cure SMA

2025 INTERNATIONAL SMA PATIENT ADVOCACY GROUP MEETING

CURRENT TREATMENTS AND GUIDELINE, PATHWAYS FROM TRIALS AND RWE TO GLOBAL ACCESS

Kenneth Hobby

President, Cure SMA

Countries Represented

We are honored to have SMA families, researchers, and clinicians attend this conference from all over the world! There are individuals attending from 40 countries, including: Argentina, Australia, Bangladesh, Belgium, Brazil, Bulgaria, Canada, Chile, Colombia, Costa Rica, Czech Republic, Estonia, Finland, France, Germany, Hungary, India, Ireland, Italy, Japan, Latvia, Malaysia, Mexico, Netherlands, New Zealand, Norway, Panama, Paraguay, Philippines, Poland, Portugal, Slovakia, Slovenia, South Africa, Spain, Switzerland, Taiwan, Turkey, United Kingdom, and United States.

2025 Approach and Themes

- **Following other sessions and activities**
  - Current updates

- **General Rare Disease Approach**
  - **Take results and findings from a small group**
    - **Expand to all**
- **International Approach**
  - Results from one country
    - Expand to others
    - Avoid duplication

SMA is The Same Everywhere

SPECIAL THANK YOU TO OUR SPONSORS

Thank you to our generous sponsors for their support.

PRESENTING SPONSORS

Biogen

Roche

TITLE SPONSOR

ScholarRock

The SMA Model

- **Investments in Disease Modifying Research**
  - Target genetic cause first, not just symptoms
- **Incremental Steps**
  - First Slow, then Stop, then Cure
- **Approach for Trials**
  - Robust Natural History
  - Placebo Controlled
  - Narrow Inclusion Criteria
- **Gave**
  - Strong Conclusive Clinical Trial Data

Shared Data and Resources

2025 International SMA Patient Advocacy Group Meeting

Resources

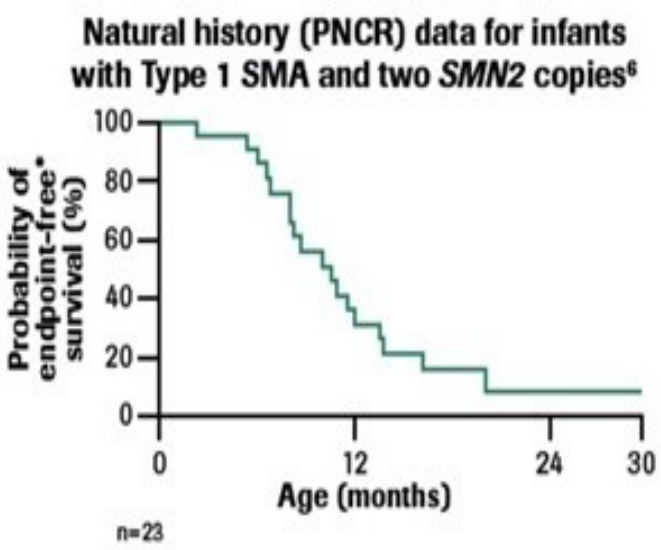
- Check out our translated Care Series Booklets, which provide patients and families the information you need to make decisions about treatment and care.
- SMA Update in Best Practices Summary Report - Recommendations for Diagnosis Considerations. This report is also available in French, Mandarin, and Spanish.
- SMA Update in Best Practices Summary Report - Recommendations for Treatment Considerations. This report is also available in French, Mandarin, and Spanish.
- SMArt Moves - Healthcare Provider Quick Reference Guide.
- SMArt Moves - Parent Checklist 0-6 Months. Also available in Spanish.
- SMArt Moves - Parents Checklist 7-12 Months. Also available in Spanish.
- 2024 State of SMA Report.
- 2025 Annual Conference Booklet.
- SMA Community Risk Tolerance Update.
- NBS Birth Prevalence of SMA.
- Cure SMA Everyday Living Survey.
- SMA Update in Best Practices Full Report - Recommendations for Diagnosis Considerations.
- SMA Update in Best Practices Full Report - Recommendations for Treatment Considerations.
- Inspired by Homer's epic Odyssey adventure, OdySMA is a bold initiative to reveal the 'quest for access' of people living with SMA by mapping, visualizing, and centralizing knowledge and data around access issues.
- SMAcademy is a SMA Europe capacity-building initiative for patient advocates in SMA. SMAcademy provides patient advocates with tools to amplify their efficacy and impact when advocating for a better life for people living with SMA.
- Global SMAdvocacy Event with the Activity Report 2024.
- Documentary: "One community. Shared dreams".
- NBS Alliance | Home with its resources NBS Alliance | Resources & Tools.
- SMArt Moves Video Playlist: Learn to Spot to Spot the Warning Signs of SMA (English). Also available in Spanish.

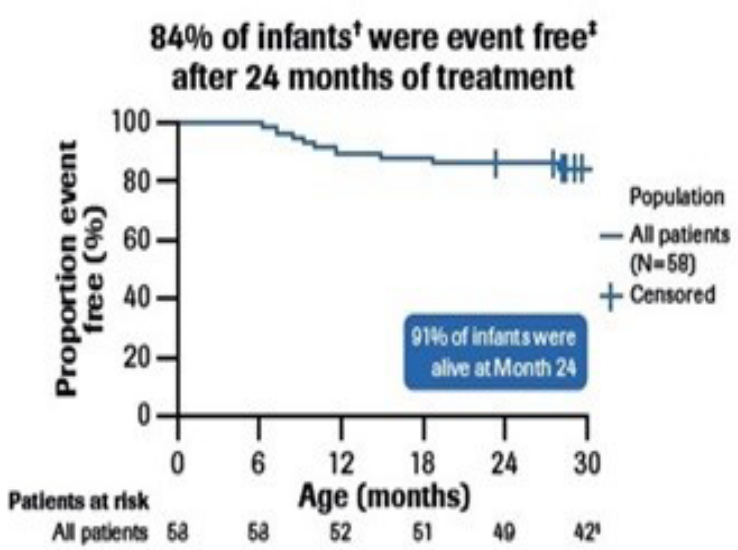
Shared Data and Resources

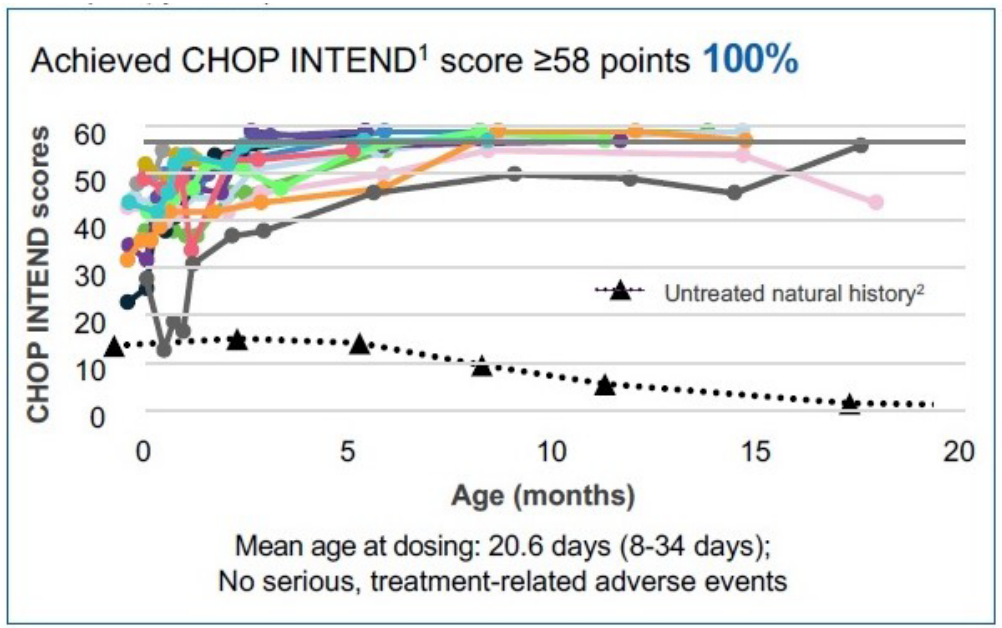
- Natural History
- Clinical Trials
- Real World Evidence
- Patient Data

- Patient Voice

Clinical Data
Clear Conclusive Signals







Clinical Real World Impact Data

J Neuromuscul Dis. 2023;10(2):199-209. doi: 10.3233/JND-221573.

Assessing Bulbar Function in Spinal Muscular Atrophy Using Patient-Reported Outcomes

Sally Dunaway Young [1], Amy Pasternak [2 3], Tina Duong [1], Katlyn E McGrattan [4], Sarah Stranberg [5], Elizabeth Maczek [2 3], Courtney Dias [2 3], Whitney Tang [1], Dana Parker [1], Alexis Levine [2], Alyssa Rohan [2], Connie Wolford [1], William Martens [6], Michael P McDermott [6 7], Basil T Darras [2], John W Day [1]

Affiliations + expand

PMID: 36776075 PMCID: PMC10258884 DOI: 10.3233/JND-221573

Abstract

Background: Novel Spinal Muscular Atrophy (SMA) treatments have demonstrated improvements on motor measures that are clearly distinct from the natural history of progressive decline. Comparable measures are needed to monitor bulbar function, which is affected in severe SMA.

Case Reports > Pediatr Phys Ther. 2025 Apr 1;37(2):282-287.
doi: 10.1097/PEP.0000000000001188. Epub 2025 Feb 13.

Therapeutic Scoliosis-Specific Exercises for a Child With Spinal Muscular Atrophy: A Case Report

Cara H Kanner [1], Rafael Rodriguez-Torres, Rebekah Wallach, Prachi Bakarania, Jacqueline Montes

Affiliations + expand

PMID: 39961029 DOI: 10.1097/PEP.0000000000001188

Abstract

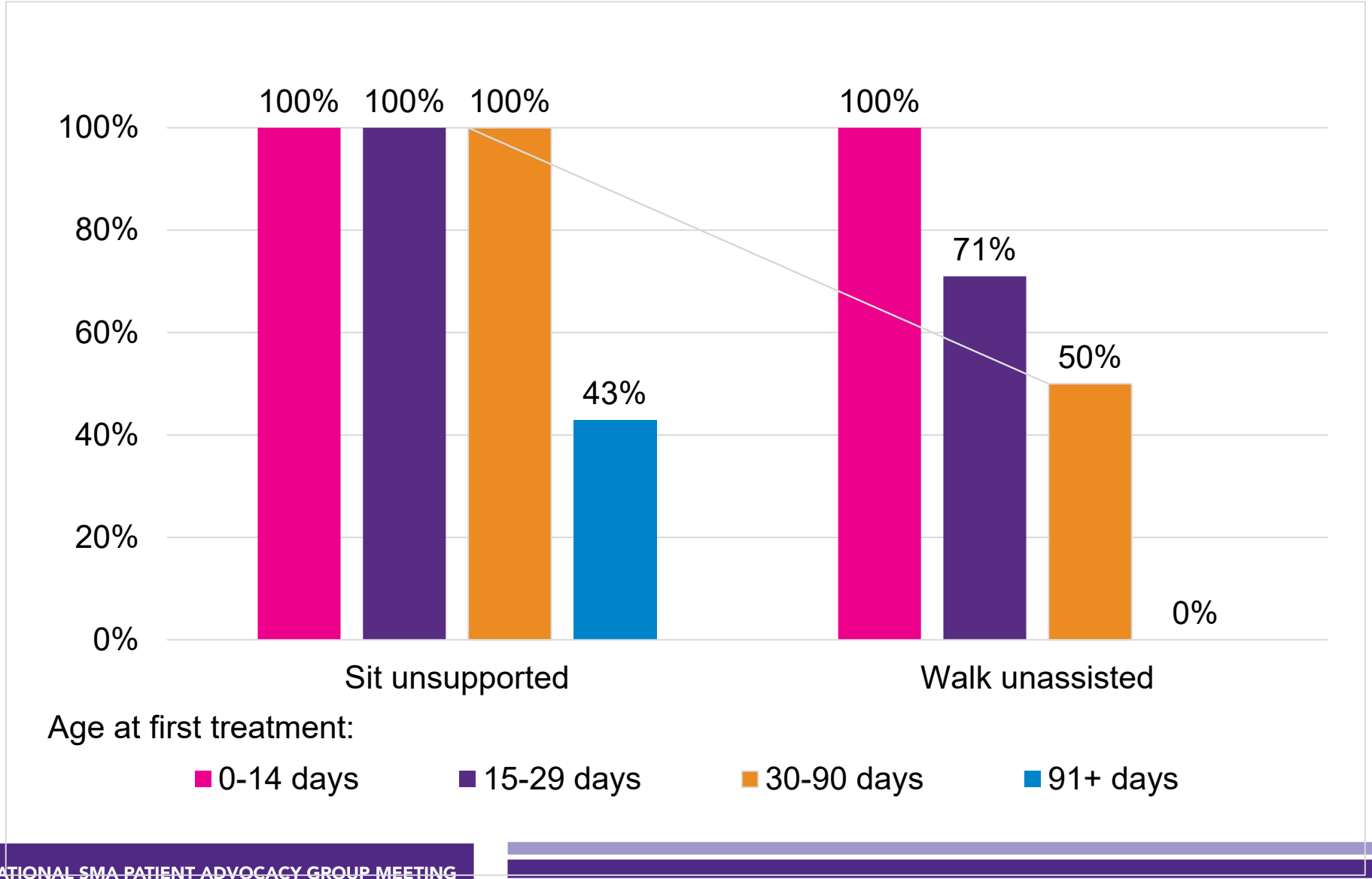
Purpose: The purpose of this study is to report on therapeutic scoliosis-specific exercises (PSSE) for a child with spinal muscular atrophy (SMA) who had spinal fusion.

J Clin Med. 2024 Apr 30;13(9):2634. doi: 10.3390/jcm13092634.

Beyond Contractures in Spinal Muscular Atrophy: Identifying Lower-Limb Joint Hypermobility

Elizabeth R Harding [1], Cara H Kanner [1], Amy Pasternak [2 3], Allan M Glanzman [4], Sally Dunaway Young [5], Ashwini K Rao [1], Michael P McDermott [6], Zarazuela Zolkipli-Cunningham [7], John W Day [5], Richard S Finkel [8], Basil T Darras [2], Darryl C De Vivo [9], Jacqueline Montes [1]

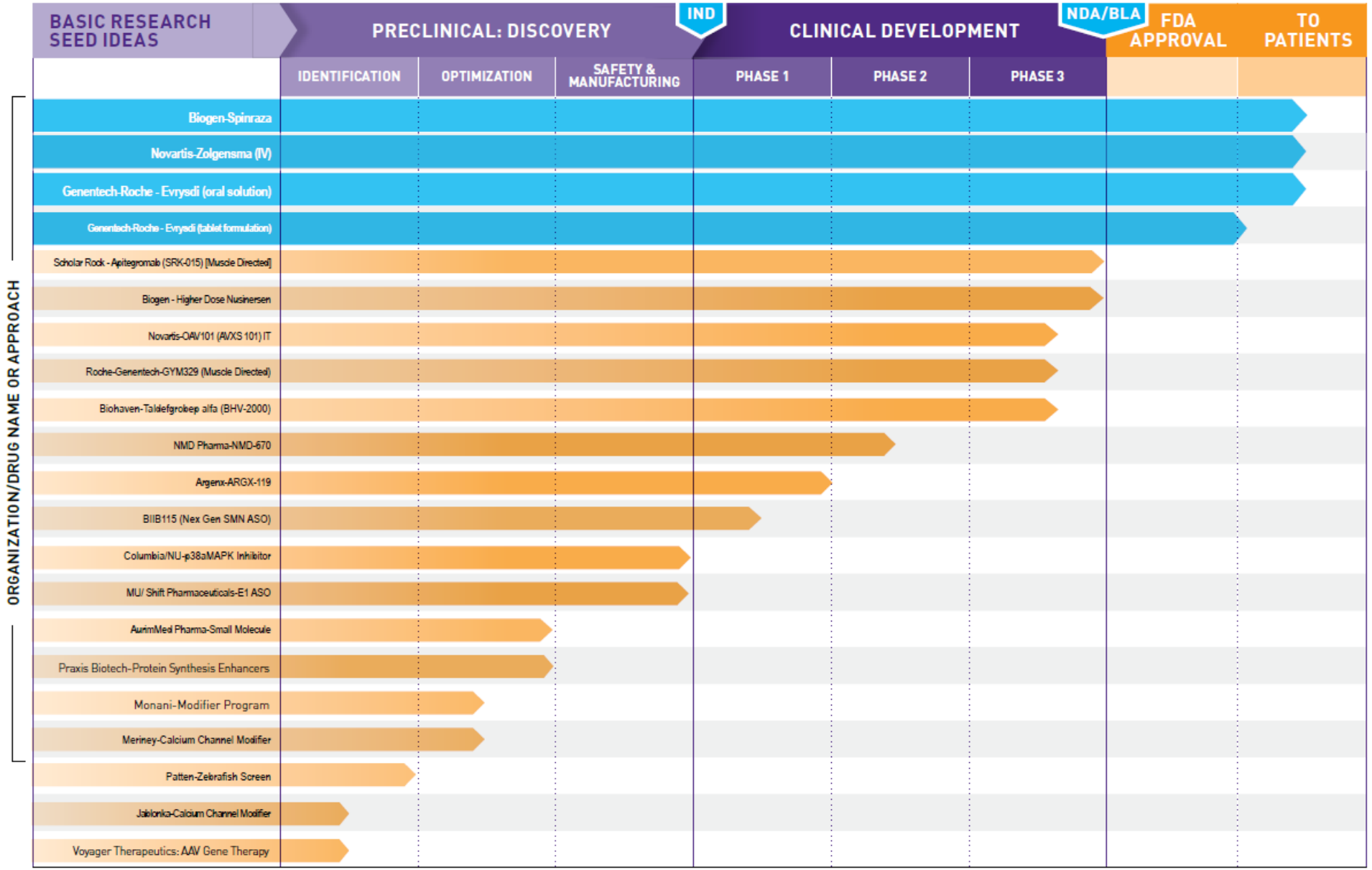
Patient Data – Real World Impact



Patient Data (and Voice)

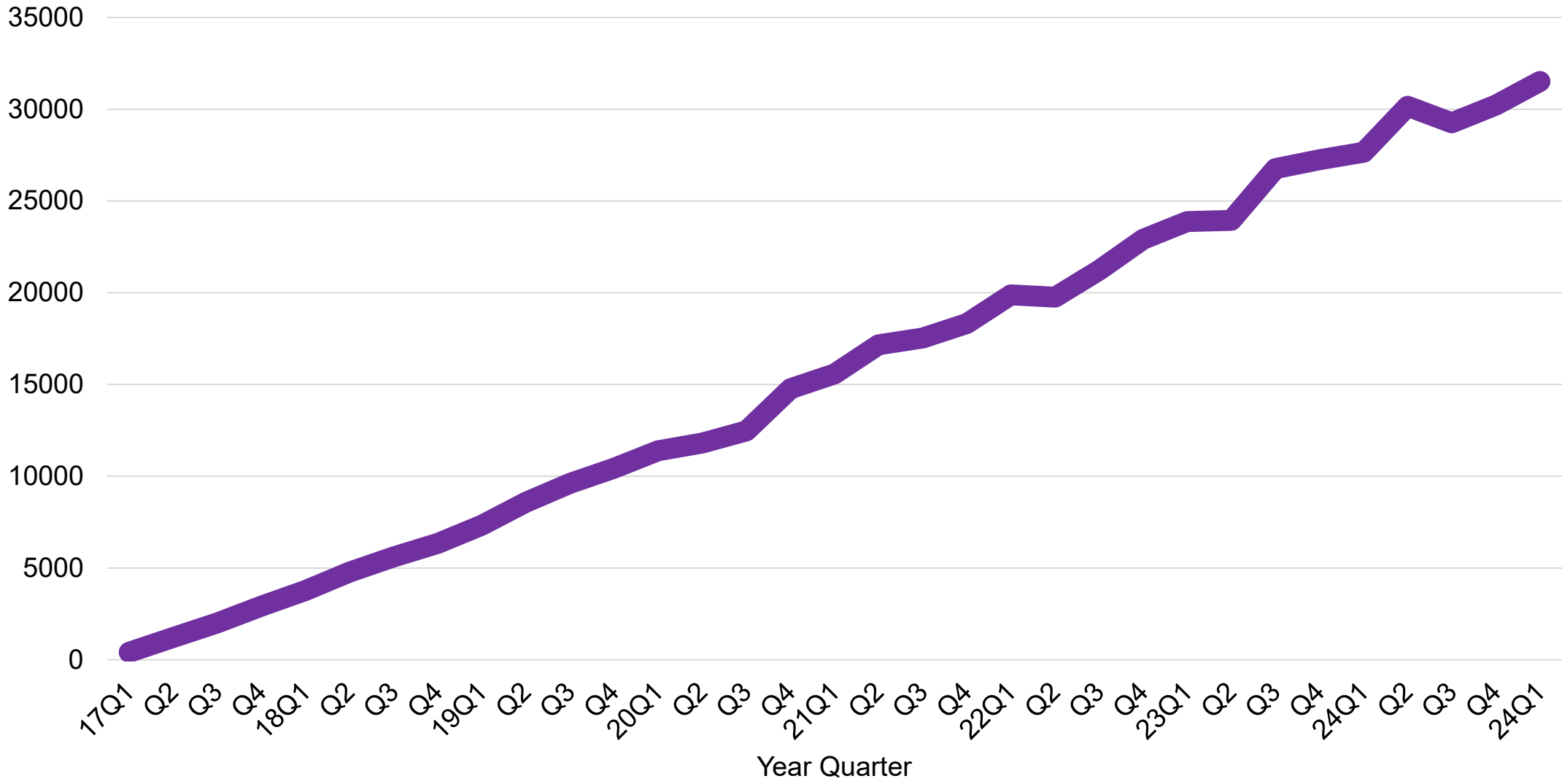
SMA DRUG PIPELINE

We're funding and directing research with more breadth and depth than ever before. We know what we need to do to develop and deliver new therapies, which could also work in combination, to reach our goal of treatments for all ages and types. And we're on the verge of further breakthroughs that will continue to change the course of SMA, and eventually lead to a cure.



