops new or worsening fatigue. In a person with MS, the presence of thyroid disease may be overlooked because the fatigue is assumed to be MS-related. Some MS therapies, such as alemtuzumab, increase the risk for thyroid disease.

Osteoporosis

Osteoporosis, a condition that makes bones more fragile, is about three times more common in people with MS. This is a concern especially because people with MS are at greater risk for falls that lead to bone fractures.

Repeated use of high-dose corticosteroids (such as those used to treat MS relapses) increases the risk for osteoporosis. So does physical inactivity—being seated or sedentary most of the time. Screening for low bone density is an important step to assess osteoporosis risk. Use of vitamin D and calcium supplements is also recommended for prevention. Engaging in regular weight-bearing exercise is a great way to strengthen bones. This can involve walking or running, using a recumbent bicycle, or even seated exercises involving weights (see Resource list on page 9).

Cancer

Current data show that about 2.2% of people with MS also have a diagnosis of cancer. Regular skin checks for skin cancer, mammograms, colonoscopies, and other preventive measures are important for detecting some cancers early, before they have a chance to spread. For some people, these basic preventive steps are neglected because they must expend so much of their time and energy focusing on and managing their MS.

Is MS to Blame? Or Something Else?

If anything goes wrong in the body, it must be due to MS, right? MS tends to “get the blame” even when symptoms are caused by another health problem. Jane, a woman with longstanding MS, shared a recent experience with *NARCOMS Now*. She needed to use a wheelchair for several months due to sharp shooting pains and weakness in her leg. Initially she (and her neurologist) thought her condition was due to MS-related disability progression. But a neurosurgeon diagnosed spinal stenosis and initiated treatment that helped her get back on her feet. “It may look

like a duck and quack like a duck...but it’s not always a duck—especially for those of us with MS!” Jane recounted. Another person with MS said she had developed symptoms of tingling and nerve pain that were initially assumed to be MS-related, but turned out to be a case of herpes zoster, or “shingles.” Others have said that their primary care doctors may be hesitant to manage routine health conditions, because they are concerned about potential complications from MS.

Comorbid conditions do not exist in isolation, Dr. Marrie stressed. One disease may affect the other. People with MS may have a more severe course if other diseases are present. “We know that there is a large variation among individuals in terms of how MS progresses,” she said. “We now believe that the presence of comorbid conditions plays an important role in the variability that we see in MS.”

Impact of Healthy Habits

The information gained from NARCOMS surveys has been invaluable in studying the impact of comorbid health conditions in MS. People with MS may have a greater susceptibility to some diseases, but others crop up as they might in any other individual regardless of MS. It is important to work on any modifiable risk factors to maintain overall health to the degree possible, Dr. Marrie noted. Preventive care is essential, but may be overlooked. “We focus a lot on treatment of MS using disease-modifying drugs. But MS is also affected by comorbid conditions and behaviors such as diet and physical activity,” Dr. Marrie explained. “This is why a comprehensive, or holistic approach to the disease is helpful.”



Experimental Agent May Help Slow Brain Atrophy in People with Progressive MS

Results of a newly published study suggest that an investigative oral drug, ibudilast, may have the potential to help patients with progressive forms of multiple sclerosis (MS). The SPRINT-MS trial compared ibudilast (pronounced “eye-BYOO-di-last”) and placebo in 255 people with MS. About half had primary progressive (PPMS) and half had secondary progressive (SPMS). Other characteristics of the study population were:

- Age between 18 and 65
- Average disease duration 12 years
- Expanded Disability Status Scale (EDSS) score between 3.0 and 6.5
- Evidence of disability progression in the previous 2 years

Participants took either ibudilast (orally once or twice a day) or a placebo for a period of 96 weeks (about 21 months). Some continued to take an injectable drug for MS such as interferon beta or glatiramer acetate (Copaxone) during the trial.

