

The background of the cover is an abstract composition of numerous three-dimensional cubes. The cubes are rendered in various shades of blue and purple, creating a sense of depth and perspective. They are scattered across the frame, with some appearing in the foreground and others receding into the background. The lighting is soft, casting gentle shadows and highlights on the faces of the cubes, which adds to the three-dimensional effect.

PROGRESSIVE MS: A SHARPER FOCUS

WHERE IN THE WORLD IS THE NARCOMS DATA?

Between 2010 and 2015 researchers published 44 research articles utilizing the NARCOMS registry data that you provide.

SOME QUICK FACTS ABOUT THESE RESEARCH PROJECTS:

- » **97.8% used enrollment data**
- » **86.4% used update data**
- » **63.6% used the Patient-Determined Disease Steps (PDDS)**
- » **59.1% also used a special section or ancillary study**
- » **11.4% used all available data**
- » **22.7% used multiple years with enrollment (3 or more updates)**
- » **63.6% used a single year with enrollment (1-2 updates)**

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THE CONSORTIUM OF
MULTIPLE SCLEROSIS CENTERS

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A Letter from the Director - Summer 2015

Greetings,

Progressive MS—the less-talked-about form of MS—is seeing a resurgence of focus by researchers, by caregivers, and more. While rarer and currently more confounding than the relapsing-remitting form of the disease, today progressive MS is being studied with renewed effort.

In our **“Feature Focus”** article, we examine some of the most recent research efforts to better understand progressive MS and potentially treat it. These include clinical trials and longer term research studies. In addition, international alliances have been formed to foster collaborative research and treatment for progressive MS, uniting MS professionals from around the world to gain insight into this rare form of the disease.

“MS News” this issue highlights several research studies presented at the recent American Academy of Neurology annual meeting (in April, 2015), where progressive MS research featured prominently. The meeting is a forum for internationally known researchers and clinicians to present the most up-to-date study results. From remyelination in optic neuritis, to antiepileptic drugs and a high-dose form of vitamin B to treat progressive MS, you can read about the research here. **“MS Blogs”** takes a closer look at blogs by MS-related organizations.

“Snapshot” too hits on progressive MS in NARCOMS participants, as well as where you fall on the Patient-determined Disease Steps (PDDS) scale, and spasticity, with numbers based information you provided on the Fall 2014 survey.

In **“MS Reflections,”** **Dr. Gary Cutter**, Deputy Director, NARCOMS Data Coordinating Center, addresses secondary progressive MS, specifically, looking at changes in disease progression as measured by the PDDS in NARCOMS surveys.

Welcome to summer, and thank you for taking part in our most recent Spring Survey. As this issue goes to press, our research and editorial teams will be presenting NARCOMS research at the **Consortium of Multiple Sclerosis Centers** annual meeting, May 27–30, a great way to kick off a summer of the latest MS news and research.



Dr. Ruth Ann Marrie is a Don Paty Career Scientist, practicing neurologist and Director of MS Clinic at University of Manitoba Health Sciences Center in Winnipeg, Canada.

Best,



Dr. Ruth Ann Marrie
Managing Director, NARCOMS

NARCOMS INFORMATION CORNER



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Reminder When Completing Paper Surveys:

Please use pen rather than pencil when filling out NARCOMS paper surveys. Responses are scanned to electronic files for data capture and pen is easier to read. Thanks!

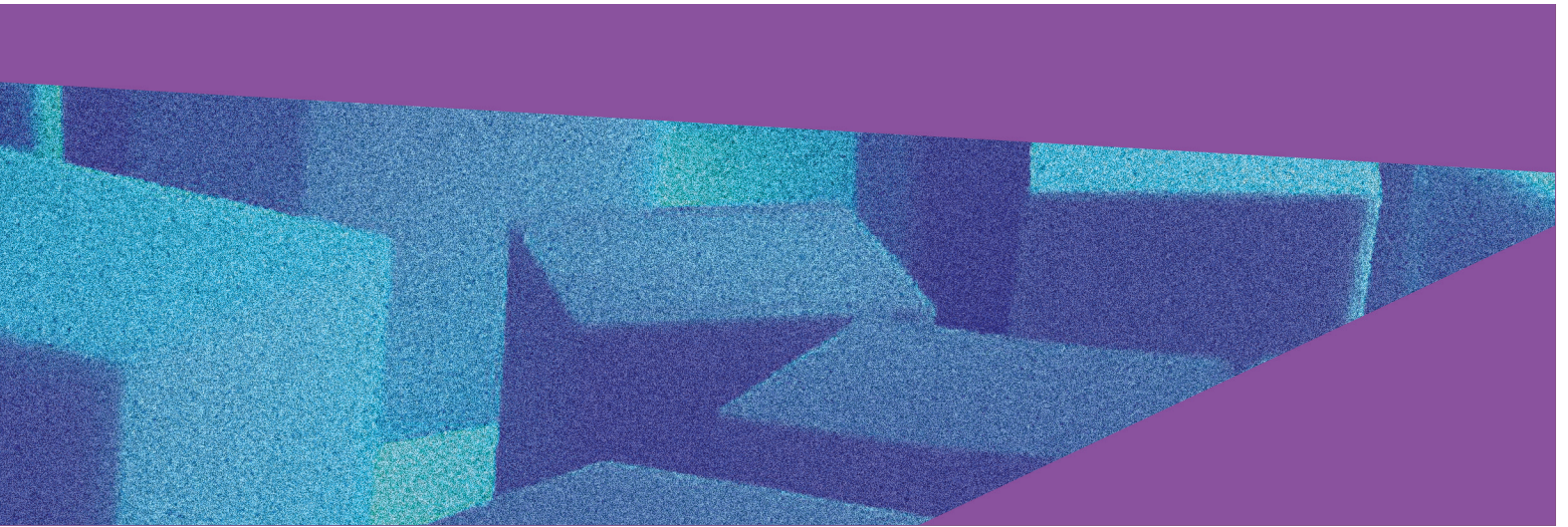
PROGRESSIVE MS: A SHARPER FOCUS

Progressive multiple sclerosis is an unique form of multiple sclerosis distinguished from the relapsing-remitting forms of the disease by nerve degeneration (the breakdown of nerves), rather than inflammation (the swelling of nerves). Researchers funded by grants from places such as the National Institutes of Health (NIH), the National Multiple Sclerosis Society (NMSS), the International Progressive MS Alliance, and more are working to answer these common questions about progressive MS:

- **What causes degeneration of nerve fibers—thought to be the cause of long-term disability—and how can that be stopped or reversed?**
- **What factors influence the transition from relapsing stages of MS to progressive MS?**
- **Can disease-modifying therapies prevent, delay, or slow long-term MS progression?**
- **And ultimately, what new therapies will stop progressive MS?**

THERE ARE THREE TYPES OF PROGRESSIVE MS:

1. Primary-progressive multiple sclerosis (PPMS) is characterized by steady worsening of neurologic functioning, without any distinct relapses (attacks or exacerbations) or periods of remission. The rate of disease progression may vary over time, but it is continuous.
2. Secondary progressive MS (SPMS) comes on after the relapsing-remitting disease course (RRMS).
3. Progressive-relapsing MS (PRMS) is the least common of the disease courses, occurring in approximately five percent of those with MS. PRMS is recognized by the same progression as PPMS, with occasional relapses—thus individuals with PPMS are re-diagnosed with PRMS when they experience a relapse.



OTHER WAYS IN WHICH PROGRESSIVE MS IS UNIQUE:

- Individuals with PPMS tend to be older at the time of diagnosis, averaging age 40.
- Nearly equal numbers of women and men develop PPMS, whereas in other types of MS, women outnumber men three to one.

Despite recent advances in the treatment and understanding of relapsing-remitting MS, progressive MS remains largely unknown. There are 12 FDA-approved treatments for RRMS, yet researchers are still on the hunt for a treatment for progressive MS. Several recent efforts, including funding for research and international alliances to foster collaboration, are targeting this rare form of multiple sclerosis.

“Treatment options in progressive MS are extremely limited in the absence of relapses,” said NARCOMS researcher Dr. Robert Fox, Medical Director, Mellen Center for MS at the Cleveland Clinic. “There is great need for safe, effective, and conveniently-administered therapies for progressive MS.”

Renewed Research Efforts

Nearly every treatment approved for relapsing-remitting MS has been studied or is undergoing testing for effectiveness in progressive MS. In progressive MS, the degrees by which the disease worsens often aren’t as well known or as easily measured as in other forms of the disease. This can make it hard to determine which therapies are impacting progression.

The results of several new studies on progressive MS were presented at the recent **American Academy of Neurology (AAN)** annual meeting in April 2015. For more information, read “MS News,” page 18.

The **Serial Unified MS Multicenter InvesTigation, or SUMMIT**, study began in 2010 with sponsorship from the National Multiple Sclerosis Society. It aims to accelerate MS research by establishing an international consortium of researchers based at MS centers in Boston; San Francisco; Basel, Switzerland; and Amsterdam. Collectively, the consortium is following 1,500 people with MS, with a goal of distinguishing what causes the disease to progress more rapidly in some people than in others.

“The big unanswered question is why MS sometimes progresses and sometimes does not,” says SUMMIT consortium leader Dr. Howard Weiner, Brigham and Women’s Hospital, an expert on MS research and clinical care. “We’re going to find those answers, and it will mark an important step toward understanding how to approach a cure.”

Researchers at each of the four participating institutions are looking at potential disease triggers and risk factors for MS by testing patients using MRI scans, blood tests, genetic analyses and physical exams. They are also considering environmental factors such as smoking and sun exposure, plus the influence of family history and hormone levels.

The **SPRINT MS trial** is a clinical trial in progressive MS looking at the effectiveness of the drug ibudilast, an anti-inflammatory drug traditionally used in to treat asthma and stroke. The trial also compares five different imaging metrics to see which is the best measurement in progressive MS. If that can be understood, it may ease the way to conducting phase 2 trials in progressive MS. (Phase 2 moves testing of a drug or treatment from a small number of individuals to a larger group, to evaluate

safety and effectiveness). Dr. Robert Fox is the principle investigator for this study, which is being conducted by the NeuroNEXT Network for Excellence in Neuroscience Centers, established in 2011 by the National Institute of Neurological Disorders and Stroke (NINDS; www.neuronext.org).

Dr. Fox also points out that despite the effectiveness of MRI in relapsing-remitting MS to diagnose and monitor changes, “new lesions aren’t developed in progressive MS. And so we need to have a different metric, a different measurement stick of what therapy looks potentially promising,” he said.

Stem cells are another area of intense research in all types of MS. In another phase II study of 21 patients with MS whose symptoms were not improving, all of the participants received medications to suppress immune system activity. Then 12 of the participants received the drug mitoxantrone, which reduces immune system activity. For the other nine participants, stem cells were harvested from their bone marrow. After the immune system was suppressed, the stem cells were reintroduced through a vein.

Over time, the cells migrated to the bone marrow and produced new cells that became immune cells. The participants were followed for up to four years, in a study supported by the Italian Multiple Sclerosis Foundation.

“This process appears to reset the immune system,” said lead author Dr. Giovanni Mancardi of the University of Genova in Italy, in a news release from the American Academy of Neurology. “With these results, we can speculate that stem cell treatment may profoundly affect the course of the disease.”

Results appeared in “Autologous Hematopoietic Stem Cell Transplantation in Multiple Sclerosis,” published in the journal *Neurology* in February 2015.

The International Progressive MS Alliance is a recent effort targeted at understanding progressive MS. Established in 2012, the goal of the alliance is to speed the development of treatment for progressive MS by removing scientific and technology barriers.

NARCOMS researcher Dr. Fox sits on the alliance’s Scientific Steering Committee, which guides its scientific direction and research activities. In July 2014, the alliance funded 20 Challenge Awards, covering topics such as new diagnostic tests, rehabilitation, and the repurposing of existing drugs to treat progressive MS. To see the list of all 20 studies funded by the alliance, visit: <http://tinyurl.com/o5oggwv>.

In March 2015, the alliance held a two-day conference in Boston. On March 4, Dr. Fox, joined by panelists Dr. Alan Thompson, Dr. Bruce Bebo, and Dr. Riley Bove and moderated by Kate Milliken (herself an MS patient), participated in a NMSS webcast entitled, “Finding Answers for Progressive MS.” One of the messages from the webcast was that people with progressive MS are not forgotten.