BLA = Biologics License Application **IND** = Investigational New Drug **NDA** = New Drug Application Last updated: May 2025

Global Patients on Treatment (200,000)



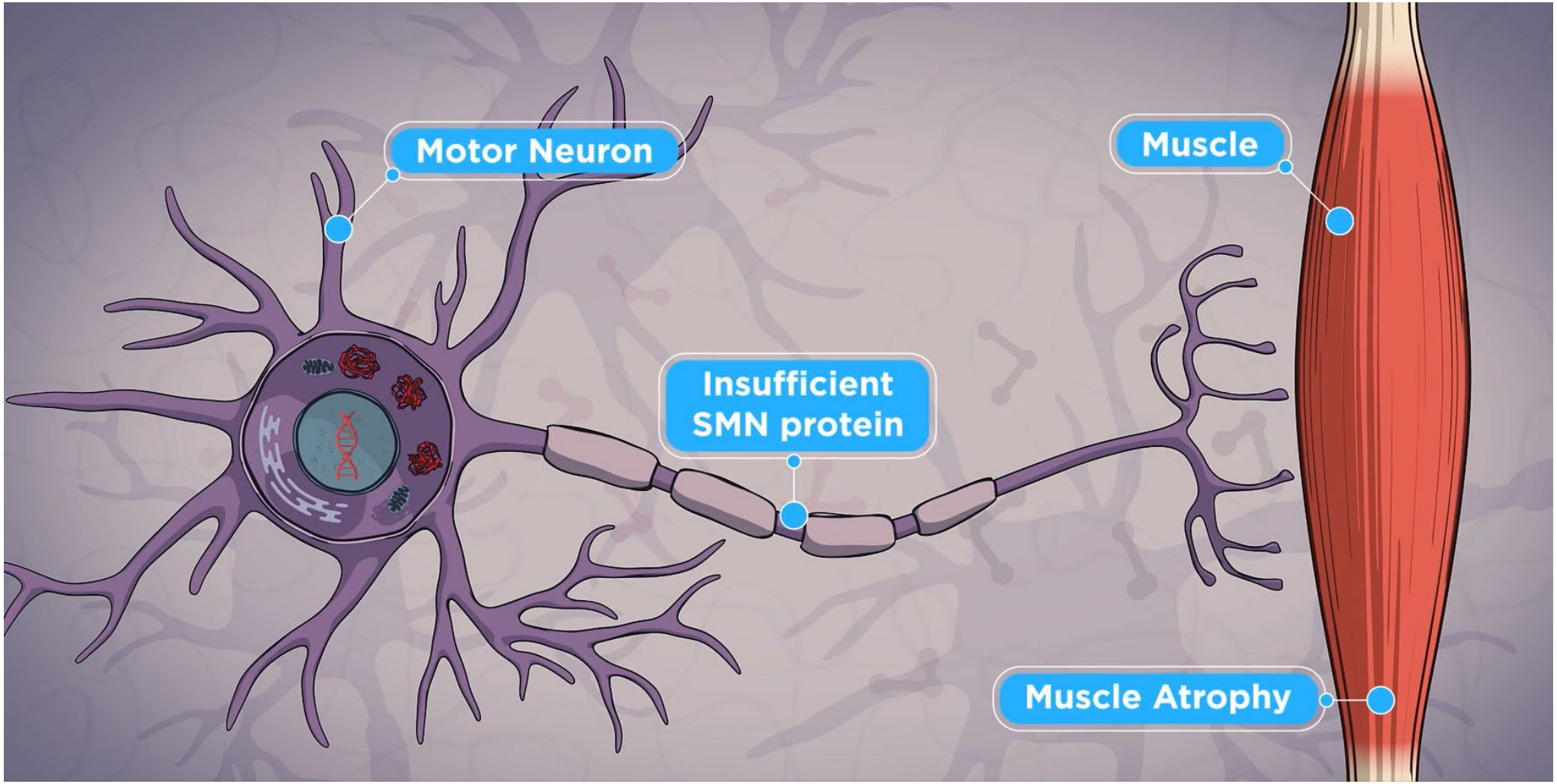
Global Patients on Treatment – 200,000

- **Zero To 30,000**
  - 8 years

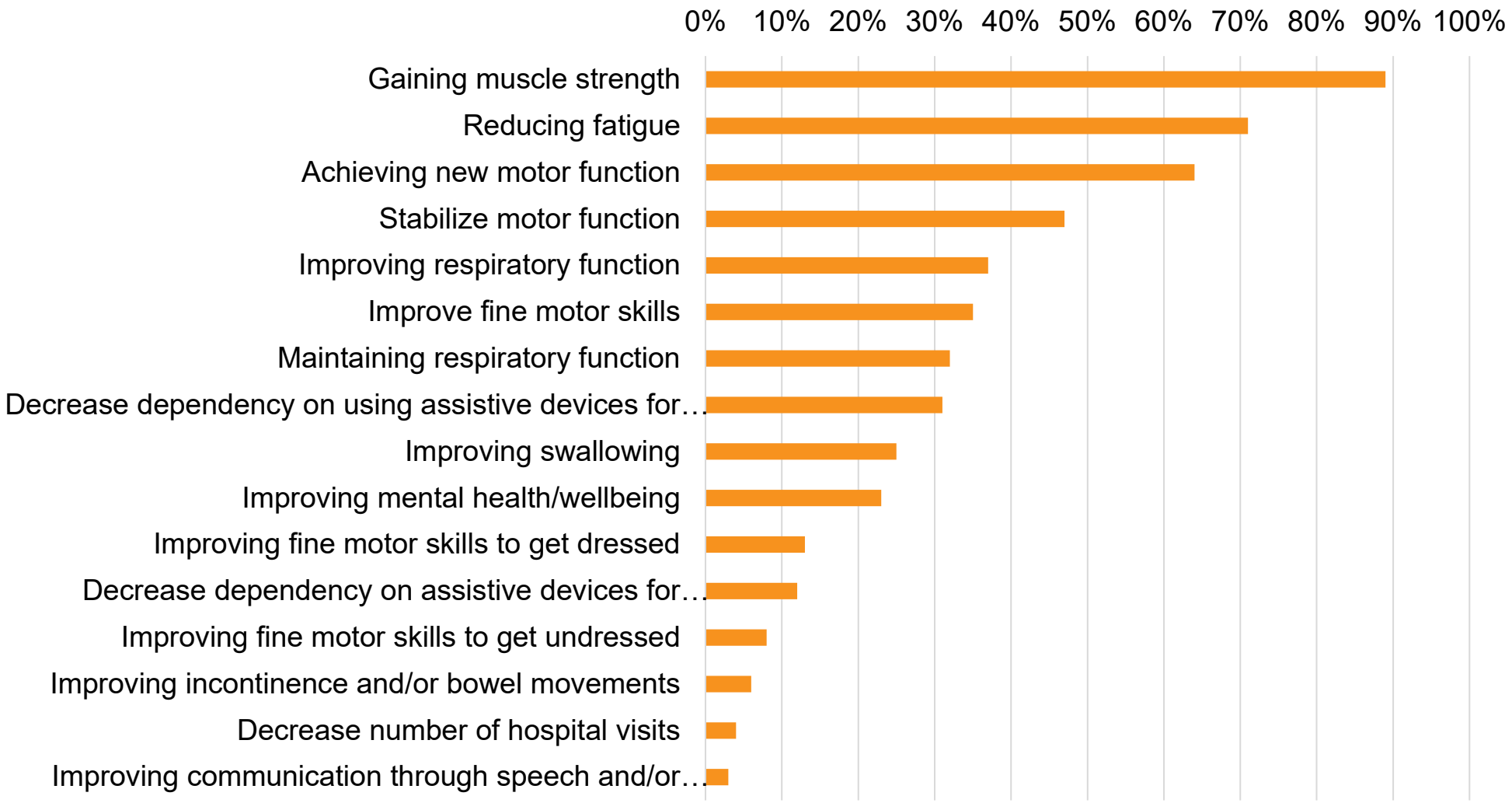
- **How Do We Now Accelerate The Rate**
  - 50 years at same rate…

- **Genetic Treatment First**
- **Then Early Diagnosis**
  - Add on Combinations Next

SMA Genes, Muscles, Nerves

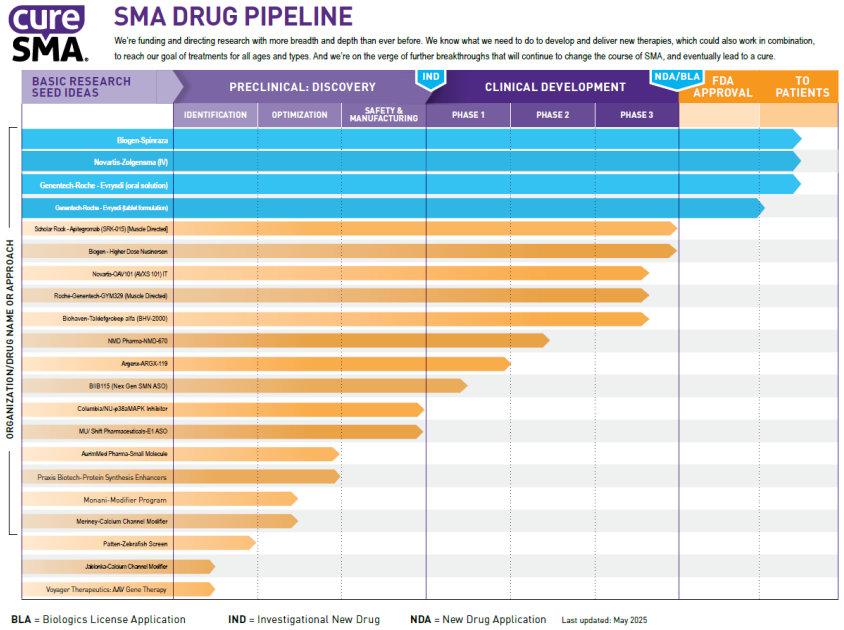


Unmet Needs That We Need to Address



Future Clinical Trials

- **How to Measure Changes**
  - Slower and smaller changes
    - For older, symptomatic patients
    - For combinations
    - Biomarkers (internal signals before external symptoms)



- **Research not Access**
  - Focus is on getting the best data to get the broadest approval as quickly as possible

Real World Evidence

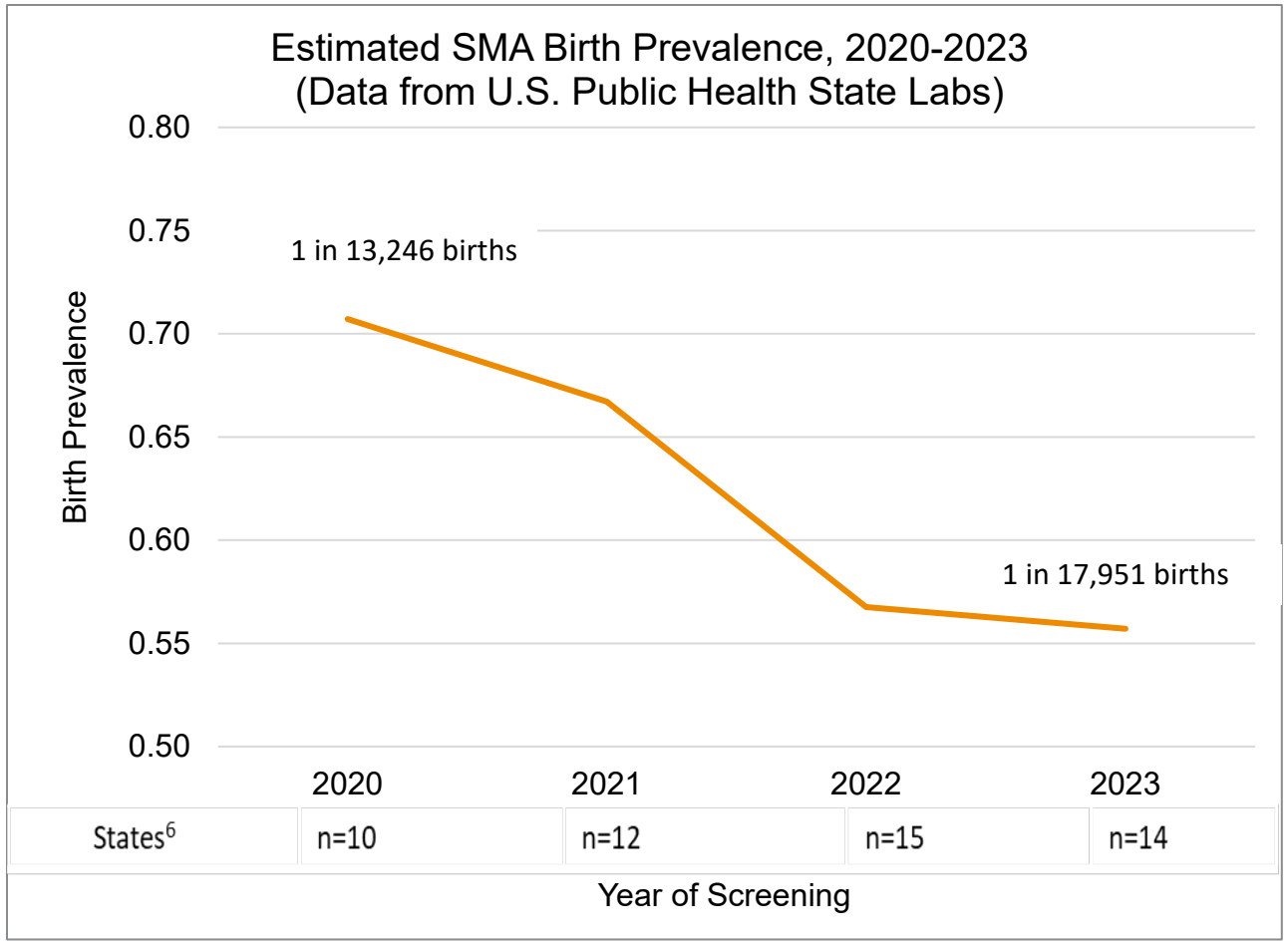
- **Different Than Natural History**
  - And different than clinical trials
  - Reinforces impact in all of the community
- **Patient and Doctors**
  - Personal choices and decisions
  - Treatments and care
- **PNCR Network and ISMAC**
  - US, UK, Italy

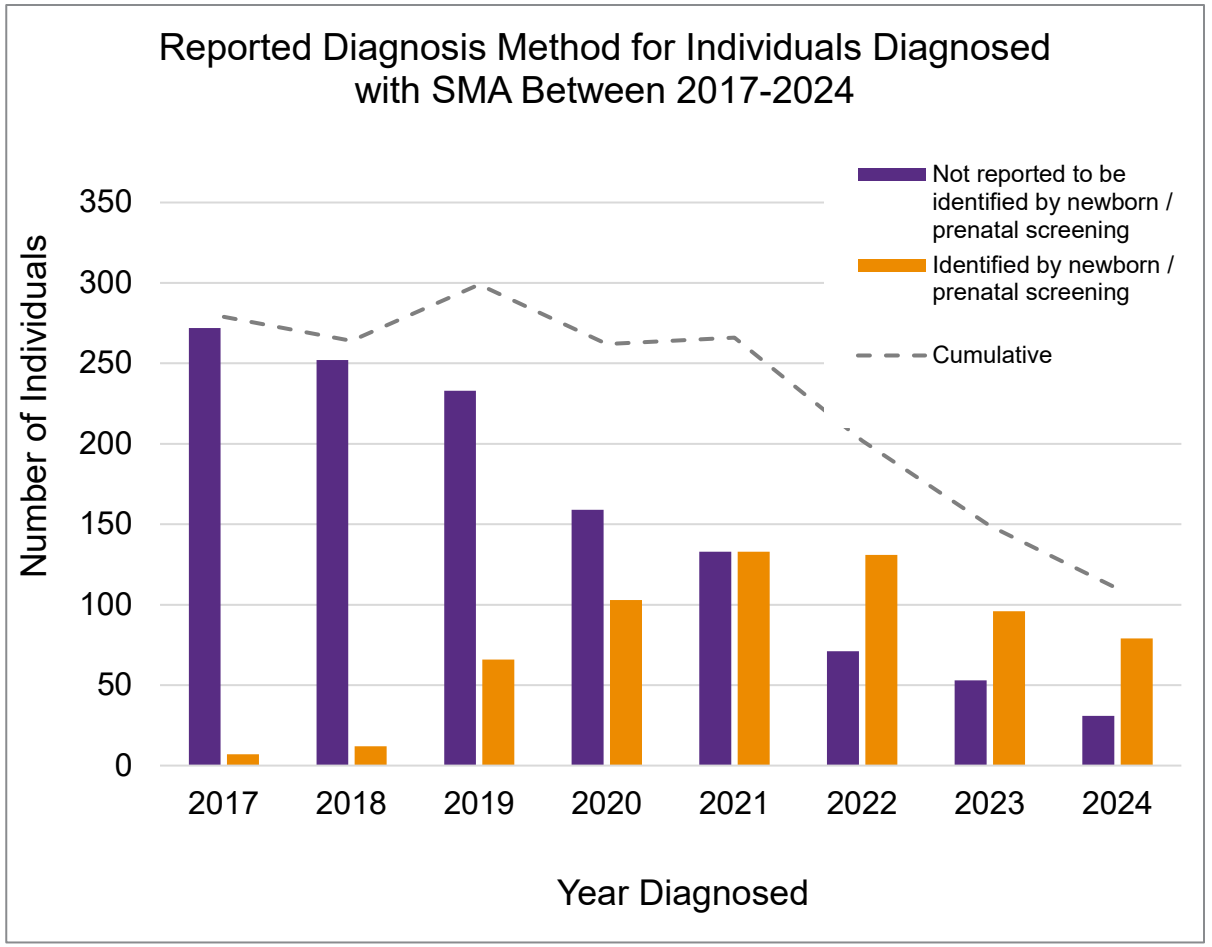
Changing Community: Needs and Makeup

- **Treatment and Early Diagnosis**
  - Change lives
  - Change the community
  - Change priorities

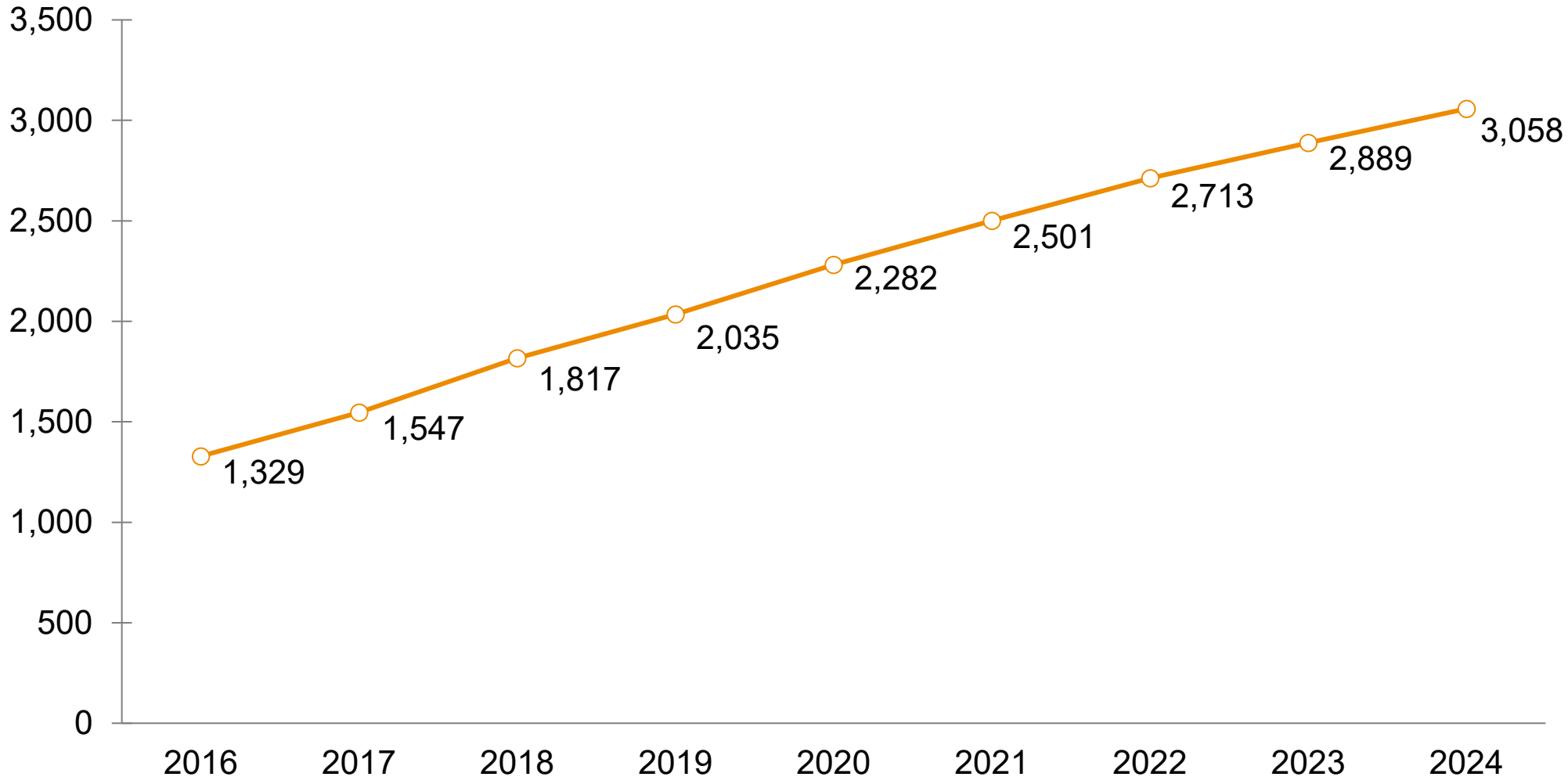
- **The Needs of Older and Symptomatic Individuals and Community**
- **Beyond medical and health**

