

# A Bright Path Forward

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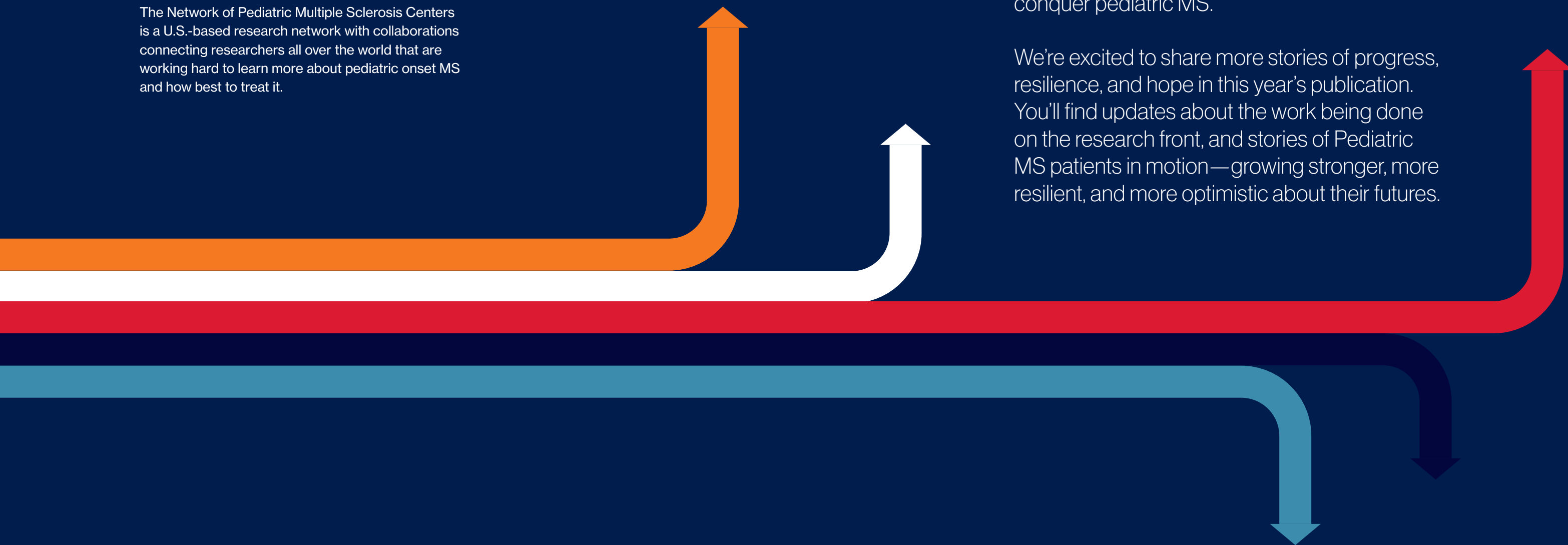
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The Network of Pediatric Multiple Sclerosis Centers is a U.S.-based research network with collaborations connecting researchers all over the world that are working hard to learn more about pediatric onset MS and how best to treat it.

Young people with MS are finding their voices, pursuing their dreams, and leading the way for others. Researchers are gaining new insights about MS and opening new doors to knowledge. Partnerships are bringing patients, caregivers, and researchers together to search for solutions. Over the past year, we've continued to see momentum in the fight to conquer pediatric MS.