“Ironically, every time there’s a new treatment licensed for relapsing-remitting MS, people with progressive MS feel they’re being left out, they’re not being thought about,” said Thompson. “That’s not the case. There’s a lot of research going on worldwide, but until that research translates into a treatment, it says nothing. People want treatment...if you do assessments across the world—this is very much what people with MS want us to be doing.”



Robert Fox, MD, *Managing Director of NARCOMS*

Several important messages came from the alliance conference, Fox said, including the identification of six to eight mechanisms or explanations for what may be driving progressive MS, “different cells that may be going awry or different pathways within the cells that may be going awry.” In addition, researchers are looking beyond progressive MS to learn lessons from other diseases that may translate into a better understanding of how progressive MS develops, and how to treat it.

Dr. Fox emphasizes that while there may not be a progressive MS-specific treatment available to patients yet, many of the lifestyle choices made by any individual living with MS can positively affect his or her daily life. These include routine exercise, quitting smoking, and managing other medical illnesses, such as diabetes, hypertension, and obesity. As for the future of treatments for progressive MS, Fox said he thinks in the next five to ten years, treatments will be available that can fully control the progression of MS.

Read the article online to see articles and resources referenced in this story:
www.narcoms.org/narcomsnow

Have you ever wondered what is involved in getting a NARCOMS update survey up and running? With Spring and Fall update cycles repeating every year, the Coordinating Center is constantly working on some aspect of the update cycle. Here's a look at our year!

Spring Update	Fall Update	Coordinating Center Activities
January	& July	Finalize survey-specific questions for update; get all required approvals for research
February	& August	Program online update survey; order supplies for paper printing
March	& September	Start printing paper update, test online survey (check functionality on different types of computers and internet browsers)
April	& October	Mail out paper surveys, finalize online survey, send emails to online participants
May	& November	Begin data entry for paper surveys received, send postcard & email reminders
June	& December	Continue data entry, send out final reminders to participants, close update

Should you ever have a question about NARCOMS or an update survey, please call or email us at: 1-800-253- 7884 (toll-free US) and narcomsnow@narcoms.org.
Thank you for your continued participation!

MS APPS (& BLOGS)

This installment of MS-related apps and blogs focuses on multiple sclerosis-themed blogs. This first installment will look at organization-based blogs; look for coverage of personal blogs in our Fall issue. *NARCOMS* and *NARCOMS Now* do not endorse the use of any particular drugs or treatments for multiple sclerosis.

MS Connection Blog — www.msconnection.org

The MS Connection Blog is a recent addition by the National MS Society to their web offerings. Featuring articles and columns written by clinicians, patients, caregivers and more, MS Connection provides up-to-date coverage of conferences and the latest MS news, as well as personal stories of how individuals cope with MS. The blog provides an online platform for additional information not already covered in the NMSS website or in their magazine, *Momentum*. A recent article, “The Plot Thickens on Diet and MS,” by clinical psychologist Nicolas LaRocca, PhD, for example, follows up on an earlier piece about diet and nutrition in treating or preventing MS. (See *NARCOMS Now*’s own interview with NMSS nutritionist Denise Nowack on the topic: <http://www.narcoms.org/narcomsnow/featurefocus/winter2015/page1>)

MultipleSclerosis.net — www.multiplesclerosis.net

This blog is designed to provide tools and resources for disease management. It features articles and information contributed by caregivers, patients, and healthcare professionals, with the aim of improving patients’ quality of life.

The blog’s editorial content is Health On the Net Code certified—a foundation that reviews health content for accuracy. “Guest Experts” contribute articles on specific topics featured in the MultipleSclerosis.Net “Newsfeed.” The author of each of these articles is clearly marked

along with a link to the author’s profile. These are unedited by MultipleSclerosis.net, as they represent the thoughts, opinions and judgment of their authors. The blog is run by Health Union, a for-profit company creating online “communities” for individuals living with chronic illnesses. Any sponsored content (while minimal) is clearly marked as such.

MS Conversations — blog.mymysaa.org

MS Conversations is the official blog of the Multiple Sclerosis Association of America (MSAA), a nonprofit organization “dedicated to enriching the quality of life for everyone affected by multiple sclerosis (MS).” Posts are written in large part by MSAA volunteers and employees, on topics ranging from how to tell someone you have MS or how to stay organized, to recaps of recent MSAA events or research updates.

Multiple Sclerosis Research — multiple-sclerosis-research.blogspot.com

The **Multiple Sclerosis Research** blog for the Blizard Institute of Barts and The London School of Medicine and Dentistry is spearheaded by Dr. Gavin Giovannoni. This blog posts and interprets MS research information from the London School for the layperson.

Here you can learn about new developments in treatments and medications. There’s even a helpful “Junk-the-Jargon Bell,” a form where you can submit medical and professional jargon you don’t understand for bloggers to interpret.



Q: How does NARCOMS pick who gets interviewed or what research gets featured in *NARCOMS Now*?

A: The process starts with a *NARCOMS Now* production meeting every January, where we plan the themes and topics for the next 4 issues. From there we look for three main types of articles that fit with the theme of each issue:

1. Interviews with experts on the topic, such as the interview with Dr. Jerry Wolinsky on MRIs:

<http://www.narcoms.org/narcomsnow/pdfs/NARCOMSNowSpring2013.pdf>

2. Articles about MS research (that may also contain interviews), such as the review of 20 years of interferon:

<http://www.narcoms.org/narcomsnow/pdfs/NARCOMSNowWinter2013.pdf>

3. Articles summarizing NARCOMS research, such as the MS Reflections on switching therapies:

<http://www.narcoms.org/narcomsnow/pdfs/NARCOMSNowFall2014.pdf>

What about the other sections?

- “Q&A” comes from questions we get from NARCOMS participants (that’s you!) either in update survey comments, email, or telephone calls.
- “Survey 101” generally focuses on changes or upcoming topics in the updates
- “MS News & Clinical Trials” are selected based on what is new and what is relevant to the NARCOMS participants – there is so much news to report that we recently expanded this section to 4 pages!
- The same goes for “MS Apps & Blogs” – we try to feature a variety of topics that fit with the theme and are likely to appeal to a wide number of participants.
- Most importantly “Faces of NARCOMS” features personal reflections from NARCOMS participants about their own MS stories. We encourage you to submit yours and let our staff help you fit it into one page, so you can inform and inspire others living with MS!
- Remember, if you ever have an idea or question relating to *NARCOMS Now*, please feel free to call or email us at: 1-800-253-7884 (toll-free US) and narcomsnow@narcoms.org.

