



# STATE OF SMA

DECEMBER 2021



---

## ACKNOWLEDGMENTS

---

**Cure SMA is thankful for all the members of the SMA community who have generously shared their data. Their willingness to share details about how SMA impacts their families and daily lives allows us to advance understanding of this disease and lay the foundation for continued progress on behalf of our community.**

**Cure SMA is grateful for the support and funding provided by the Cure SMA Industry Collaboration (SMA-IC), the Cure SMA Real World Evidence Collaboration (RWEC) and the Cure SMA Newborn Screening Coalition (NBSC).**

**Cure SMA is also grateful to the SMA Care Center Network for their commitment to improving care for people with SMA and contributing consented patient data.**

### The Cure SMA Industry Collaboration

---

The Cure SMA Industry Collaboration (SMA-IC) was established in 2016 to leverage the experience, expertise, and resources of pharmaceutical and biotechnology companies, as well as other nonprofit organizations involved in the development of spinal muscular atrophy (SMA) therapeutics to more effectively address a range of scientific, clinical, and regulatory challenges. It is currently comprised of our partners at Biogen, Genentech/Roche Pharmaceuticals, Scholar Rock, Novartis Gene Therapies, Biohaven Pharmaceuticals, Epirium Bio, and SMA Europe. Additionally, the work of the Collaboration is supported by funds provided by Biogen, Genentech/Roche Pharmaceuticals, Scholar Rock, Novartis Gene Therapies, Biohaven Pharmaceuticals, and Epirium Bio.

### The Cure SMA Real World Evidence Collaboration

---

The Cure SMA Real World Evidence Collaboration (RWEC) was established in 2021 to leverage the experience, expertise and resources of pharmaceutical and biotechnology companies and nonprofit organizations involved in the development of SMA therapeutics to guide the future direction of real world evidence collection and use in SMA. Members of the RWEC include Biogen, Novartis Gene Therapies, Genentech/Roche Pharmaceuticals, and SMA Europe.

### The Cure SMA Newborn Screening Coalition

---

The Cure SMA Newborn Screening Coalition (NBSC) was established in 2017 to leverage the experience, expertise and resources of pharmaceutical and biotechnology companies and nonprofit organizations involved in the development of SMA therapeutics to advance newborn screening for SMA. Members of the NBSC include Novartis Gene Therapies, Genentech/Roche Pharmaceuticals, and Biogen.

# ACKNOWLEDGMENTS

## Cure SMA Care Center Network

Cure SMA has partnered with 19 SMA Care Centers across the U.S. who provide multidisciplinary care for people with SMA. These centers are committed to establishing and implementing an evidence-based standard of care for SMA through a centralized registry collection of real world data on SMA care and treatment. Consented patient electronic medical record (EMR) data is electronically transferred from the Care Center to the SMA Clinical Data Registry (CDR).

The SMA Care Center Network includes the following 19 sites:

Advocate Children's Hospital  
Park Ridge, IL

Arkansas Children's Hospital  
Little Rock, AR

Boston Children's Hospital  
Boston, MA

Children's of Alabama  
Birmingham, AL

Children's National Medical Center  
Washington, DC

Columbia University  
New York, NY

Connecticut Children's Medical Center  
Hartford, CT

Duke University Medical Center  
Durham, NC

Gillette Children's Specialty Healthcare  
St. Paul, MN

Phoenix Children's Hospital  
Phoenix, AZ

Stanford Health  
Palo Alto, CA

Stanford Children's Health  
Palo Alto, CA

Seattle Children's Hospital  
Seattle, WA

University of Missouri Health Care  
Columbia, MO

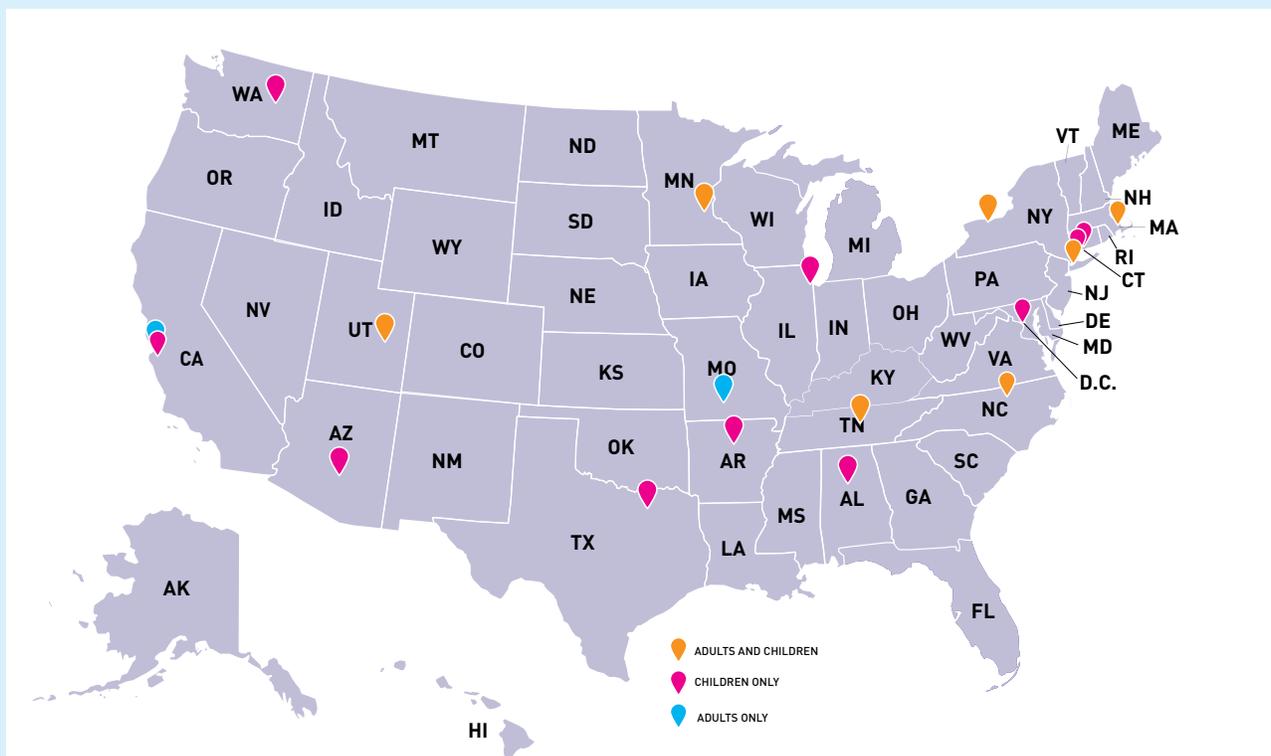
University of Rochester Medical Center  
Rochester, NY

University of Utah, Utah Program  
for Inherited Neuromuscular Disorders  
Salt Lake City, UT

University of Texas Southwestern/  
Children's Health  
Dallas, TX

Vanderbilt University Medical Center  
Nashville, TN

Yale Pediatric Neuromuscular Clinic  
New Haven, CT



## Additional Acknowledgments

We acknowledge the Oscar G. and Elsa S. Mayer Family Foundation and an endowment from Bill and Susan Orr and the Tyler William Orr Memorial Fund for their support.

## DEAR CURE SMA COMMUNITY,

We are pleased to share with you the first annual State of SMA report. The purpose of this report is to share highlights, data, and stories that people with SMA and their family members have generously contributed over the years. It reflects the current landscape of the SMA community, and we hope it will foster future research, programs, and therapies.

Cure SMA proudly hosts three databases: a patient reported outcomes database with data on over 9,700 affected individuals worldwide that also incorporates longitudinal data from our annual community update survey; an electronic medical record (EMR) sourced registry that compiles clinical data from 19 U.S.-based SMA Care Center Network sites; and a newborn screening registry with data from parents of babies with SMA identified through statewide SMA newborn screening.

The last five years have witnessed a whirlwind of exciting changes within the SMA community, from the availability of SMA treatments to a robust drug pipeline that continues to develop to widespread adoption of statewide newborn screening. Our data shows more and more individuals achieving motor function atypical for their SMA type, infants being diagnosed and receiving treatment within days of their birth and decreasing mortality rates within our community. We are excited to see what the next five years hold for SMA.

Many thanks to of you who contribute to the Cure SMA databases. This report is a community effort and would not be possible without your contributions. This work celebrates you.

Thank you all for your commitment to Cure SMA.

Sincerely,



Lisa Belter  
Director, Data Analytics



Sarah Whitmire  
Senior Manager, Data Analytics



Dr. Mary Schroth  
Chief Medical Officer

# TABLE OF CONTENTS

About This Report

Cure SMA Databases

Demographics and Clinical Characteristics

Patient Journey

Diagnosis

Newborn Screening

Treatment

Treatment Impact



# ABOUT THIS REPORT

## This report is based on data from:

1. The Cure SMA Membership Database,
2. The Annual Community Update Survey,
3. The Clinical Data Registry, and
4. The Newborn Screening Registry

Individuals have consented to provide their information through the Community Update Survey, SMA Clinical Data Registry, and the SMA Newborn Screening Registry. The consents are governed by WIRB-Copernicus Group Institutional Review Board (WCG IRB).