The primary outcome of the SPRINT-MS study was the progression of brain atrophy, or, how fast brain tissue is shrinking. Brain shrinkage occurs in everyone as we age, but is more rapid in people with MS and is one way to measure change in progressive MS. SPRINT-MS participants who received ibudilast had a

48% reduction in the progression of whole brain atrophy during the study, a significant improvement compared with placebo. Side effects of ibudilast included gastrointestinal symptoms, headache, and depression.

NARCOMS Managing Director Robert Fox, MD, was a lead investigator in the SPRINT-MS study. Dr. Fox said that ibudilast acts in part by inhibiting phosphodiesterase or “PDE.” Ibudilast is available in Korea and Japan for treatment of asthma and other conditions. Different types of PDE inhibitors are approved in the U.S. for other diseases—such as lung disease and erectile dysfunction—but none has been used previously in MS. The results of this trial suggest that ibudilast may have a “neuroprotective” effect on the brain, although it is unclear whether the benefit seen on brain atrophy will translate into slower progression of disability.

The ibudilast trial was conducted through the NeuroNEXT clinical trial network, which is an effort by the National Institutes of Health (NIH) to bring promising neurological therapies further along in the testing phases.

“These findings are preliminary, but they are encouraging because we have so few treatments available to slow the progression of disability in people with progressive MS,” Dr. Fox stated.

Reference: Fox RJ, Coffey CS, Conwit R, et al. Phase 2 trial of ibudilast in progressive multiple sclerosis. *New Engl J Med.* Aug 30, 2018;379:846-855.

Fatigue and Other MS Symptoms Interfere With Regular Exercise, But Special Programs Can Help People with MS Overcome Barriers

Exercise may help people with multiple sclerosis (MS) to manage symptoms such as fatigue, walking impairment, and depression. It's challenging for anyone to stick with a regular fitness program, but people with MS face additional challenges that often get in the way of exercise.

To identify specific barriers and seek solutions, a research team from Scotland surveyed 35 people with MS (most over age 50) who were not physically active. Fatigue was shown to be the number one barrier to exercise. MS-related impairment, such as bladder problems or fear of falling, also got in the way of exercise goals. Lack of support and the need

for extra time were other barriers that affected people with MS.

The researchers also identified three factors to help improve exercise habits. The first was exercising in a group with other people who face similar challenges. This creates a positive, understanding environment, and avoids the need to be compared with "fitness fanatics who have nothing wrong with them," one survey participant noted. Second was support from instructors who are aware of the limitations brought on by MS and can provide targeted help. Finally, the person's mindset and attitudes about exercise and fitness had an impact on ability to achieve exercise goals. See Resources below for ideas on fitness programs designed for people with MS.

Reference: Moffat F, Paul L. Barriers and solutions to participation in exercise for moderately disabled people with multiple sclerosis not currently exercising: a consensus development study using nominal group technique. *Disabil Rehabil.* 2018 Jun 29. E-pub ahead of print.

Resources for MS-Specific Fitness Programs

- **Aquatic exercise:** MSAA Swim for MS. National initiative to encourage water exercises for people with MS. Website: www.mymsaa.org. Phone: 800-532-7667.
- **Exercise videos for people with MS:** MS Trust, Staying Active with MS. Online videos for aerobic training, strength training, endurance exercises. Website: www.mstrust.org.uk/
- **Seated exercises:** 5-minute exercise videos developed by a physical therapist with experience in MS. On Youtube, search ChairFit with Nancy.
- **Yoga and non-cardio exercises:** National MS Society (NMSS) and Can Do MS initiative. Website: www.nationalMSSociety.org. In Living Well with MS section, click tab for Diet, Exercise, and Healthy Behaviors. Or contact NMSS at 800-344-4867.
- **Stress reduction:** Workout Your Worries: Anxiety and Exercise in MS. NMSS and Can Do MS. Website: www.cando-ms.org, search "Workout your worries" for more info and links to webinar.
- **Other seated exercises:** The Summer 2018 issue of *NARCOMS Now* provided a series of illustrated exercises to perform while seated. Website: www.NARCOMS.org. Click tab for *NARCOMS Now*.