**To submit a question for Q&A please email
narcomsnow@narcoms.org**

Cost of DMTs in US Soaring, Study Shows

We do not need to tell you that the cost of MS medications—and disease-modifying therapies in particular—is extremely high. A recent study of the cost of MS medications in the United States verifies that MS drugs cost a lot, and prices may be rising higher than the cost of drugs for other chronic illnesses.

The study results were published April 24 in the journal *Neurology*, and presented at the American Academy of Neurology annual meeting in April. The study looked at the cost of disease-modifying therapies, or DMTs, over the last 20 years. It compared changes in DMT costs to general and prescription drug inflation during the same period.

The results suggest that first-generation DMTs, which originally cost \$8,000–\$11,000 per year, now cost about \$60,000 per year. Their costs have increased annually at rates five to seven times higher than overall prescription drug inflation. And newer DMTs commonly entered the market with a cost 25–60 percent higher than existing DMTs. Costs went up significantly among first-generation DMTs following the FDA’s approval of interferon Beta 1-a (IFN-β-1a SC; 2002) and natalizumab (reintroduced 2006). Costs remained high following introduction of fingolimod (2010). DMT costs in the United States currently are two to three times higher than in other comparable countries such as Canada.

“The issue of astronomical drug costs, especially for newer drugs or rare conditions, is more and more common,” study author Daniel Hartung, an associate professor at Oregon State University’s College of Pharmacy, said in an Oregon State release.

Conducted by researchers at Oregon State University/Oregon Health & Science University, this study concluded that costs for MS DMTs have risen at rates “well beyond inflation and substantially above rates observed for drugs in a similar biologic class.” The authors, led by Daniel M. Hartung, PharmD, MPH, Oregon Health & Science University, suggest there is an “urgent” need for patients, drug manufacturers, and clinicians in the US to confront these soaring costs.

The full text of the article can be found here:
<http://tinyurl.com/lcvb4s3>

NARCOMS at the CMSC Annual Meeting, May 27–30, Indianapolis, IN

As you read this the NARCOMS crew is likely hosting a booth and presenting research based on information provided by you in our biannual surveys at the 2015 meeting of the Consortium of Multiple Sclerosis Centers (CMSC), held May 27–30 in Indianapolis, Indiana. Our researchers will present two posters, on “Patient Perspectives on Insurance Changes and Therapy Decisions in NARCOMS” and “Disease Modifying Therapy & the Decision Making Process for MS patients in NARCOMS.”

In addition, Dr. Stacey Cofield will lead a platform presentation on “Current Marijuana Usage By MS Status and Disability in the NARCOMS Registry,” based on data you provided in our separate survey on marijuana last summer. Look for interviews with individuals presenting at CMSC’s meeting in the Fall and Winter issues of *NARCOMS Now*.

CHARACTERISTICS ASSOCIATED WITH SUSTAINED DISEASE PROGRESSION IN PREVIOUSLY RELAPSING MS PATIENTS — Presented at 2014 CMSC Annual Meeting

Gary Cutter, PhD, Professor of Biostatistics, University of Alabama at Birmingham

BACKGROUND

The new view of secondary progressive multiple sclerosis (SPMS) is based on the idea that MS is a two-part disease: An inflammatory phase that now is widely treated with one of nearly a dozen drugs, and phase with continual worsening called progression.

To manage MS over a lifetime requires a better understanding of the nature and timing of the gradual transition from the relapsing-remitting phase to the continual worsening, progressive phase.

In terms of important long-term research, NARCOMS surveys are an excellent source of information about changes in disease progression as measured by the self-reported Patient-determined Disease Steps (PDDS), this is what is reported by the NARCOMS participants.

STUDY PURPOSE

The goals of this project were:

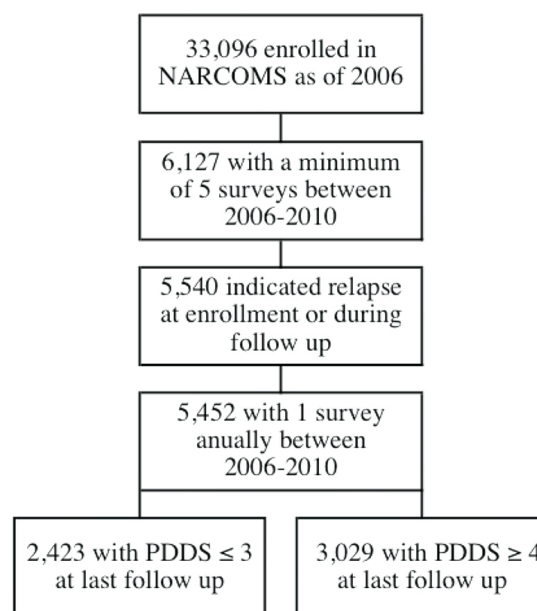
- Describe the characteristics of relapsing-remitting MS (RRMS) in NARCOMS participants who have changes in their PDDS—who are the people that have relapses and changes in the PDDS?
- Estimate change in PDDS over a 5-year period and total follow-up based on starting PDDS and other participant characteristics, such as gender and age—see if changes in the PDDS over 5 years can be predicted based on information provided by NARCOMS participants.
- Determine patterns of PDDS changes and the durability of these changes (how long the change in PDDS lasts), answering questions such as: is this irreversible progression or is this a transient worsening? That is, are the changes reported in PDDS by NARCOMS participants from a relapse or are they progression?

THE PATIENT-DETERMINED DISEASE STEPS SCALE

0	1	2	3	4	5	6	7	8
Mild symptoms, return to normal after an attack	Noticeable symptoms with small effect on my life	No limitations in my walking, significant problems limit daily activities	Do not need a cane, but might need assistance during an attack	Need assistance to walk as far as 3 blocks	Cane to walk 25 feet, scooter or wheelchair for further distances	Two canes, crutches or a walker, scooter or wheelchair for further distances	My main form of mobility is wheelchair	Unable to sit in a wheelchair for more than one hour
Normal	Mild Disability	Moderate Disability	Gait Disability	Early Cane	Late Cane	Bilateral Support	Wheelchair/ Scooter	Bedridden

What NARCOMS information was included?