## Our analyses within this report include individuals who are:

- Diagnosed (both self-reported and clinically confirmed) with 5q SMA
- Included in one or more of our databases as of December 31, 2021
- Residents of the United States
- Living at time of data cut

**The “SMA Model” was created by Cure SMA to estimate characteristics of the US SMA population. Results from the model are based on internal and external real-world inputs, and the following assumptions were made:**

- SMA incidence 1 in 11,000<sup>1</sup>
- SMA subtype incidence of 60% for Type 1, 30% for Type 2, and 10% for Type 3/4<sup>1</sup>
- Median age of survival of 4 years, 40 years, and 78 years for SMA type 1, type 2, and type 3, respectively<sup>2</sup>
- Race and ethnicity estimates adjusted based on SMA carrier rates described by Sugarman et al.<sup>3</sup>; and the 2020 US Census<sup>4</sup>

1. Verhaart IEC, Robertson A, Wilson IJ, Aartsma-Rus A, Cameron S, Jones CC, Cook SF, Lochmüller H. Prevalence, incidence and carrier frequency of 5q-linked spinal muscular atrophy - a literature review. *Orphanet J Rare Dis.* 2017 Jul 4;12(1):124.

2. Based on Cure SMA internal assumptions

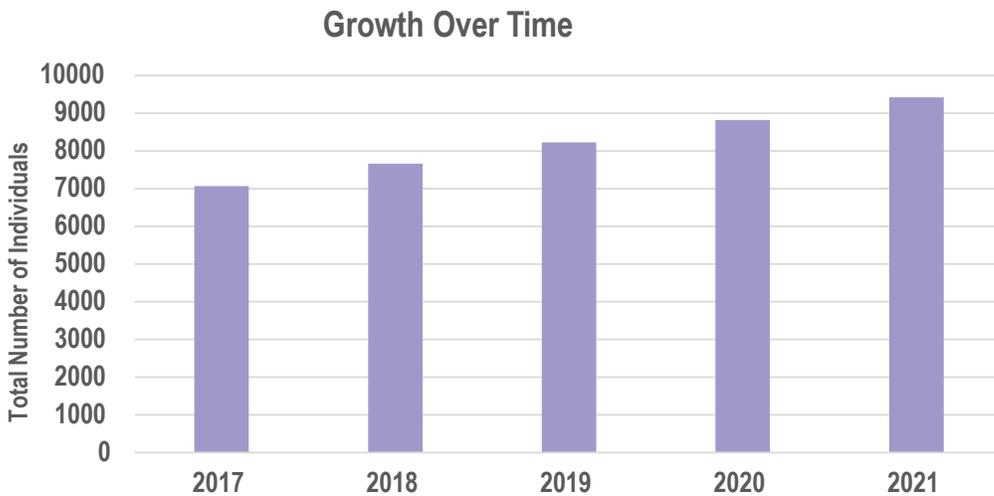
3. Sugarman EA, Nagan N, Zhu H, Akmaev VR, Zhou Z, Rohlf s EM, et al. Pan-ethnic carrier screening and prenatal diagnosis for spinal muscular atrophy: clinical laboratory analysis of >72,400 specimens. *Eur J Hum Genet.* 2012 Jan;20(1):27-32.

4. <https://www.census.gov/quickfacts/fact/table/US/PST045221>

# CURE SMA DATABASES

## CURE SMA MEMBERSHIP DATABASE

The Cure SMA membership database constitutes one of the largest patient-reported data repositories for SMA patients worldwide. It was launched in 1996. Since then, an average of 50 newly diagnosed individuals have contacted Cure SMA each month to share information. Patient reported data captures real world patient experiences and can represent a broad spectrum of patients. Research projects using patient level data from the membership database receive IRB approval prior to project start.



**DATA TYPE:** Patient – and caregiver provided data

**YEARS:** 1996-Present

**SIZE:** >9,500 individuals

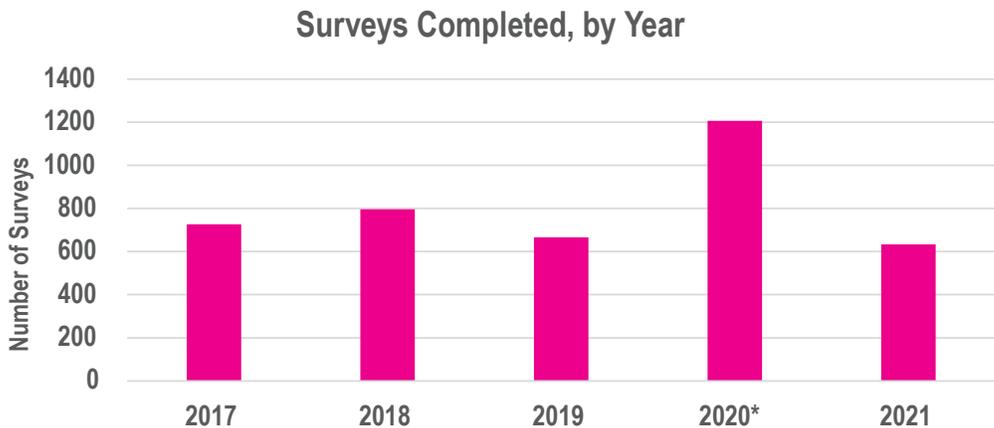
**GEOGRAPHIC SPAN:** International

**CORE DATA FIELDS:**

Name, address, birthdate, diagnosis date, SMA type, number of SMN2 copies, deceased date (if applicable)

## THE COMMUNITY UPDATE SURVEY

Since 2017, Cure SMA has conducted an annual online Community Update Survey to capture natural history data from the patient’s perspective and develop additional data that can support assessment of SMA’s impact. Survey participants include both new and existing Cure SMA members.



**DATA TYPE:** Patient and caregiver survey

**YEARS:** 2017-2021

**SIZE:** 2,277 individuals

**GEOGRAPHIC SPAN:** International

**CORE DATA FIELDS:**

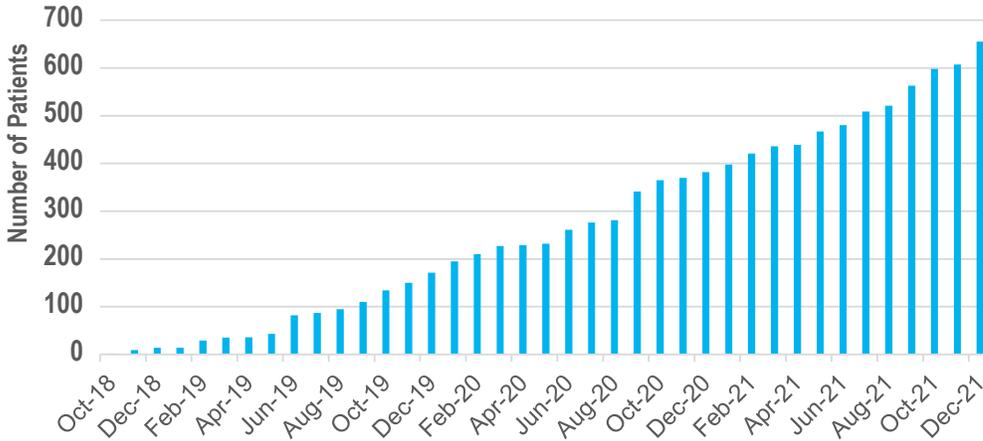
Demographics, surgeries, hospitalizations, motor function, treatment, and quality of life

\* The Community Update Survey had the largest response rate in 2020 at the start of the COVID-19 pandemic.

# CLINICAL DATA REGISTRY (CDR)

The Clinical Data Registry (CDR) is an IRB governed database for individuals with SMA comprised of electronic medical records (EMR) sourced data from 19 care sites and clinician-entered electronic case report form to gather additional information that is not easily found in the EMR. The registry was launched in October 2018.

Growth Over Time



**DATA TYPE:** Electronic medical records + Clinician Survey

**YEARS:** 2018-Present

**SIZE:** ~700 individuals

**GEOGRAPHIC SPAN:** United States\*

**CORE DATA FIELDS:**  
Demographics, SMA type, genetic information, diagnoses, medications, procedures, laboratory tests and vital signs.

*\*a few international patients are included in this data that receive care in the U.S.*

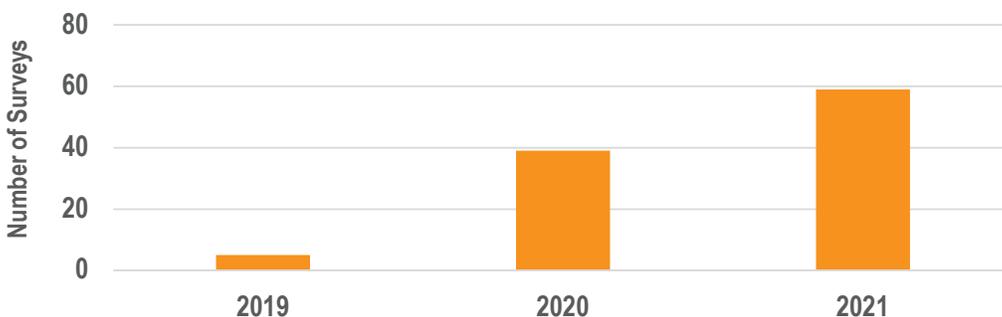
## HIGHLIGHTS

- > 46,000 encounters from 1999 to present
- > 30,000 diagnoses recorded
- > 94,000 procedures
- > 275,000 lab/vital measurements
- Clinician entered electronic case report form (eCRF) data for 87% of patients, including:
  - SMN2 copy number
  - Diagnostic testing
  - Current and maximum motor function

# THE NEWBORN SCREENING REGISTRY DATABASE

The newborn screening registry (NBSR) database is a caregiver-reported data repository comprised of individuals with SMA identified via newborn screening. This database was launched in 2019 and allows for the collection of real-world data that can be used to track outcomes in this population.