Diagnosis Trends – Lower Incidence





Adults Joining the Community




Q
A

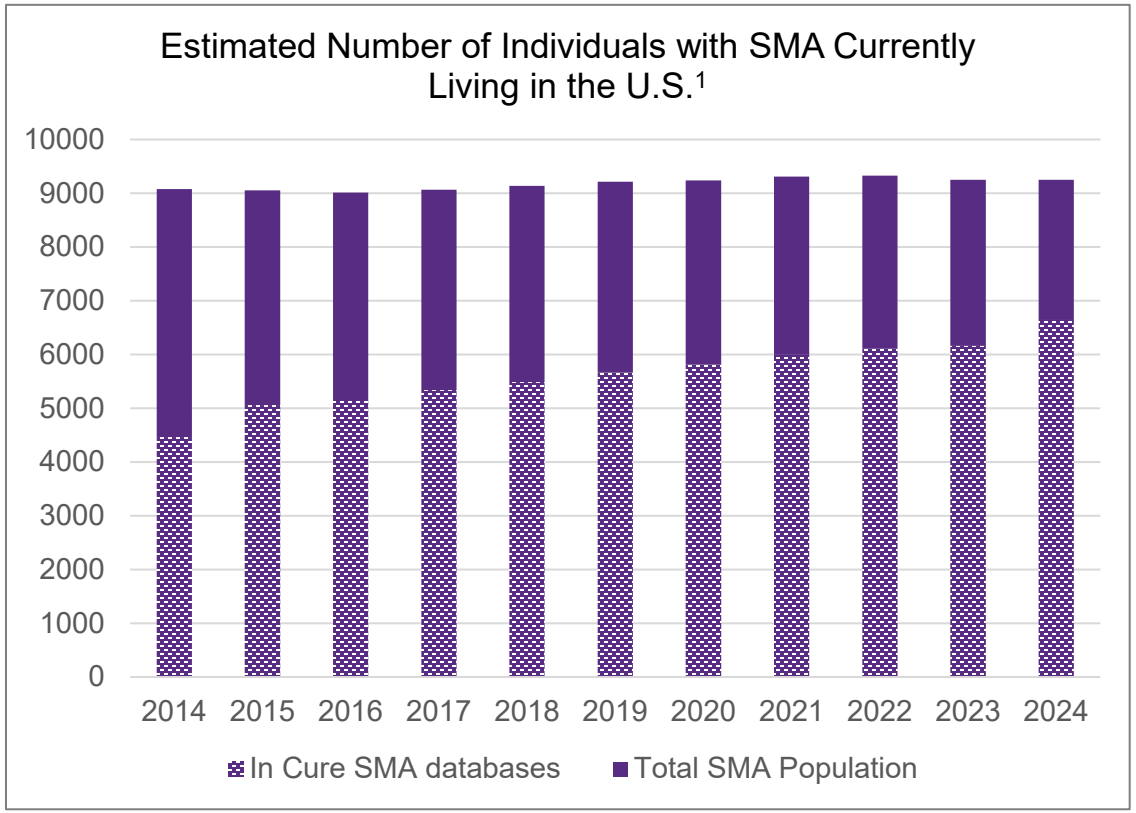
KEY COMMUNITY CHANGES AND TRENDS DATA COLLECTION PROCESSES AND SHARED RESOURCES

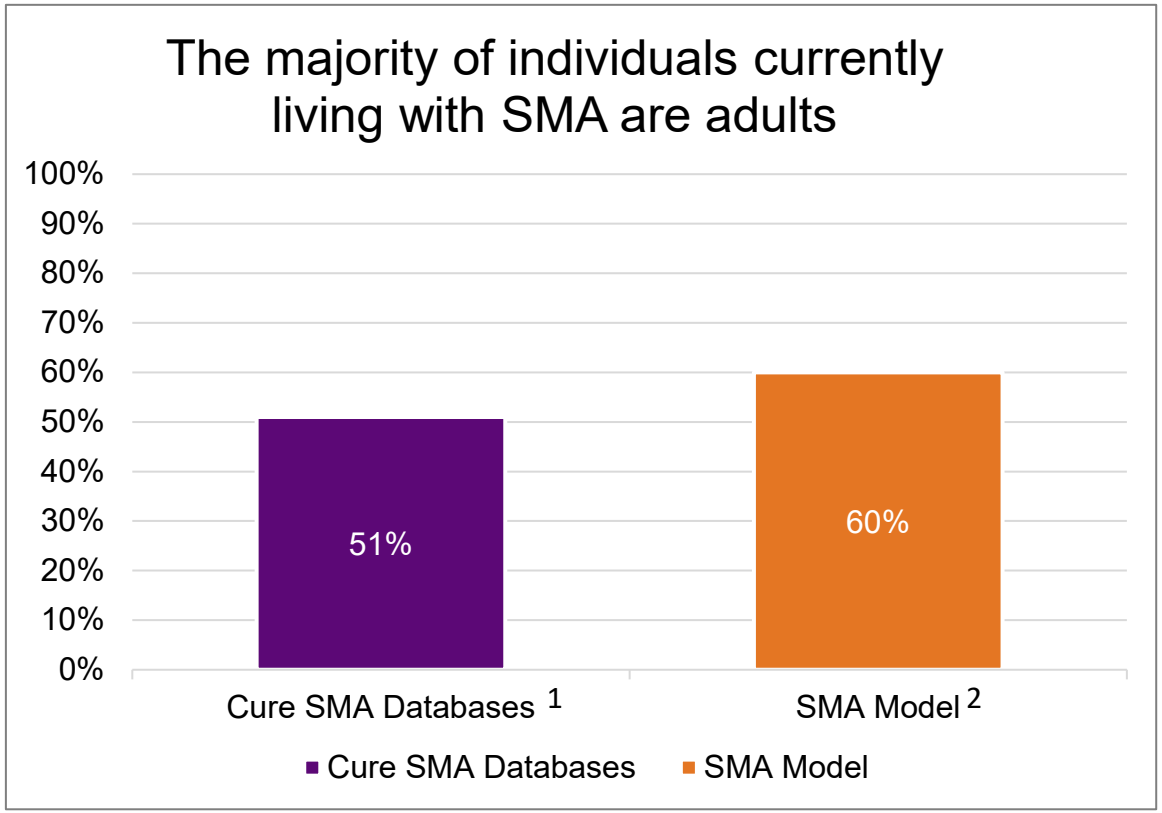
Lisa Belter, MPH

Vice President, Research Data Analytics, Cure SMA

The U.S. SMA Population

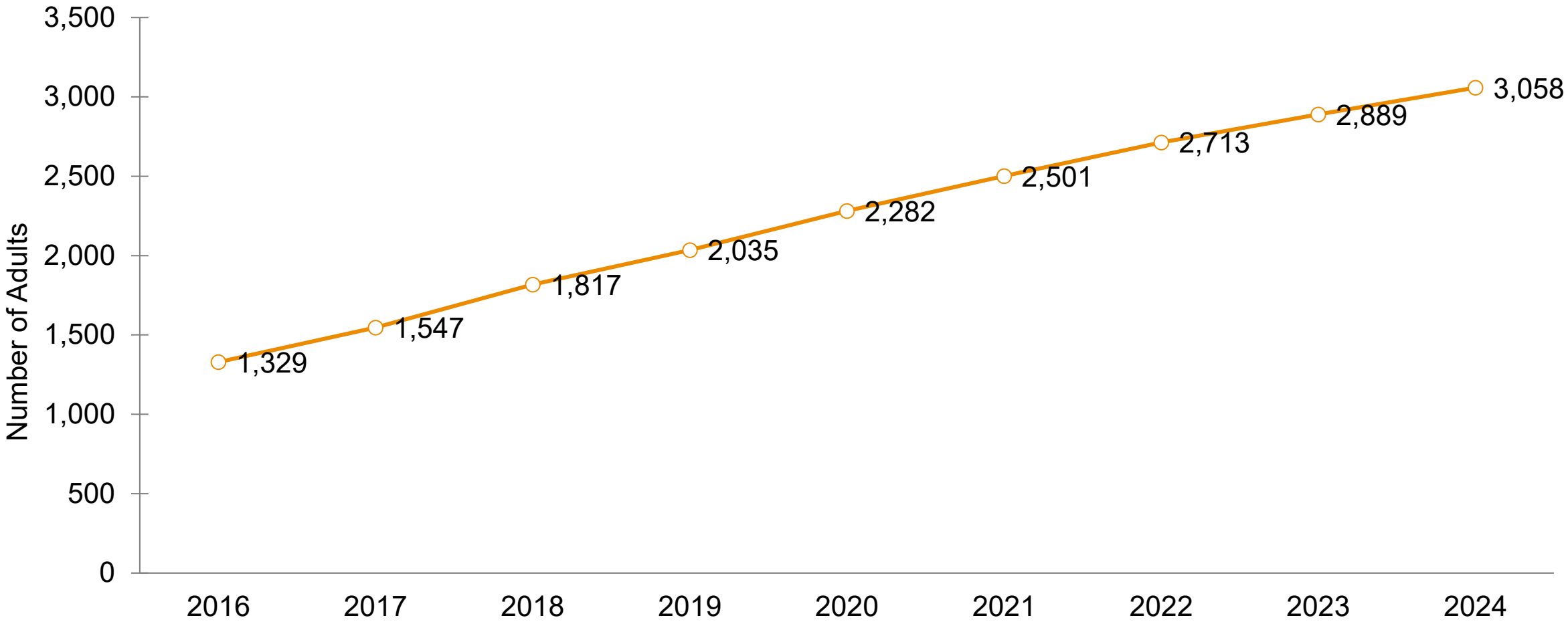
Cure SMA estimates there are currently **9,000-9,500** individuals with SMA currently living in the U.S.



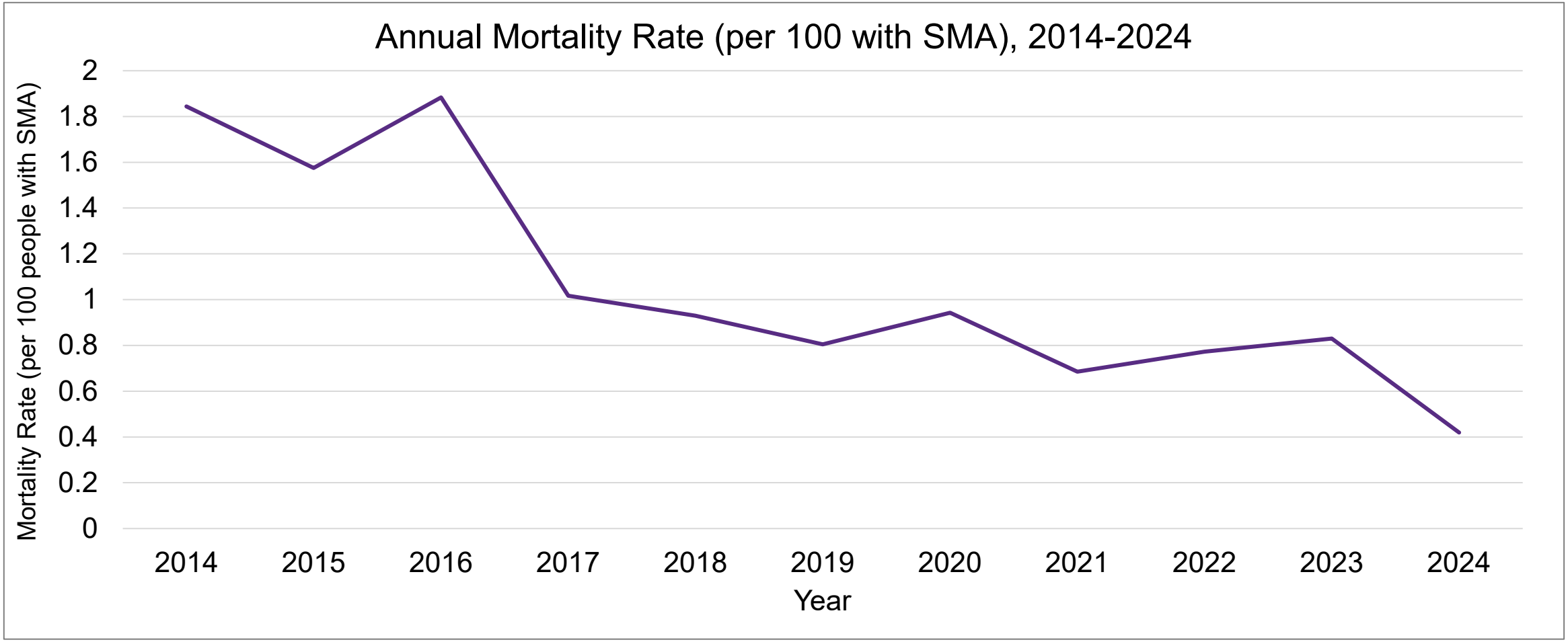


[1] Cure SMA 2024 State of SMA https://www.curesma.org/wp-content/uploads/2025/04/State-of-SMA-Report2024_vWeb-4.pdf
[2] Data from the 2022 State of SMA https://www.curesma.org/wp-content/uploads/2023/06/9062023_State-of-SMA_vWeb.pdf

The number of adults living with SMA in the Cure SMA databases have also steadily increased each year



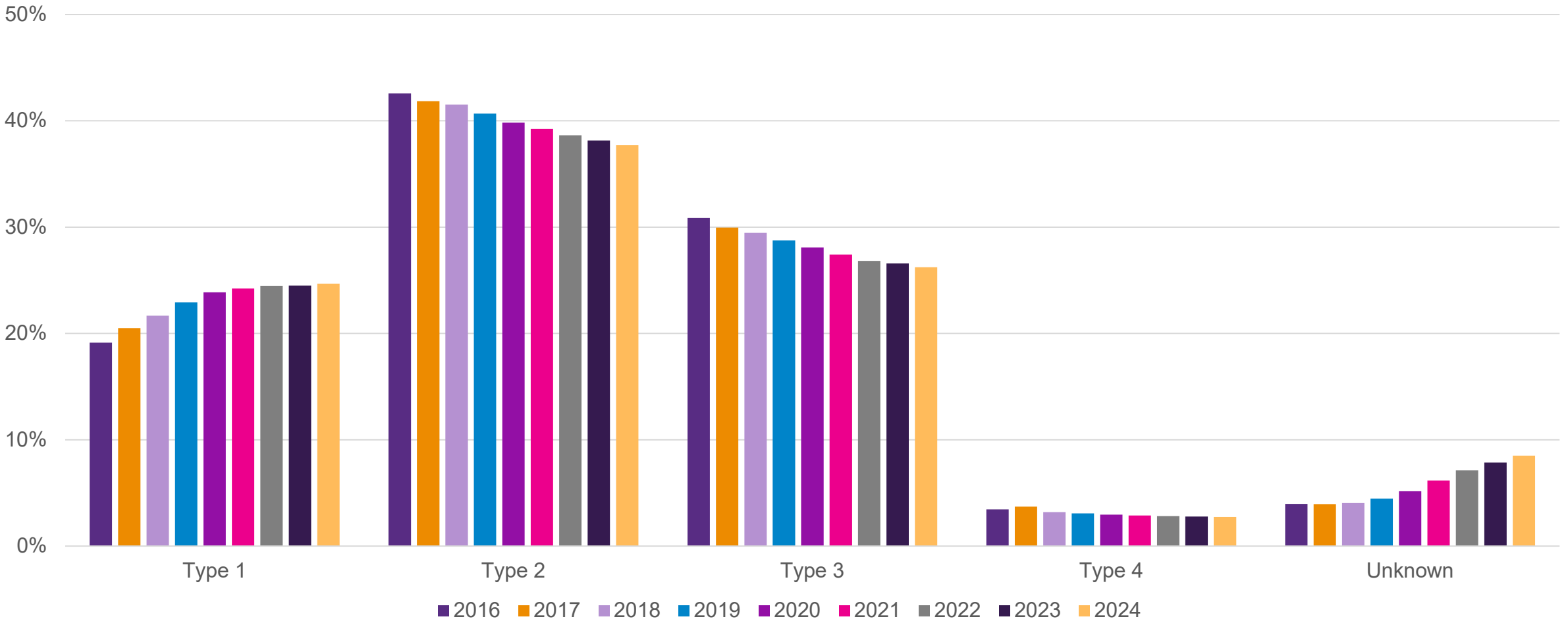
The mortality rate of SMA in 2024 has dropped nearly 80% since 2014, having decreased from 1.84 per 100 individuals to 0.42 per 100 individuals with SMA.



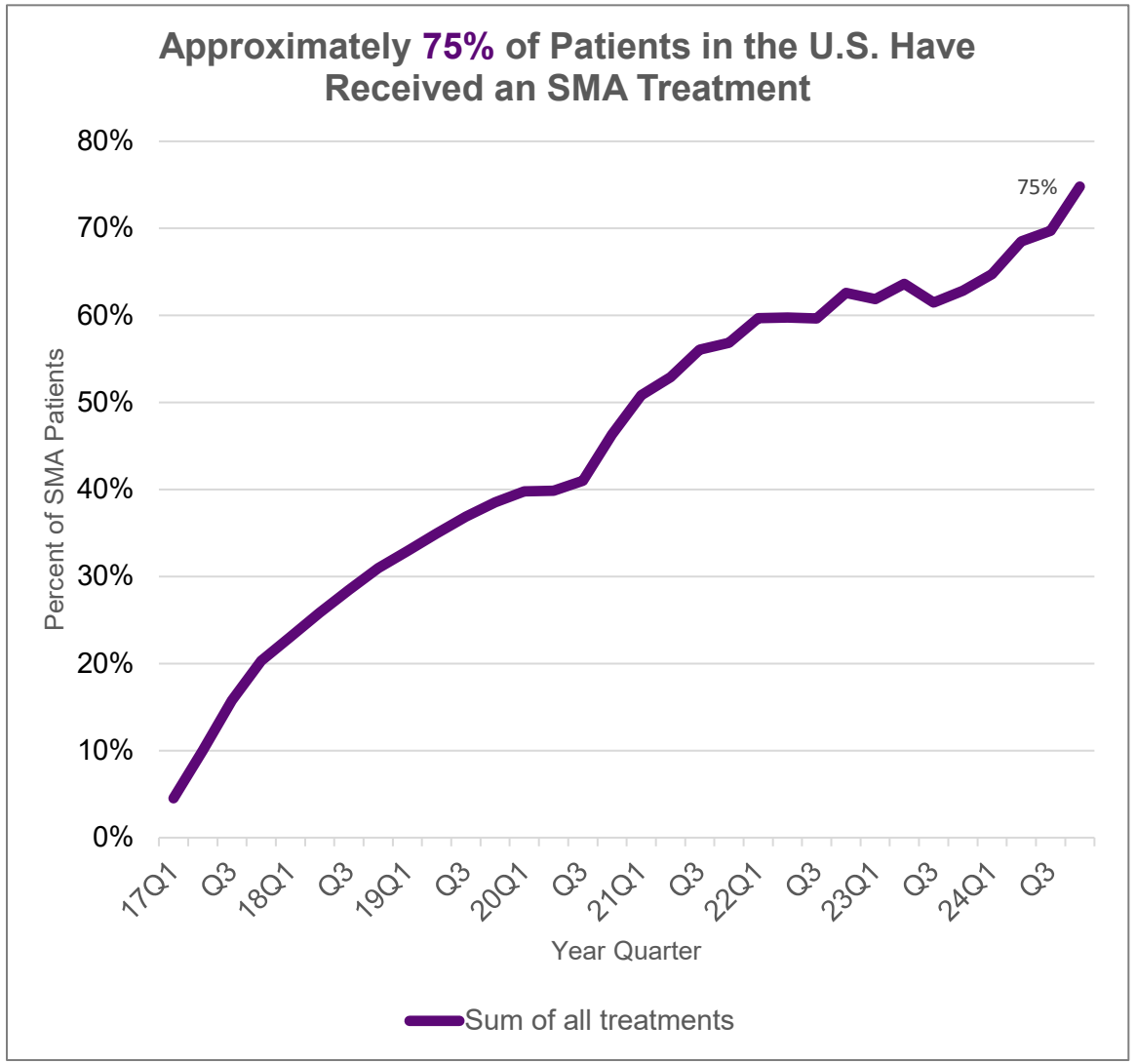
[1] Cure SMA 2024 State of SMA https://www.curesma.org/wp-content/uploads/2025/04/State-of-SMA-Report2024_vWeb-4.pdf

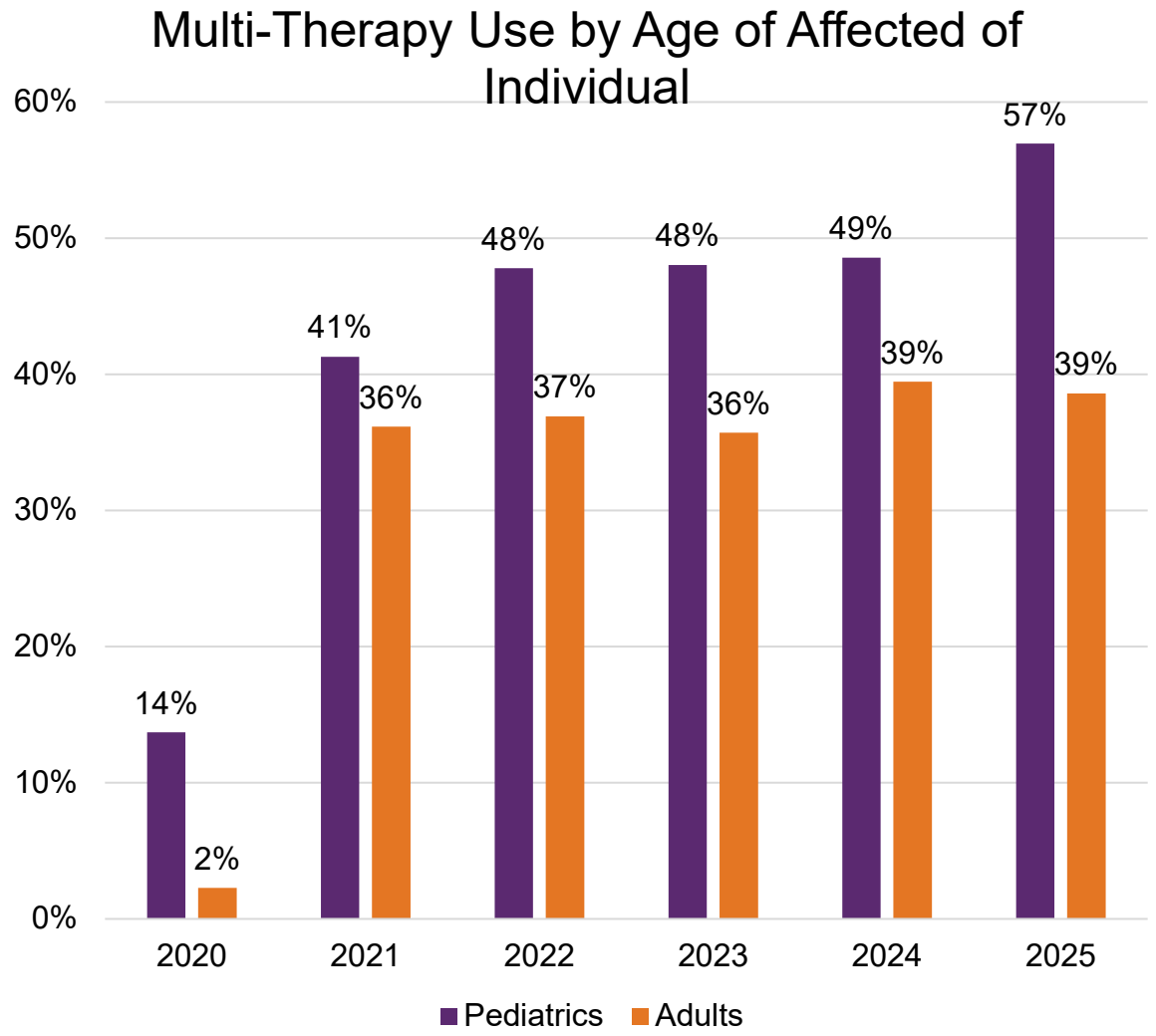
Prevalence of SMA Type Over Time

Cure SMA is observing an increasing proportion of individuals living with SMA type 1 and unknown SMA type over time



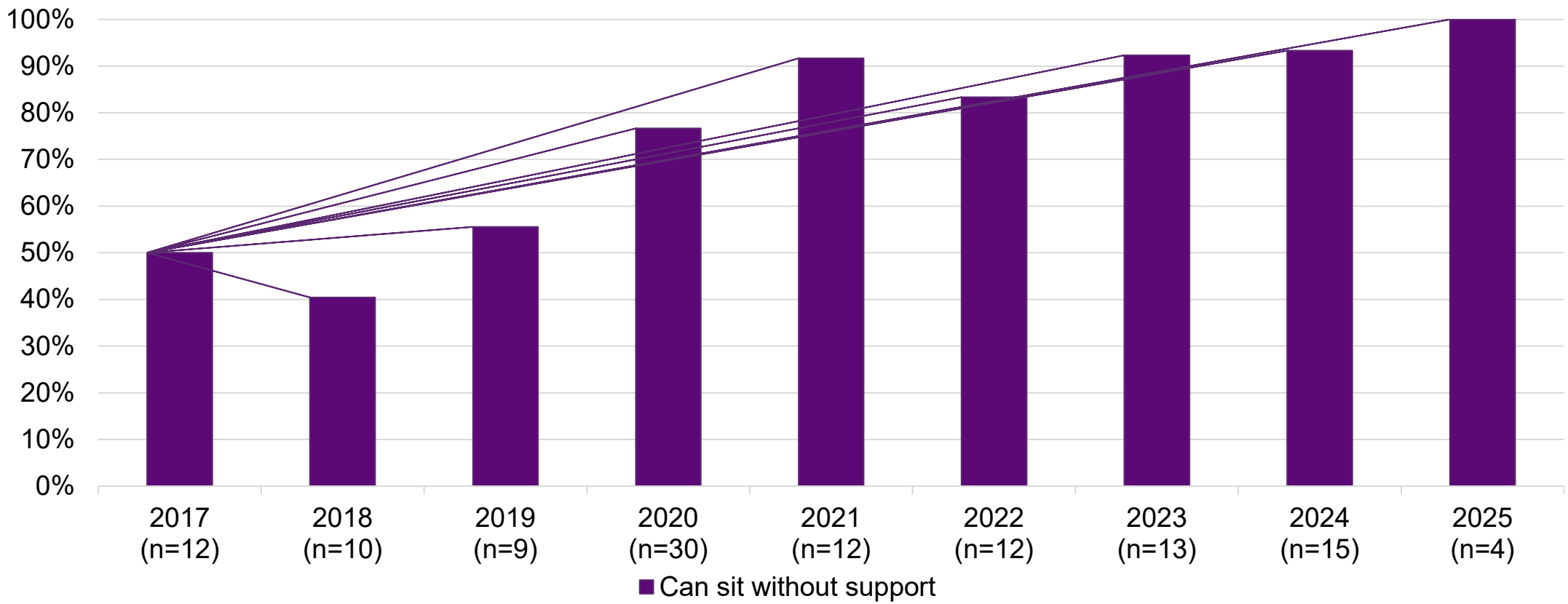
Patients Receiving SMA Treatment in the U.S.