For this study we included individuals who reported a having a relapse ever (even once) when they enrolled or who reported a relapse between 2006 and 2010. Participants must have completed at least one update survey each year during 2006–2010; been US residents in 2006, and be at least 18 years old. Of all those taking part in NARCOMS as of 2006, 18.5 percent had completed at least one survey in each of five years. Ninety percent of participants had had a relapse and 98.4 percent were US residents. Forty-four percent reported a PDDS score greater than 3 (Gait Disability, see PDDS Figure); while 55.6 percent reported a PDDS less than 3 in 2010.



Participants were mostly women (77 percent), with an average age of 30 years old when MS symptoms started, and average age at diagnosis of 38 years. The average age in 2006 when this project began was 53 years. The PDDS went from a median of 3.4 (just higher than “Gait Disability”) in 2006, to 3.8 in 2010 (just below “Early Cane Use”). The average number of reported relapses in that five-year period was 3.6 over 5 years, or less than 1 per year.

FINDINGS

Several important findings resulted from this research, including the following:

Variable	Improved	No Change	Got Worse	Total
	N=696 (12.8%)	N=2956 (54.2%)	N=1799 (33.0%)	N=5451
Age in 2006	51.72	52.78	52.91	52.69
Disease Duration	7.65	9.42	8.73	8.97
Total Relapses	3.64	3.46	3.70	3.56
Rate of PDDS Change	-0.07	0.05	0.19	0.08
Mean Change in PDDS	-1.43	0	1.46	0.30
% w/Confirmed	11.6%	17.1%	92.2%	41.2%

MS REFLECTIONS

- Those who had had MS the longest had fewer relapses, pointing to relapses decreasing over time.
- Those with the shortest duration of MS were more likely to improve after reporting an increase in their PDDS. Those with MS the longest were the most likely to have fewer disease changes. This can of course be due to the fact that individuals, once their condition worsens, remain there, and those with the least disease duration have a more relapsing remitting course of the disease.
- Of those who started at a PDDS score of less than 4 (“Early Cane”) in 2006 (2,895 individuals), one in three were at or above PDDS 4 in 2010 (~33 percent began using a cane in 4 years). Of those who started at or above PDDS 4, nine out of ten were found to remain at or above this level in 2010 (90 percent were not able to stop using a cane).

CHANGES OVER TIME 2006–2010

In 2010, participants with a PDDS of less than or equal to 4 were more likely to be male, and be older at diagnosis and at enrollment in NARCOMS. They were, however, slightly younger at symptom onset. The younger a patient is, the more quickly they seem to worsen. However, the PDDS does not detect small changes very well once participants reach a score of 4.

The PDDS scale was developed to mimic the clinician-measured Expanded Disability Status Scale (EDSS). The EDSS is a scale to monitor disability changes in MS. Once an individual with MS reaches a higher score on the EDSS, the EDSS mainly focuses on ambulation, or ability to walk and move about.

Gary Cutter, Ph.D.

Dr. Cutter is a Professor of Biostatistics and Head of the Section on Research Methods and Clinical Trials (RMCT Section) at the UAB School of Public Health. Dr. Cutter has a major interest in design, analysis and interpretation of clinical trials, epidemiologic studies and evaluation research.

He directs three multinational coordinating centers; the CombiRx - combination therapy trial in MS; MGTX - a surgical trial in Myasthenia Gravis, both funded by NINDS, and the NARCOMS registry.



CONCLUSIONS

Over an average of almost five years, two-thirds of participants starting at or below PDDS 3 remained less than 3. Males changed more than females, but the amount of change was reduced as participants got older. The amount of change per year in PDDS dropped with age, that is, the measurement of changes in the PDDS was greater at younger ages. The amount of time the worsening lasted (durability of change) increased with PDDS and was unaffected by relapses, that is as the PDDS gets higher, people tended to stay at the higher PDDS with or without relapses. That durability mirrors that reported by Dr. Fred Lublin et.al for the EDSS (“Measuring Enduring Worsening in the CombiRx Study,” presented at the American Academy of Neurology 2014 annual meeting; abstract here: www.neurology.org/content/82/10_Supplement/S34.007).

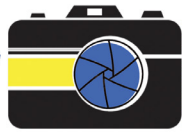
So, while PDDS greater than or equal to 4 and EDSS greater than or equal to 6 are considered a particular hallmark of the disease course (needing a cane to walk)—because once people with MS reach this level they are likely to remain at or above this level (in this study, over 90 percent)—the benchmark is really based solely on walking. More attention needs to be placed on aspects of later disease, not just walking, that can better assess if improvements are occurring, or are possible to achieve with treatment in walking, as well as in other aspects of the lives of people living with MS.

Further research using the individual scales for measuring change, rather than the overall PDDS score, will provide a more complete picture of how the disease affects individuals over time.

WELCOMING NARCOMS FELLOW GUOQIAO “PETER” WANG, PHD

NARCOMS is proud to welcome a new member to our team. Guoqiao “Peter” Wang comes to work with us after completing his PhD in Biostatistics at the University of Alabama at Birmingham (UAB) and joins the staff at NARCOMS’ Data Coordinating Center, based at UAB. Dr. Wang will be presenting “Patient Perspectives Patient Perspectives on Insurance Changes and Therapy Decisions in NARCOMS” at the CMSC meeting in May, discussing how insurance changes affect choice of disease-modifying therapy (DMT), including not taking a DMT.