Growth Over Time



**DATA TYPE:** Caregiver survey

**YEARS:** 2019-Present

**SIZE:** ~50 individuals

**GEOGRAPHIC SPAN:** United States

**CORE DATA FIELDS:**  
Demographics, SMN2 copy number, diagnosis date, treatment, treatment date, motor function milestones, equipment needs and symptoms



# DEMOGRAPHICS AND CLINICAL CHARACTERISTICS

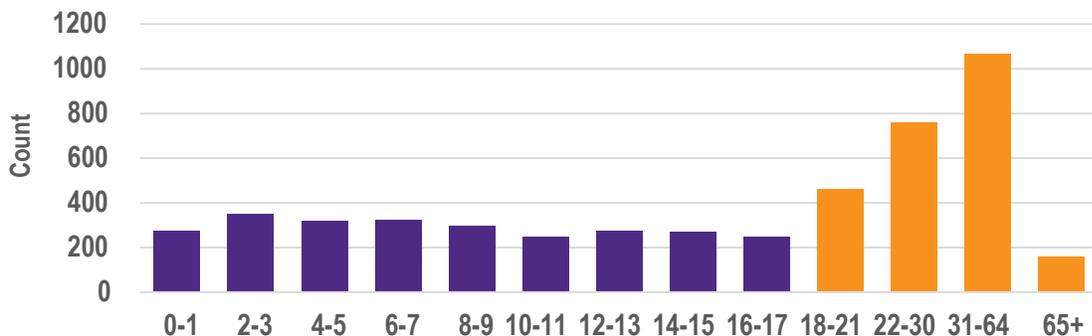
Cure SMA seeks to collect data that is representative of the whole SMA community. An annual review evaluates gaps in representativeness of our data and informs initiatives to address these gaps.

## **Recent initiatives have included:**

- Care packages to support the teen and adult population
- Updating survey fields and other data collection efforts to include additional gender options
- Expanding current support packages and programs to the SMA Community living in Puerto Rico

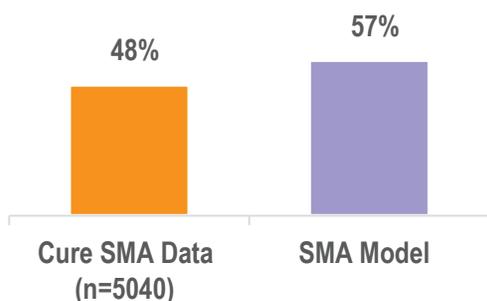
**Mean Age:**  
 21.3 years  
  
**Min Age:**  
 30 days  
  
**Max Age:**  
 90 years

### Age Categories

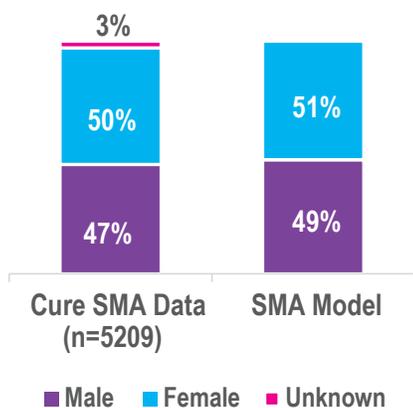


### ADULTS ARE UNDER-REPRESENTED IN CURE SMA DATABASES (48%)

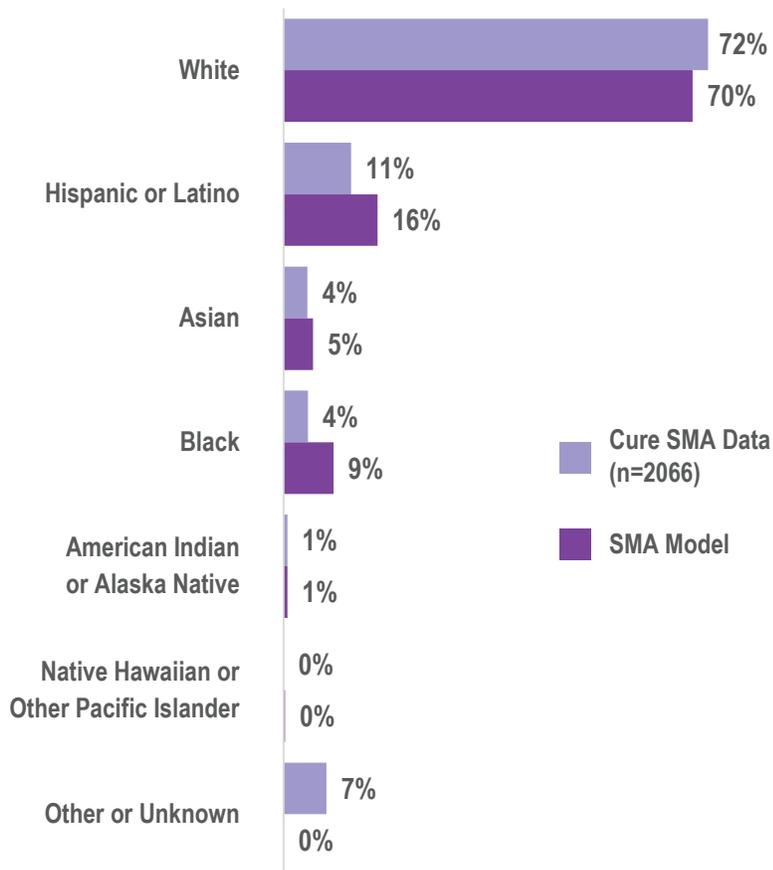
#### Percent of Adults



#### Sex Assigned at Birth



#### Race and Ethnicity



Data from the Newborn Screening Registry is not presented here as newborn screening registry demographics are captured in membership database.

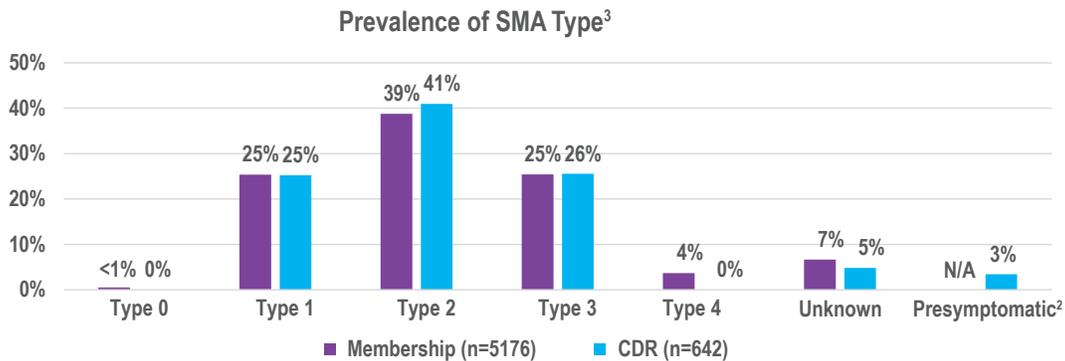
In this report, adult is defined as an individual who is 18 years or older.

## AN ESTIMATED 9,000 INDIVIDUALS CURRENTLY LIVE IN THE U.S. WITH SMA<sup>1</sup>

In the membership database, SMA Type is self or caregiver reported.

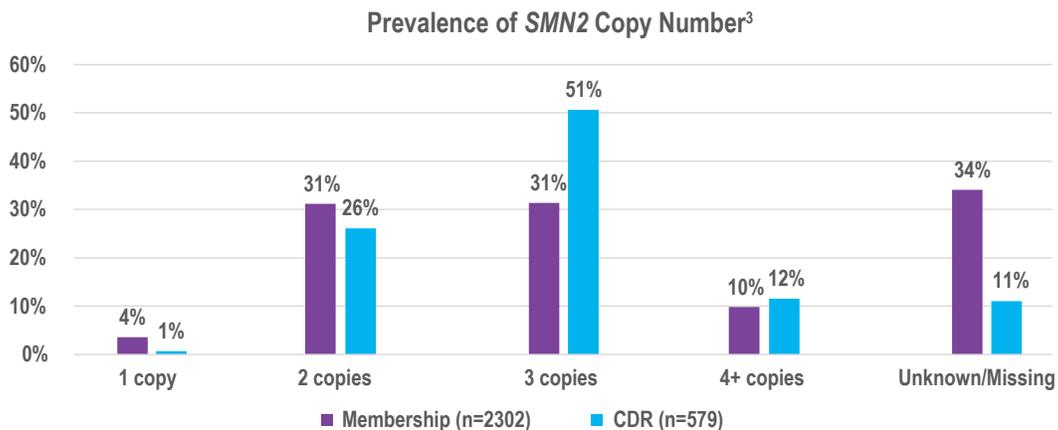
In the CDR, SMA Type is clinician-reported. If SMA Type was not reported, it was pulled from the electronic medical records (if available).