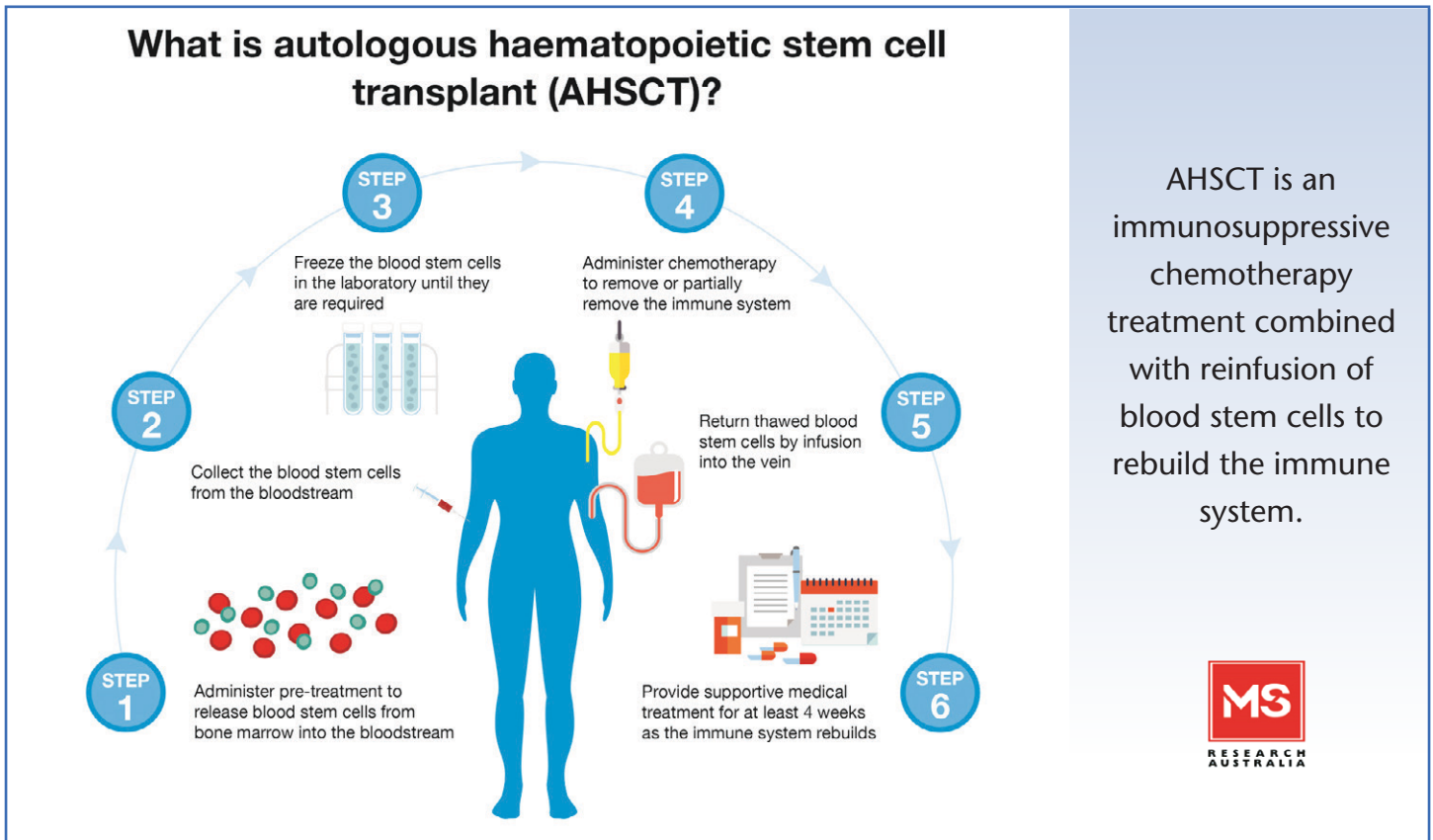
Clarification on Stem Cell Therapies for Multiple Sclerosis

Stem cell procedures are a hot topic in the multiple sclerosis (MS) community. At the 2018 Annual Meeting of the Consortium of Multiple Sclerosis Centers (CMSC) in Nashville, Canadian neurologist Mark Freedman, MSc, MD, urged caution about non-scientific stem cell procedures that offer little or no benefit for people with MS.

