

MS-Related Pain



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INFOCORNER



What is NARCOMS?

NARCOMS is a registry for people who have multiple sclerosis (MS). Registry participants complete two surveys each year to provide information about themselves and their experience of having MS. Data from these surveys are used in research studies and to help further our understanding of MS. Participation in the registry is voluntary, and responders' identity and privacy are carefully secured.



What is the Goal of NARCOMS?

The NARCOMS Global MS Patient Registry helps to facilitate research about multiple sclerosis 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.



How Private Is My Information?

We will keep the information that you provide us private and confidential by storing your data in a secure database. All information will be used for research purposes only. We do not share any personally identifying information with any person or research institution. We follow all Federal (HIPAA) laws regarding confidentiality.



Not Yet a NARCOMS Participant?

Please contact us at www.NARCOMS.org to enroll online, or call toll free at 1-800-253-7884.



Tell Us Your Thoughts!

Have an idea? We would love to hear from you!
Send us your questions, comments, and suggestions.

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This publication is supported
by grants from:



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NARCOMS is a project of the Consortium of Multiple Sclerosis Centers (CMSC).

For more information on the CMSC visit www.ms-care.org.

NARCOMS Now acknowledges and appreciates the companies listed on the bottom of page 2, which have provided unrestricted educational grants through the Foundation of the CMSC toward production costs of NARCOMS Now, including printing and mailing. None of these companies have any control or influence over the content of NARCOMS Now and are not provided access to NARCOMS data in return for their support. For any questions regarding NARCOMS Now funding please call 1-800-253-7884.

DIRECTOR'S LETTER

Dear NARCOMS Now Readers:

Pain is a common symptom reported by a large proportion of people with multiple sclerosis (MS). To find out more about the pain that occurs in MS, NARCOMS Now interviewed two experts from the University of Washington in Seattle. Neurologist Brett Stacey, head of the Center for Pain Relief, describes how some of the pain experienced by people with MS is neuropathic, or related to faulty nerve signaling. This pain often does not respond to the usual pain-relieving medicines, but there are other treatments that can help. MS nurse practitioner Pamela Davies discusses how treating the whole person may help to calm overly sensitized nerve signaling and reduce some of the triggers that can cause pain or make it worse. We hope you will find this topic informative.



Ruth Ann Marrie, MD, PhD

The NARCOMS surveys ask about the experience of pain to find out more about how this symptom may impact your employment, quality of life and other aspects of your life. We report on the level of pain among NARCOMS participants in the *Snapshot* column in this issue.

As always, thank you for taking the time to complete the NARCOMS surveys and for your ongoing participation in the registry. We value your contributions highly and we are always open to hearing from you.

Sincerely,

Ruth Ann Marrie, MD, PhD
Scientific Director, NARCOMS



Pain in Multiple Sclerosis

What Causes It? What Can Be Done to Manage It?

Margot, age 62 years, has had multiple sclerosis (MS) for over 20 years. She uses a cane or occasionally a walker to help her get around. Recently, pain has become one of her more noticeable symptoms. This took her by surprise because she had thought MS was not supposed to cause pain.

Brett Stacey, MD, Medical Director at the University of Washington Center for Pain Relief, frequently treats people with MS. "About 30 years ago, we were taught that MS was not a particularly painful condition," Dr. Stacey said in an interview with *NARCOMS Now*. Pain in MS still tends to be overlooked or under-treated. However, there is now more awareness about what causes pain in MS and what can be done to manage it.

Moderate to severe pain affects about 40% to 60% of people with MS, according to

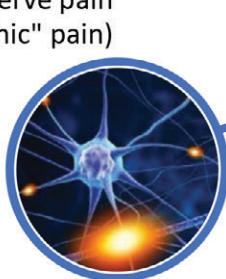
NARCOMS data. People with advanced MS are more likely to have pain, and to have more severe pain. The sources of pain can vary, Dr. Stacey explained, because multiple types of pain can occur in people with MS (See **Figure 1**). One of the more common types is neuropathic pain (nerve pain), brought on by damage to the nervous system. But people with MS also may have pain due to other causes, such as spasticity or musculoskeletal problems.

Neuropathic Pain

The brain acts as the control center for pain, with the job of interpreting sensations from the body. Pain can serve to signal danger: touching a hot stove, for example, or trying to stand on a sprained or broken ankle. Sometimes, the pain signaling system is overly sensitive or does not work properly. This is the case for

Figure 1. Types of Pain in MS

Nerve pain
("Neuropathic" pain)



Trigeminal neuralgia



Spasticity



Muscle or joint pain
("Nociceptive")

neuropathic pain, which is thought to be due to faulty or overly sensitive signaling of the pain messaging system in the spinal cord or brain. In MS, the faulty signal may be caused or made worse by inflammation in the nervous system.