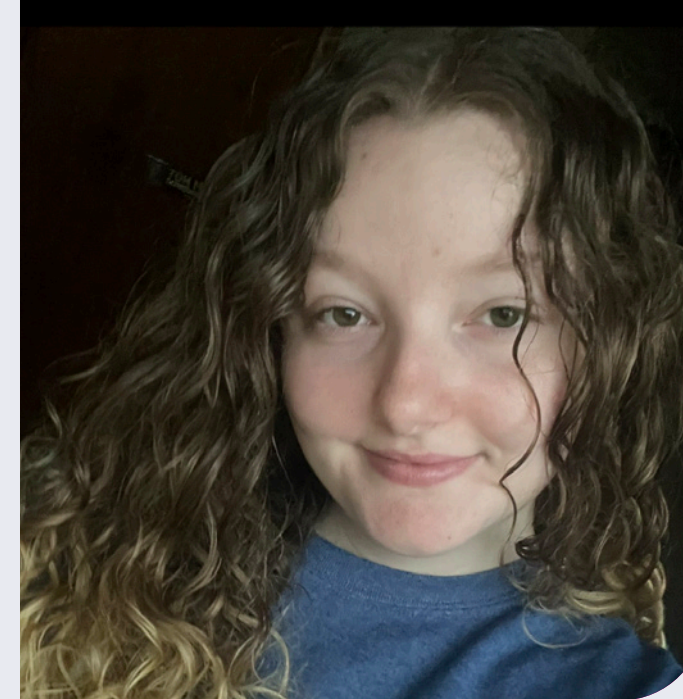
We're excited to share more stories of progress, resilience, and hope in this year's publication. You'll find updates about the work being done on the research front, and stories of Pediatric MS patients in motion—growing stronger, more resilient, and more optimistic about their futures.





**Adventure, chocolate ice cream, and Spider-Man movies – these are a few of Ashlie’s favorite things. She’s also no stranger to the thrills of kayaking and the artistic allure of diamond painting, although those pastimes have taken a backseat to her current focus: nursing school.**

The course of Ashlie's life shifted in January 2022 when she received her official MS diagnosis. Just before her eighteenth birthday, she began to experience neurological issues like tingling sensations, nerve problems, and persistent headaches. An MRI revealed her first lesion, prompting swift treatment with steroids. When a subsequent MRI revealed a second lesion near her brain stem, she was admitted to the hospital for a two week stay.



**“ I stay positive by keeping the people I love, and who understand my diagnosis, close to me.”**

Despite the challenges posed by an MS diagnosis, Ashlie's passions and pursuits continue to fuel her drive. She remains committed to an active lifestyle while also incorporating adaptations to her routines, sometimes turning to indoor hobbies, like board games, when the going gets tough. Ashlie's advice to those newly initiated into the world of MS echoes with a message of courage – cling to your passions and dreams, continue savoring life, even on the most challenging days.

The invisible nature of MS has taught Ashlie a profound truth – the unseen battles can be the most formidable. With MS, outward appearances often mask the internal struggle. In her opinion, one of the best things a loved one can do is research MS for their own understanding. Empathy makes a world of difference in the lives of those on this journey.