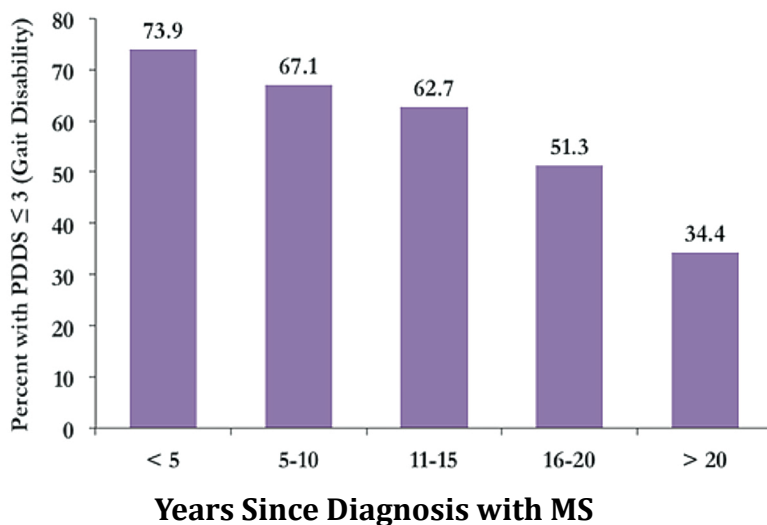
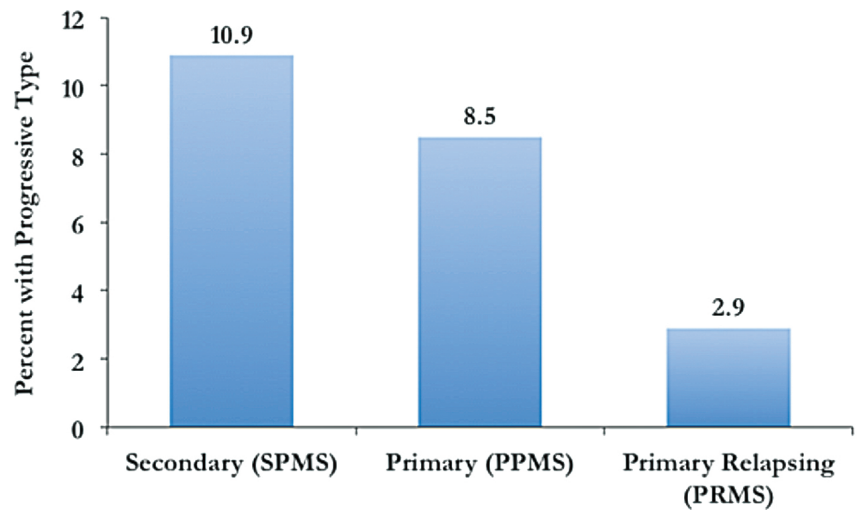




In this issue of *NARCOMS Now*, we present research results on progressive MS (“Feature Focus,” page 4), PDDS and disease duration (“MS Reflections,” p. 12), optic neuritis (“MS News,” p. 18), and a new clinical trial on spasticity (“MS News Clinical Trials,” p. 22). So what do the participants who responded to the Fall 2014 Update look like with respect to these topics?

Progressive MS in NARCOMS

In each survey you tell us about your current MS type. Nearly one in three NARCOMS responders classify themselves into one of the three progressive types of MS.



PDDS and Duration of MS

Overall most of the responders reported a PDDS score between 0 (Normal) and 3 (Gait Disability). The proportion of responders with a score of 0–3 decreases with more years since MS diagnosis.

Those with a more recent diagnosis are more likely to report lower PDDS scores.



Initial MS Symptoms

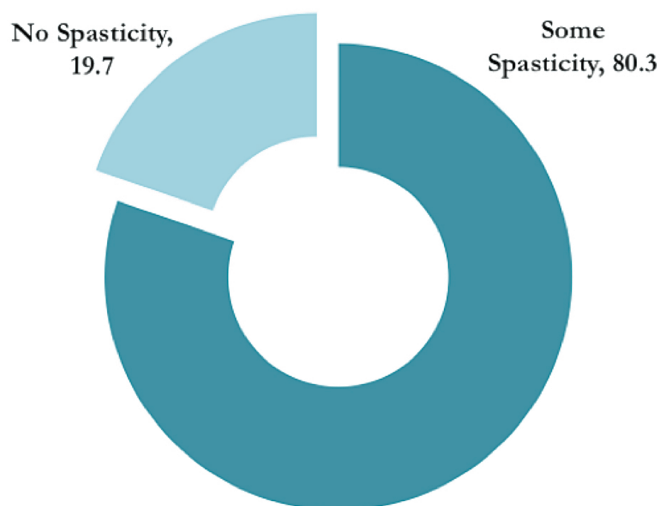
Among those who completed the Fall 2014 update survey, the most common initial MS symptom reported at enrollment was numbness (72 percent). At 31 percent, optic neuritis was the fifth most common first symptom of MS for the Fall 2014 NARCOMS responders.

Percent with Any Level of Spasticity

Spasticity

Spasticity is defined as:

“Unusual tightening of muscles that feels like leg stiffness, jumping of legs, a repetitive bouncing of the foot, muscle cramping in legs or arms or legs going out tight and straight or drawing up”



AAN Roundup

The 67th annual meeting of the **American Academy of Neurology** took place April 18–25 in Washington, DC, with the results of several major MS studies and research announced. We'll cover a few of the highlights here; you can browse abstracts of all research presented at AAN online at: <http://abstracts2view.com/aan/>

Remyelination in MS: First Clinical Evidence (Abstract 9208)

A research team from Biogen Inc., reported that patients with optic neuritis—often one of the first reported symptoms of MS—who were given BIIB033, a monoclonal antibody, saw improved conduction of electrical impulses along the optic nerve between the brain and retina.

Eyes normally transmit visual information to the brain in around 100 milliseconds. Optic neuritis slows this process by 15–40 milliseconds, a delay known as latency, caused by loss of myelin in the optic nerve.

“Patients in this study who were given BIIB033 had an improvement of 40 percent in latency compared with placebo, and they were twice as likely to get back to normal times,” said lead author Diego Cadavid, MD, with Biogen Inc, Cambridge, Massachusetts. “This is giving us confidence that the drug is active and remyelination is occurring. This is the first time that evidence has been seen in humans that we might be able to repair myelin with a drug treatment.”

Monoclonal antibodies are researcher-designed copies of antibodies designed to specifically target a certain antigen—a specific protein in the body.

The generic names of the monoclonal antibody drugs referenced often end with “mab,” such as natalizumab (Tysabri), rituxumab (Rituxan), and alemtuzumab (Lemtrada).

For more information on all therapies, including “mabs,” access the online brochure, “The MS Disease-Modifying Medications,” from the National Multiple Sclerosis Society, <http://tinyurl.com/k273zm6> (current as of January 2015)

“This is the first time that evidence has been seen in humans that we might be able to repair myelin with a drug treatment.” - Diego Cadavid, MD

The monoclonal antibody used in this study targets the LINGO-1 protein expressed only in the central nervous system in axons of neurons and oligodendrocyte progenitor cells (OPCs), which produce myelin.