“There isn’t a hallmark, or typical description, for neuropathic pain in MS,” Dr. Stacey noted. “Other nerve pain conditions, like migraine, tend to have typical patterns. But in MS each person’s experience is quite different.” This could mean feeling extra-sensitive to touch in some areas, a stabbing sensation, or an overall feeling of achiness (See Figure 2).

“Treatment for neuropathic pain, at least for now, involves trying to calm down or adjust the behavior of the nervous system that is sending the faulty pain signals,” Dr. Stacey said. Some antidepressant drugs are effective in treating neuropathic pain. This is not because the pain is thought to be caused by stress or depression, he cautioned. Antidepressant drugs act on the neurotransmitters (chemical signals) that are involved in faulty pain signals. Other treatments which may be used to treat pain are shown in Table 1 on page 6.

Spasticity

Spasticity is a common and debilitating MS symptom. Spasticity affects over 80% of people with MS and can happen at any stage of the disease. Spasticity in MS is caused by lesions that damage the brain cells controlling motor function. This results in involuntary activation of the muscles, or abnormal muscle tightness. A person with MS experiences spasticity as persistent muscle stiffness, often in combination with spasms

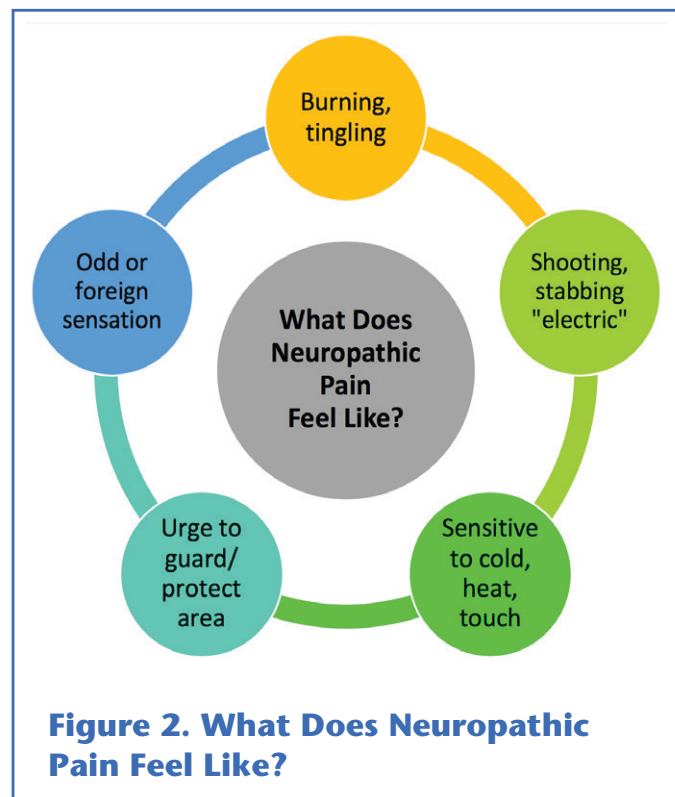


Figure 2. What Does Neuropathic Pain Feel Like?

or jerking. This painful condition can often be managed at the source, by treating the underlying spasticity. Baclofen is a medication often used to treat spasticity. There are other medications that can be used if baclofen is not helpful. A regular stretching program and exercise can be very helpful in treating spasticity, to improve movement and posture, and prevent permanent shortening of muscles (contractures).

Trigeminal Neuralgia

Trigeminal neuralgia (TGN) is a neuropathic pain syndrome that affects the face. The trigeminal nerve is responsible for sensation (feeling) in the face (See Figure 3). It also controls the muscles in the jaw. With MS, the myelin or insulation lining the trigeminal nerve may be damaged. The pain is sudden, and shoots into the face most often along the cheek or jaw. Pain from TGN may be triggered

Table 1. Medications Used for Pain in Multiple Sclerosis

Type of Pain	Drug Categories Used	Comments
Neuropathic Pain Preferred Choices	Some antidepressants <ul style="list-style-type: none"> • Selective norepinephrine reuptake inhibitors (SNRIs) • Tricyclics Some antiseizure drugs	Combine with wellness approaches. Selective serotonin reuptake inhibitors (SSRIs) are usually not effective for neuropathic pain.
Neuropathic Pain Other Options	<ul style="list-style-type: none"> • Lidocaine patch • Capsaicin 8% patch • Tramadol (similar to an opioid) • Botulinum toxin 	Opioids usually not recommended except in cases of severe pain
Trigeminal Neuralgia (a type of neuropathic pain)	Antiseizure drugs	Surgical options may be appropriate for some people
Musculoskeletal Pain	<ul style="list-style-type: none"> • Anti-inflammatory drugs • Antidepressants • Muscle relaxants (short term) 	
Spasticity	<ul style="list-style-type: none"> • Baclofen (oral or pump) • Botulinum toxin 	

by drinking, chewing, tooth brushing, shaving, vibrations from riding in car, or others. Pain also may occur with no trigger, and at times can be severe and disruptive.