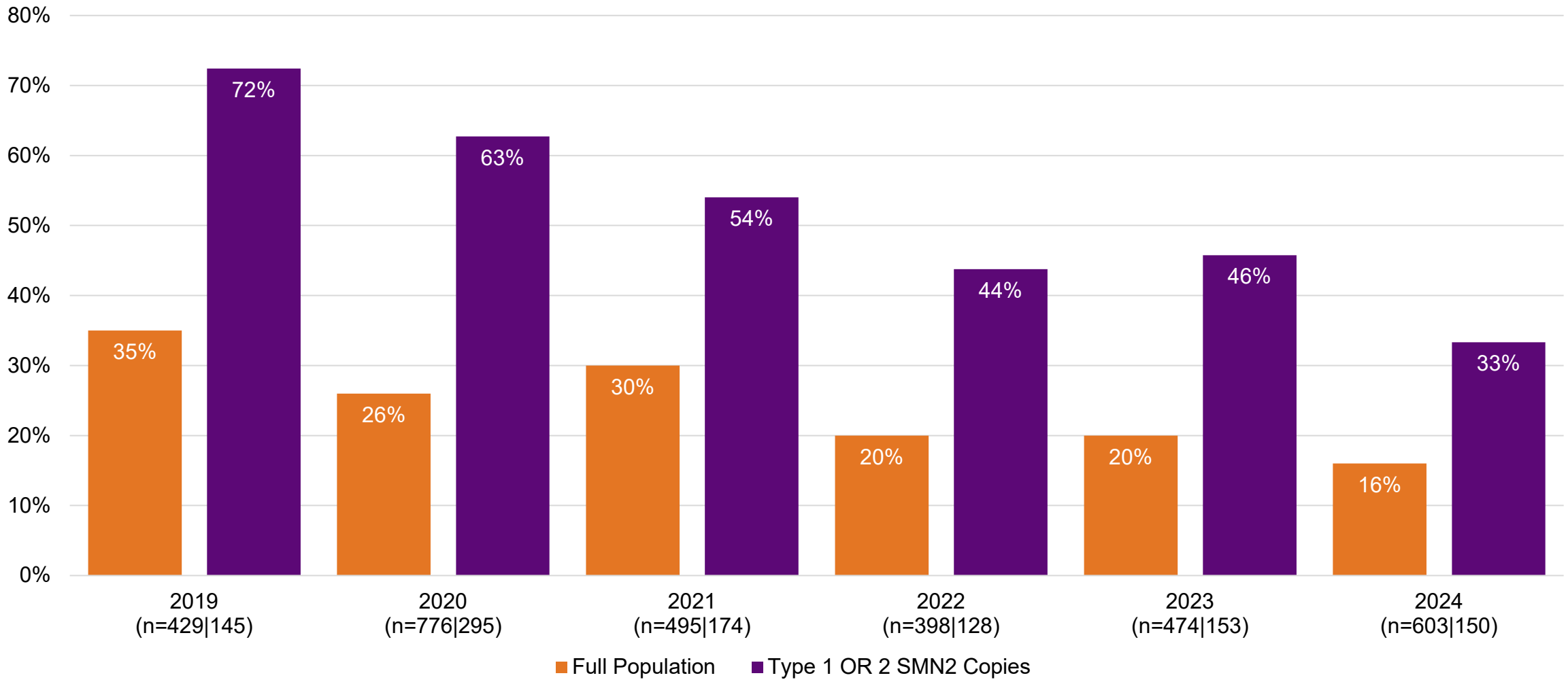
Impact – Sitting – Copy

The proportion of individuals 2 years of age with 2 *SMN2* copies sitting without support has **increased** since 2017

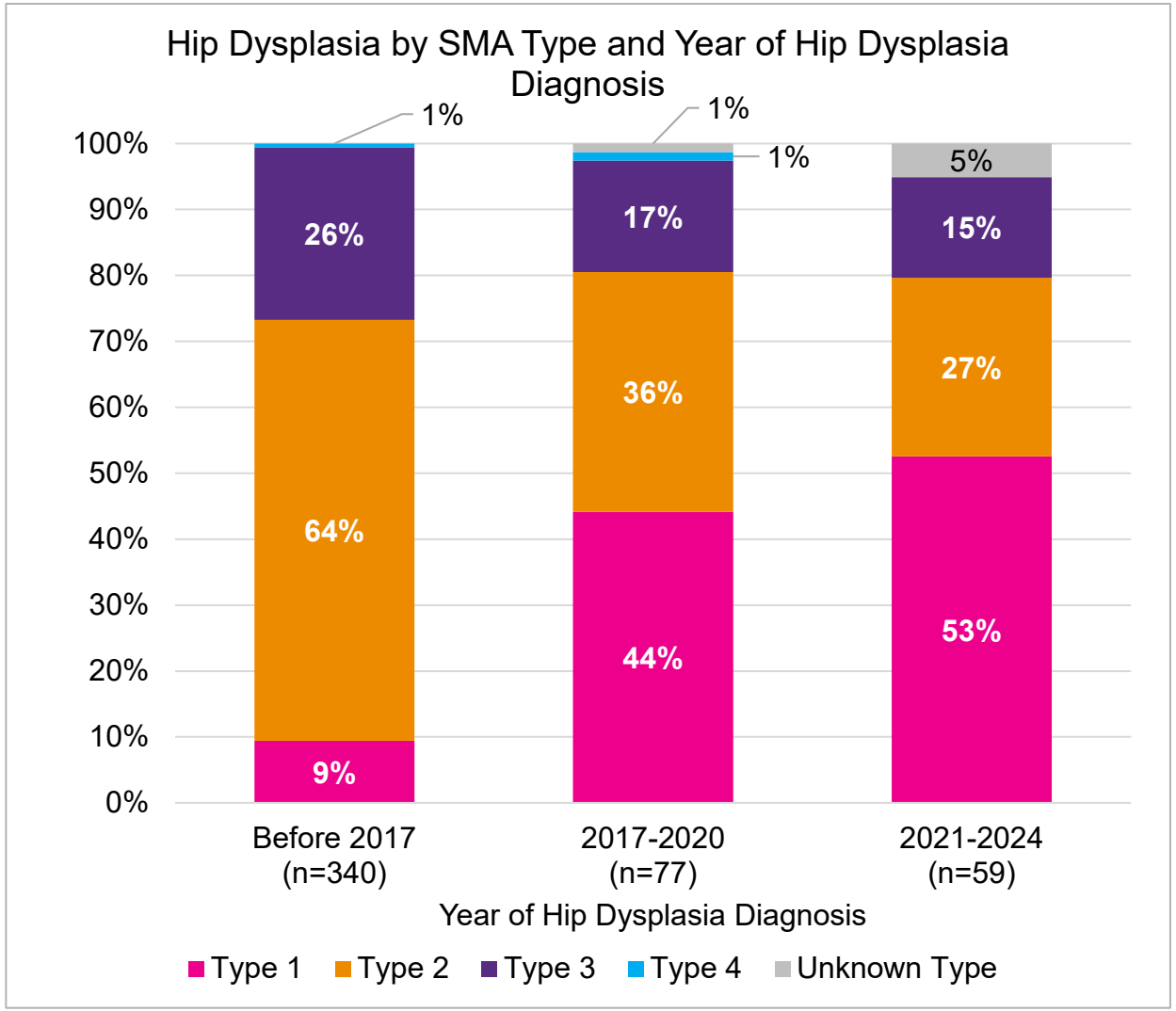


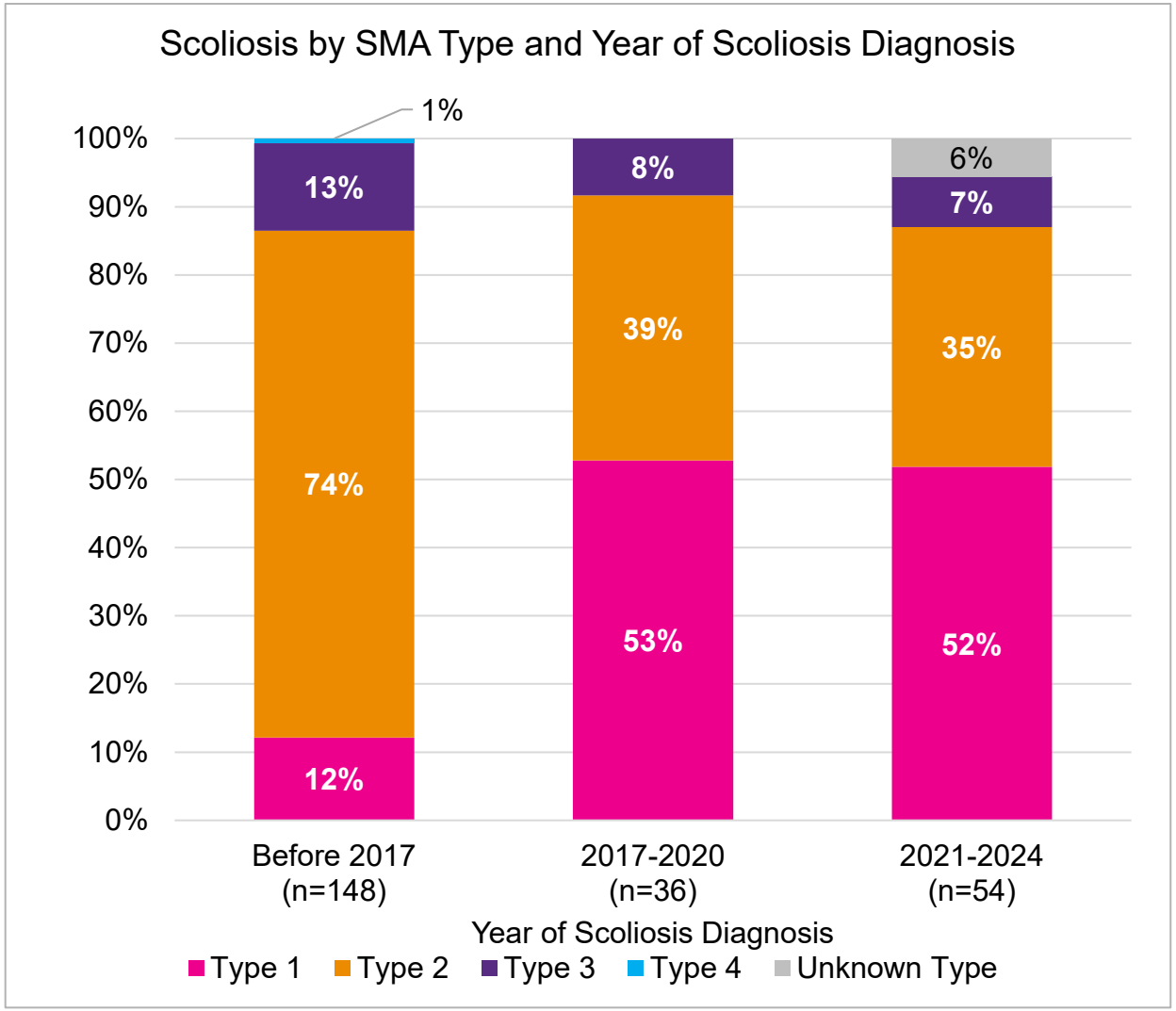
Feeding Tube Utilization

The proportion of individuals using a feeding tube has been **decreasing** since 2019.



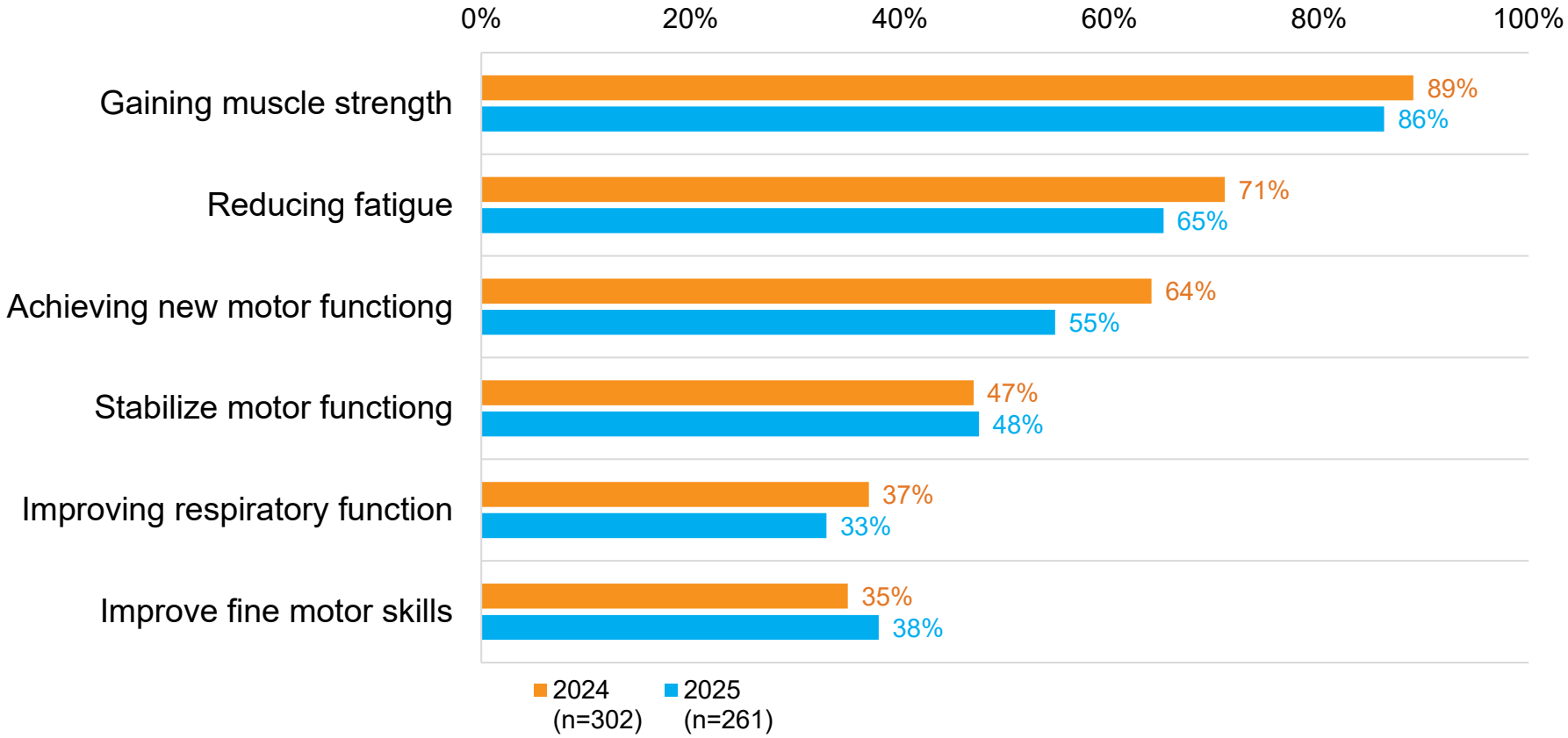
Orthopedic concerns have increased among individuals living with SMA Type 1 over time[1]



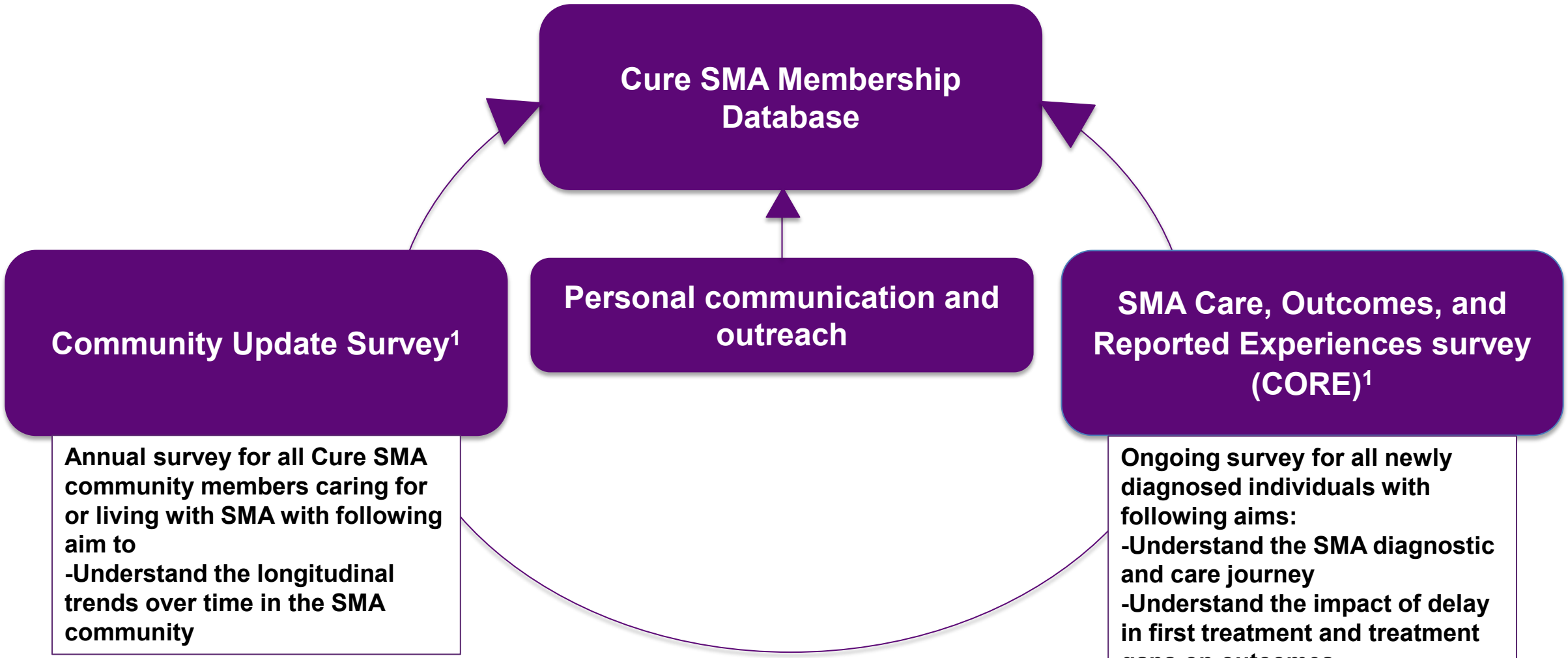


[1]Data source: 2024 & 2025 Community Update Survey

Unmet Needs of Adults Living With SMA from 2024 to 2025



Cure SMA Data Sources

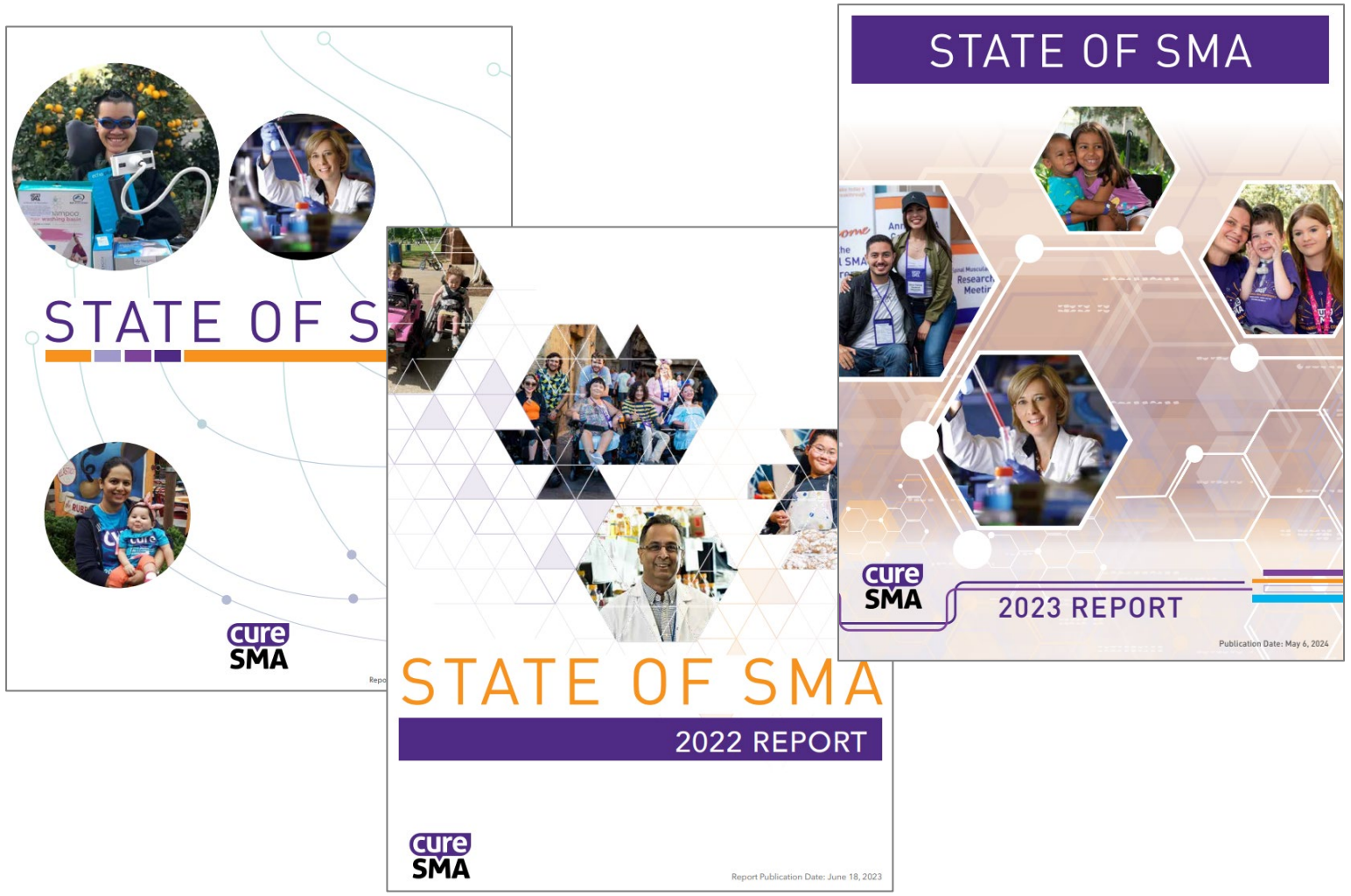


[1] Funding for these surveys are provided by the Cure SMA Industry Collaboration.