## THE PREVALENCE OF SMA TYPE IS PREDOMINATELY SMA TYPE 2 IN BOTH THE MEMBERSHIP DATABASE AND THE CDR



*SMN<sub>2</sub>* is an inefficient variant of the *SMN<sub>1</sub>* gene because it produces significantly less SMN protein.

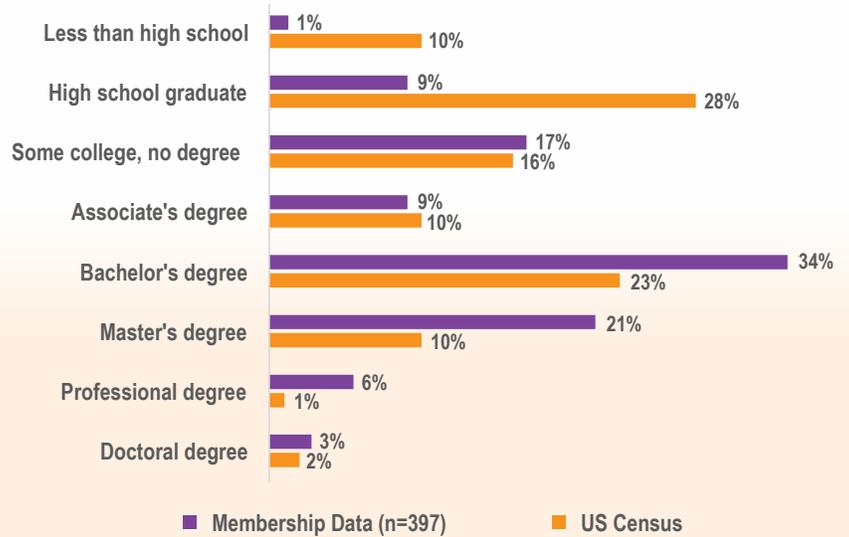
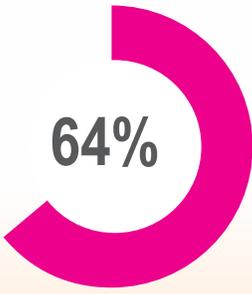
## 34% OF AFFECTED INDIVIDUALS IN THE MEMBERSHIP DATABASE AND 11% IN THE CDR HAVE NOT BEEN TESTED OR DO NOT KNOW THEIR SMN2 COPY NUMBER



**Cure SMA membership database and CDR. Data from the Newborn Screening Registry is not presented here as newborn screening registry demographics are captured in membership database.**

1. Based on the Cure SMA "SMA Model"
2. Presymptomatic SMA type is not collected in the Cure SMA membership database
3. Prevalence refers to the number of people currently alive with the specified characteristic such as SMA type or SMN2 copy number

## HIGHEST LEVEL OF EDUCATION OBTAINED<sup>1</sup>



## HOUSEHOLD INCOME<sup>2</sup>



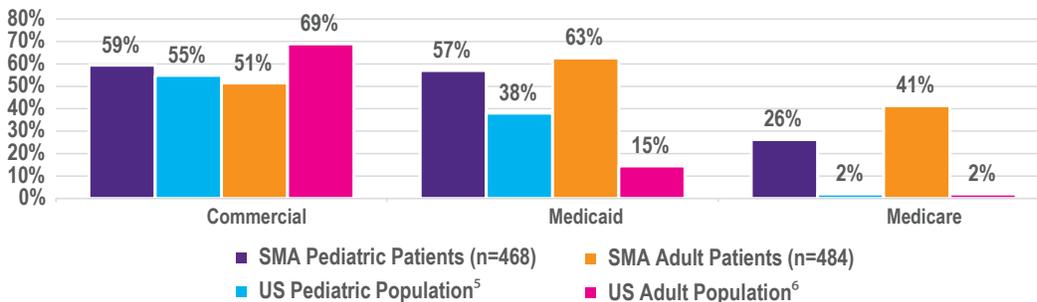
## EMPLOYMENT AMONG ADULTS AFFECTED WITH SMA<sup>3</sup>



## INSURANCE COVERAGE<sup>4</sup>

SMA care is expensive and includes many out-of-pocket costs for outpatient medical care, hospitalizations, and medications. Most children with SMA are enrolled in government-funded insurance programs. In 2019, over 50% of families reported to Cure SMA spending more than \$5,000 a year on SMA related expenses.

Types of insurance among children (ages 0-17) and adults (ages 18-64)



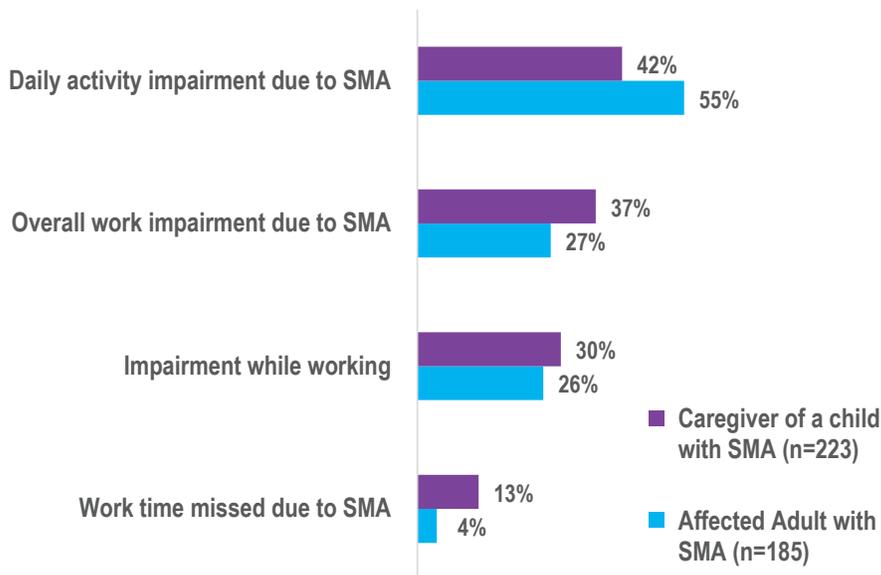
### Membership Data

1. Data out of 396 affected individuals 25 years of age and older
2. Data out of 517 affected individuals
3. Data out of 276 affected individuals 25 years of age and older
4. Data out of 470 affected individuals with health insurance
5. <https://www.kff.org/other/state-indicator/children-0-18/?currentTimeframe=0&sortModel=%7B%22collid%22:%22Location%22,%22sort%22:%22asc%22%7D>
6. <https://www.kff.org/other/state-indicator/adults-19-64/?currentTimeframe=0&sortModel=%7B%22collid%22:%22Location%22,%22sort%22:%22asc%22%7D>

## WORK PRODUCTIVITY AND ACTIVITY IMPAIRMENT (WPAI) QUESTIONNAIRE: SPECIFIC HEALTH PROBLEM V2.0

A six-item questionnaire to measure the effect of a specific health problem on your ability to work and perform regular activities<sup>1</sup>. Scoring procedures are based on responses regarding the seven days prior to the administering of the questionnaire. WPAI outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity.

### Both affected adults and caregivers report extensive impact on their lives



In the last 12 months 90.6% of children and 72.2% of adults with SMA have seen an SMA specialist in the last 12 months.<sup>2</sup>

61.5% of individuals treated with an SMA therapy have received an insurance denial.<sup>3</sup>

34.4%, 35.9% and 41.8% of individuals with Type 1, 2, and 3, respectively, who have seen a physical therapist in the last year have physical therapy needs that exceed their health insurance coverage.<sup>4</sup>