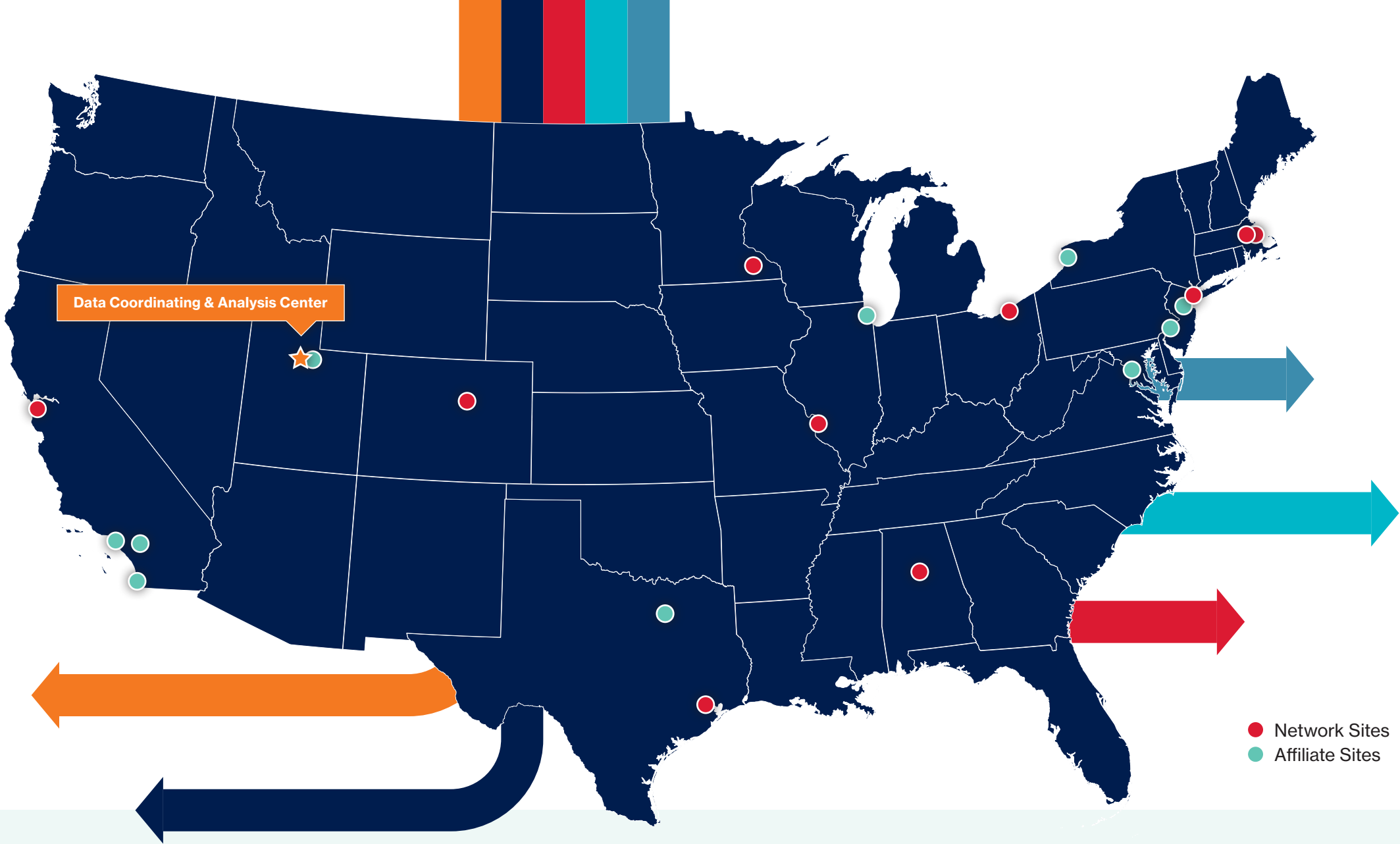
Like the rest of us, Ashlie dreams of a future where MS has been conquered. In the interim, she places her faith in the power of research to unlock new possibilities, learn what causes MS, and perhaps one day, lead to preventive measures. Ashlie's optimism mirrors the collective spirit of the MS community, all of us united in a determination to sculpt a brighter future. Her story is a reminder that amidst life's challenges, the blend of courage, determination, and hope can guide us forward.

**“I hope in research we can learn more options, what causes it, if it’s preventable.”**



# What is the Network of Pediatric Multiple Sclerosis Centers?

The Network of Pediatric Multiple Sclerosis Centers (NPMSC) is a collective of adult and child neurologists, seasoned scientists, and dedicated research professionals who are united in a shared mission to confront the complexities of Pediatric Multiple Sclerosis head-on. Comprising ten Clinical Centers and a Data Coordinating and Analysis Center (DCAC), the NPMSC functions as a cohesive unit where each contributor plays a vital role in advancing our understanding of Pediatric MS.



## Here are a few of our key players:

**Steering Committee:** At the forefront of our collective efforts is the NPMSC Steering Committee—an assembly of medical doctors and Ph.D. scientists drawn from our Clinical Centers and the DCAC. These dedicated individuals provide the strategic direction necessary to navigate the intricate waters of Pediatric MS research.

**“As an NPMSC principal investigator, I enjoy providing care to youths with MS & other demyelinating diseases. Research allows me to expand that care by initiating grants for multicenter projects, developing concept proposals for manuscripts, and mentoring junior faculty.”**

Soe Mar, MD, Washington University

**Statisticians:** Behind the scenes, statisticians stand as unsung heroes, transforming raw data into actionable knowledge. Their expertise shapes evidence-based medical decisions and propels our understanding of health and disease forward, contributing significantly to the integrity and reliability of our research outcomes.