Annual State of SMA Report

Data from the Community Update Survey highlights the changing landscape and unmet needs from the community.

The State of SMA report is shared with families, payers, regulators, researchers, healthcare providers, and biotech partners

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THE NEXT BREAKTHROUGHS: TREATMENT FORECAST, NEXT STEPS, AND THE NEED FOR CONTINUED RESEARCH

Jackie Glascock, PhD

Chief Scientific Officer, Cure SMA

SMA DRUG PIPELINE

BLA = Biologics License Application **IND** = Investigational New Drug **NDA** = New Drug Application Last updated: May 2025

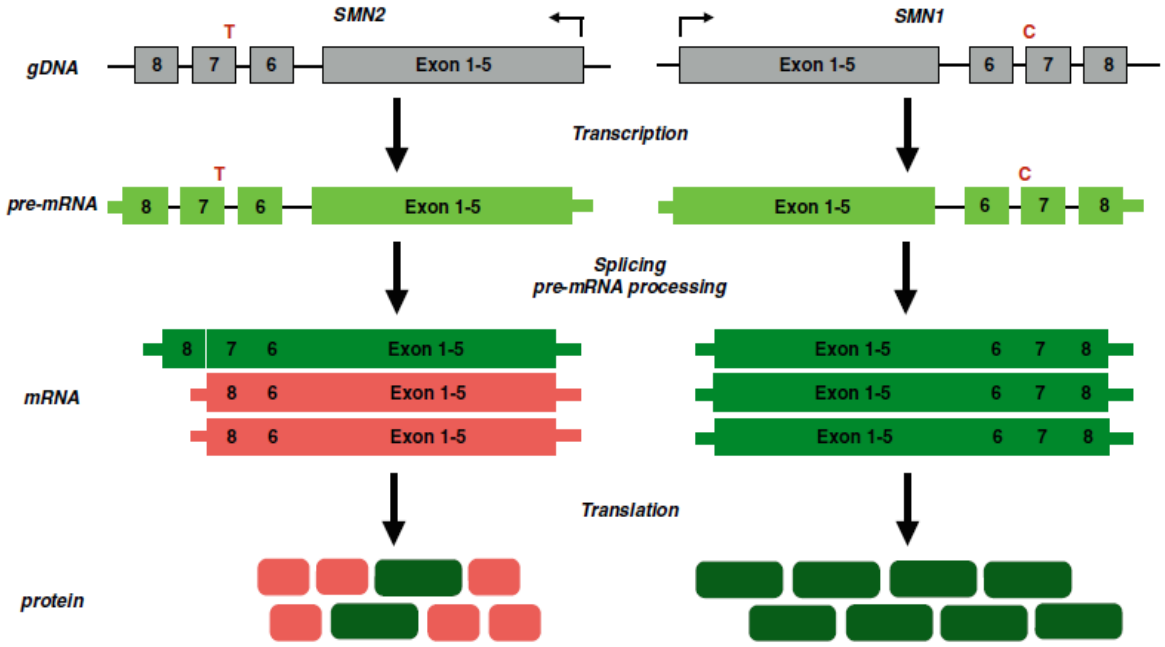
The Evolving Landscape in Spinal Muscular Atrophy

- The FDA-approval of 3 new therapies has revolutionized and dramatically changed the natural history of SMA
- Early identification and treatment dramatically alter long-term outcomes, most strikingly presymptomatically
- Symptomatic treatment providing improvements through increases, stabilization, and slowing
- However, ~50% of all SMA patients in US currently remain untreated

- **Multiple Opportunities for new drugs in 2025**
  - New combination treatments
  - Improvements to our existing drugs
  - If successful, move through
    - FDA approvals
      - And then roll-out for access to patients in the US, and then around the world
        - » Coverage
        - » Delivery
      - **Last 7 years**
        - » 3, and just one at a time

Therapeutic Strategies – SMN Dependent

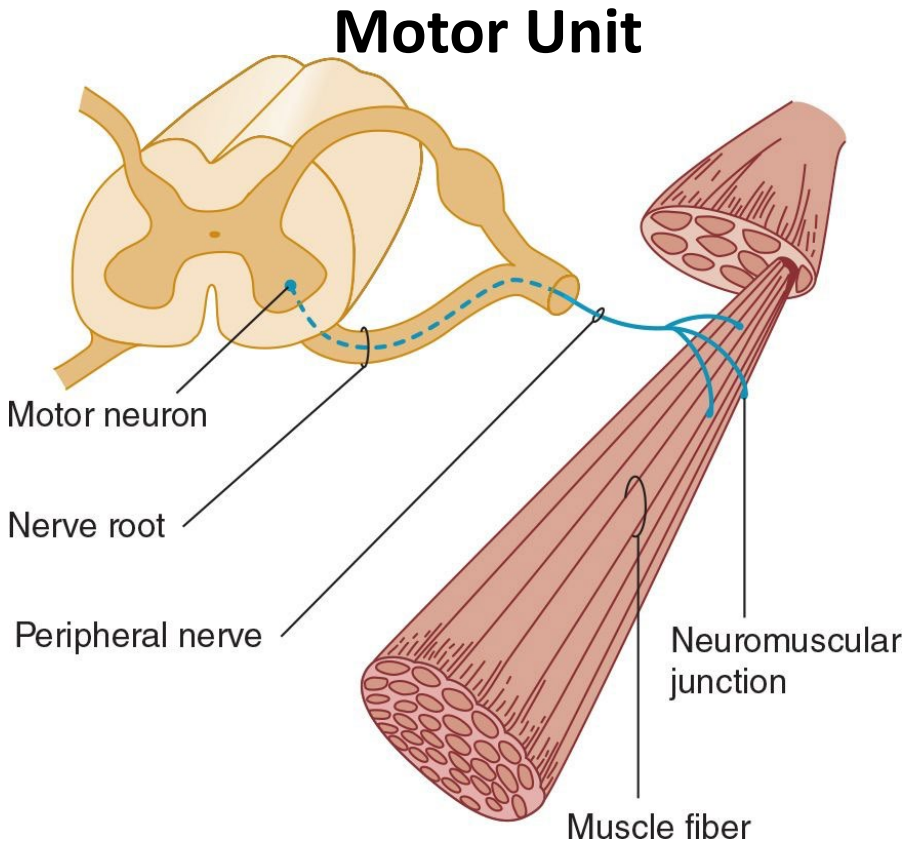
- **Gene Therapy**
  - Replace the missing SMN1 gene via a viral vector
  - Ex. Zolgensma (Novartis)
- **SMN2 splicing modulation**
  - Redirect splicing of SMN2 to make more full-length transcripts containing exon 7
  - Antisense Oligonucleotides (ASOs) or small molecules
  - Ex. Spinraza (Biogen)
  - Ex. Evrysdi (Roche-Genentech)



Van Meerbeke JP et, Discov Med, 2011

Therapeutic Strategies – SMN Independent

- **Neuroprotection**
  - Protect against neuronal injury or degradation
- **Neural transmission**
  - Novel calcium channel agonist
    - Meriney at Univ of Pittsburgh
- **Regenerative targets**
  - Promote axonal growth/nerve terminal sprouting
  - Promote muscle regeneration
- **Muscle enhancement**
  - Ex. SRK-015/Apitegromab (Scholar Rock)
  - Ex. Taldefgrobep Alfa (Biohaven)
  - Ex. RO7204239/GYM329 (Roche/Genentech)
  - Ex. NMD-670 (NMD Pharma)
- **Genetic Modifiers**
  - Broader functionality
    - Monani at Columbia
- **Combinations of above or with SMN dependent therapies**



Chapter 9 Motor Disorders, Simon RP, Aminoff MJ, Greenberg DA. Clinical Neurology, 10e; 2017. Available at: https://accessmedicine.mhmedical.com/content.aspx?bookid=2274&sectionid=176233445 Accessed: August 22, 2024

Next Treatment Breakthroughs

- **Improvements to Our Existing Treatments**
  - Higher dose of Spinraza (Biogen)
    - May increase **benefits and longevity of treatment effect**
  - New formulation of Evrysdi (Genentech)
    - May allow easier **administration at home and during travel**
  - Different (IT) delivery route for Zolgensma (Novartis)
    - Could expand **availability to more people over the age of 2**
  - New device to deliver Spinraza (Alcyone/Biogen)
    - Could make Spinraza **delivery easier to repeat**
- **Brand New Combination Treatments Focused on the Muscles**
  - Anti-myostatin combination treatment (Scholar Rock)
    - Aims to **restore muscle strength and function** in addition to SMN upregulating therapies
  - Anti-myostatin combination treatment from (Biohaven)
    - Aims to **restore muscle strength and function** in addition to SMN upregulating therapies
  - Anti-myostatin combination treatment from (Genentech)
    - Aims to **restore muscle strength and function** in addition to SMN upregulating therapies

Update on New and Investigational Drugs

- **Genentech/Roche – tablet formulation of Evrysdi**
  - Recently approved
- **Scholar Rock – Apitegromab**
  - Under regulatory review
- **Biogen – higher dose nusinersen (Spinraza)**
  - Under regulatory review
- **Novartis – IT gene therapy**
- **Biohaven - Taldefgrobep alfa**

Genentech/Roche (Tablet Formulation of Evrysdi)

- **Evrysdi alters the splicing of SMN2 to produce more fully functional SMN protein.**
- Currently available as a liquid medication given daily, by mouth or G-tube
- Tablet formulation eliminates need for refrigeration and increases ease of travel

Genentech
A Member of the Roche Group

Scholar Rock (Apitegromab)

- **Apitegromab is an investigational fully human monoclonal antibody inhibiting myostatin activation by selectively binding the pro- and latent forms of myostatin in the skeletal muscle**
- **SAPPHIRE study is now complete (phase 3)**
  - Evaluating the safety and efficacy of apitegromab in nonambulatory patients with Types 2 and 3 spinal muscular atrophy (SMA) who are receiving SMN therapy (either nusinersen or risdiplam)
  - Patients 2 to 21 years of age
  - Met Primary Endpoint
    - Significant and clinically meaningful improvement in motor function as measured by the gold standard Hammersmith Functional Motor Scale Expanded (HFMSE) for patients with SMA receiving apitegromab versus placebo (current standard of care) at week 52

ScholarRock™

Biogen (Higher Dose Nusinersen)

- **Nusinersen is an antisense oligonucleotide administered intrathecally that alters the splicing of the *SMN2* pre-messenger RNA (mRNA), promoting the expression of SMN protein**
- **DEVOTE study is completed (phase 3)**
  - Evaluating the clinical efficacy, safety, and tolerability of higher-dose regimens of nusinersen intrathecally administered to participants with SMA
  - Ages 7 days and older
  - Met Primary Endpoint
    - Significant improvement in motor function in infants who received the higher dose regimen as compared to a prespecified matched sham (untreated) control group from the ENDEAR study

Biogen

Novartis (OAV101)

- **OAV101 is an investigational gene therapy**
- **STEER study is active, not enrolling (phase 3)**
  - Intrathecal administration of OAV101
  - Evaluating the clinical efficacy, safety and tolerability of OAV101 IT in patients with SMA Type 2 between 2 to <18 years of age who are able to sit but never walked, and have never received treatment for SMA
  - Met Primary Endpoint
    - Increase from baseline in HFMSE total score in patients with SMA treated with intrathecal onasemnogene abeparvovec (OAV101 IT)
- **STRENGTH study is complete (phase 3)**
  - Intrathecal administration of OAV101
  - Evaluating safety, tolerability, and efficacy of OAV101 IT in patients with SMA between 2 to <18 years of age who discontinued treatment with nusinersen or risdiplam.
  - Met Primary Endpoint
    - OAV101 IT demonstrated a favorable safety profile that was consistent with STEER study.
    - The motor endpoint of efficacy, HFMSE, demonstrated stabilization for the overall study population over 52 weeks.
    - The increase from baseline to 52 weeks in HFMSE least squares (LS) total score was 1.05.

NOVARTIS

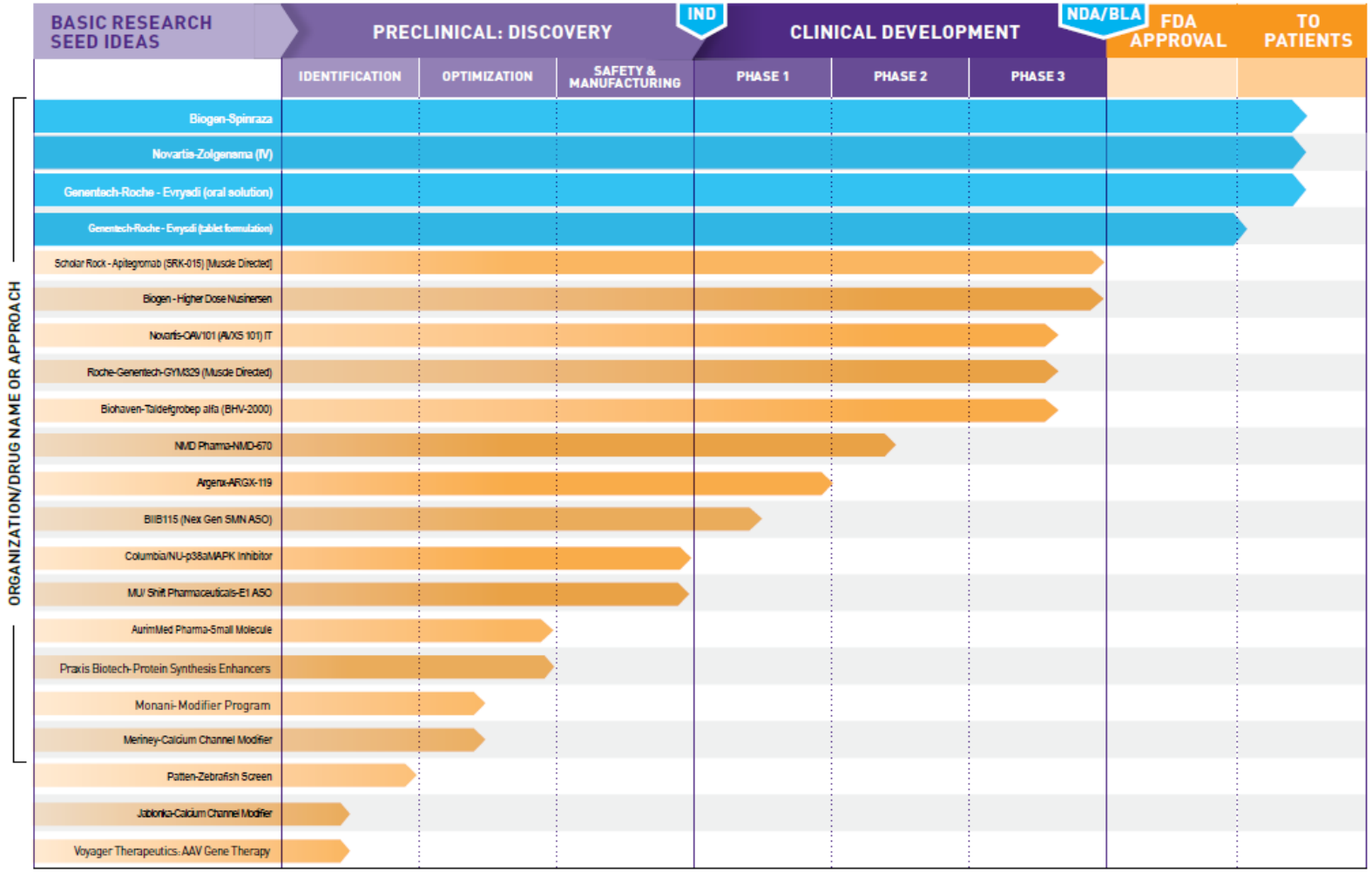
Biohaven (Taldefgrobep alfa)

- **Taldefgrobep alfa is a myostatin inhibitor in clinical development that targets both myostatin and activin A signaling, two key regulators of muscle mass and adipose tissue**
- **RESILIENT study is ongoing (phase 3)**
  - Evaluating the efficacy and safety of taldefgrobep alfa as adjunctive therapy to increase muscle in SMA patients treated with standard of care nusinersen, risdiplam or onasemnogene abeparvovec-xioi
  - Ages 4 to 21

biohaven pharmaceuticals

SMA DRUG PIPELINE

We're funding and directing research with more breadth and depth than ever before. We know what we need to do to develop and deliver new therapies, which could also work in combination, to reach our goal of treatments for all ages and types. And we're on the verge of further breakthroughs that will continue to change the course of SMA, and eventually lead to a cure.

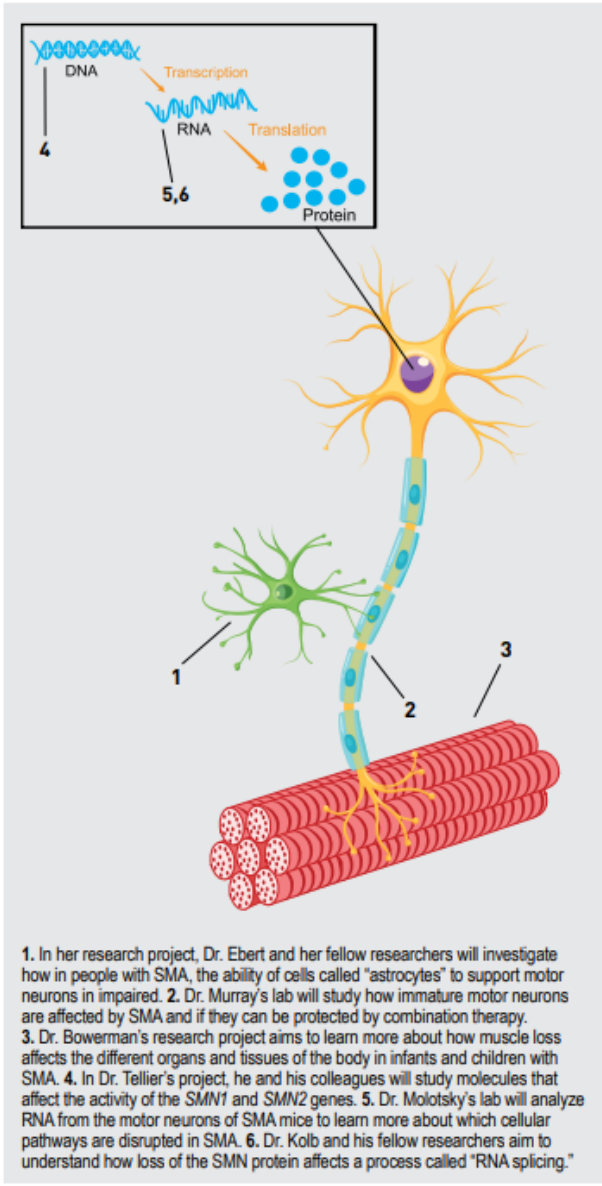


BLA = Biologics License Application **IND** = Investigational New Drug **NDA** = New Drug Application Last updated: May 2025

Continued Need For Basic Research

- **More Treatments**
  - Identification of new druggable targets
  - More options for all ages/stages of SMA

- **SMN Independent – New Targets**
  - Neuroprotection
  - Regenerative targets
  - Muscle enhancement
  - In combination with SMN Dependent approaches



1. In her research project, Dr. Ebert and her fellow researchers will investigate how in people with SMA, the ability of cells called "astrocytes" to support motor neurons in impaired. **2.** Dr. Murray's lab will study how immature motor neurons are affected by SMA and if they can be protected by combination therapy. **3.** Dr. Bowerman's research project aims to learn more about how muscle loss affects the different organs and tissues of the body in infants and children with SMA. **4.** In Dr. Tellier's project, he and his colleagues will study molecules that affect the activity of the *SMN1* and *SMN2* genes. **5.** Dr. Molotsky's lab will analyze RNA from the motor neurons of SMA mice to learn more about which cellular pathways are disrupted in SMA. **6.** Dr. Kolb and his fellow researchers aim to understand how loss of the SMN protein affects a process called "RNA splicing."

Figure 1. Cure SMA Basic Research Grant recipients plan to use a variety of approaches to learn more about SMA disease and treatment.

Current Basic Research Grant Funding

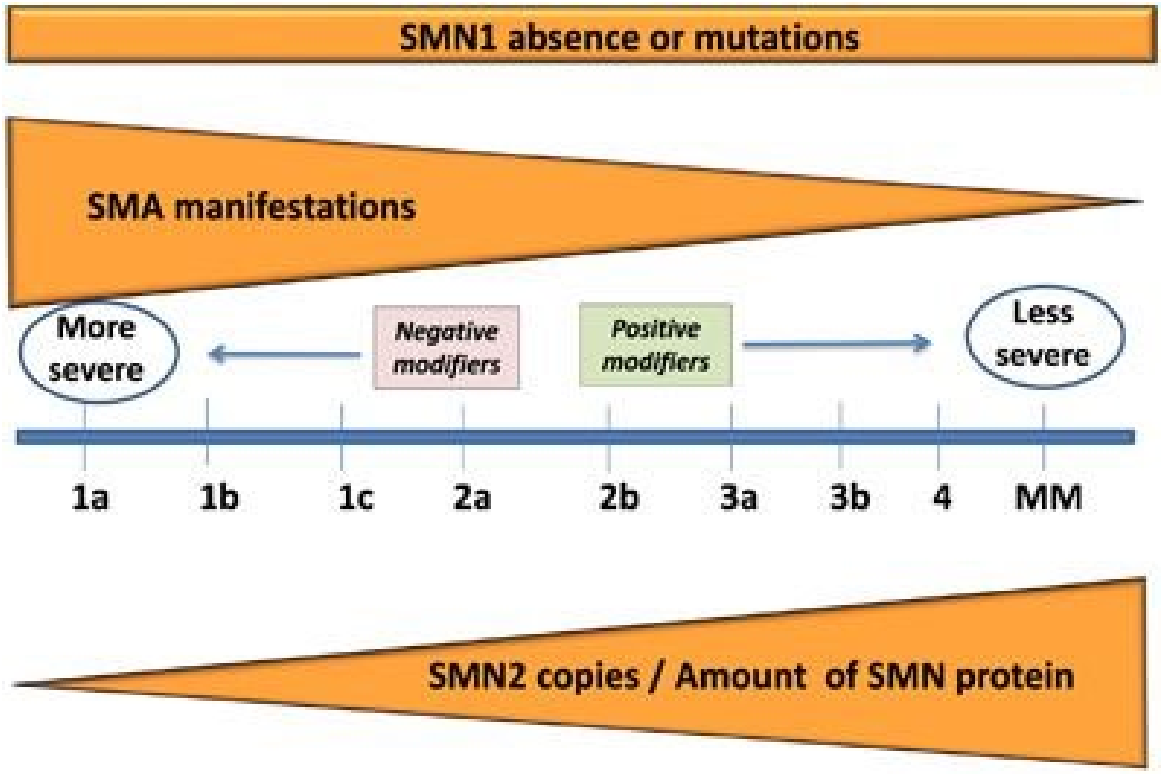
Asking key, unanswered questions:

- When and where is SMN protein needed in the body?
- How is SMN expression controlled?
- Why do low levels of SMN protein cause motor neuron dysfunction and death?
- How is expression of SMN regulated?
- What are the function(s) of SMN within cells?
- What other targets (beyond SMN) could be druggable?