1. Reilly Associates Health Outcomes Research. [<http://www.reillyassociates.net>]

2. Data out of 267 affected children and 266 affected adults

3. Data from our 2021 Community Update Survey from 377 affected individuals on treatment

4. Data out of 291 affected individuals from the 2021 Community Update Survey



# PATIENT JOURNEY

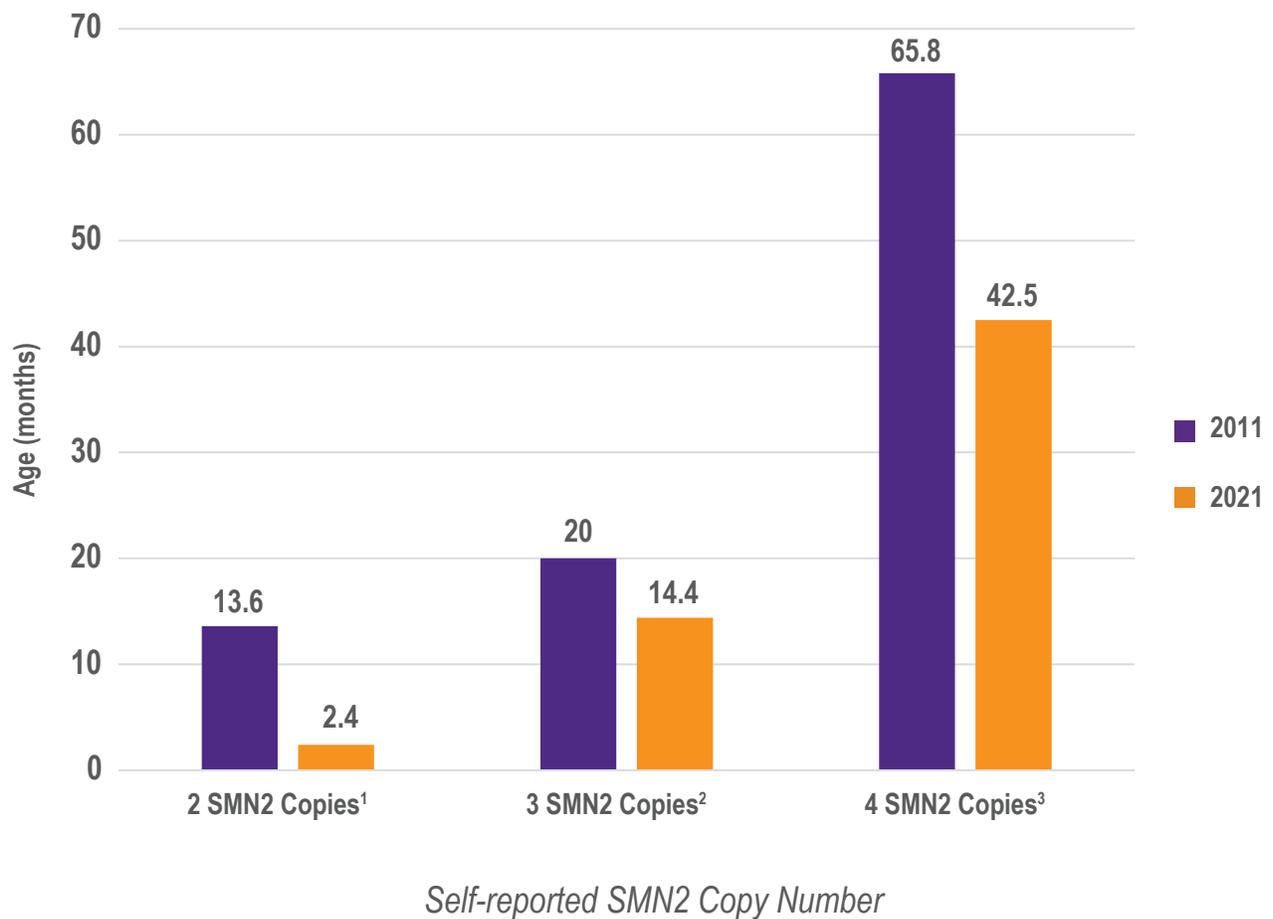


**The patient journey encompasses experiences from diagnosis to treatment and ongoing management**



WITHIN OUR DATABASE, THE AVERAGE AGE AT DIAGNOSIS DECREASED SINCE 2011.

Average Age (Months) at SMA Diagnosis by SMN2 copy number in 2011 and 2021



**Membership Data**

- 1. n=19 for 2011 and n=35 for 2021
- 2. n=19 for 2011 and n=36 for 2021
- 3. n=5 for 2011 and n=13 for 2021

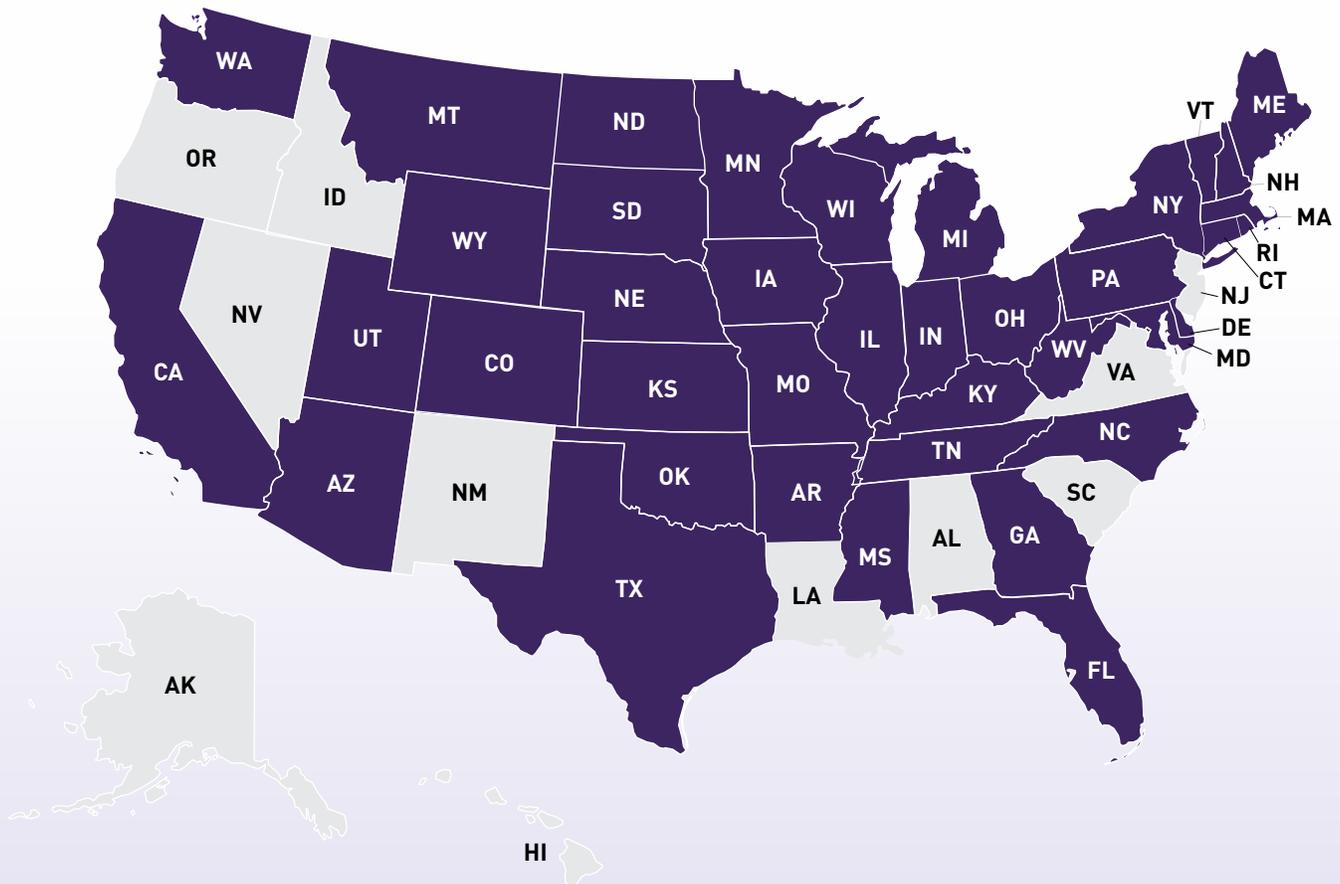
# NEWBORN SCREENING

AS OF DECEMBER 2021, WITH 36 STATES SCREENING AND 32 STATES REPORTING:  
MORE THAN **4.5 MILLION** INFANTS HAVE BEEN SCREENED FOR SMA  
AN ESTIMATED **301** INFANTS SCREENED POSITIVE AND SMA DIAGNOSIS CONFIRMED  
PRELIMINARY ESTIMATED INCIDENCE IS APPROXIMATELY **1 IN 15,000**<sup>1</sup>