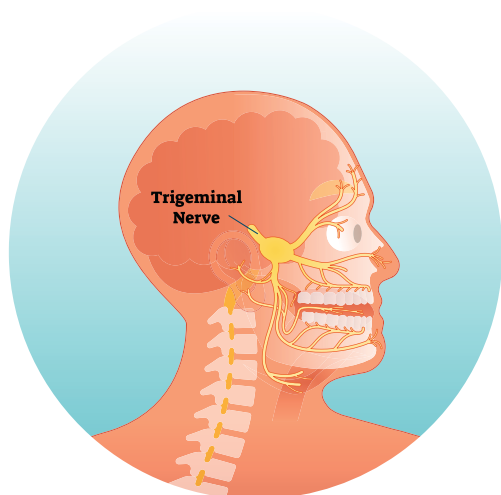
TGN is more common in people with MS than in people without MS. In 2009, almost 1 in 10 participants in the NARCOMS Fall survey reported having TGN. An antiseizure drug

called carbamazepine is one method used to treat TGN, Dr. Stacey said. There are surgical approaches as well, including “gamma knife” radiosurgery and nerve decompression. Dr. Stacey noted that surgery tends to be most successful if the TGN pain is intermittent, rather than constant.

What About Musculoskeletal Pain?

Everyone has experienced pain from an injury or damage to part of the body. This can include anything from a sports injury such as a pulled muscle or ligament, to skin damage or tooth pain. This type of pain is called “nociceptive.” In many cases, this pain goes away gradually as the affected area heals. According to Dr. Stacey, pain should not always be “blamed” on MS or assumed to be neuropathic. The pain may be caused—or made worse—by joint damage, or a postural or seating problem that can be addressed.

Figure 3. Trigeminal Nerve



Nociceptive Pain

Injury or Tissue Damage

- Postoperative pain
- Low back pain (due to injury)
- Muscle, bone, or ligament damage
- Skin damage or disease
- Arthritis (joint pain)

Neuropathic Pain

Lesion or Dysfunction in Nervous System

- Postherpetic neuralgia (with herpes zoster or “shingles”)
- Multiple sclerosis
- Low back pain (chronic, neuropathic)
- Trigeminal neuralgia
- Diabetes
- Other chronic pain syndromes

In fact, many people with MS have what is called “mixed” pain from multiple sources, and need treatment that uses a combination of approaches.

Evaluating and Treating The Whole Person

It is very important for the possible sources of pain to be evaluated properly, stressed Pamela Davies, MS, ARNP, a neurology nurse practitioner at the University of Washington’s Multiple Sclerosis Center in Seattle. Pain “scales” that ask people to rate their pain from 0 to 10 are sometimes used. But what is more helpful is to find out how the pain affects the person’s daily life. Does it keep you from sleeping? Functioning at work and in daily activities?

“I tell my patients that their pain may be due to pain signals that are misfiring, rather than a structural problem,” she said. “So we need to try to change how that pain signal is being sent from the brain into the body, instead of the other way around.” This concept focuses

on trying to turn down or calm those pain signals. Or, as Ms. Davies explains it, “Turn down the signal on the radio dial.

“Treating the factors that can bring on pain or make it worse is an important part of treating pain in MS and chronic pain in general,” she noted. Instead of focusing on one approach, like a drug treatment, she prefers a whole-body approach. This may include exercise or physical therapy, stress management, or methods that include a bit of both, such as yoga. These treatments help many people adapt to and cope with pain, she explained, but they do not mean that the pain does not have a physical cause. “We know that pain can be aggravated or brought on by stress or poor conditioning, so it is reasonable that working on these issues can help the nervous system’s response and help the body to adapt.

“I tell people with MS, we want to help you to get your body in the best possible condition to support the things that you want to do,” she said.