“The monoclonal antibody targets the LINGO-1 protein so allows the cells to differentiate better and produce myelin again,” Cadavid said.

Laboratory and animal studies have shown enhancement of myelination with the monoclonal antibody, and a phase 1 safety study has also been completed, Cadavid reported.

The current study—known as RENEW—is a phase 2 study looking at whether the drug facilitates new myelin production. These results suggest it does. RENEW involved 82 patients with a first acute optic neuritis episode in one eye.

A second phase 2 study—SYNERGY—is now examining the use of BIIB033 in patients with definite MS of different severities. “This will tell us which population this drug may help the most,” Cadavid said.

NARCOMS researchers published an article about vision-related quality of life in the June 19, 2013, issue of the journal *Multiple Sclerosis*; <http://www.ncbi.nlm.nih.gov/pubmed/23257618>

Antiepileptic Drug Neuroprotective in MS (Abstract # PL2.005)

The antiepilepsy drug phenytoin has been shown to protect retinal nerve cells from degeneration in a new study in patients with optic neuritis. Phenytoin and other sodium channel blockers may be protective against MS, the study suggests.

“While there have been other studies of neuroprotectant agents in MS, our results are the most convincing demonstration of neuroprotection for MS to date,” said lead author Raju Kapoor, MD, National Hospital for Neurology and Neurosurgery, London, United Kingdom. “We’ve been looking for something like this for a long time. This is a big step forward.”

This research on ways to protect neurons from damage represents an advance on existing therapies now available for delaying MS relapses. Kapoor and his research team examined the effect of phenytoin, which is known to be a partial blocker of sodium channels, on the thickness of the nerve fiber layer in the retina after an optic neuritis attack.

“In inflamed areas, the axons of nerve cells get flooded with sodium, which causes an influx of calcium, which in turn causes cell death,” he elaborated. “If we can block sodium entry into

the cell, we may be able to prevent this. Optic neuritis, which is an inflammatory event and is often the first symptom of MS, gives us a window of opportunity to study active inflammation early on in the disease process.”

For the study, 86 patients with acute optic neuritis were randomly assigned within 2 weeks of symptom onset to receive either phenytoin (4 mg/kg/day) or placebo for 3 months.

Researchers measured retinal nerve fiber layer thickness and macular volume at baseline and then six months later, using optical coherence tomography.

Results showed that the average retinal nerve fiber layer thickness at six months was higher in the active group than in the placebo group, showing a 30 percent protective treatment effect. Adjusted macular volume was higher in the active group, showing a 34 percent protective treatment effect.

“The drug appeared to prevent about one third of the damage caused by an optic neuritis attack,” Kapoor said.

When researchers used MRI to measure the width of the optic nerve, they found near-significant protection with phenytoin—less shrinkage in the treated group.

Kapoor said that drugs such as phenytoin would complement existing immunomodulating therapies and potential remyelination approaches. “If you don’t have any nerve fibers, you can’t remyelinate them,” Kapoor said. “The ideal would be to protect the nerve cells with therapies like phenytoin and repair them with a remyelination approach, using several strategies to preserve function.”

Vitamin B Shows Promise in Progressive MS (Abstract #PL2.002)

Emerging research shows a regimen of high doses of biotin, a water-soluble B vitamin, appears to be effective in patients with primary or secondary progressive multiple sclerosis.

A new phase 3 study of the investigational drug MD1003 (MedDay Pharmaceuticals), a highly concentrated pharmaceutical-grade biotin, found that patients with progressive MS taking the drug had significant improvement at 9 months, which was confirmed at 12 months, compared with those taking placebo. (In a phase 3 study, the drug or treatment is given to large groups of people to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow the drug or treatment to be used safely.)

A total of 154 patients with a baseline EDSS (Expanded Disability Status Scale) score of between 4.5 and 7 were enrolled from 16 MS centers across France. Treatment duration was one year. The study's primary endpoint was defined as the proportion of patients who improved at nine months, with confirmation at 12 months. Improvement was defined as either a decrease in EDSS (by at least 1 point for baseline EDSS greater than or equal to 5.5 and 0.5 points for EDSS of less than or equal to 6) or an improvement in a timed 25-foot walk of at least 20 percent.

"We are encouraged that the primary endpoint was met despite the very high bar for treatment response," said the study's principal investigator, Professor Ayman Tourbah, of CHU de Reims, Neurology, France, in a press release.

The results, he said, suggest that MD1003 "could be an important and efficacious treatment for primary and secondary progressive multiple sclerosis."

Currently, there are no effective therapies for progressive MS.

Topical Drugs Show Promise Against MS

Two common topical drugs—the antifungal miconazole, used to treat athlete's foot, and the steroid clobetasol, used for eczema—may have applications in treating MS, as shown by research designed to repurpose approved drugs for other uses.

Miconazole and clobetasol may stimulate mouse and human oligodendrocyte progenitor cells (OPCs) into generating myelin-producing cells in culture, according to research published online April 20 in *Nature*. Myelin is the protective layer around the nerves in the central nervous system and brain.

A multidisciplinary team of researchers from Case Western Reserve School of Medicine stimulated the regeneration of damaged brain cells and reversed paralysis when administered systemically to animal models of multiple sclerosis.

Tests to analyze immune response, called assays, suggest that miconazole functions directly as a remyelinating drug with no effect on the immune system, while clobetasol is a potent immunosuppressant, as well as a remyelinating agent.

“To replace damaged cells, the scientific field has focused on direct transplantation of stem cell-derived tissues for regenerative medicine, and that approach is likely to provide enormous benefit down the road,” said Paul Tesar, PhD, co-senior author, from Case Western Reserve School of Medicine in Cleveland, Ohio, in a news release.

“We asked if we could find a faster and less invasive approach by using drugs to activate native nervous system stem cells and direct them to form new myelin. Our ultimate goal was to enhance the body’s ability to repair itself,” Tesar said.

The researchers hit on miconazole and clobetasol as potential MS treatments by screening hundreds of approved compounds in a drug library maintained by the National Center for Advancing Translational Sciences (NCATS), part of the National Institutes of Health. Tesar and colleagues said they plan to expand the library of drugs screened against OPCs in the near future to identify other promising compounds.