**“As a biostatistician it feels good knowing my data analysis provides a better understanding of pediatric MS.”**

Michael Waltz, Biostatistician, University of Utah

**Data Managers:** Playing a pivotal role, data managers construct and maintain the databases housing our research data. Simultaneously, they diligently query and validate the data to guarantee accuracy and consistency—an essential contribution that forms the bedrock of reliable research findings.

**Project Managers:** Project managers, with their multifaceted role, coordinate diverse teams, oversee regulatory compliance, and manage project timelines. Fostering collaboration among investigators, sponsors, and regulatory bodies, they are key players in ensuring the success of the clinical research process.

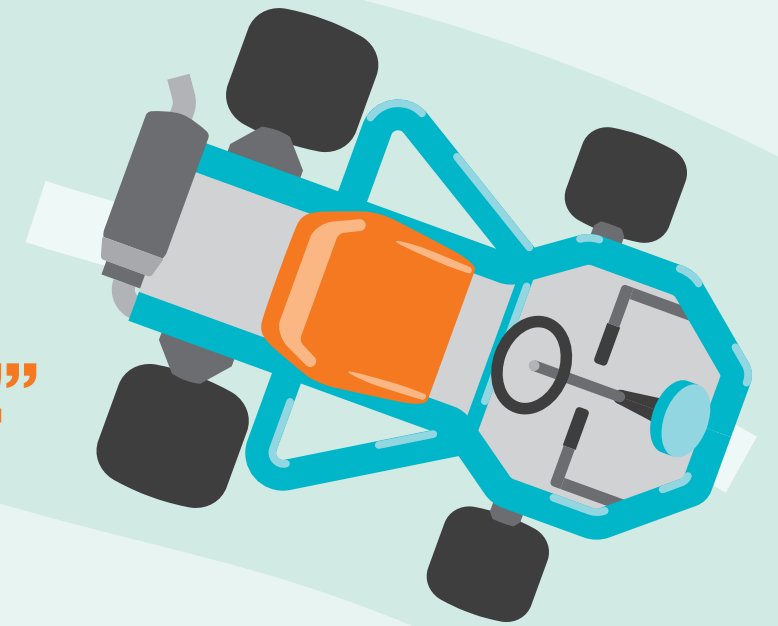
**Clinical Research Coordinators:** Often serving as the face of our research to participants, clinical research coordinators play a pivotal role in guiding participants through studies. They explain protocols, address concerns, and ensure adherence to ethical standards, embodying the human connection essential for the ethical conduct of clinical research.

**“It is rewarding to be part of a nationwide team of researchers helping to find improved outcomes for patients with pediatric MS.”**

Janace, Research Projects Manager, University of California San Francisco

# Unbreakable Spirit

“MS messed with the wrong girl!”



**When MaKayla isn't busy pursuing her nursing degree, she's embracing life with enthusiasm. Whether spending quality time with her family, enjoying mani/pedis with her mom, go-kart racing or playing with her beloved dogs, she approaches every day with an infectious zest for life.**

Her dreams of becoming a Neonatal Intensive Care Unit (NICU) nurse and later a nurse practitioner speak to her passion for making a positive impact on others.

MaKayla's path took an unexpected turn in July 2020, when she was just 17 years old. A sudden dizzy spell and fall led to a series of doctor visits and tests, culminating in the life-altering diagnosis of MS. Instead of letting this define her, MaKayla chose to redefine what was possible. She began listening to her body and recognizing the reservoir of strength within her. Despite the challenges, she remains dedicated to doing what she loves, adapting her activities to her body's needs. Her belief that everything happens for a reason has fueled her determination. While she acknowledges the tougher days, she never loses sight of her goal: to rise, fight, and show the world that MS cannot deter her dreams.