## STATES SCREENING & NOT SCREENING FOR SMA

38 States Currently Screen for SMA | 85% of Newborn Babies in the U.S. are Screened

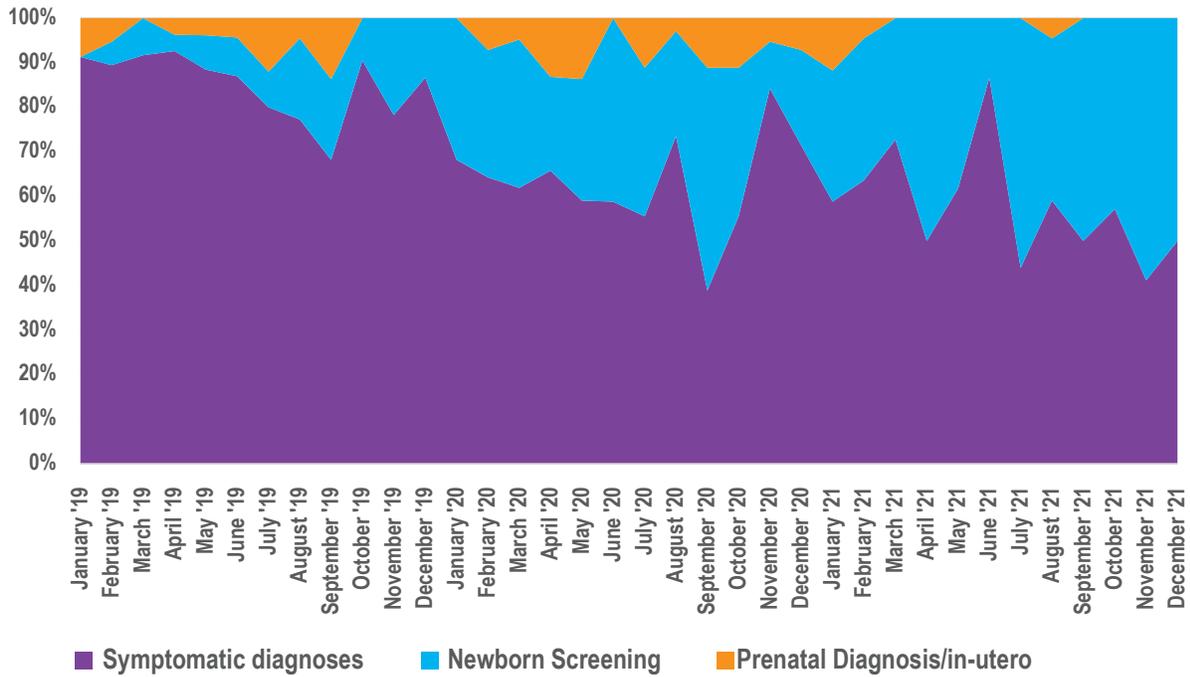
As of December 2021



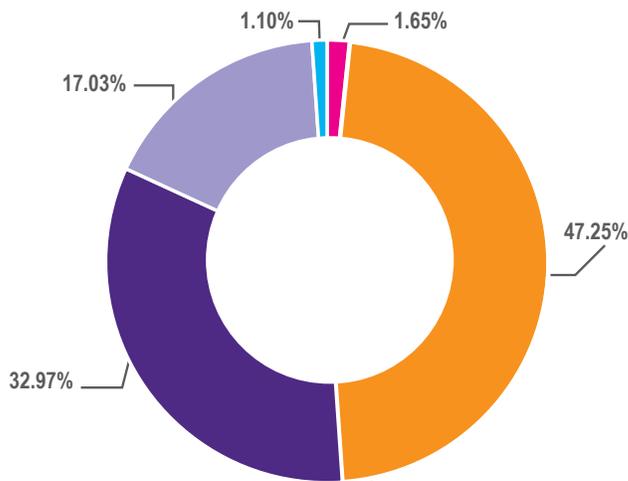
Since December 2021, the following states have added SMA newborn screening: Alabama, Arizona, Idaho, Louisiana, New Jersey, Virginia.

1. Data based on state lab screening rates as of December 31, 2021. These numbers are estimates.

## INCREASED NEWBORN SCREENING HAS BEEN ACCOMPANIED BY A DECREASING FREQUENCY OF SYMPTOMATIC DIAGNOSES



### Incidence<sup>1</sup> of SMN2 Copy Number for Individuals Identified via NBS<sup>2</sup>



Nearly half of newborns with SMA have 2 copies of SMN2, which is common for individuals with SMA type 1

Legend: 1 copy (pink), 2 copies (orange), 3 copies (purple), 4 copies (light purple), 5 or more copies (cyan)

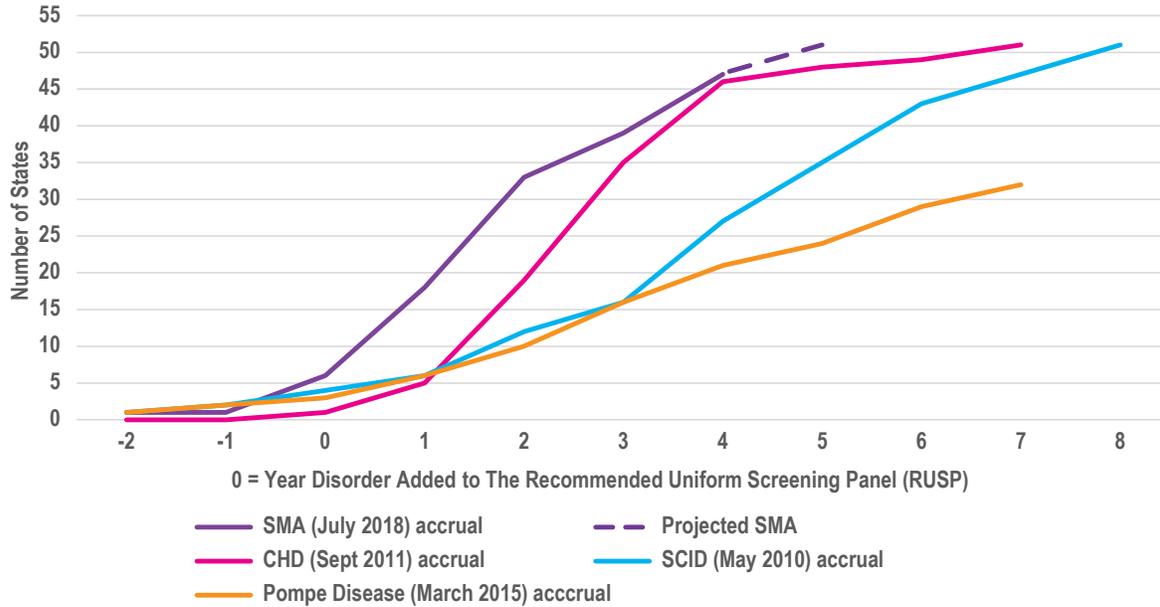
#### Membership Data

1. Incidence is the number of new cases of SMA per year.

2. Data from the membership database among those identified with SMA through newborn screening, n=182.

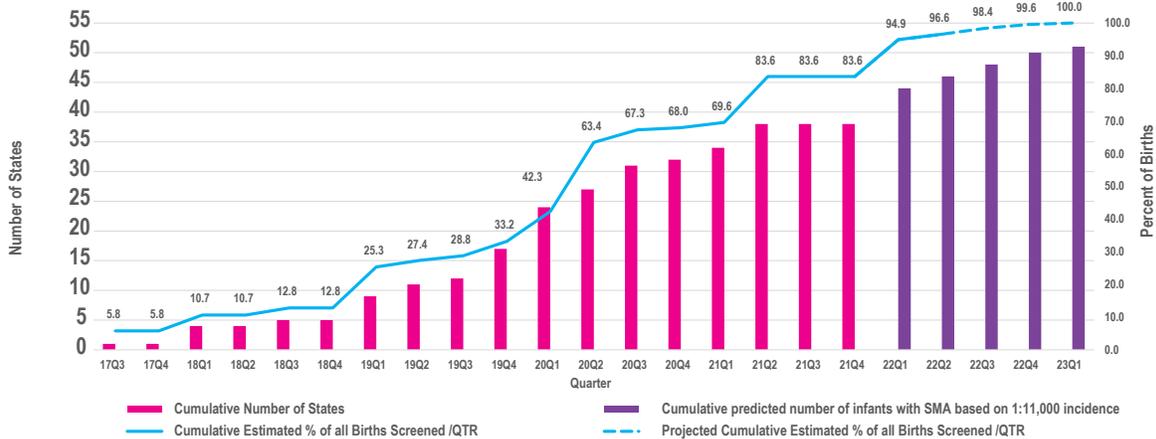
# NEWBORN SCREENING FOR SMA HAS INCREASED RAPIDLY SINCE 2017, MUCH FASTER THAN MANY OTHER RARE DISEASES

State and District of Columbia SMA NBS Implementation<sup>1</sup> Over Time Compared to Congenital Heart Disease (CHD)<sup>2</sup>, SCID<sup>3</sup> and Pompe Disease<sup>4</sup> NBS Implementation



## Quarterly Growth:

Number of States Screening for SMA and Percent of Infant Births Screened in the US



1. SMA information per Cure SMA State NBS implementation tracking
2. CHD information per Glidewell J, Grosse SD, Riehle-Colarusso T, et al. Actions in Support of Newborn Screening for Critical Congenital Heart Disease — United States, 2011–2018. MMWR; <https://www.cdc.gov/mmwr/volumes/68/wr/mm6805a3.htm>
3. SCID information per the Immune Deficiency Foundation; <https://primaryimmune.org/scid-compass/idf-scid-newborn-screening-campaign>
4. Pompe information per Hale, K., Kellar-Guenther, et al (2020). Expanding Newborn Screening for Pompe Disease in the United States. International Journal of Neonatal Screening. 6(2);48; <https://www.newsteps.org/resources/data-visualizations/newborn-screening-status-all-disorders>; <https://www.babysfirsttest.org/newborn-screening/states>
5. 2020 CDC Birth Rate

# THE IMPACT OF NEWBORN SCREENING

## WITHIN CURE SMA NEWBORN SCREENING REGISTRY, N=52:

### MEDIAN AGE AT DIAGNOSIS CONFIRMATION:

**7 DAYS<sup>1</sup>**

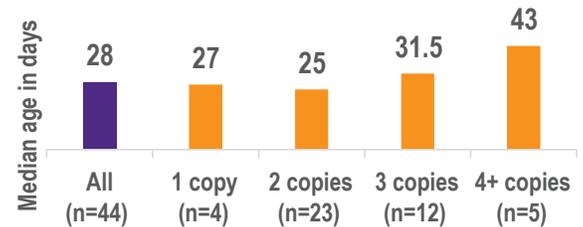
(RANGE 1 -22 DAYS)