“Some clinics have set up shop for no other reason than to take advantage of vulnerable people,” Dr. Freedman explained. The clinics charge fees ranging from \$5,000 to \$20,000 for procedures that involve withdrawal of fat cells, usually from abdominal tissue. These cells have very minimal stem cell content, Dr. Freedman stressed. The lab then processes the cells in some fashion and reinfuses them

into the patient. But without suppressing the immune system first, these procedures are very unlikely to reset the immune system. With a medically based stem cell transplant, strong immunosuppressant drugs are used in a controlled environment after the cells are harvested to ensure that the newly introduced immune cells can take effect.

Dr. Freedman discussed results of his studies on autologous hematopoietic stem cell transplant in people with MS. *Autologous* means that cells are taken from the same person who is undergoing the transplant (See box for more key terms). A study based at the Ottawa Research Institute and other Canadian medical centers showed generally positive results in 24 people with aggressive MS, although there was one death in the group. In over 13 years of follow-up, all of the surviving patients had no MS relapses, no new lesions on MRI scans,



Hematopoietic stem cell. A young stem cell that can become any kind of blood cell. It is usually harvested from bone marrow.

Mesenchymal stem cell. A mature stem cell present in many different body tissues. It can differentiate into many different types of tissue cells.

reduced levels of brain atrophy, and long-lasting improvement in disability scores.

Because of the risks, the decision to undergo a stem cell transplant involves careful consideration. Women must accept that they will be infertile, but some have had successful pregnancies using stored or donor eggs after recovery. The data suggest that

stem cell procedures work best for people with aggressive MS who do not yet have extensive disability, but Dr. Freedman says he has some patients with severe deficits who have done well. Interest in stem cell technology is increasing rapidly, Dr. Freedman said, but people with MS should be cautious about commercial stem-cell centers, and should carefully consider the risks involved in medically based stem cell procedures. “Stem Cell Clinics – Questions to Ask” is a useful article on the National Multiple Sclerosis Society (NMSS) website. Or call NMSS to request the article.

Report from “Stem Cells for MS: An Update” chaired by Mark Freedman, MD, at the CMSC 2018 Annual Meeting, June 1, 2018, Nashville, TN.

Eye-Movement Technology May Help Correct Balance Problems in People With MS

Impaired balance is a major factor that interferes with walking, sitting, and most routine tasks. Poor balance is also one of the main culprits contributing to falls in people with MS. Balance is influenced by many body systems, including vision, the inner ear, muscle function, and the brain. But, treatments to correct balance problems in people with MS often rely on strength-building exercises and most do not target individual problems.

A newer program for people with MS uses special technology that measures eye movements as a way to find and correct specific balance problems. The program, called “Balance and Eye-Movement Exercises for Persons With Multiple Sclerosis” or BEEMS, has 3 main components: 1) balance practice while

standing on different surfaces, 2) balance while walking, with or without head movements, and 3) improving visual stability, which includes eye exercises that affect balance.

A study at the University of Colorado in 88 people with MS evaluated the BEEMS method, offering sessions two times a week with a trainer plus a daily home exercise program. This was compared with a control group who did not receive BEEMS training. After a 6-week program, the BEEMS group had improvements in balance, dizziness or unsteadiness, and fatigue compared to controls. These improvements were still present at a three-month follow up. The program may be one way to improve balance by targeting specific problems but further research is needed to understand the long-term benefits.

