The Creation of a Rare Disease Registry to Improve Understanding and Clinical Management of Marshall-Smith Syndrome

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Background and Significance

Marshall-Smith Syndrome (MSS) is an ultra-rare disorder caused by mutations to exons 6-10 on the NFIX gene. The syndrome is characterized by a set of classic physical characteristics which are present at birth and affect nearly every body system. People with MSS have complex medical needs and intellectual disability.(1). Fewer than 100 cases have been officially described in literature; MSS birth rate is <1:1,000,000; and locally, the United States is home to 28 MSS families in less than 200 that have been identified globally. A simple PubMed search brings forth 75 total articles, much of which is supported by a world-renowned specialist, Dr. Raoul Hennekam. An existing research foundation was established in 2007 by an MSS family in the Netherlands, this foundation is currently the only one raising funds to generate awareness and research. In order to accelerate research and advocate for MSS awareness worldwide, a rare disease patient registry is necessary and will contribute to equity and diversity in research by connecting patients with experts. (2,3).

Specific Aims

- Establish official representation of MSS in the U.S. by creating a nonprofit that represents individuals with MSS, their families and caregivers, and provides a vessel for connecting clinicians, researchers, and international collaborators.
- Establish and coordinate a rare disease registry.
- Explore the relationship between patient advocacy groups and the rare disease community (individuals, caregivers, clinicians, researchers, legislators, and other councils that represent rare disease entities). Utilize resources and provide leadership for a nonprofit that operates at the highest ethical and equitable standards for the people it serves.
- Educate families on the research process and disseminate useful, vetted, streamlined information about Marshall-Smith Syndrome for public use.

Creating a Patient Advocacy Group

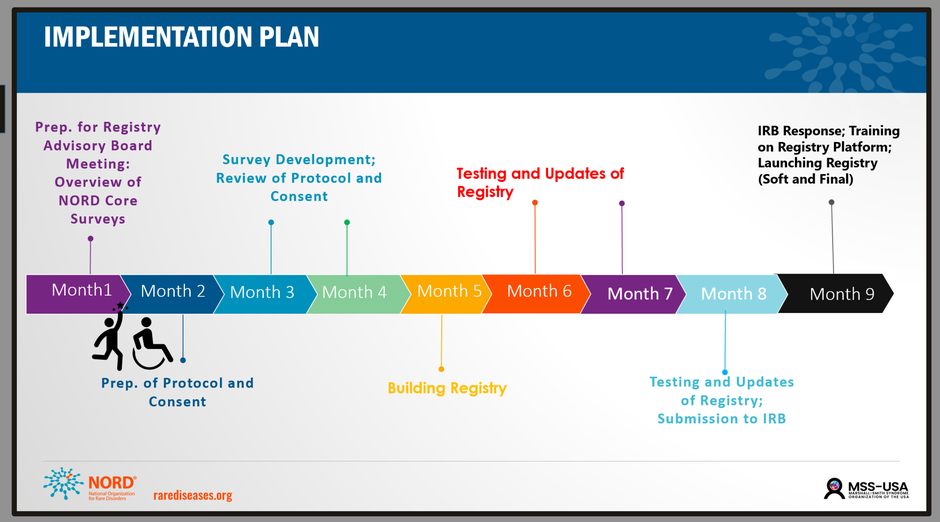
The Marshall-Smith Syndrome Organization of the USA, Inc. (MSS-USA) was incorporated in June of 2023 after a group of MSS moms came together to establish a U.S.-based operation that represents individuals and families with the rare disease.

- In phase one, the formalization of a nonprofit required approximately 200 hours of learning, developing bylaws, seating members of the executive board and generating buy-in from family members of the Marshall-Smith Syndrome in the U.S. and globally.
- In phase two, approximately 100 hours of investigation and learning the optimal pathway to establish a basis for research through a patient registry. Common data elements library and National Center for Translational Science information was utilized, and interviews were conducted with multiple online registries hosted by various entities who conduct biomedical research. The Medical Advisory Board and Research Advisory Board were seated by special invitation and families were notified of open seats.
- In phase three, MSS-USA formalized our membership as a Platinum Level NORD partner and are sharing our intentions with the larger community to generate awareness, reduce isolation, and encourage knowledge sharing while developing formal research protocols and communication channels.

THE MISSION OF MSS-USA IS TO PROVIDE SUPPORT TO INDIVIDUALS WITH MARSHALL-SMITH SYNDROME AND THEIR FAMILIES BY CREATING CONNECTION, RAISING AWARENESS THROUGH ADVOCACY, AND INCREASING UNDERSTANDING OF THE ULTRA-RARE DISORDER THROUGH RESEARCH. www.mss-usa.org

Getting Research Ready

- Establish an organization that has representatives who reflect the voice and concerns of those who are affected. Establish solid operational policies and procedures. Generate funding and community buy-in. Assure compliance.
- Define roles and processes on the Executive, Medical Advisory, and Research Advisory Boards. Host meetings to establish goals and processes.
- Explore data registry platform options. MSS-USA voted to purchase the National Organization for Rare Disorders IAMRARE© data platform Nov. '23.
- Perform literature review, current studies in disease spill-over, and validated tools. Design and develop a registry protocol with input from all parties. (4).



Resources

- Operational nonprofit with the ability to accept donations and grants. Website and transparency.
- Identify patients nationally and abroad. Collaborate with existing interested parties. Create connections that promote knowledge sharing and expert collaborations.
- Build a Medical Advisory Board and Registry Advisory Board with experts from relevant domains.
- Partner with the National Organization for Rare Disorders (NORD).
- Fundraise and purchase data platform and hire an IRB.
- Commitment to the larger mission and ability to create awareness and generate advocacy through leadership, mentorship, and feedback/ feedforward processes.

Summary and Conclusions

- Establishing a nonprofit organization's structure, mission, and functional operations was the primary time investment for phase one of the project. Special consideration is given to developing equity for MSS patients and their families in the organization and connecting with international researchers to streamline priorities and goals.
- Creating buy-in and establishing a line of communication amongst the patient, medical, and research community is essential to establishing a registry and promoting awareness for MSS. NORD's platforms and connections are an accelerant for rare disease patient advocacy groups. Many agencies involved in the care and management of rare disease are siloed, taking decades for correlation and adoption of new information. By harnessing the power of technology and communication in today's digital age, MSS-USA is in a prime position to connect experts, families, and organizations from across the globe.
- Long term coordination and management is required to sustain the project. Family members who serve board roles add to representation and relevance of ongoing pursuits to develop clinical standards and review potential prospects for research studies, therapeutic development, and assessments. Ongoing leadership is needed to promote the needs of the MSS community. Mentorship and team-building are essential.

Future Directions

- February 2025 is the expected launch date for the Marshall-Smith Syndrome Rare Disease Registry (MSSRDR). Data will be available by request of MSS-USA. We expect to contribute to the publication of an updated living history study as well as connect MSS families with research opportunities.
- Ongoing collaboration will increase global outreach and awareness.
- MSS-USA team members are connecting various professionals in the rare disease community to engage further support for rare disease patients.
- Fundraising continues as MSS-USA is a nonprofit organization that is 100% donation-based, including the time and skills of our professional boards. All proceeds are used to support individuals and families affected by MSS.
- Long term interests include the creation of an U.S. based MSS Expert Clinic, therapeutic development for musculoskeletal disease, and continued advocacy to improve the lives of MSS patients and their families.

References

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