MaKayla's involvement in MS clinical research is another testament to her commitment to making a difference. By actively participating in research efforts, she contributes to a better future for those living with MS. Her ultimate dream is to witness the day when a cure is found, but she also wishes for greater awareness and understanding of MS, particularly its invisible nature – the pain she endures, the heaviness of constant fatigue, and the challenge of keeping her memory sharp. Even so, her tenacity serves as an inspiration, showing that individuals with MS are far from weak; they are warriors battling a formidable opponent.

For those recently diagnosed, MaKayla wants them to know their dreams are still attainable, and that listening to their bodies, resting when needed, and seeking support are essential steps on this journey. MS transforms individuals into fighters, fortifying their inner strength and determination. She encourages families to stand by their fighters, reminding them of their unbreakable strength and love.

MaKayla's achievements are nothing short of remarkable. From being on the Dean's list and a member of the Honor's Society in college to earning the Daktronics NAIA Competitive Cheer Scholar Athlete award, her dedication to excellence shines brightly. Her participation in the Nurse's Association, both locally and nationally, along with her achievement as the Box Stock Go-Kart champion, highlight her wide-ranging talents and indomitable spirit. She serves as an embodiment of resilience, a living testament to the power of determination, and a reminder that MS may try, but it will never break her spirit.



**“I would want a newly diagnosed person to know to keep fighting and never give up!”**

# Movement on the Research Front.

Our goal at NPMSC is to connect adult and child neurologists and other research professionals whose mission is to discover the causes, investigate determinants of remyelination and neuroprotection, advance therapeutics, and improve outcomes for those with Pediatric MS. We're pleased to share updates on our current studies and our latest manuscript publications.

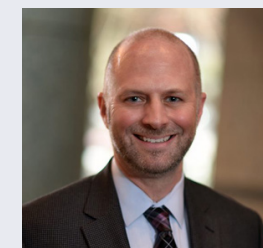


## The Pediatric Multiple Sclerosis and other Demyelinating Diseases Database – Ongoing Study

This long-standing data collection project aims to describe the number and characteristics of pediatric patients with suspected early onset of demyelinating disease of the central nervous system. These characteristics include things like a patient's demographics, environmental history, disease history, diagnostic information, and medical management decisions. The data are provided to our network investigators to support hypothesis generation and study design development for clinical trials and observational studies. Over the course of the last decade, the database has added over three thousand participants who have been enrolled at our network centers. The data have been used to produce many abstracts and manuscripts for journals and national meetings while also being leveraged for industry projects. If you're interested in contributing to this important database, ask your doctor about participating.

### Some of the research projects currently studying these data include:

- Biological Age in the Pediatric MS Population: Measuring biological age in pediatric participants' samples and data to study whether or not MS pathology may relate to premature aging
- Metabolic Correlates: Utilizing previously collected stool and plasma samples to determine whether lipids and fatty acids are related to relapses and lesions in pediatric participants
- Effects of Avonex & Plegridy: The amount of time between certain treatments and relapses is being analyzed on approximately 250 pediatric subjects in the database.