Understanding these key biological questions helps to:

- Optimize current therapies
- Identify targets for new therapies
- Understand how to best use SMN-dependent and independent therapies in combination.

Identification of Modifiers as Drug Targets



Talbot and Tizzano, 2017.

Committed to Increased Basic Research

- **Large remaining unmet needs**
  - In both pediatric and adult populations
- **Need to understand foundational biology in order to generate new therapies**
- **750K in new basic research grants in 2025**
- **Increased funding for more basic research and reintroduction of translational research program**

Special thanks to the Concepcion Family, Nunemaker Family, Weisman Family, Luke 18:1 Foundation and Dhont Foundation for their generosity to Cure SMA in our quest to invest in basic research that will ultimately drive the next generation of SMA treatments


Q
A

SMA EUROPE

From Dreams to Reality:

How Research Makes It Possible

Anaheim, June 2025

Nicole Gusset, CEO SMA Europe

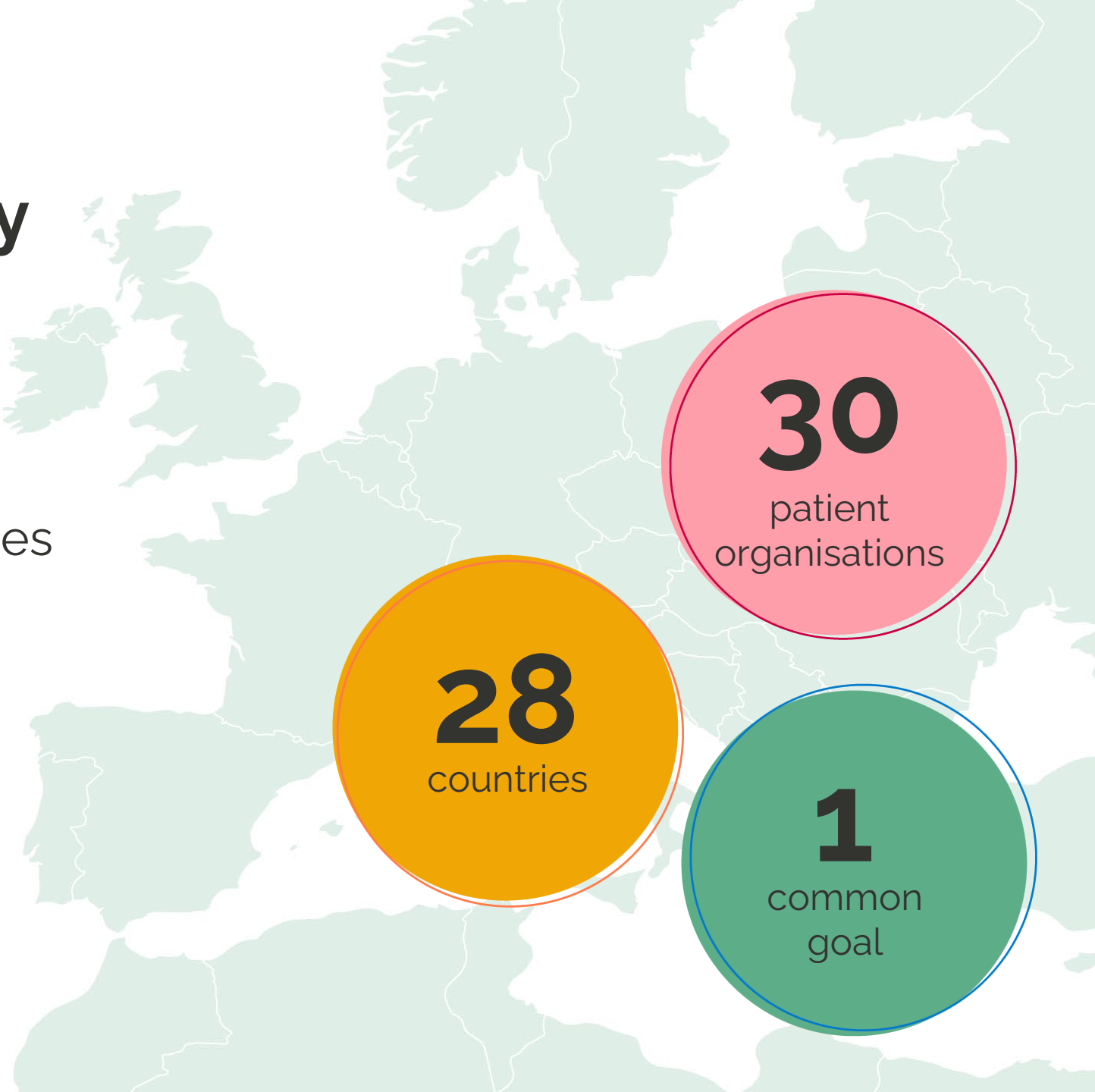
Our SMA Europe Family

28 countries

30 members with over 40 delegates

7 Board members

7 Staff members



"The future belongs to those who believe in the beauty of their dreams."

— Eleanor Roosevelt

SMA EUROPE

How Research Turns Hope into Reality

"Hope fuels vision. Research builds the bridge."

SMA EUROPE

Our Voices, our Priorities

"Those closest to the problem are closest to the solution."

SMA Research Priorities

TOP 10 FUTURE RESEARCH PRIORITIES
#1
Regenerating motoneurons

TOP 10 FUTURE RESEARCH PRIORITIES
#2
Identifying biomarkers

TOP 10 FUTURE RESEARCH PRIORITIES
#3
Rebuilding and strengthening damaged muscles

TOP 10 FUTURE RESEARCH PRIORITIES
#4
Exploring metabolism and diet

TOP 10 FUTURE RESEARCH PRIORITIES
#5
Tailoring physiotherapy

TOP 10 FUTURE RESEARCH PRIORITIES
#6
Understanding the impact of SMA on the body

TOP 10 FUTURE RESEARCH PRIORITIES
#7
Developing innovative therapies such as spinal cord stimulation

TOP 10 FUTURE RESEARCH PRIORITIES
#8
Advancing treatments for the skeletal system

TOP 10 FUTURE RESEARCH PRIORITIES
#9
Finding solutions to manage fatigue

TOP 10 FUTURE RESEARCH PRIORITIES
#10
Leveraging technology and assistive devices

What You Can Do

"Act as if what you do, makes a difference. It does."

The Next Chapter Starts with us!

"The best way to predict the future is to create it."

Towards a new disease description for SMA

Yasemin Erbas, PhD
President, SMA Europe

Yasemin.erbas@sma-Europe.eu
sma-europe.eu

All together. One goal.

CURRENT DESCRIPTION

SMA EUROPE

SMA is a neuromuscular disorder caused by mutations in the *SMN1 gene*, characterised by **progressive weakness and atrophy** of muscles due to the **degeneration** of motor neurons in the spinal cord and brainstem.

SMA is **classified in types**, based on the **age of onset** and the **motor milestones** achieved at the time of **diagnosis**:

- **Type 0:** symptom onset prior to birth.
- **Type 1:** symptom onset before 6 months of age, no independent sitting.
- **Type 2:** symptom onset between 6 and 18 months of age, can **sit** without support but unable to stand or walk without help
- **Type 3:** symptom onset after 18 months of age, can **walk** independently but may have difficulty doing so. They may also have trouble running, rising from a chair or climbing stairs
- **Type 4:** symptom onset after 18 years of age.

ISSUES WITH THE CURRENT DESCRIPTION

SMA EUROPE

- Artificial; no biological difference
- No clear borders (e.g., sitting with or without feet on the floor; sitting for 5 or 30 seconds)
- Current clinical status is not taken into account (e.g., a non-sitter type 2)
- Limited to motor milestones, not considering other dimensions:
  - Activities of daily living, motor function
  - Breathing, eating, swallowing, smiling, talking, osteoporosis, skeletal deformities, joint contractures, pain, fatigue/endurance, metabolism, fertility, liver, heart, brain, (social) cognition, language, seizures, eyes
- No prognostic value
  - DMTs, timing of treatment initiation, symptom severity, SMN2 copy nr…

HOW SHOULD WE DESCRIBE OUR COMMUNITY?

SMA EUROPE

- One disease!
- Spectrum, symptoms ranging from no/minimal to very severe, on all dimensions
- Room for individualisation
- Prognostic value

Question:

How does the current disease description limit access to treatments and care?


Biogen

Committed to the SMA Community

ADVANCING research and development.

PARTNERING with the patient and caregiver community.

RETHINKING the way we view and talk about SMA.

Biogen

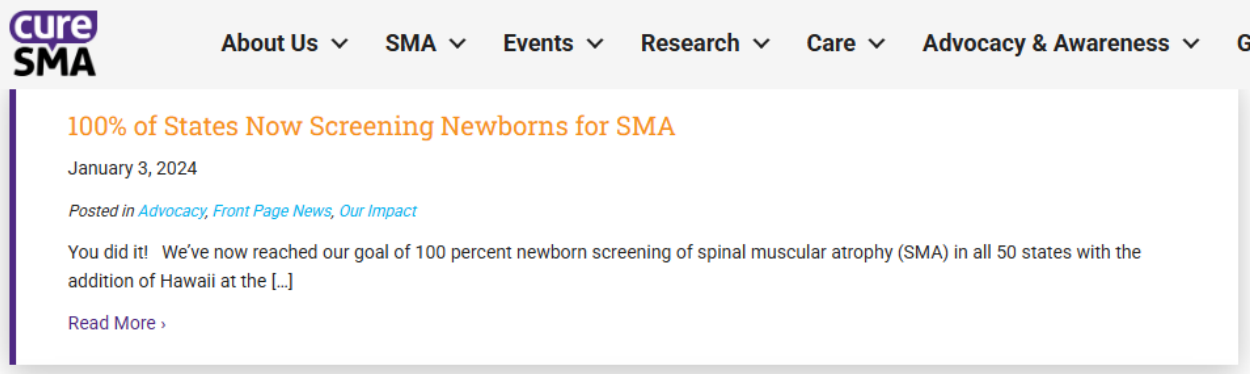
EVERY MOTOR NEURON MATTERS

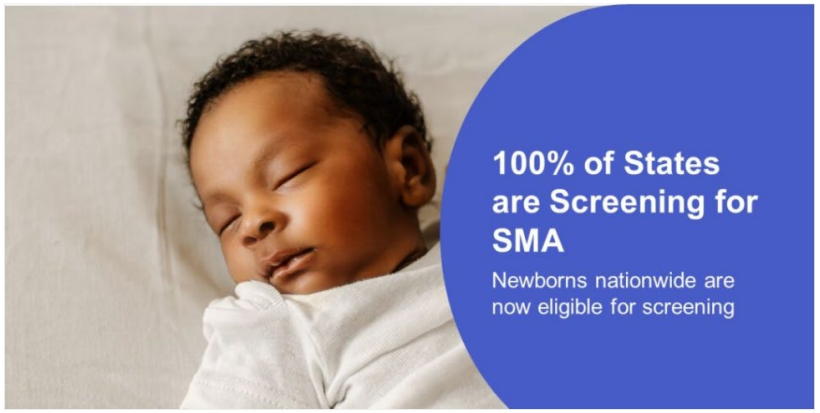

Biogen®

NEWBORN SCREENING (NBS) AND EARLY TREATMENT DATA

Sarah Whitmire MS
Director, Data Analytics
Cure SMA

January 2024: 100% of U.S. States are Screening for SMA



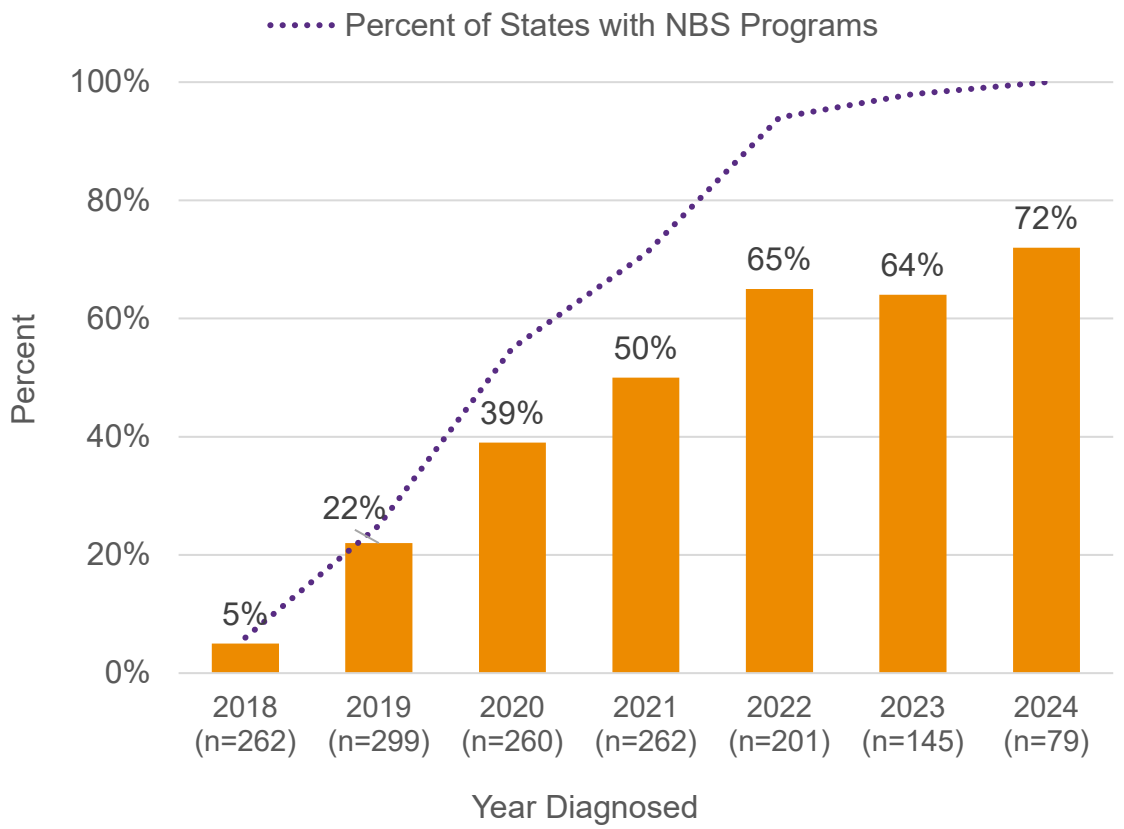


All 50 States and DC Implement Spinal Muscular Atrophy Newborn Screening

By Jori Houck | Friday, February 23, 2024

Topics
> Advocacy
> Finding a Diagnosis

Percent of Individuals Identified by Screening in Combined Cure SMA Databases, by Year of Diagnosis



Source: Combined Cure SMA Databases (de-duplicated), 2024 State of SMA

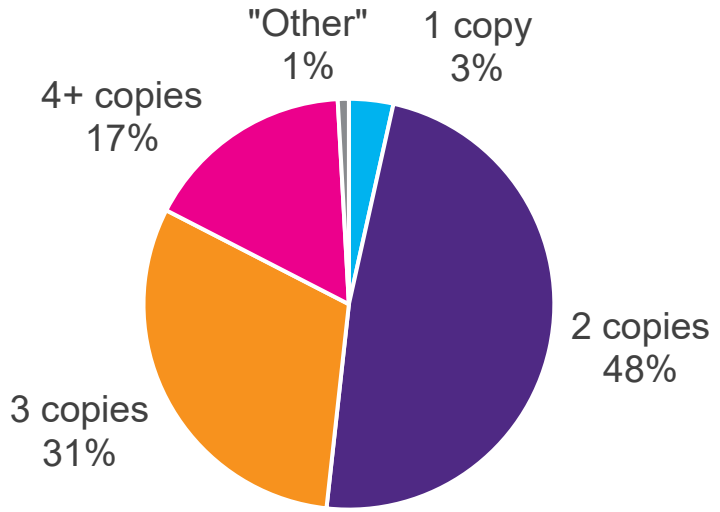
NBS Data from U.S. State Public Health Labs

Estimated Birth Prevalence of SMA

Birth prevalence: the proportion of individuals born in a specific time period that have SMA

Data from 2018-2023	
Number of states that provided data	26
Infants screened for SMA	7,269,749
Infants with a confirmed positive SMA diagnosis	460
Estimated birth prevalence (2018-2023)	1 in 15,804 births

SMN2 Copy Number Distribution, n=344*

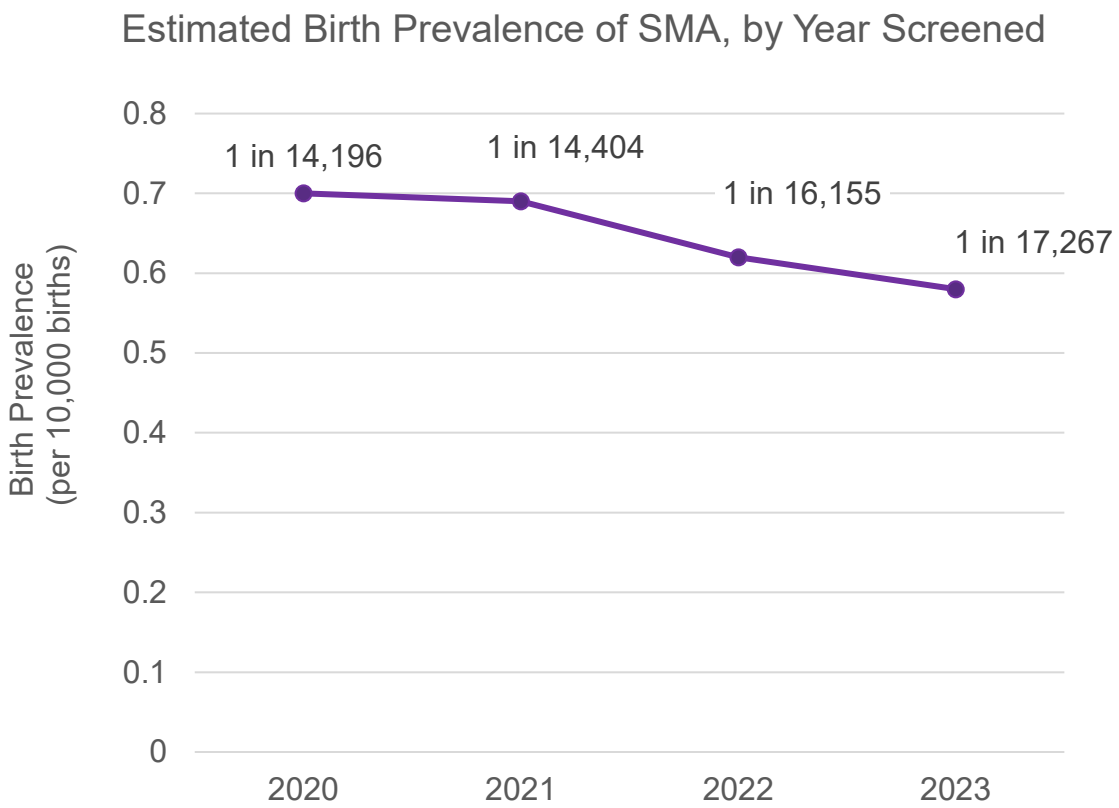


*All states did not provide *SMN2* copy number data

Source: Aggregated NBS Data from US State Public Health Labs

Decreasing Trends in the Number of SMA Diagnoses

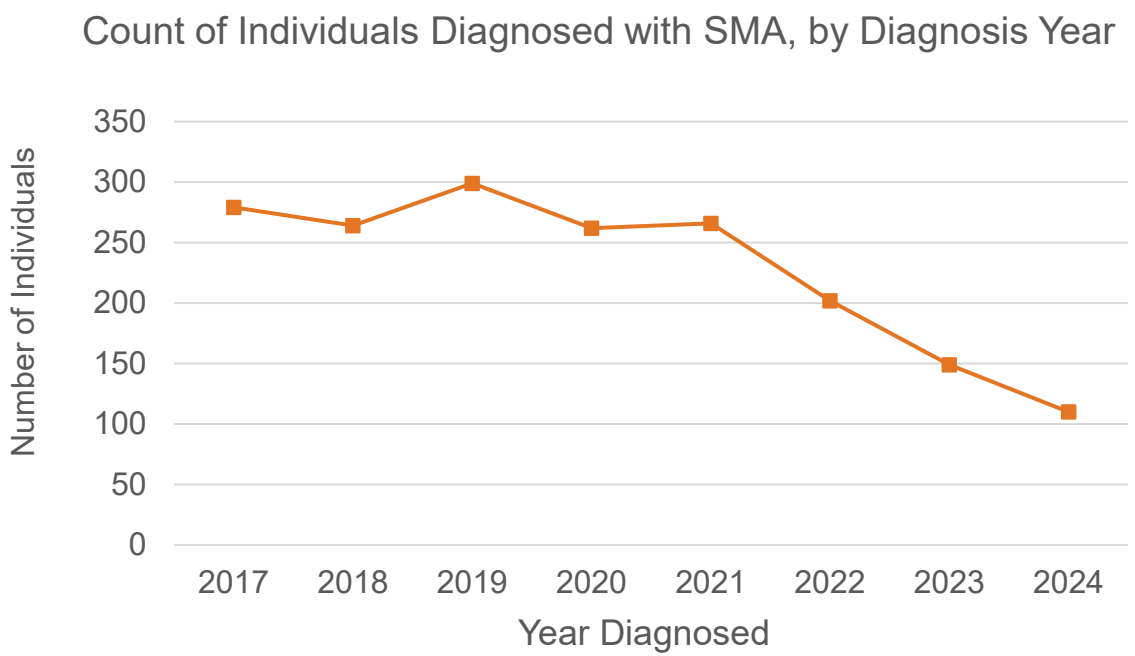
Trends from U.S. State Public Health Labs