15-Year Study Suggests Early MRI Signs May Predict How MS Will Progress

Being able to predict early on how a person's multiple sclerosis (MS) might progress over the long term is a problem that has eluded MS experts for many years. A recent long-term study report may provide clues to help answer that question. Investigators from England recruited a group of 178 patients with clinically isolated syndrome (CIS) between 1995 and 2004. Having CIS means that these persons experienced a single clinical attack that appeared to be MS, but they did not meet full criteria for a diagnosis. Magnetic resonance imaging (MRI) scans and clinical evaluations such as Expanded Disability Status Scale (EDSS) were done at the start of the study, after 1 year, and after 3 years to look for early changes.

Dr. Wallace Brownlee of University College London followed up with this same group of people 15 years later to see if any of those early changes could be indicators of how the person's MS had progressed. Of the 166 people (93%) who were able to be evaluated, 72% had developed MS, 27% remained in the CIS stage, and 1% had conditions other than MS. Overall, the patients did well and many of them had not received any disease-modifying treatment, even after diagnosis.

Among people who developed MS, having

“Being able to predict how a person's MS might progress will mean more certainty, better treatment choices, and hopefully better long-term outcomes for everyone living with the condition.”

— Wallace Brownlee, PhD

more gadolinium-enhancing lesions in the brain or even a single lesion on the spinal cord at the start of the study helped predict whether the person would have greater disability after 15 years, or have secondary progressive MS (SPMS). The risk of SPMS was especially high for those who had any lesions on the spinal cord. Risk for reaching SPMS in 15 years was:

- 45.5% for those who had at least two brain lesions and one spinal cord lesion at the beginning of the study
- 5.3% for those with no brain or spinal cord lesions at the study's start.

These findings offer important information about treatment, Dr. Brownlee noted in an interview, because they can be useful in counseling patients with early MS about long-term prognosis, and personalizing treatment plans based on predictions of disease severity.

Reference: Brownlee WJ, Altmann DR, Prados F, et al. Early imaging predictors of long-term outcomes in relapse-onset MS. *Brain*. 2019 Aug 1;142(8):2276-2287.

Update from Consortium of Multiple Sclerosis Centers Annual Meeting

Earlier this year, over 2,200 people involved in the care and treatment of multiple sclerosis (MS) met in Seattle, Washington for the Consortium of Multiple Sclerosis Centers (CMSC) 33rd Annual Meeting. Each year, the CMSC meeting focuses on educating MS care professionals and encouraging collaboration in research and treatment of MS.

New Program for People with MS

For the first time, the CMSC meeting offered a special educational program, “More About MS.” This program was designed especially for people with MS and their care partners. Several local NARCOMS participants were among those attending. Led by veteran MS professionals, the program included an extensive discussion session for exchange of questions and ideas. “Our goal for this program is to help people affected by MS to gain an objective understanding of the most up-to-date information in this rapidly changing field,” said program chair Randall T. Schapiro, MD. “It makes sense to combine the expertise of MS care professionals with the unique insights of people with MS and their care partners.”

Future of MS Imaging

In a scientific session, “The Future of MS Imaging,” Andrew Solomon, MD, of the University of Vermont reported on a new MRI technique to locate a central blood vessel or “central vessel sign” within MS lesions. “MS lesions typically form around small veins,

or venules, in the brain,” explained CMSC educational chair Corey Ford, MD, PhD, in an interview following the session. “With advanced imaging techniques, we can actually see those veins inside of the lesions.” This can help to differentiate MS from other conditions, he said, because similar-looking lesions in conditions such as migraine do not have that central vein.

Genetic Risk

Sergio Baranzini, PhD, of the University of California San Francisco Institute for Human Genetics chaired a symposium on genetic risk. “MS is one of the success stories of modern genetics,” he noted. “While the exact origins of MS still remain a mystery, new information about the human genome has aided in our understanding of the root causes of MS.” Researchers have been able to identify specific gene variants that may be responsible for at least some of the genetic susceptibility of MS. We are pleased to report that over the years hundreds of NARCOMS participants and their family members have submitted DNA samples for some of this research and thus contributed to the recent breakthroughs.

Myelocortical MS

Cleveland Clinic researcher Bruce Trapp, PhD, described the latest findings on myelocortical MS. This is a newly discovered form of the disease in which nerve damage occurs in the absence of inflammation. “This suggests that neurodegeneration and demyelination in MS are independent events,” Dr. Trapp said. “If so, we should consider development of therapies that protect those neurons that still have myelinated axons [nerve fibers].”

Fatigue is Common in MS But May Be Improved By Exercise and Rehabilitation, Studies Show

Fatigue is considered the most common symptom in multiple sclerosis (MS). It affects over 75% of people with MS. Fatigue also impairs quality of life for people with MS.

