

COMPASS

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Understanding the Impact of Newborn Screening for SMA

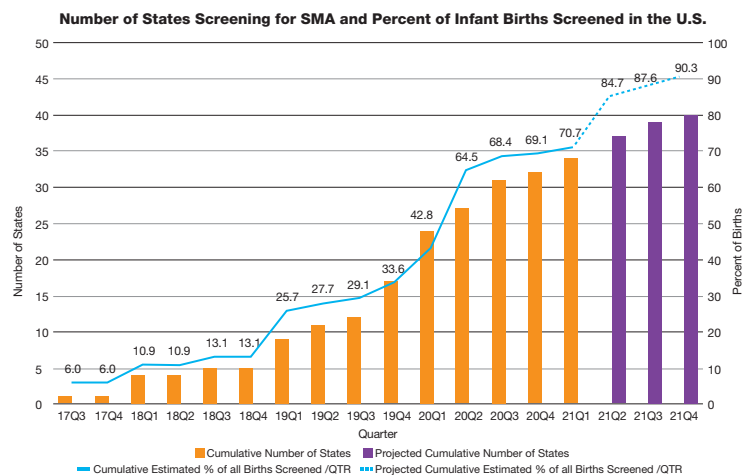
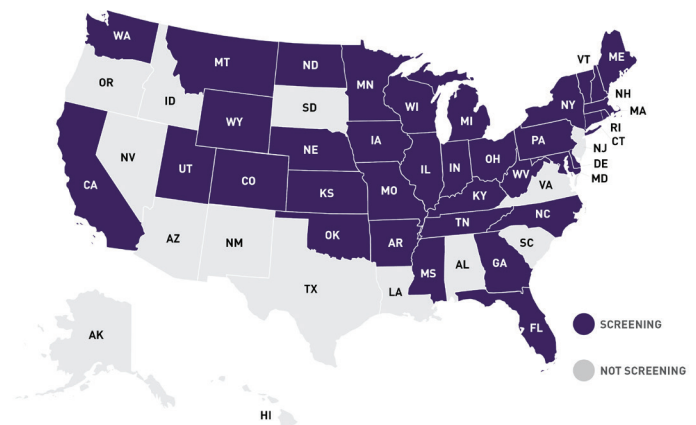
Newborn screening for spinal muscular atrophy (SMA) has taken hold in the United States. The U.S. Food and Drug Administration’s (FDA) approval of the first disease-modifying therapy for SMA in 2016 provided an effective early treatment. This approval opened the path to adding SMA to the federal [Recommended Uniform Screening Panel \(RUSP\)](#) in 2018, making it one of the disorders the Secretary of the U.S. Department of Health and Human Services (HHS) recommends for states to screen as part of their state universal newborn screening programs.

How We Got Here

In 2008, the first nomination to consider SMA for newborn screening was denied because there was not an effective treatment for SMA at the time, and no state pilot programs had been initiated. However, in February 2017, a multidisciplinary team led by Cure SMA resubmitted a nomination for SMA, which was accepted for full evidence review. This was supported by an SMA newborn screening pilot program that was initiated in New York State in 2016, in addition to having an FDA-approved treatment. The Condition Review Workgroup completed their review, and in February 2018, the Advisory Committee on Heritable Disorders in Newborns and Children met to deliberate the evidence and voted to recommend adding SMA to the RUSP. The HHS Secretary signed the recommendation in July 2018, officially adding SMA to the RUSP.

In January 2018, just prior to adding SMA to the RUSP, the state of Utah began permanent SMA newborn screening, followed shortly after by Minnesota and later by the state of New York. That same year, pilot SMA newborn screening studies began in Massachusetts, Indiana, and North Carolina. By the end of 2019, 10 states in the U.S. had implemented

permanent screening and three additional states began pilot programs. In 2020, 17 new states implemented SMA newborn screening, making it the most successful year to date in implementing newborn screening for SMA. As of April 2021, 36 states are screening for SMA (see map below), through permanent SMA screening programs and pilot or population screening programs. This means that more than 74 percent of all infants born in the U.S. are now screened for SMA. Cure SMA, in partnership with the SMA community in non-screening states, continues to advocate for and support implementation, with a goal of 90 percent of U.S. newborns being screened for SMA by the end of 2021.