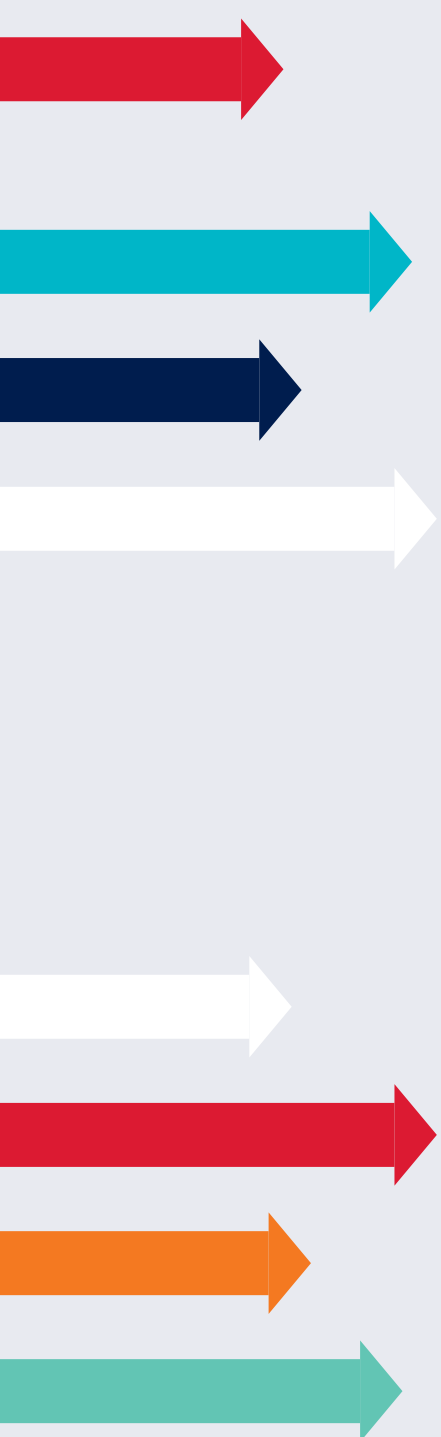


**“The collection of data from patients in this ongoing study is a key method by which the Network is fostering the discoveries needed to Stop demyelinating diseases from further progression, to Restore what functions that have been lost, and to End the development of such diseases forever. These three pillars (Stop, Restore, and End) are what the National MS Society has identified as the Pathways to Cures for MS, and are they important across a range of other demyelinating conditions, as well. Every patient has their own story to tell, and through collecting all the details from as many stories as possible, we hope to better understand how we can finally Stop, Restore, and End them all.”**

**Tim Lotze**, NPMSC Chair, Professor of Pediatrics and Neurology,  
Baylor College of Medicine



**Read more about the National  
MS Society's Pathways to Cures.**



### Diet and Relapses in Pediatric MS – Wrapping Up

Families often ask if there are specific diets that could trigger the onset of Pediatric MS or later relapses. This study began in 2018 to better understand the role that diet and metabolism play in the amount of MS relapses and disease progression. Participants completed a questionnaire about their food and vitamin intake as well as their physical activity three times during the study: at enrollment, six months later, and 12 months after enrollment. Study participation concluded in October 2022. 226 participants were enrolled in the study, and of these, 90% completed their baseline food frequency questionnaire, 72% completed their 6-month follow-up questionnaire and 74% completed their 12-month follow-up questionnaire. Final analysis for the study is still in progress.

### Patient Family Views on Pediatric MS – Wrapping Up

This study was designed to understand what research is important to those living with the disease, and what barriers keep them from participating in clinical research and clinical trials. It began with a series of focus groups in three areas of the country. Taking what we learned from the groups, we then launched a study in eight centers across the U.S., with questionnaires for three different groups: Teens with MS, their parents, and young adults with MS. We will use the insights gained to better guide future research priorities and design. Enrollment in the survey phase of the study ended in October 2022. In total there were 55 parents, 47 teens, and 96 young adults who completed their survey. A manuscript utilizing information from the focus group phase of the project has been published and one based on data from patient and caregiver surveys is currently being written.

## Recent NPMSC Publications and Abstracts

### Silent findings: Examination of asymptomatic demyelination in a pediatric US cohort (Bhise et al. 2023)

We identified 38 patients in the US Network of Pediatric Multiple Sclerosis Centers database with MRI images, and examined risk factors for development of first clinical event or new MRI activity. MRI were rated based on published MS and radiologically isolated syndrome (RIS) imaging diagnostic criteria. We found that one-third had a clinical attack and three-fourths developed new MRI activity over a mean follow-up time of 3.7 years. Individuals in our cohort shared similar demographics to those with clinically definite pediatric-onset MS. We show that sex, presence of infratentorial lesions, T1 hypointense lesions, juxtacortical lesion count, and callosal lesions were predictors of disease progression.

**Patient impact:** Children without symptoms, but with evidence of demyelination on MRI are at increased risk for developing MS.