Three recent studies by researchers from Glasgow, Scotland looked more closely at the relationship between fatigue and other aspects of MS. In a survey of 412 people with MS, fatigue was reported by 64% of people with relapsing MS and 81% of those with progressive MS. In both groups, worse fatigue was associated with cognitive problems, more

anxiety and depression, and poorer quality of life. Fatigue was also associated with poor sleep quality.

For people who suffer from fatigue, the very idea of exercising may seem impossible. However, these researchers found that higher aerobic capacity was associated with lower levels of fatigue. Aerobic capacity refers to the amount of oxygen available for muscle cells during sustained activities involving large muscles, such as running, cycling or swimming. "This finding highlights the potential role of aerobic exercise interventions in managing fatigue," reported lead author Scott Rooney of Glasgow Caledonian University.

Rehabilitation is another way to help relieve fatigue in people with MS. Most of these studies have been done in people with relapsing MS. Rooney and colleagues found some studies that showed beneficial effects of exercise, rehabilitation, and behavioral interventions in people with progressive MS as well. These findings suggest that exercise programs and rehabilitation efforts should be considered to manage fatigue regardless of the stage of MS.

References:

Rooney S, Wood L, Moffat F, Paul L. Prevalence of fatigue and its association with clinical features in progressive and non-progressive forms of multiple sclerosis. *Mult Scler Relat Disord*. 2019 Feb;28:276-282.

Rooney S, Wood L, Moffat F, Paul L. Is fatigue associated with aerobic capacity and muscle strength in people with multiple sclerosis: a systematic review and meta-analysis. *Arch Phys Med Rehabil*. 2019 Aug 6.

Rooney S, Moffat F, Wood L, Paul L. Effectiveness of fatigue management interventions in reducing severity and impact of fatigue in people with progressive multiple sclerosis: a systematic review. *Int J MS Care*. 2019 Jan-Feb;21(1):35-46.





MS MESSENGER

WHAT TO EXPECT ON THE NEXT NARCOMS SURVEY

Fall 2019 Survey Preview

In the NARCOMS Registry Fall 2019 update survey, scheduled for early October, you can look forward to seeing some much-requested changes! After reviewing comments from many registry participants, we have decided to remove the Performance Scales® (PS) from the questionnaire. Many of you reported that those scales did not adequately represent your experiences and it was hard to remember the time before you had MS. We have chosen to replace the PS with the more concise SymptoMScreen. Most of you are already familiar with these questions because we have tested this instrument over the past two years.



The SymptoMScreen is a tool developed to quickly screen for the severity of 12 different symptoms commonly affected by MS. Using the SymptoMScreen allows us to shorten the survey length while still being able to assess how each symptom area affects you.

You will also notice the new Health Utilities Index® (HUI) in this survey. We

are considering this measure for use in future NARCOMS surveys as well. The HUI is used by many research groups to evaluate functional abilities and health-related quality of life across different chronic conditions. The HUI is also used to evaluate the cost benefit of treatments that improve quality of life. Responses to the HUI will allow us compare your individual experiences not only with those reported by others with MS, but also with experiences among people who live with a variety of other chronic conditions.

In addition to some new questions in the fall survey, there are some “oldies but goodies” in this round as well. We have included questions about the use of medications that are not directly related to MS. We will also ask about other health conditions that might affect your lifestyle. Please be on the lookout for this upcoming survey. If you need to update your contact information, please call or email us as soon as convenient. Thank you!

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Performance Scales Questions Copyright Registration Number/Date: TXu000743629 / 1996-04-04; assigned to DeltaQuest Foundation, Inc., effective October 1, 2005. U.S. Copyright law governs terms of use.



SNAPSHOT

WHAT WE CAN LEARN FROM NARCOMS SURVEYS

Pain Assessment: Asking About a Complex Symptom With Simple Questions

Pain is a common symptom reported by persons with MS. Table 1 lists some of the ways pain is described. How often the pain occurs and for how long are also important aspects of pain. Pain is hard to assess because no two people perceive pain in the same way. Sometimes it can also be hard to figure out the cause of the pain, such as whether it is due to MS or another health condition.

In 2005 NARCOMS did a study to see how well the single-item pain question, used in the NARCOMS surveys for decades, would compare to pain questionnaires using more questions.² The single-item pain question worked well. Recently we added the Health Utilities Index® (HUI) to the semi-annual surveys. The HUI includes two questions on pain. This highlights the importance of pain in health-related quality of life.³ Here we summarize nearly 7,000 responses to two of the three pain questions included in the NARCOMS spring 2018 update survey.