Newborn Screening Diagnosis & Treatment

Shortly after birth, infants are tested for multiple serious disorders that may not present clinically at birth. Early diagnosis facilitates early treatments before harmful effects occur. To screen for diseases, such as SMA, a blood test is performed 24 to 48 hours after birth. If a condition is identified, parents are immediately notified, and follow-up diagnostic testing is conducted. This public health process for early diagnosis provides both medical care teams and families with the ability to seek out resources and treatments before the onset of serious and often irreversible symptoms that could drastically affect a child’s life.

SMA is caused by a mutation in the survival motor neuron gene 1 (*SMN1*). In a healthy person, this gene produces a protein—called survival motor neuron protein or SMN protein—that is critical to the function of the nerves that control our muscles. Without it, those nerve cells cannot properly function and eventually die, leading to debilitating and sometimes fatal muscle weakness. The newborn screening assay detects the presence or absence of deletion of the *survival motor neuron 1 (SMN1)* gene at exon 7 and does not detect point mutations. Therefore, approximately 3 to 5 percent of infants with SMA will not be detected via newborn screening and will present with symptoms of [hypotonia](#).

Newborn screening is essential to providing early SMN-enhancing treatment and achieving the best possible outcomes for infants born with SMA. Clinical trials of each SMN-enhancing treatment in symptomatic SMA infants younger than 6 months of age have demonstrated significant motor function improvement and survival compared to natural history. Ongoing clinical trials of infants with SMA treated prior to the development of symptoms have also yielded significantly altered disease outcomes compared to natural history. Because the loss of motor neurons that impact a baby’s motor function is irreversible with SMA, SMA healthcare providers often say that “time is neurons.”

Diagnosing a child with suspected SMA, or presenting as newborn screening positive, requires emergent evaluation by a neuromuscular specialist, confirmatory genetic testing, counseling about SMA disease, and discussion of treatment options. If symptomatic and identified to have just one copy of *SMN1*, further testing via *SMN1* gene sequencing is indicated to look for a point mutation. Consensus expert opinion recommends offering and efficiently providing [treatment for infants with 1-4 copies of *SMN2*](#) (often referred to as the SMA “back-up gene”).

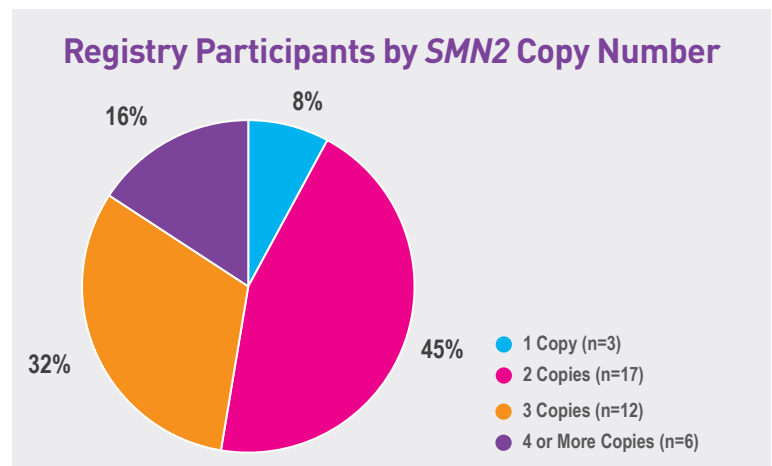


SMART MOVES
EARLY ACTION, EARLY TREATMENT, SAVES LIVES.