FDA Approves Generic Form of Copaxone® for Relapsing MS

On April 17, the U.S. Food and Drug Administration approved a generic form of the drug Copaxone® (glatiramer acetate, made in Israel by Sandoz, a Novartis company). The generic, called Glatopa™ (developed in collaboration with Momenta and produced in the US), is a disease-modifying therapy for people with relapsing forms of MS, including those who have experienced a first clinical episode and have MRI features consistent with MS.



photo: www.pharmafile.com

The generic medication is a 20mg dose daily subcutaneous (under the skin) injection. Glatopa is chemically equivalent to the brand-name drug (Copaxone), but Glatopa (20mg per mL) and glatiramer acetate injection (40 mg per mL) are not interchangeable.

Patients should speak to their treating physician about what this means for them. There is no information yet on when Glatopa will be available by prescription in the United States, or what it might cost.

NARCOMS and NARCOMS Now do not endorse the use of any particular drugs or treatments for multiple sclerosis.

CLINICAL TRIALS IN MS

Following are several clinical trials recently announced for individuals with MS. We know you are loyal supporters of and participants in NARCOMS, which is a research study. Here we'll highlight some of the latest information about clinical trials in MS. Considering participation in a clinical trial? The National Multiple Sclerosis Society offers an online guide: <http://tinyurl.com/q9z6nuu>

MARCH 2015:

Investigators Recruiting People with MS-Related Muscle Spasticity for a Study of Extended-Release Baclofen

Summary: Investigators nationwide are recruiting 135 people with any form of multiple sclerosis for a research study to determine the effectiveness of extended-release baclofen capsules (a high dose, a low dose, or inactive placebo) in relieving muscle spasticity related to MS.

Study sponsor: Sun Pharma Advanced Research Company Limited

Rationale: Spasticity refers to feelings of stiffness and a wide range of involuntary muscle spasms (sustained muscle contractions or sudden movements). Spasticity is one of the more common and troublesome symptoms of MS. Baclofen is an available medication that acts on the central nervous system to relieve spasms, cramping, and tightness of muscles caused by spasticity. This study will evaluate the potential benefits of an extended-release form of baclofen. Extended release form (the drug is released over a period of time) may allow for it to be taken less often.

Eligibility and Details: Participants must be at least 18 years old, have any form of MS and a known history of spasticity. Participants should have no history of hypersensitivity to baclofen and should not have been treated with intrathecal baclofen (a system wherein an implantable pump delivers liquid baclofen directly into the spinal canal) previously.

Participants will be randomly assigned to receive immediate release capsules of high-dose baclofen, low-dose baclofen, or inactive placebo, daily by mouth for 22 days.

The primary outcome being measured is improvement in the Ashworth Scale, which measures spasticity. Secondary outcomes include spasm frequency, participants' assessment of their overall spasm frequency, and nighttime awakening.

Contact: To learn more visit www.basisstudy.com.

APRIL 2015:

Study of Teleconference Intervention to Increase Exercise and Decrease Fatigue

Summary: Investigators at Case Western Reserve University are recruiting 215 people from seven states (see list below) for a study to determine whether rehabilitation centers can distribute methods of fatigue management and increasing physical activity often provided by physical and/or occupational therapists via a series of teleconferences and phone interviews. Matthew Plow, PhD, the primary investigator, is conducting this randomized controlled trial funded by a research grant from the National MS Society.

Rationale: Many people with MS describe fatigue as one of their most disabling symptoms. MS fatigue can be chronic, severe, and it often interferes with the ability to maintain employment or engage in leisure activities. The reduced physical activity that results from MS fatigue can lower physical conditioning. This can lead to higher than normal levels of fatigue from normal activities of daily living, setting up a “vicious cycle” in which fatigue and physical inactivity enhance each other.

Eligibility and Details: Participants should be ages 18 to 65, with a diagnosis of MS and the ability to walk 25 feet with or without a cane. Among those excluded are people who exercise more than 90 minutes per week, are pregnant, have metabolic or cardiopulmonary disease that puts them at high risk for engaging in a home exercise program, or have had 4 or more falls in the past 6 months.

Participants will be randomly assigned to one of three groups receiving support through weekly phone conferences: an educational program that combines fatigue management with physical activity promotion; a physical activity promotion program alone; or an educational social support group.

The primary outcomes being measured are changes in physical activity levels over 24 weeks, and secondary outcomes include fatigue levels and quality of life.

To learn more contact:

Arielle Tucker, MS,
(216) 368-0510,
arielle.tucker@UHhospitals.org.

The Case Western Reserve University is enrolling participants from the following states:

Illinois
Indiana
Kentucky
Michigan
Ohio
Pennsylvania
West Virginia



Find the following hidden words:

myelin, antibody, therapy, neuron, immune, relapsing,
remitting, injection, oral, alliance, progress, clinical,
mobility, diagnosis, treatment, trial

U	N	O	K	Y	S	O	G	L	M	N	A	W	B	N	S
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FIND THE ANSWERS TO THIS WORD PUZZLE ONLINE:

www.narcoms.org/narcomsnow/play/answers

FACES *of* NARCOMS

Hands-on MS Healing

I am 70 years old and in 1987 was diagnosed with a mild case of relapsing remitting MS. For the first five years after my diagnosis, my fatigue was so bad that I could barely walk from one side of my small bedroom to the other to lie across my bed. I was an accountant at the time I was diagnosed and worked long, stressful hours during tax season. I was tired, grumpy and not a pleasant person to work with or be around. Numbness and fatigue have been my ongoing symptoms. I knew if I wanted to keep my job, which I desperately needed, I had to make some changes.

I sold my home and moved into a condo complex that offered a full-service spa. I started getting a one-hour massage every Sunday (my only day off) during tax season, and would rest the remainder of the day in preparation for the pending six-day work week. I started walking to and from work (a 15- to 20-minute trip each way) no matter how tired I was, increased my intake of water, took the supplements recommended for MS, and ate more vegetables.

The results I saw from the massages alone impressed me so much that when I had the opportunity to take a buy-out from the financial world, I went to school to become a massage therapist. I had the intimate experience of learning what balancing the body can do for the body and mind. With my massage license in hand, I worked as a therapist for a top resort in my city for 11 years.

It was a wonderful privilege to be licensed to assist people in their journeys to better health. I have since retired completely, and will be forever grateful for having MS, because it led me to the wonderful world of touch!

—Geraldine T.

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