The figures here show that men and women report similar pain severity at all disability levels. Overall, increased pain levels are more commonly reported starting at Patient Determined Disease Steps (PDDS) level 2 (moderate disability) and upward. Reports of more intense pain increase at PDDS level 8, especially among women. The difference may be due to the small number of male responders at this level.

The fall 2019 survey questions on medications and co-existing health conditions will help us look at pain in more detail. Thank you for your participation in the NARCOMS registry!

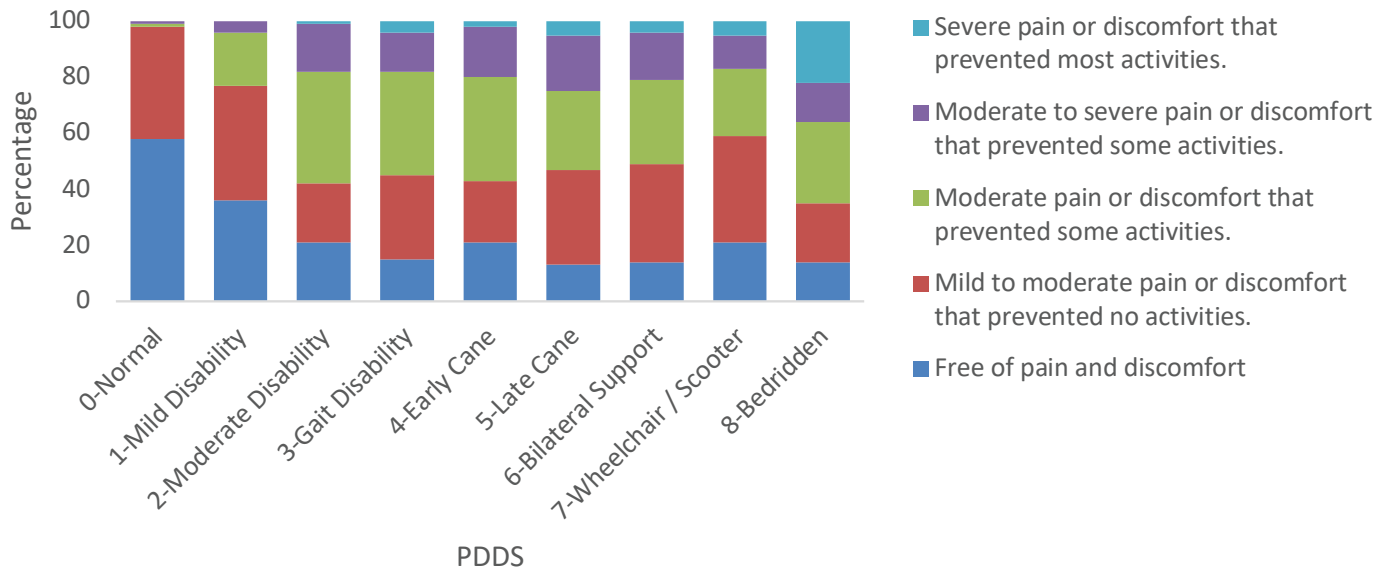
References:

1. Svendsen KB, Jensen TS, Overvad K, et al. Pain in patients with multiple sclerosis: a population-based study. *Arch Neurol.* 2003;60(8):1089-1094.
2. Marrie RA, Cutter G, Tyry T, et al. Validation of the NARCOMS Registry: pain assessment. *Mult Scler.* 2005;11(3): 338-342.
3. Health Utilities Inc. (HUIInc), Dundas, Ontario.