	2020	2021	2022	2023
States (n)	16	18	22	21
Infants screened (n)	1,121,461	1,569,982	1,809,394	1,813,016

Source: Aggregated NBS Data from US State Public Health Labs

Trends in Combined Cure SMA Databases

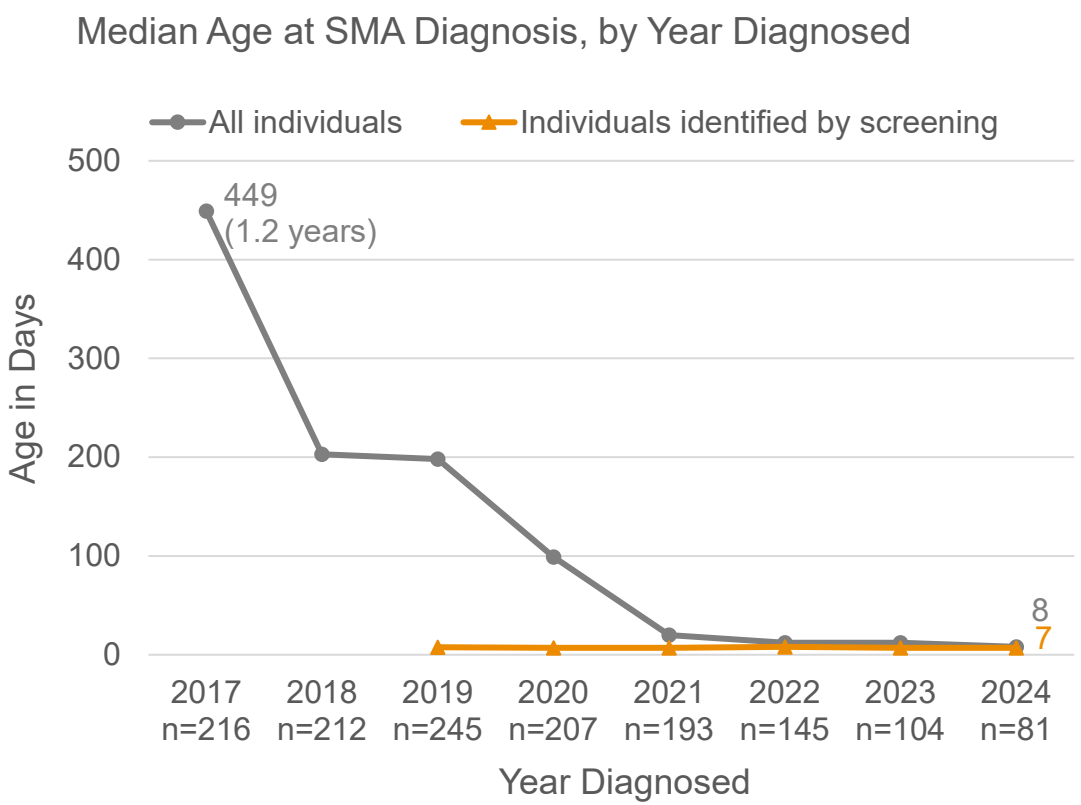


Source: Combined Cure SMA Databases (de-duplicated)
Graph adapted from the 2024 State of SMA

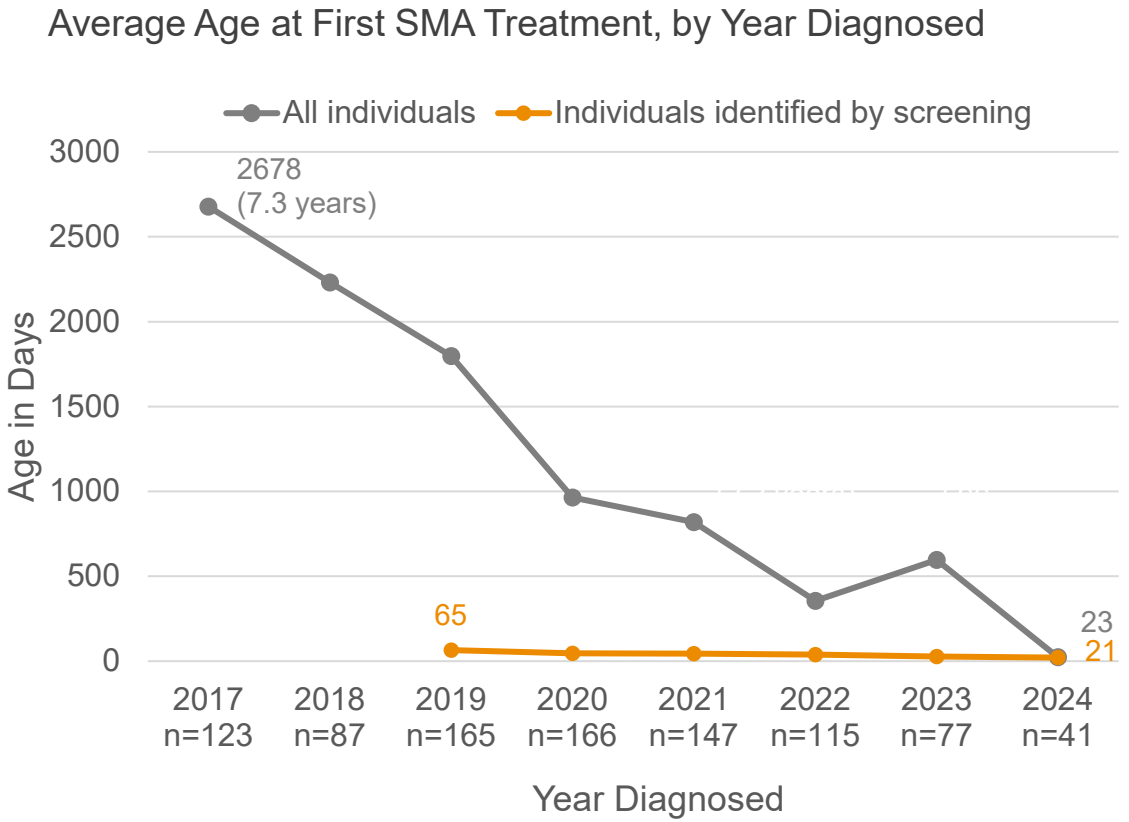
Why?
- Increase in carrier screening?
- Increase in prenatal screening?
- Greater awareness of SMA?

Impact of Screening Programs: Diagnosis & Treatment

Time to Diagnosis



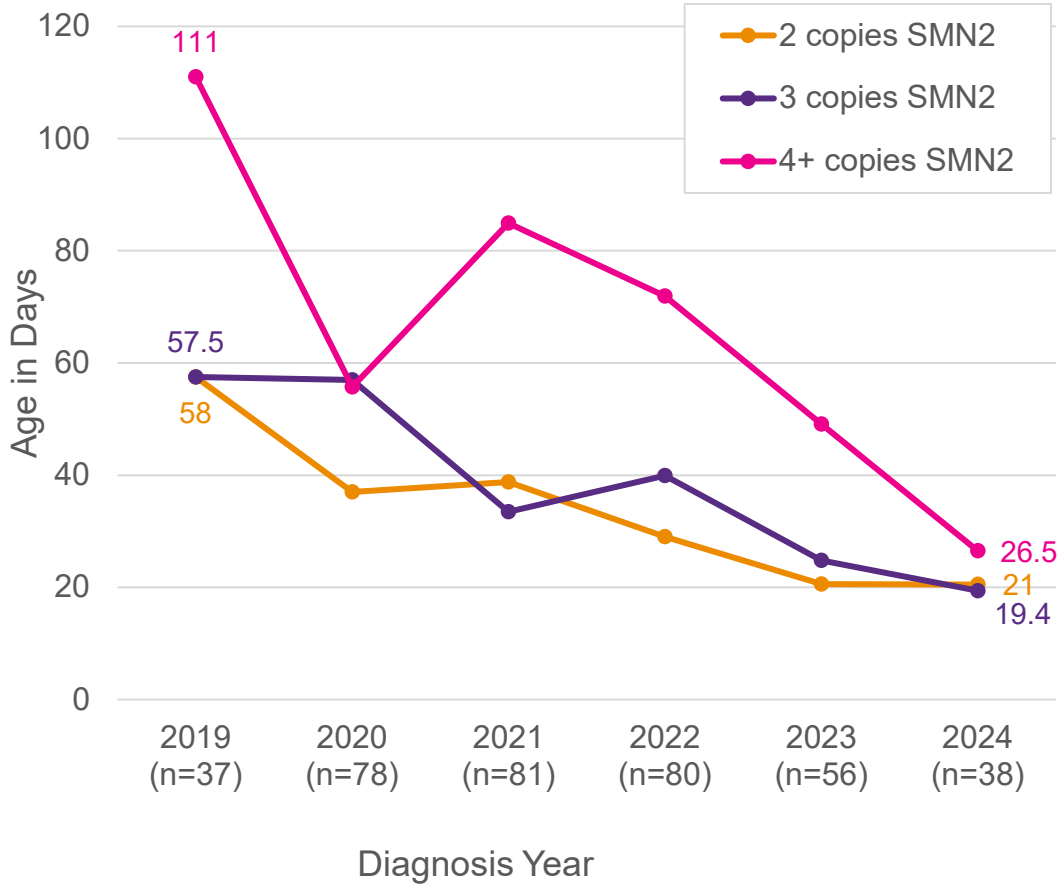
Time to First Treatment



Source: Combined Cure SMA Databases (de-duplicated), 2024 State of SMA Report

Impact of Screening Programs: Treatment Timing

Median Age at First SMA Treatment, by Year Diagnosed and *SMN2* Copy Number

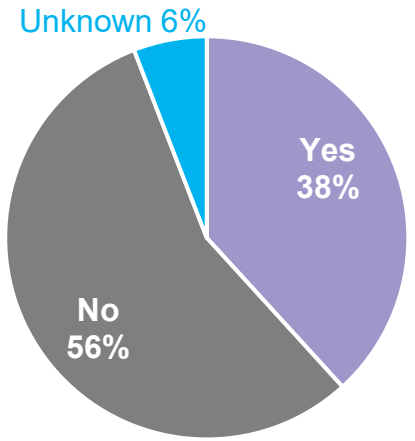


Source: Combined Cure SMA Databases (de-duplicated)

Treatment Bridging

Source: 2023 State of SMA

Use of "Bridging" Treatment (n=34)

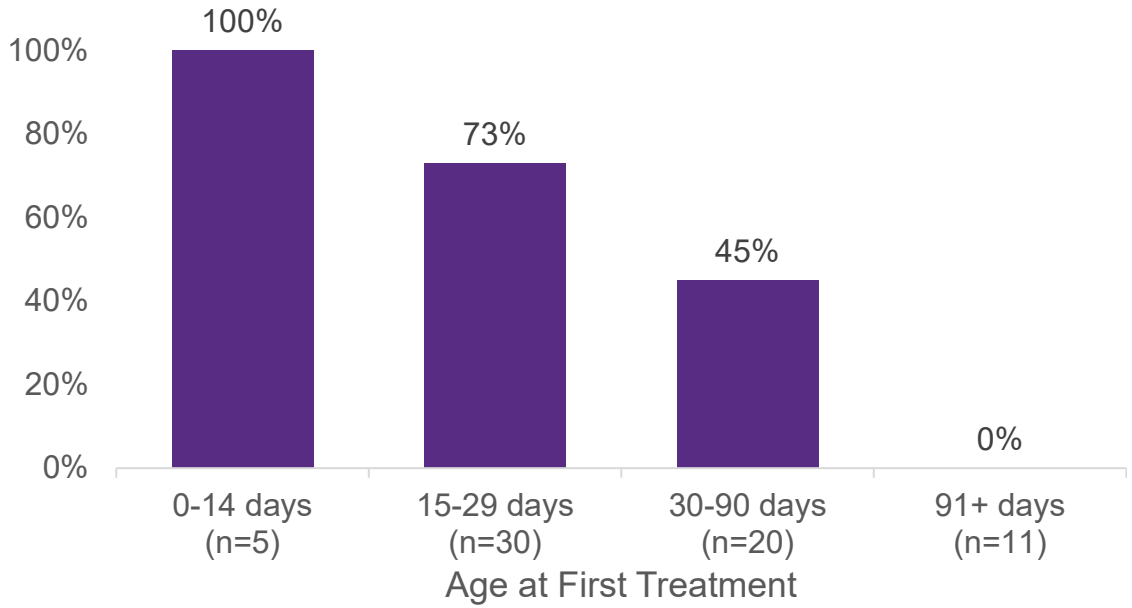


Source: SMA CORE data (caregiver-reported)

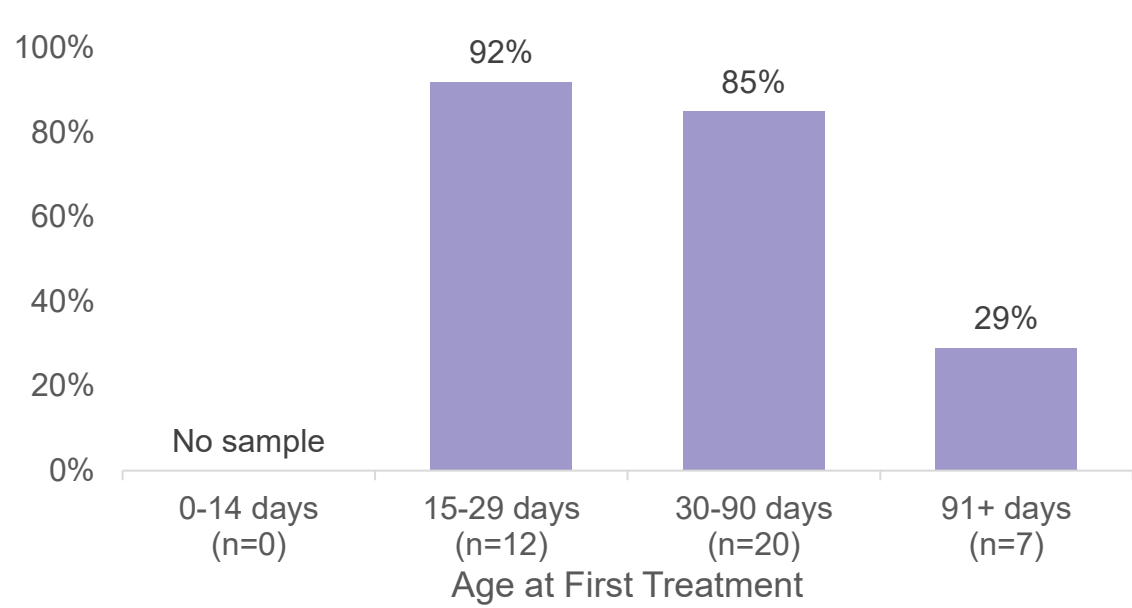
Impact of Early Treatment: Motor Function

This analysis included unique individuals with 5q SMA that resided in the United States (U.S.) who were 2 years old at the time of data collection and had a known current motor milestone achievement reported:

Individuals with 2 copies of *SMN2*, n=66



Individuals with 3 copies of *SMN2*, n=39



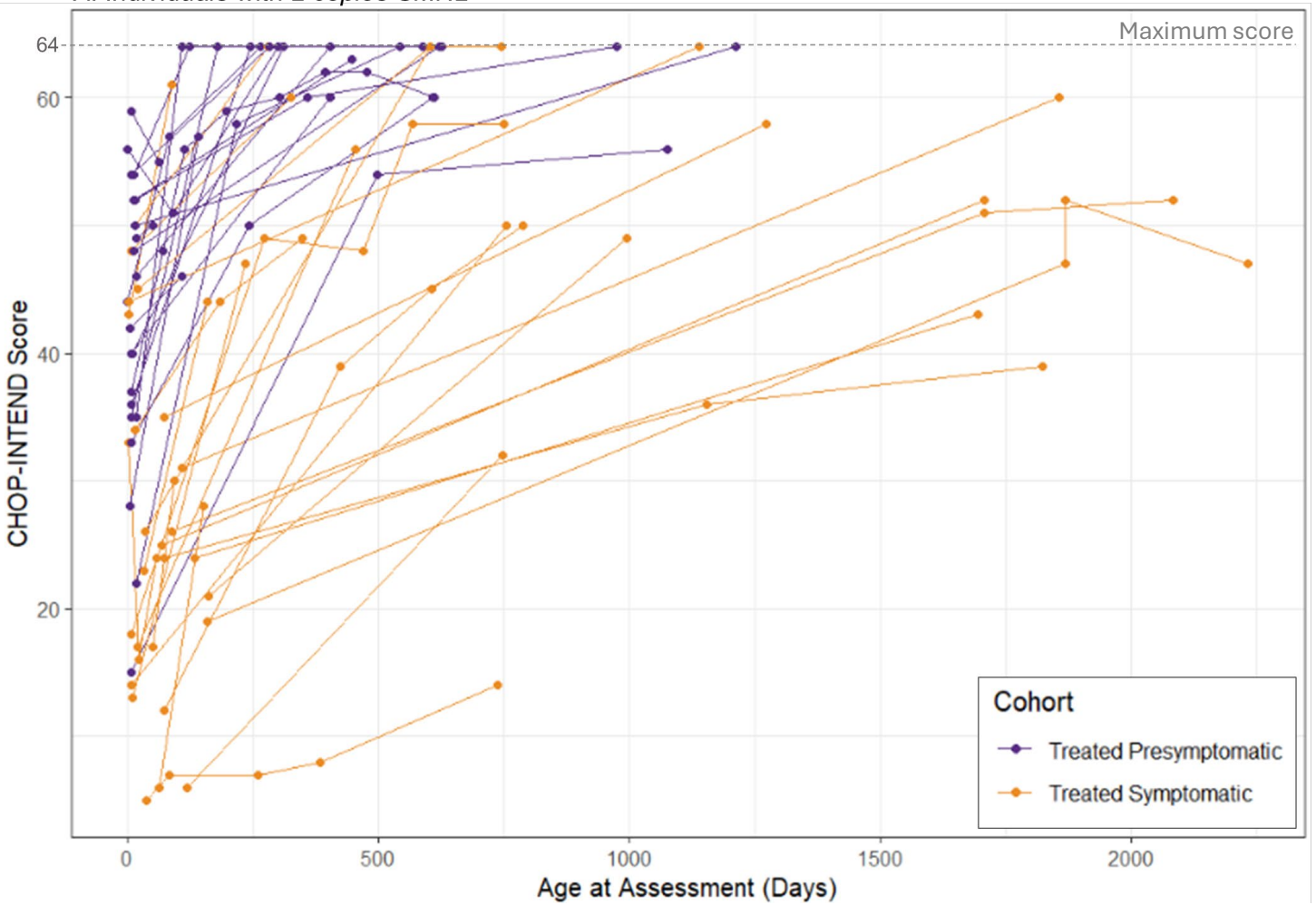
These results are based on observations in our data and results may not be generalizable to all individuals with SMA as the overall clinical course for an individual patient is complex and multifactorial.

Source: CDR (2021-2024) and CUS (2021-2025) data (de-duplicated)

Impact of Early Treatment: Motor Function

Longitudinal CHOP-INTEND Scores, by Treatment Timing

A. Individuals with 2 copies SMN2



Analysis Notes:

- All individuals were treated < 6 months of age
- The sample was divided into individuals who received their first SMA treatment before clinician-reported clinical manifestation of SMA (**"Treated Presymptomatic"**) and those that received their first SMA treatment after clinical manifestation of SMA (**"Treated Symptomatic"**)
- No statistical testing or adjustments were done

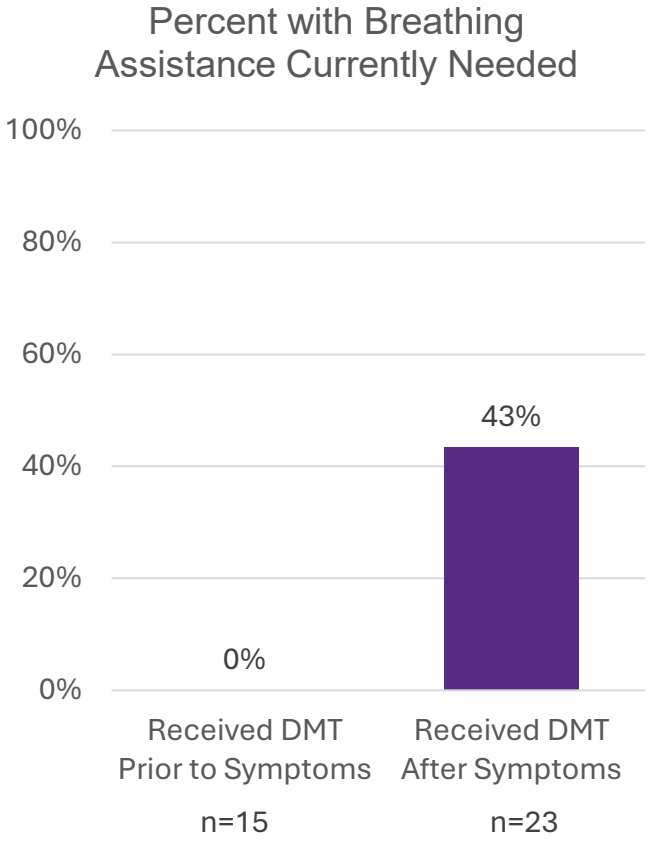
What is the CHOP-INTEND?

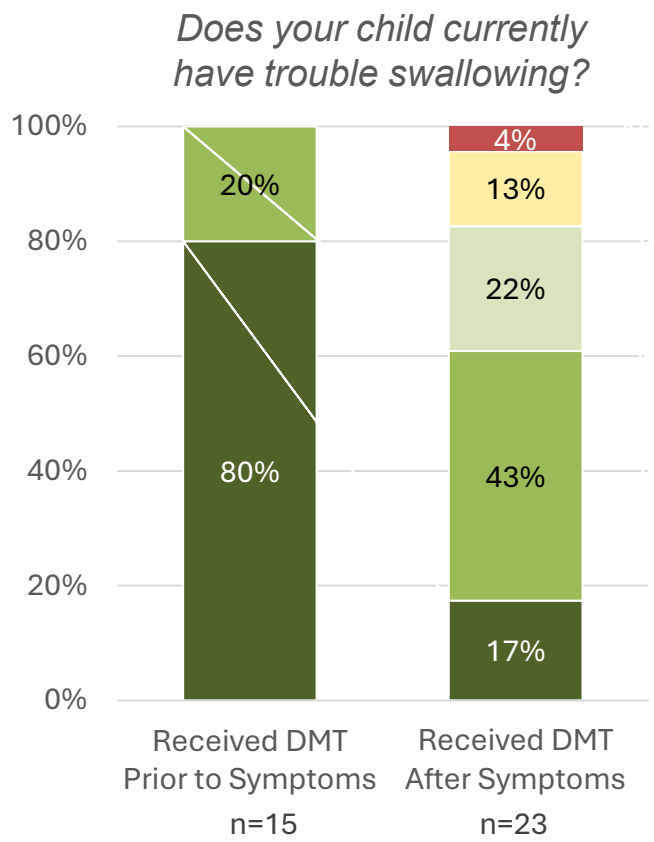
- The Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND) was developed to measure the motor skills of infants and young children with SMA Type 1 and other neuromuscular disorders of infancy.
- The test is scored from 0-64, with 64 indicating higher strength and motor function.