### Gene-environment interactions increase the risk of pediatric-onset multiple sclerosis associated with household chemical exposures (Nasr et al. 2022)

We previously reported an association between household chemical exposures and an increased risk of pediatric-onset multiple sclerosis. In this new investigation, 490 pediatric-onset multiple sclerosis cases and 716 controls were included in the analyses. Exposures to insect repellent for ticks or mosquitos, weed control products and plant/tree insect or disease control products were associated with increased odds of pediatric-onset multiple sclerosis. There was a multiplicative interaction between exposure to weed control products and NFKB1 SNP GG genotype. The presence of gene-environment interactions with household toxins supports their possible causal role in pediatric-onset multiple sclerosis.

**Patient Impact:** Toxic exposures and genetic background interact to increase risk of developing pediatric onset MS

### Characteristics of pediatric patients with multiple sclerosis and related disorders infected with SARS-CoV-2 (Schreiner et al. 2023)

Pediatric patients with multiple sclerosis (POMS) and related disorders, clinically isolated syndrome (CIS), myelin oligodendrocyte glycoprotein antibody disorder (MOGAD), and neuromyelitis optica spectrum disorder (NMOSD), are commonly treated with immunosuppressants. To understand the impact of SARS-CoV-2 infection in these patients we surveyed 669 patients from March 2020 and August 2021. There were 73 confirmed COVID-19 infections. Eight of nine hospitalized patients (89%), and all patients admitted to the ICU were treated with B cell depleting therapy (rituximab and ocrelizumab). The results suggest that these therapies carry higher risk of severe infection in POMS and related disorders.

**Patient impact:** During the COVID Pandemic, POMS patients on B-cell depleting therapies were at increased risk of hospitalization

**MOG and AQP4 Antibodies among Children with Multiple Sclerosis and Controls (Gaudioso et al. 2022)**

The purpose of our investigation was to determine the frequency of myelin oligodendrocyte glycoprotein (MOG) and aquaporin-4 (AQP4) antibodies (IgG) among patients with pediatric-onset multiple sclerosis (POMS) and healthy controls. Patients with POMS (493) and healthy controls (703) were enrolled at 14 US sites. Serum AQP4-IgG and MOG-IgG were assessed using live cell-based assays. AQP4-IgG was negative among all 1,196 participants. MOG-IgG was positive in 30 of 493 cases (6%) and zero controls. Twenty-five of 30 patients positive with MOG-IgG (83%) had MOGAD, whereas 5 of 30 (17%) maintained a diagnosis of multiple sclerosis (MS) on re-review of records. MOG-IgG and AQP4-IgG were not identified among healthy controls confirming their high specificity for pediatric central nervous system demyelinating disease. Five percent of those with prior POMS diagnoses ultimately had MOGAD; and none had AQP4-IgG positivity. Clinical features associated with a final diagnosis of MOGAD in those with suspected MS included initial ADEM phenotype, younger age at disease onset, and lack of EBV exposure.