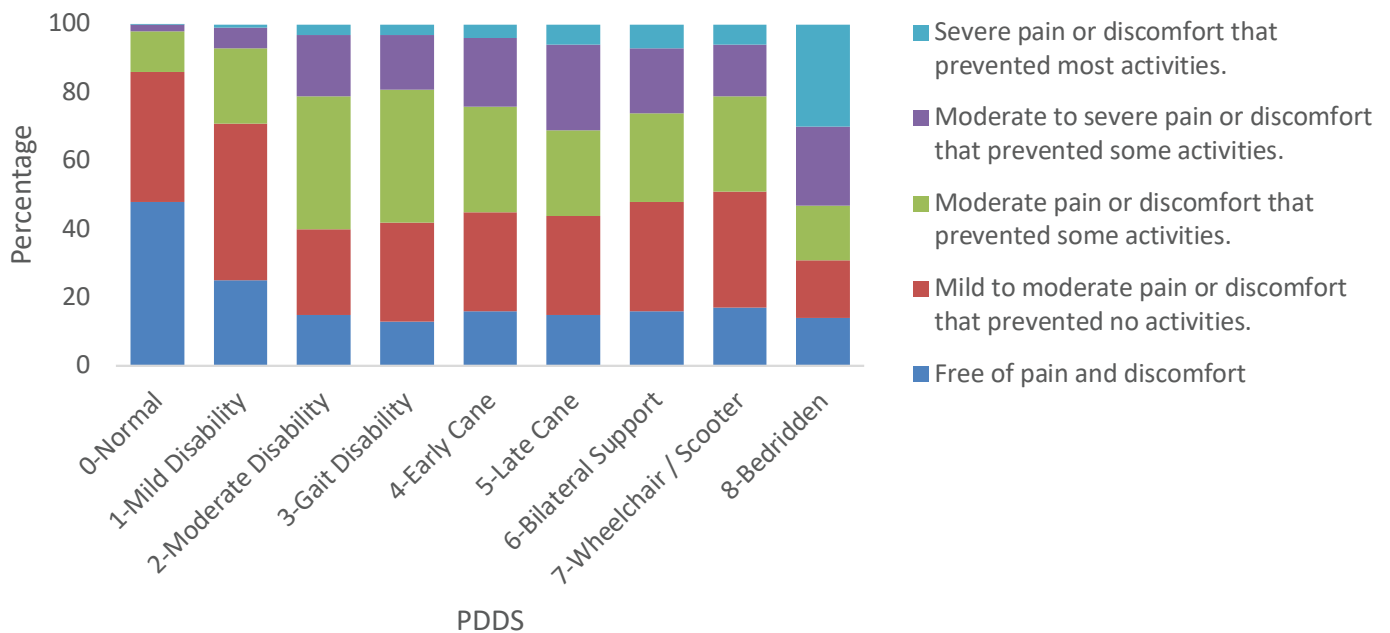
Table 1. Common Pain Descriptions¹

Throbbing	Shooting	Stabbing
Cramping	Gnawing	Hot/burning
Aching	Heavy	Tender
Splitting	Tiring/Exhausting	Sickening

1A. Pain Assessment (Men)



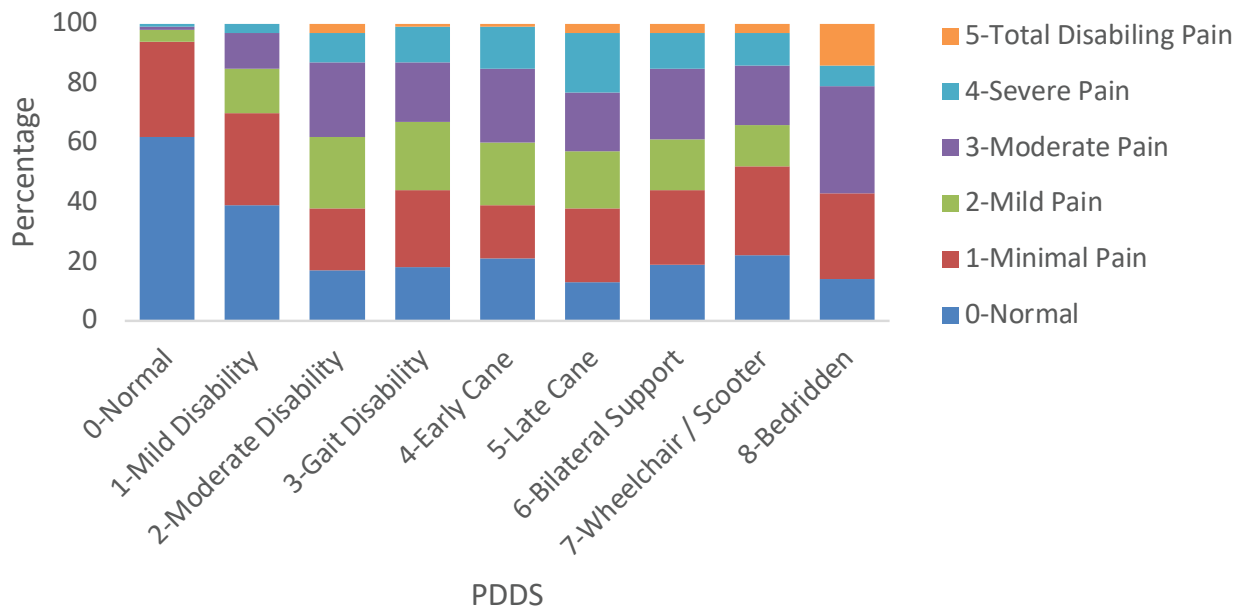
1B. Pain Assessment (Women)