Reference: Hebert JR, Corboy JR, Vollmer T, et al. Efficacy of balance and eye-movement exercises for persons with multiple sclerosis (BEEMS). *Neurology*. 2018 Feb 27;90(9):e797-e807.



SNAPSHOT

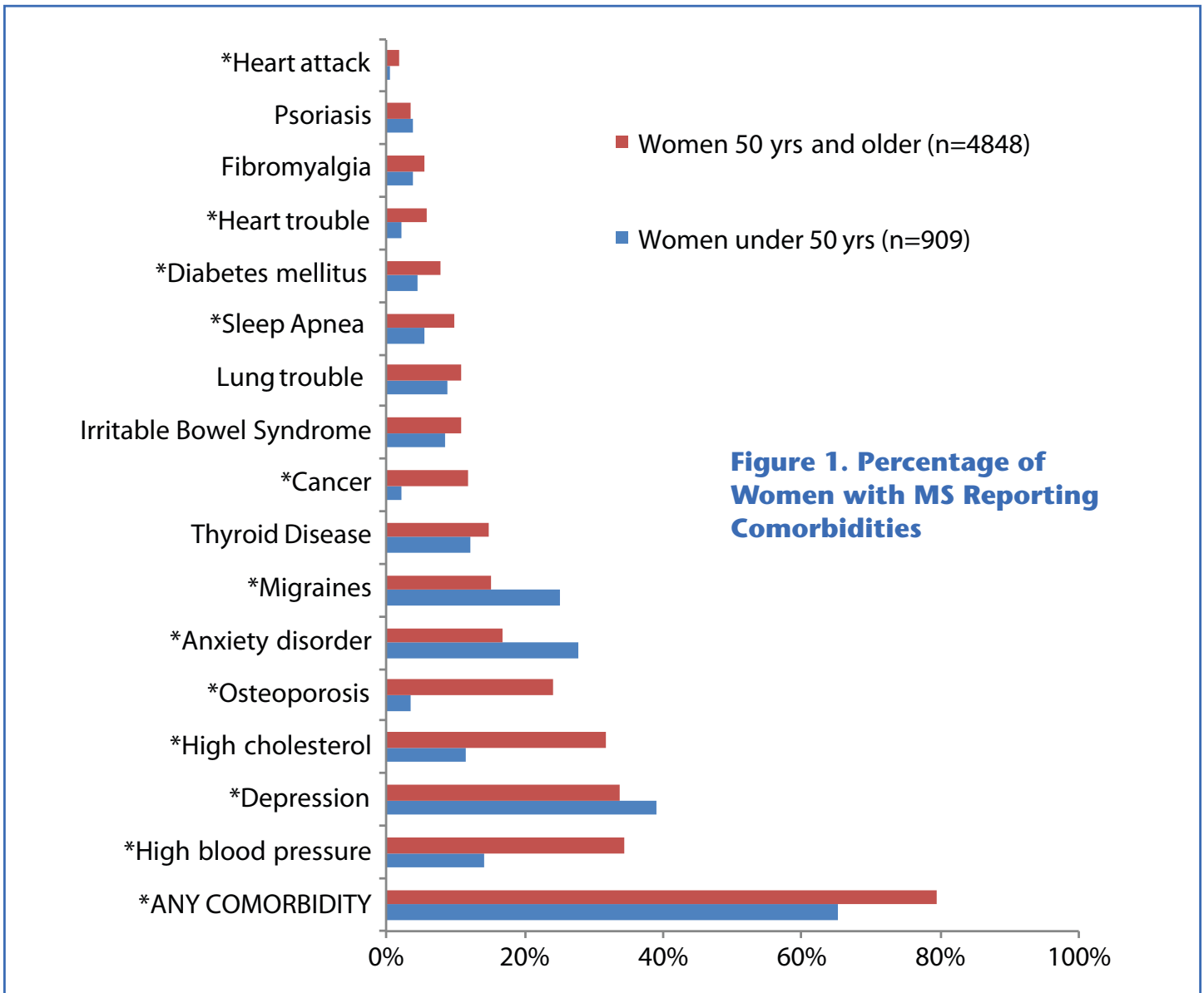
HOW WE'RE USING YOUR NARCOMS FEEDBACK

What Else is Bugging You?