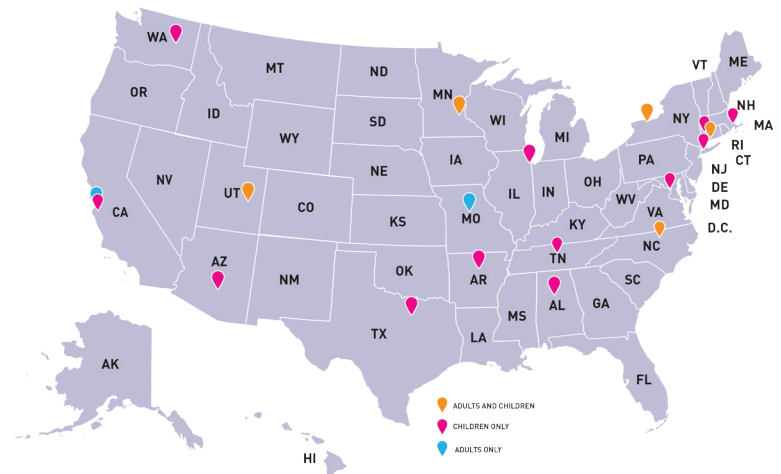
SMARt Moves is an educational online module available to bridge the gap to diagnosis for those infants for whom SMA newborn screening is not available or will not detect. SMARt Moves emphasizes the early warning signs of SMA and provides demonstration videos for healthcare providers and families, as well as a checklist and a diagnostic toolkit. More information can be found at www.curesma.org/smartmoves/.

Newborn Screening Registry

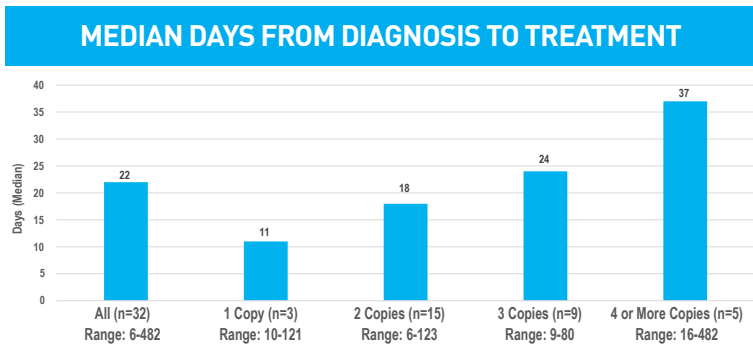
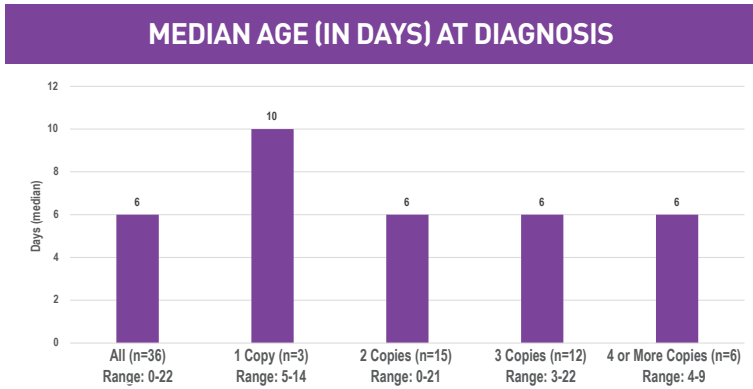
To better understand the impact of SMA newborn screening over time, Cure SMA has established an SMA Newborn Screening Registry. Families with an infant diagnosed with SMA via newborn screening, or prenatally, are encouraged to enter data in Cure SMA’s Newborn Screening Registry. Families can also consent for their providers to enter data on their behalf. As of April 9, 2021, there were 38 newborns in the Registry. More information is available at www.curesma.org/newborn-screening-for-sma/ or www.curesma.org/nbsr.



Families with an infant or child diagnosed with SMA are eligible to receive an Information Packet and Newly Diagnosed Care Package from Cure SMA. We encourage healthcare providers to share the Cure SMA website information with their patient’s families, namely our pages for [newly diagnosed families](#). If you would like to have educational materials in your clinic, please contact Cure SMA via patientcare@curesma.org to request [specific Care Series Booklets](#), including resources that have been translated into different languages.



As of today, the Cure SMA Care Center Network has 19 sites across the country (see above map), representing SMA care for both children and adults. The Network is supported in part by a grant from the Oscar G. and Elsa S. Mayer Family Foundation and an endowment from Bill and Susan Orr and the Tyler William Orr Memorial Fund.



Centers, a collection of neuromuscular clinics, provide multidisciplinary care for people with SMA and contribute consented SMA patient data transferred securely and electronically from electronic medical records to the SMA Clinical Data Registry. This clinical information is real-world evidence that will be used to guide best care and create evidence-based standards of care for SMA. The SMA Clinical Data Registry continues to grow in partnership with the Cure SMA Care Center Network, with over 500 patients included in the Registry to date.