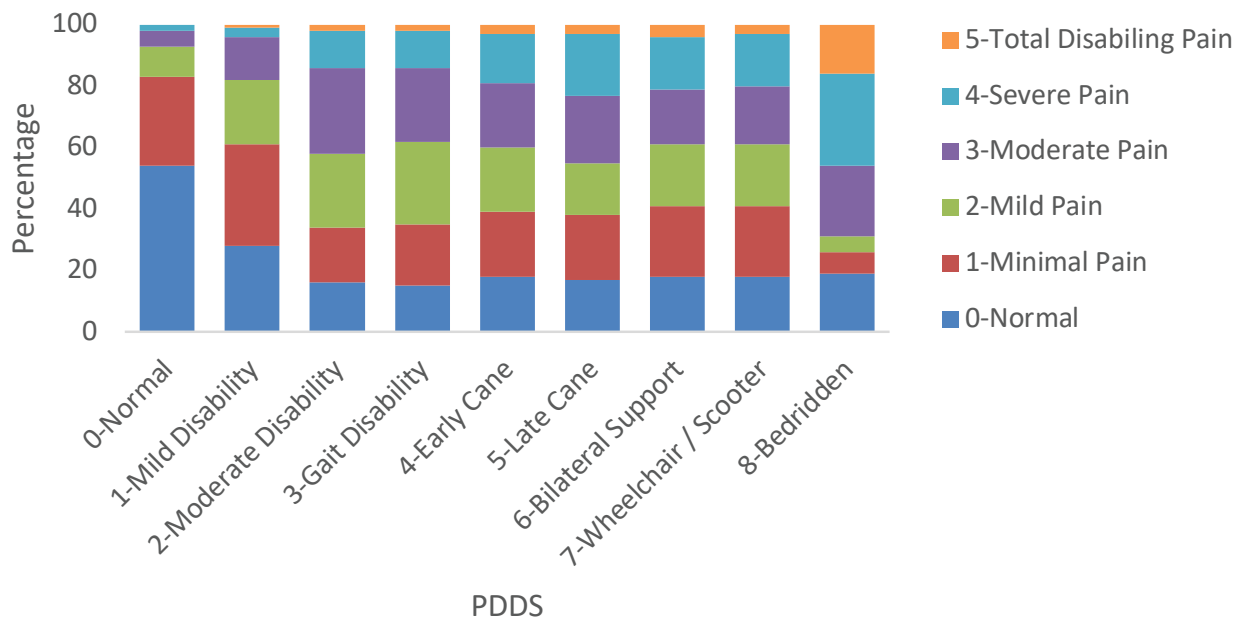
Figures 1A and 1B.

“Pain Assessment: Check the single category that most accurately describes your pain (regardless of cause) in the past month.” Percentage of responses reported at different PDDS levels for A) men (n=1384) and B) women (n=5654). © Health Utilities Inc.

2A. Pain and Discomfort (Men)



2B. Pain and Discomfort (Women)



Figures 2A and 2B:

“Which one of the following best describes the pain and discomfort you have experienced during the past 4 weeks?” Percentage of responses reported at different PDDS levels for A) men (n=1384) and B) women (n=5654).

Play WORDSEARCH

Find the following hidden words relating to Pain.

PAIN
DISCOMFORT
IBUPROFEN
ANALGESIC

ACHE
RELIEF
IRRITATION
CONTENTMENT

SYMPTOM
COMFORTABLE
TENDERNESS
WELLNESS

INFLAMMATION
SPASM
MEDICATION

P L C O M S E E C S S X D I O
P T W O Y S Y R A F Y M I B C
D V T C N T A N J S M Q B R M
R W E S V T D P C Q P N U P N
A M N E T Q E V S C T E P P R
N S D M E H B N A E O Q R N U
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G E N O S S E N L L E W E S A
E H E F E I L E R S W N N O P
S C S C A R W G Q J G Q T U N
I A S N E L B A T R O F M O C
C Q I R R I T A T I O N B E K
D I S C O M F O R T T R N Y P
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NARCOMS NOW

BE PART OF NARCOMS—HELP TO ADVANCE RESEARCH IN MS

Whether you were recently diagnosed with multiple sclerosis (MS) or have lived with it for years, your personal history with the disease helps contribute to improving the lives of others with MS.

Participation in the NARCOMS registry allows you to be part of the process. The data provided by participants gives researchers a clearer picture of how a condition like MS impacts the lives of those affected.

Participation in NARCOMS is confidential—your information is kept secure and completely private. If you have MS and are not yet participating in NARCOMS, or have been out of touch for a while, we would love to hear from you! Contact us at 1-800-253-7884 (toll-free U.S.) or via email at MSRegistry@narcoms.org.



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