### MEDIAN AGE AT 1ST TREATMENT:

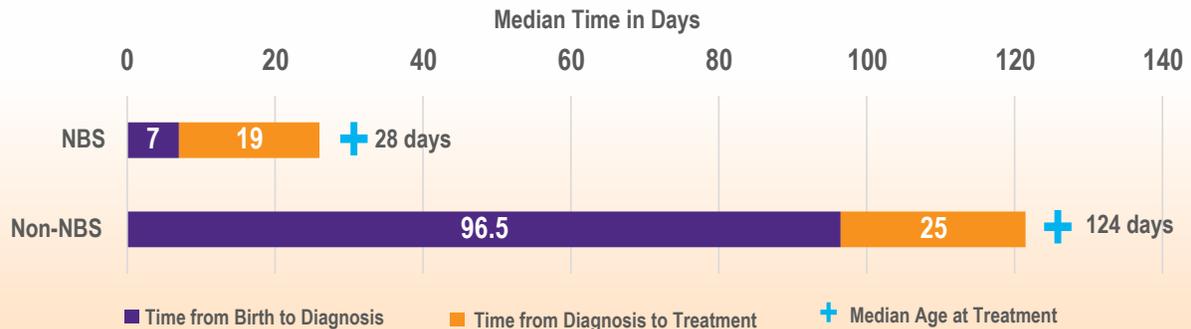
**28 DAYS<sup>2</sup>**

(RANGE 8 -487 DAYS)

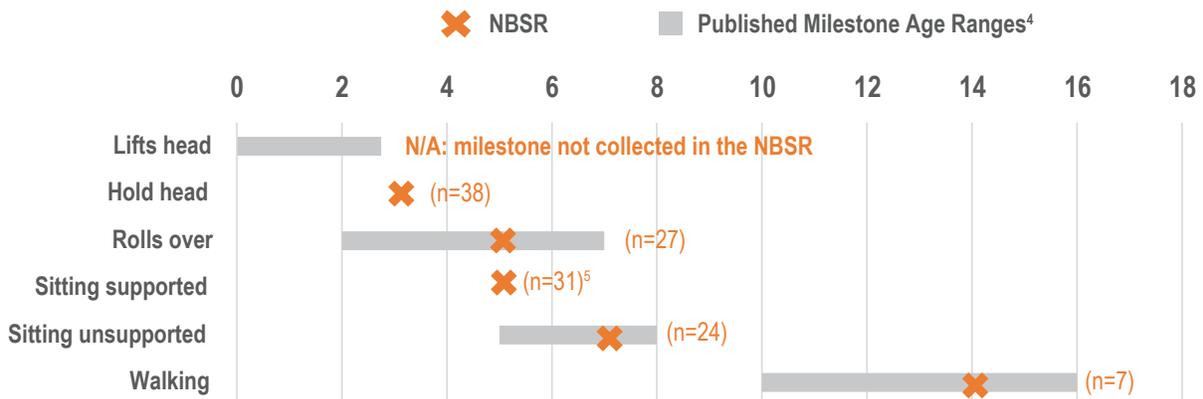
Median Age at First Treatment by SMN2 Copy Number, n=44<sup>2</sup>



### Individuals identified via newborn screening had decreased time to diagnosis and treatment<sup>3</sup>



### Median Age in Months at Developmental Milestones



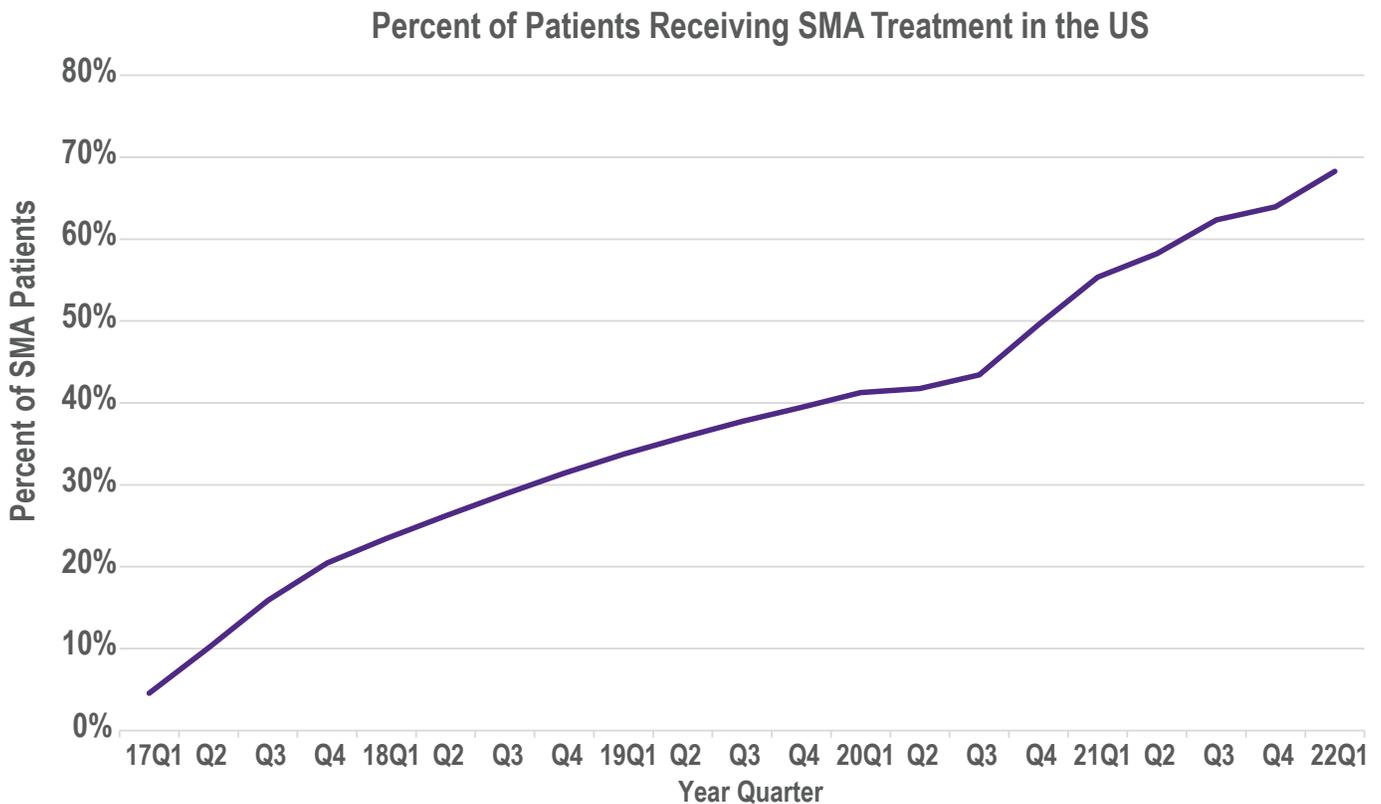
1. Individuals must have a non-blank age of diagnosis (n=52)
2. Treatment date must be a valid date and must have occurred after birth (n=44)
3. Unadjusted analysis of individuals identified via newborn screening compared to a sample from the Clinical Data Registry. CDR patients must have been born after 2017 (after first FDA approved treatment) and not identified via prenatal screening or newborn screening (n=80).
4. Adolph KE, Franchak JM. The development of motor behavior. Wiley Interdiscip Rev Cogn Sci. 2017 Jan; 8(1-2): 10.1002/wcs.1430.
5. For NBSR, combined milestone of rolling from back to stomach and rolling from stomach to back

# TREATMENT

THE SMA TREATMENT PIPELINE CONTINUES TO ADVANCE. CURRENTLY, THERE ARE MULTIPLE FDA-APPROVED TREATMENTS FOR SMA:

Treatment	Approval Date	Age Eligibility	SMA Type Eligibility
Spinraza® (nusinersen)	12/23/2016	All ages	All SMA types
Zolgensma® (onasemnogene abeparvovec -xioi)	5/24/2019	Individuals < 2 years old	All SMA types
Evrysdi® (risdiplam)	8/7/2020	All ages	All SMA types

ALMOST 70% OF INDIVIDUALS WITH SMA IN THE US HAVE RECEIVED AN FDA-APPROVED TREATMENT<sup>1</sup>



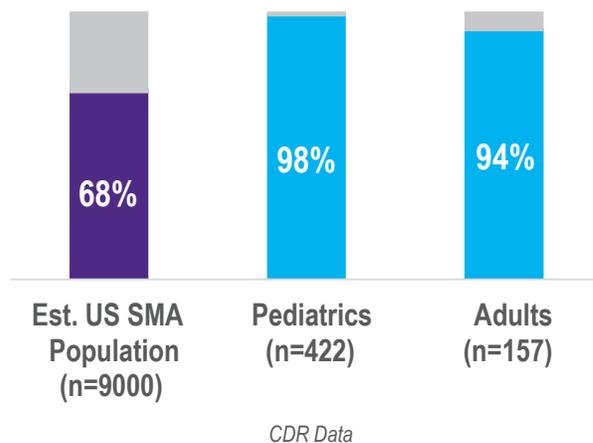
1. Modeled estimates derived from quarterly earnings reports from Biogen, Roche, and Novartis and an assumed prevalence of 9000 patients with SMA.