Comorbidity Report from NARCOMS Spring Survey

In the Spring 2017 update survey we asked NARCOMS participants to report on comorbidities (any other chronic health conditions in addition to MS). Most of the responders reported at least one such

condition. In general, women were more likely than men to report comorbidities. Participants aged 50 years or older were more likely to report comorbidities than were younger participants. The results get more interesting

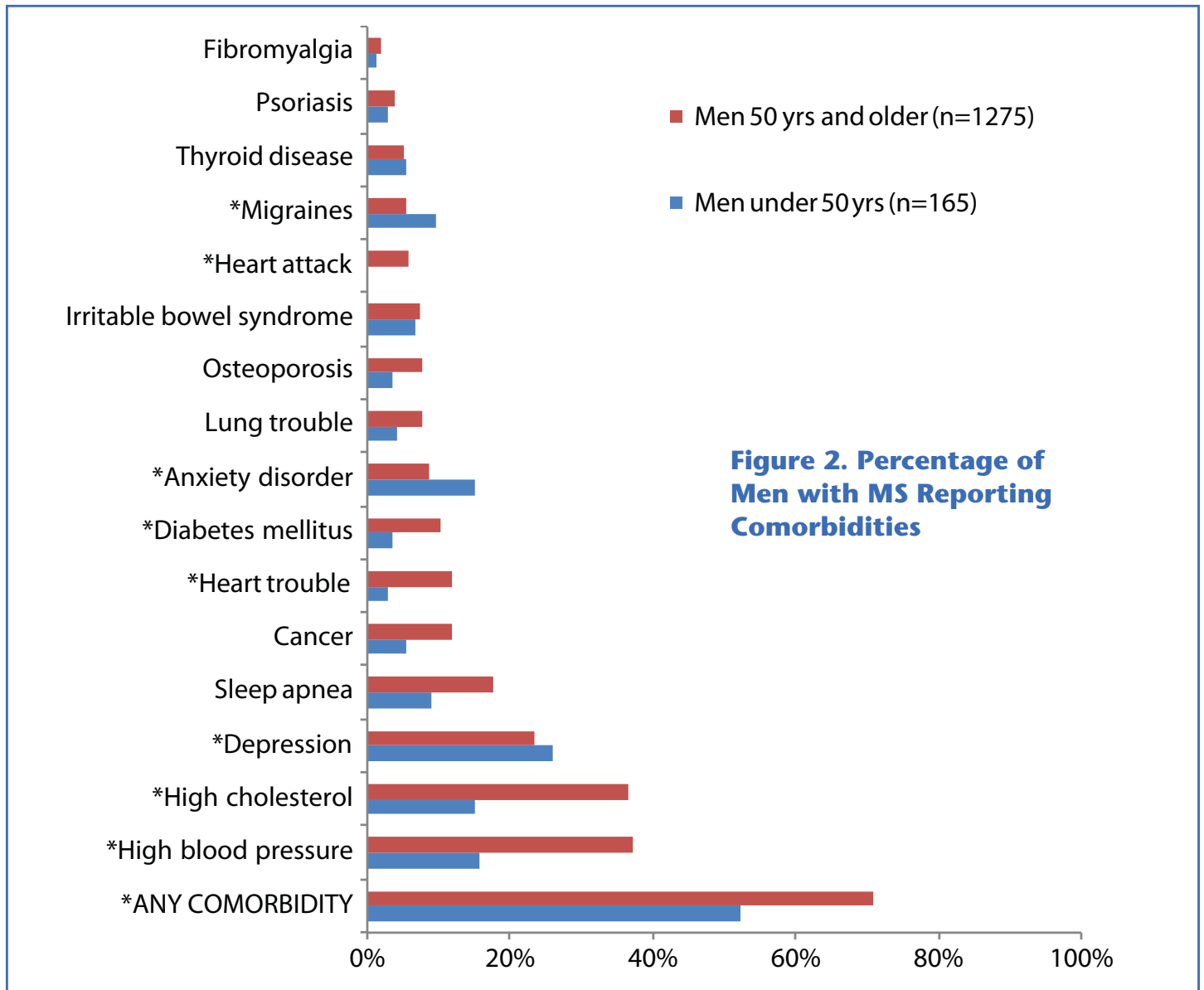


when each chronic condition is reviewed separately, as shown in Figure 1 (women) and Figure 2 (men). Reports of **anxiety**, **depression** and **migraine** are more common among people under age 50 (both men and women).

All differences that were statistically significant between the two age groups are indicated in the figures with an asterisk (*). The * means there is a less than 5% chance that the difference between the groups was due to chance alone. In some categories, the number of responses was quite low, especially among

men, so these results should be interpreted with caution.

We hope this overview will remind you to discuss all aspects of your health when you meet with your healthcare providers. MS causes many different symptoms but it should not be blamed for everything. For some symptoms there may be other causes. Treating or preventing other chronic conditions can help manage and cope with MS too, so managing these other conditions is doubly worth the effort.





MS MESSENGER

WHAT TO EXPECT ON THE NEXT NARCOMS SURVEY

The NARCOMS 2018 Fall Update Survey is scheduled to go out to participants via email or the postal service in early October. This edition of the survey is shorter than the past few update surveys. The only addition to the routinely asked core set of questions is the SymptoMScreen®, which was well received in the Fall 2017 update. We hope this shorter survey will allow you to enjoy an extra few minutes of autumn leaves, hot cider, or time to do something that makes you happy. As always, feel free to contact us with any questions or to ask for assistance.