**Patient impact:** MOG and AQP4 antibodies were respectively infrequent or negative in POMS patients

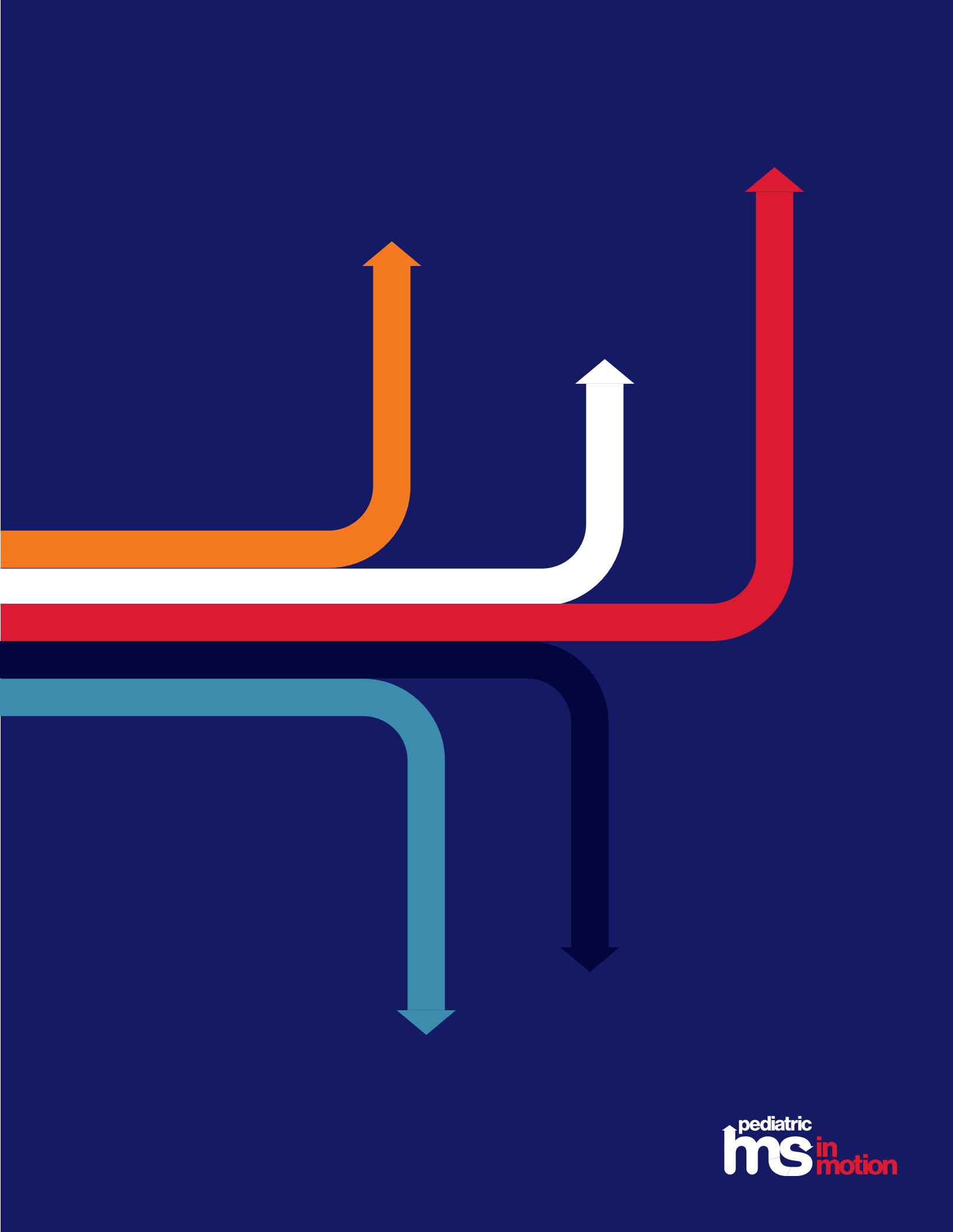
**A new look at cognitive functioning in pediatric MS (Krupp et al. 2022)**

Cognitive involvement in pediatric multiple sclerosis (MS) relative to adult MS is less defined. This study advances our understanding by measuring cognitive performances in pediatric MS, adult MS, and pediatric healthy controls. Consecutive relapsing pediatric MS participants from the United States Network of Pediatric MS Centers were compared with pediatric healthy controls and adults with relapsing MS. Participants were compared on two screening batteries: The Brief International Cognitive Assessment for MS and the Cogstate Brief Battery. The pediatric groups (MS vs. Healthy Controls) did not differ on either battery’s composite mean score or individual test scores ( $p > 0.32$ ), nor in the proportions impaired on either battery, Brief International Cognitive Assessment for MS (26% vs. 24%,  $p = 0.83$ ); Cogstate Brief Battery (26% vs. 32%,  $p = 0.41$ ).

**Patient Impact:** The full results of these studies demonstrated that Pediatric MS patients do not differ from healthy pediatric controls on cognitive screens but perform better than adults with MS.



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