Role of Cure SMA Care Center Network

Cure SMA’s primary focus is on supporting care of the highest value to individuals with SMA. In 2018, SMA standard of care guidelines were updated and approved based on consensus, due to limited evidence. With the advent of effective treatments and the implementation of newborn screening, the need for an evidence-based standard of care for people with SMA is needed now more than ever. To create the evidence needed for this, Cure SMA established the [Cure SMA Care Center Network and SMA Clinical Data Registry](#) to collect a cross section of real-world data about SMA care.

The growth of the Cure SMA Care Center Network and SMA Clinical Data Registry will also be supported by Cure SMA’s recently launched Real-World Evidence Collaboration. This Collaboration will deliver an expanded and validated clinical dataset to be used in the development of the updated standards of care on diagnosis, SMA treatment considerations, and mental and emotional health, as well as adding 10 sites to join the Cure SMA Care Center Network.

ACKNOWLEDGMENT

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- Members of the Cure SMA Real-World Evidence Collaboration include Cure SMA, Biogen, Genentech, Novartis Gene Therapies, and SMA Europe.

Cure SMA Care Center Spotlight



Russell Butterfield, M.D., Ph.D., is a pediatric neurologist and director of the Cure SMA Care Center Network site at the University of Utah and Primary Children's Hospital. Utah was the first state in the U.S. to implement permanent newborn screening for SMA, and the team at the University of Utah receives all referrals for newborn screening in Utah and advocates for the best care possible for their patients.

Cure SMA: How has newborn screening changed the SMA landscape for your patients?

Dr. Butterfield: SMA newborn screening has been transformative in identifying infants with SMA at the earliest possible time. Many of our pre-symptomatically treated patients are meeting normal developmental milestones. Still, we have been screening for three years and we still have a lot to learn. Newborn screening creates an unusual first interaction with families. Giving the news to a family that their child has SMA and then the pressure of having to make treatment decisions quickly can be difficult. We need to learn to do this better for families. We also need better tools to assess newborn patients and understand predictors of early onset. We do not really know very much about “pre-symptomatic” SMA.

Cure SMA: How has the process of newborn screening changed since Utah originally implemented newborn screening for SMA?

Dr. Butterfield: Our first case was a false positive and as a result we fine-tuned the assay and have not had a false positive subsequently. The overall process is the same. My team receives the report at five days and then we run with it. We have a great working relationship with the Newborn Screening Lab at the Department of Health, which facilitates things going smoothly.

Cure SMA: Why did the University of Utah choose to participate in the Cure SMA Care Center Network?

Dr. Butterfield: We chose to participate for three important reasons. First, to give SMA patients the best care possible. Then, we wanted to help link patients to the SMA community. At first, they may not know how badly they need each other. Finally, the Network is a way to stay up-to-speed with changes for patients and healthcare providers.

Cure SMA: What were the challenges you faced to become a Cure SMA Care Center and how did you overcome them?

Dr. Butterfield: Engagement and coordination of people and administration was the biggest challenge. The clinical team was established and ready. But we had to link together people from across the organization.

Get Involved in Newborn Screening Advocacy

Building off the most impactful year in state newborn screening for SMA, Cure SMA continues to urge [remaining non-screening states](#) to complete implementation as soon as possible. Many families from these non-screening states have stepped forward to share their personal stories with public health officials—describing how an earlier SMA diagnosis with early treatment may have dramatically changed the course of their child's life. These advocates are talking to the media, writing their local legislators, and testifying in public meetings discussing newborn screening for SMA.

As an expert or healthcare provider in SMA, you can also get involved in advocating for newborn screening for SMA in your state. For example, recently, Dr. Erika Finanger, Director, Pediatric Neuromuscular Program at the Oregon Health & Science University, testified before an Oregon legislative committee considering legislation to implement newborn screening for SMA in Oregon. She offered her perspective on treating individuals with SMA and highlighted the known value of early diagnosis and treatment.

For more information on how you can get involved or for help in getting started, contact the Cure SMA Advocacy Team at advocacy@curesma.org.