If you have not received the Fall 2018 update survey by the end of October, please contact us. In some cases your account may have been marked inactive because of an outdated email address or lack of completed surveys in the past year, or sometimes the result of spam filters blocking the survey invitations. Please note that *NARCOMS Now* will be mailed only to active registry participants.

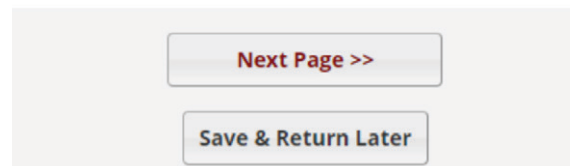
We truly appreciate your participation in the NARCOMS Registry and your commitment to MS research. Thank you!

Please use pen rather than pencil when filling out the paper survey.

Please remember to update your contact information if you move, get a new email address, or change your phone number. You can email us at MSRegistry@NARCOMS.org, or call (800) 253-7884.

SURVEY 101

As a reminder, even if you complete the surveys online, you have the option to take a break as you go. On the bottom of each survey page you will see an option to “Save and Return,” or go to the “Next Page.”



If you would like to take a break, choose “**Save and Return.**” A **Return Code** will be emailed to you, along with a link to your survey. When you are ready to continue, simply click on the link, “**Enter the Return Code when prompted**” and you will get back to the survey exactly where you stopped.

If, for some reason, your browser closes while you are completing the survey, and you do not receive that email, don’t worry! You can call (800) 253-7884 or email MSRegistry@NARCOMS.org, and we will provide the Return Code to you.

Thank you for taking the time to complete and return the Fall 2018 survey at your earliest convenience, either by mail or online!

Play **WORDSEARCH**

Find the following hidden words relating to *research*.

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DOCTOR

DONATION

HYPOTHESIS

INFORMATION

MEDICINE

MICROSCOPE

PATIENT

PROJECT

RESEARCH

RESULTS

SAMPLE

SCIENCE

STATISTICS

STUDY

TREATMENT

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