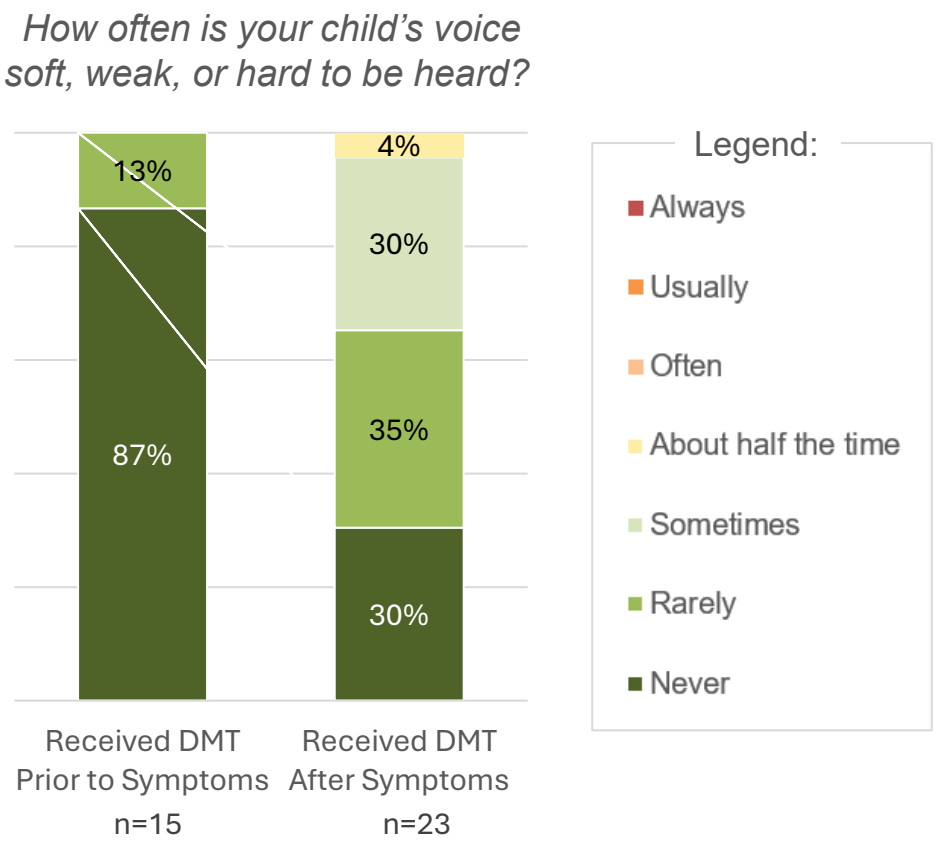
Source: SMA Clinical Data Registry
Poster presented at the 2025 Annual Research & Clinical Care Meeting

Impact of Early Treatment: Breathing and Bulbar

Individuals with 2 copies of SMN2 that are ≤ 5 years of age







Mean age at 1st treatment:
Received DMT prior to symptoms (n=15): 23.3 days
Received DMT after to symptoms (n=23): 73 days

Source: Combined SMA CORE and 2025 CUS data (de-duplicated)

DMT: Disease modifying treatment

CUS note: n=9 reported that symptoms started at "less than 1 month" and treatment occurred < 30 days. It was assumed that treatment was initiated after symptom manifestation.

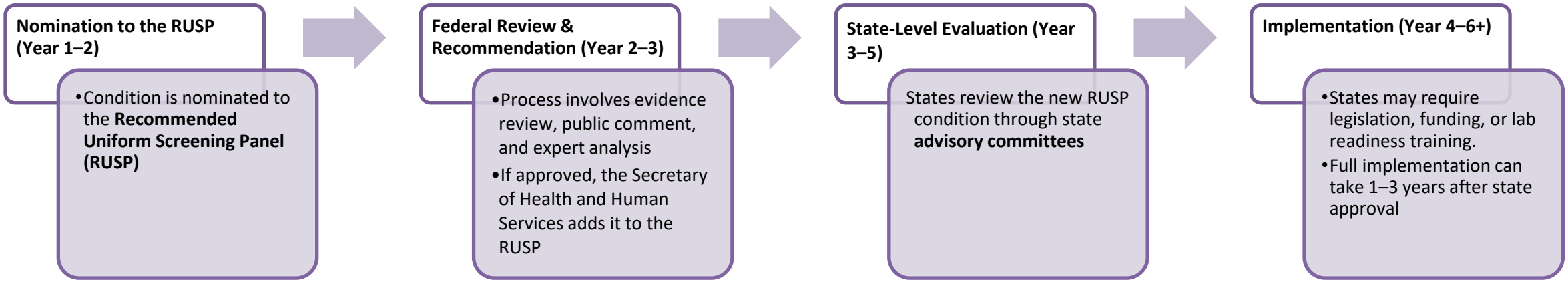

Q
A

RESOURCES TO PROMOTE EARLY DIAGNOSIS AND INTERVENTION IN SMA

Mary Curry, ND
Vice President, Clinical Research and Care
Cure SMA

SMA Newborn Screening

- **Enables early diagnosis, early treatment, and improved outcomes**
- **Adding a genetic condition to NBS panels is a multi-step process**
  - Involves a complex set of country-specific challenges
    - Lack of government support
    - Policy barriers
    - Financial limitations & resource constraints
  - Implementation may take several years
    - Avg of 6+ years for full implementation in the US
      - 7 years for SMA



Timeline for US Newborn Screening Implementation

Cure SMA's SMArt Moves

www.SMArtMoves.CureSMA.org

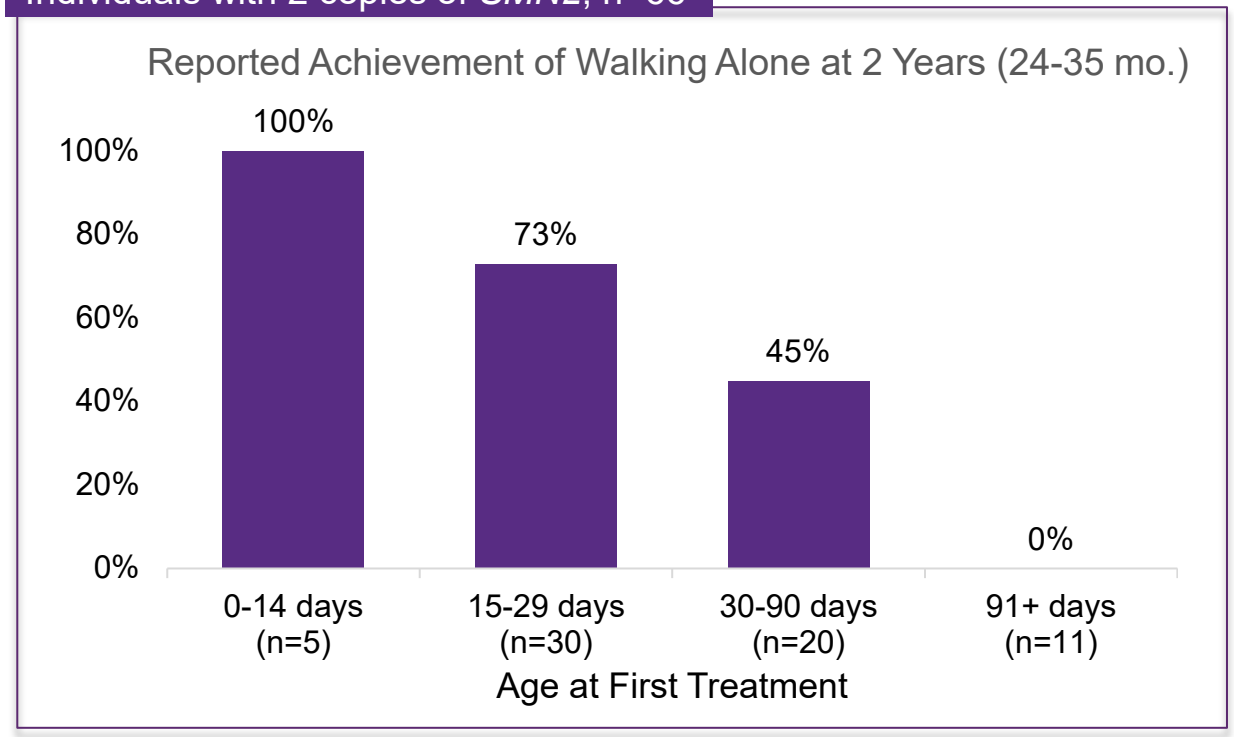
- **Designed to empower providers and parents to recognize the early signs of SMA**
- **Intended to bridge the gap until universal inclusion of SMA on NBS panels**
- **On-demand resources include**
  - Parent Checklist
  - SMA Diagnostic Toolkit
  - SMA Quick Reference Guide
  - CME Activities

SMArt Moves Video Resources

- **Highlights 8 early signs and symptoms of SMA type I**
- **Available on campaign microsite and YouTube**
  - Increase engagement & retention of core message
  - Amplify reach
- **Content may be repurposed to connect with diverse and global audiences**

SMA NBS Implemented? What's Next?

Individuals with 2 copies of *SMN2*, n=66



Source: CDR (2021-2024) and CUS (2021-2025) data (de-duplicated)

- **Time to treatment** remains critical
- Delays in **care coordination, confirmatory testing**, and **clinical evaluation** of a NBS-identified infant may impact outcomes

SMA Update in Best Practices

- **Recommendations for Diagnosis Considerations**
  - Published in *Neurology Clinical Practice*, May 24, 2024
  - Recommendations emphasize:
    - The importance of timely coordination across public health labs, primary care, and SMA care teams
    - Current best practices for the characterization of SMA infants identified by newborn screening
    - The central role of individuals with SMA and their caregivers throughout the decision-making process

Spinal Muscular Atrophy Update in Best Practices

Recommendations for Diagnosis Considerations

Abstract

SMA Update in Best Practices

- **Recommendations for Treatment Considerations**
  - Published in *Neurology Clinical Practice*, October 8, 2024
  - Recommendations highlight factors to consider when:
    - Initiating treatment for patients newly diagnosed with SMA
    - Initiating, changing, or adding treatment for patients not newly diagnosed with SMA

RESEARCH ARTICLE OPEN ACCESS

Spinal Muscular Atrophy Update in Best Practices

Recommendations for Treatment Considerations

Abstract

Background and Objectives

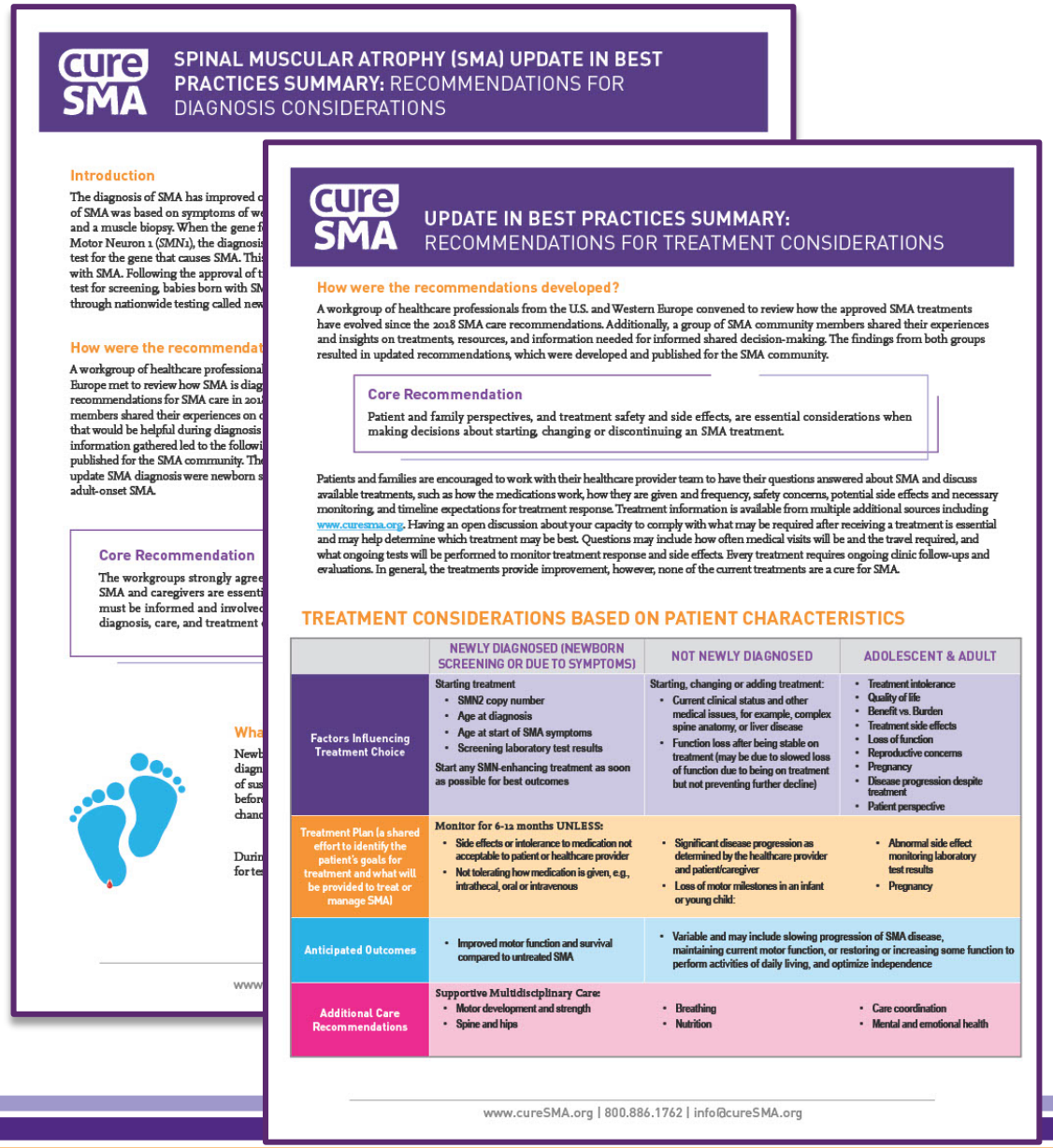
Methods

Results

Discussion

SMA Update in Best Practices

- **Community Friendly Summaries**
  - Resources aim to empower individuals with SMA, their families, and caregivers to participate in and advocate for their care and treatment
  - Also available in Spanish, French, and Mandarin



SPINAL MUSCULAR ATROPHY (SMA) UPDATE IN BEST PRACTICES SUMMARY: RECOMMENDATIONS FOR DIAGNOSIS CONSIDERATIONS

Introduction

Core Recommendation

UPDATE IN BEST PRACTICES SUMMARY: RECOMMENDATIONS FOR TREATMENT CONSIDERATIONS

How were the recommendations developed?

A workgroup of healthcare professionals from the U.S. and Western Europe convened to review how the approved SMA treatments have evolved since the 2018 SMA care recommendations. Additionally, a group of SMA community members shared their experiences and insights on treatments, resources, and information needed for informed shared decision-making. The findings from both groups resulted in updated recommendations, which were developed and published for the SMA community.

Core Recommendation

Patient and family perspectives, and treatment safety and side effects, are essential considerations when making decisions about starting, changing or discontinuing an SMA treatment.

Patients and families are encouraged to work with their healthcare provider team to have their questions answered about SMA and discuss available treatments, such as how the medications work, how they are given and frequency, safety concerns, potential side effects and necessary monitoring, and timeline expectations for treatment response. Treatment information is available from multiple additional sources including www.curesma.org. Having an open discussion about your capacity to comply with what may be required after receiving a treatment is essential and may help determine which treatment may be best. Questions may include how often medical visits will be and the travel required, and what ongoing tests will be performed to monitor treatment response and side effects. Every treatment requires ongoing clinic follow-ups and evaluations. In general, the treatments provide improvement, however, none of the current treatments are a cure for SMA.

TREATMENT CONSIDERATIONS BASED ON PATIENT CHARACTERISTICS

	NEWLY DIAGNOSED (NEWBORN SCREENING OR DUE TO SYMPTOMS)	NOT NEWLY DIAGNOSED	ADOLESCENT & ADULT
Factors Influencing Treatment Choice	Starting treatment • SMN2 copy number • Age at diagnosis • Age at start of SMA symptoms • Screening laboratory test results Start any SMN-enhancing treatment as soon as possible for best outcomes	Starting, changing or adding treatment: • Current clinical status and other medical issues, for example, complex spine anatomy, or liver disease • Function loss after being stable on treatment (may be due to slowed loss of function due to being on treatment but not preventing further decline)	• Treatment intolerance • Quality of life • Benefit vs. Burden • Treatment side effects • Loss of function • Reproductive concerns • Pregnancy • Disease progression despite treatment • Patient perspective
Treatment Plan (a shared effort to identify the patient's goals for treatment and what will be provided to treat or manage SMA)	Monitor for 6-12 months UNLESS: • Side effects or intolerance to medication not acceptable to patient or healthcare provider • Not tolerating how medication is given, e.g., intrathecal, oral or intravenous	• Significant disease progression as determined by the healthcare provider and patient/caregiver • Loss of motor milestones in an infant or young child:	• Abnormal side effect monitoring laboratory test results • Pregnancy
Anticipated Outcomes	• Improved motor function and survival compared to untreated SMA	• Variable and may include slowing progression of SMA disease, maintaining current motor function, or restoring or increasing some function to perform activities of daily living, and optimize independence	
Additional Care Recommendations	Supportive Multidisciplinary Care: • Motor development and strength • Spine and hips	• Breathing • Nutrition	• Care coordination • Mental and emotional health

www.cureSMA.org | 800.886.1762 | info@cureSMA.org


Q
A

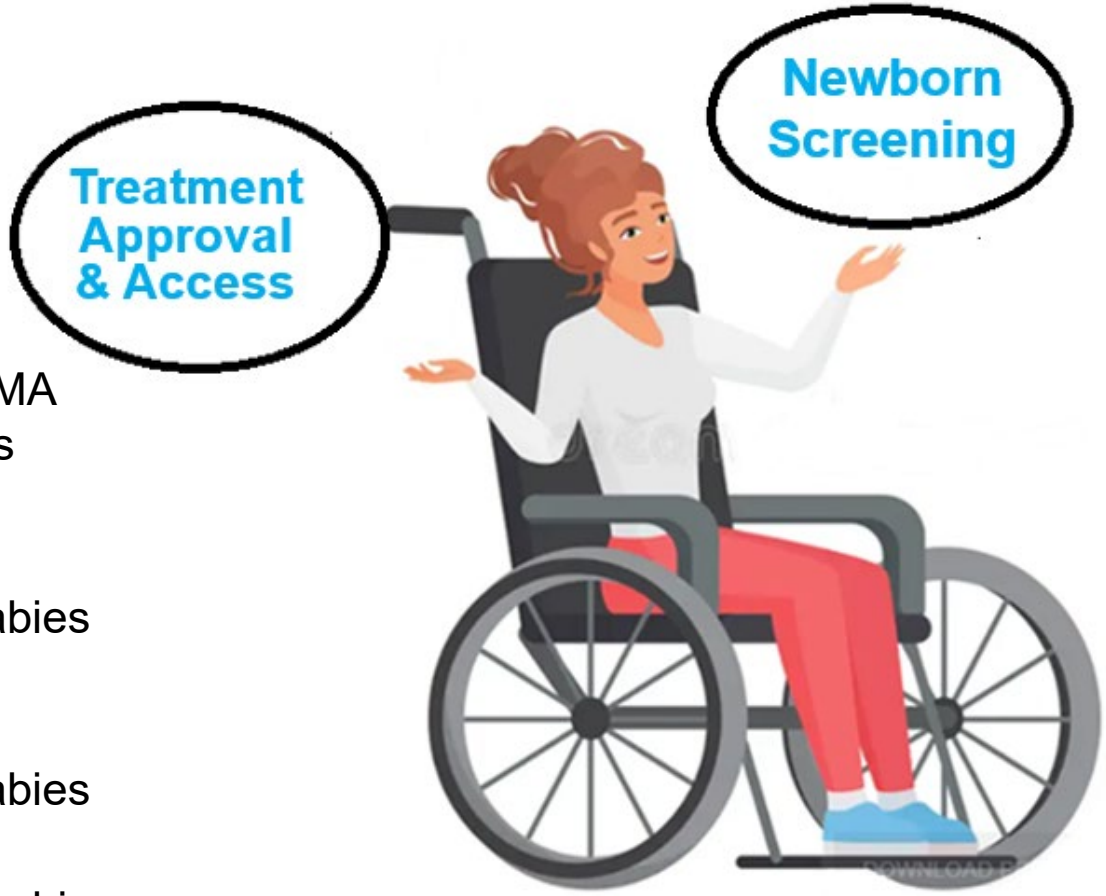
DAILY LIVING NEEDS AND SUPPORT

Maynard Friesz

Vice President of Policy & Advocacy, Cure SMA

Early Focus.... Treatments & Newborn Screening

- **2016:**
  - 1st SMA treatment approved (Spinraza)
  - 1st Newborn screening pilot (New York)
- **2018:**
  - Federal recommendation for newborn screening of SMA
  - 6 States screening for SMA covering 13% U.S. babies
- **2019**
  - 2nd SMA treatment approved (Zolgensma)
  - 20 States screening for SMA covering 37% of U.S. babies
- **2020**
  - 3rd SMA treatment approved (Evrysdi)
  - 33 States screening for SMA covering 68% of U.S. babies
- **2024**
  - 50 States screening for SMA covering 100% of U.S. babies



Recognizing other Needs & Priorities

- **Everyday living issues**
  - Community living
  - Employment
  - Healthcare access
  - Housing
  - Transportation
  - & More

- **Especially important for adults with SMA & families of older children with SMA**

What We Heard from the SMA Community

- **Top Priorities (in order)**
  - Healthcare
  - Employment & Financial Security
  - Disability Rights
  - Independent Living (i.e., Housing)
  - Transportation
  - Technology
  - Education
  - Emergency Preparedness
  - SMA Awareness

- **Same Top 5**
  - Based on Age
  - Based on SMA Type
  - Based on Gender

How to Meet the Everyday Living Needs?

- Through New Support Activities
- Through New Advocacy Activities

Support Activities - Everyday Living

- **Adult Advisory Council**
  - Created to receive ongoing feedback
- **Virtual Programming**
  - Education, employment, transportation panels
- **Conference Workshops**
  - Caregiving, housing, emergency management, & other everyday living issues
- **Resources and Packets**
  - Accessible vans, educational accommodations, home modification, financial planning
- **Support Packages**
  - Air travel, independence assistance

Advocacy Activities - Everyday Living

- **Adult Advisory Council**
  - Created to receive ongoing feedback
- **Advocacy Fact Sheets**
  - Transportation, caregiving, housing, employment and more
- **Cure SMA Direct Advocacy**
  - Statements & testimony to Congress
- **Online Advocacy Campaigns**
  - Advocacy campaigns on everyday living priorities
- **In-Person Advocacy Events**
  - Cure SMA Hill Day
  - Hope on the Hill reception


Q
A