# 97%

## 97% OF PATIENTS IN THE CLINICAL DATA REGISTRY WERE REPORTED TO HAVE RECEIVED AN SMA TREATMENT<sup>1</sup>

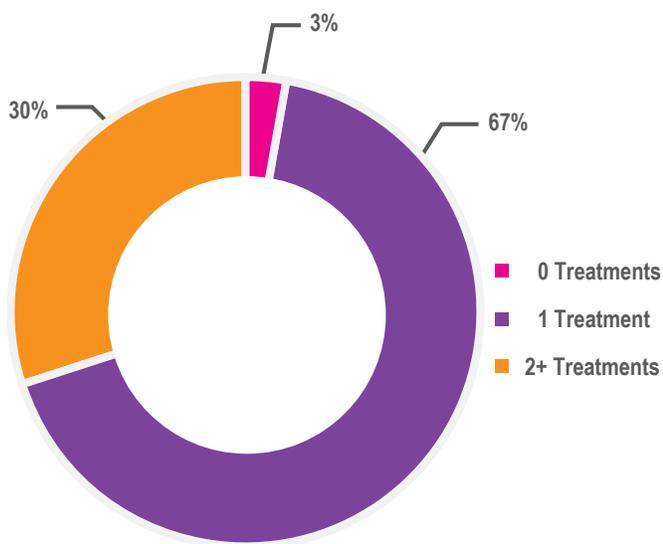
The CDR has a large proportion of individuals that have received treatment as well as pediatric individuals, which does not reflect the broader U.S. SMA population. Efforts are underway to make our databases better reflective the U.S. SMA community.

### Treatment by Age Group

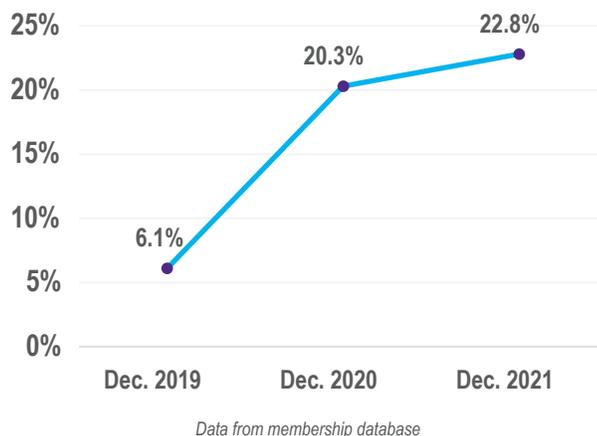


### USE OF MULTIPLE TREATMENTS (CONCURRENTLY OR SEQUENTIALLY):

30% of individuals have received multiple SMA treatments<sup>2</sup>:



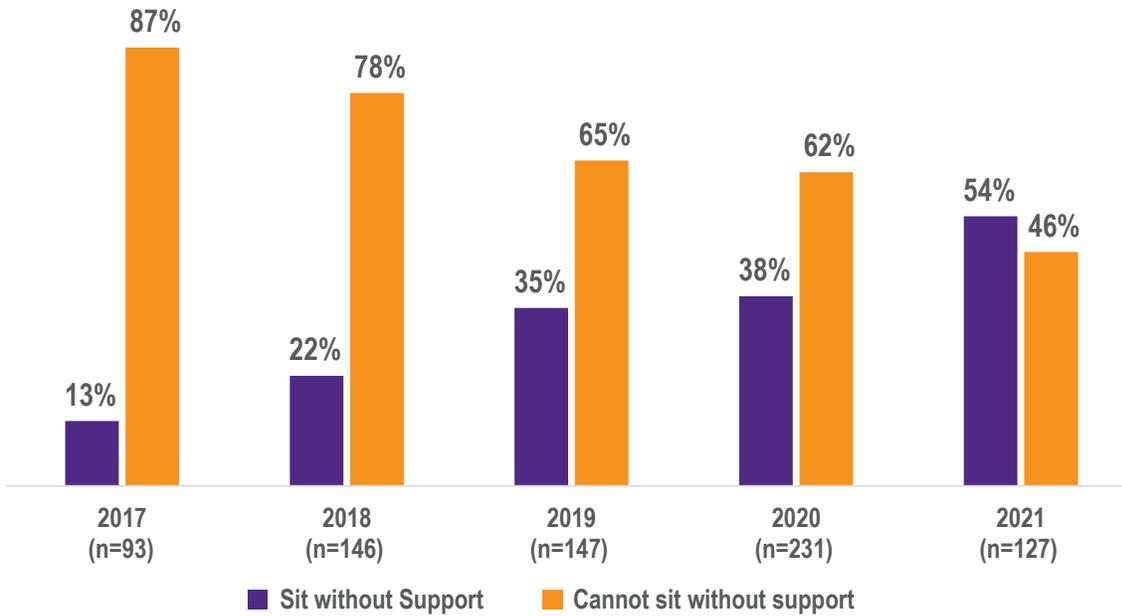
Use of multiple SMA treatments has risen since 2019<sup>3</sup>:



1. Treatment defined as an FDA approved treatment for SMA as of 2/2022. Treatment was defined as any evidence of treatment through either the EMR data or the clinician filled eCRF. Analysis was restricted to patients with a completed eCRF, n=579.  
2. Number of treatments refers to current and historical number of treatments and included both concurrent use as well as sequential use.  
3. Membership data analysis includes 689 treated individuals in 2019, 792 treated individuals in 2020 and 881 treated individuals in 2021.

# TREATMENT IMPACT

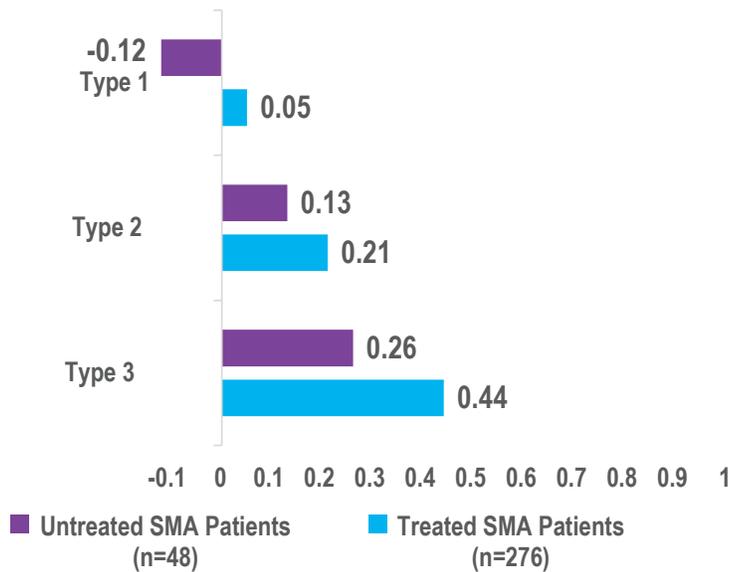
The proportion of individuals with SMA type 1 who can sit without support has increased since 2017<sup>1</sup>



Health Utilities Index measures health related quality of life on a single scale from **-0.36 to 1**. Higher scores indicate greater health-related quality of life.

Individuals treated with an SMA therapy have **higher** quality of life scores than untreated individuals.

Health Utilities Index Score <sup>2,3</sup>



### Membership Data

1. Community Update Survey year shown on x-axis
2. Among those ages greater than or equal to >5
3. Data shown is for the Health Utilities Index Mark 3 (<https://hqlo.biomedcentral.com/articles/10.1186/1477-7525-1-54>)

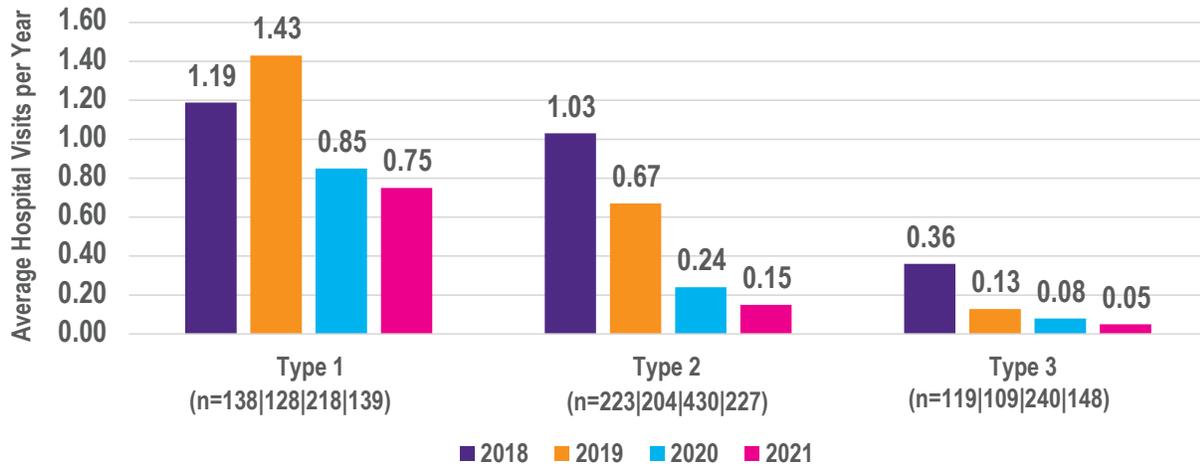
## SMA TYPE – A THING OF THE PAST?

DUE TO NEWBORN SCREENING AND THE USE OF SMA DISEASE MODIFYING THERAPIES, IT IS DIFFICULT TO CATEGORIZE THE SEVERITY OF SMA ON TYPE (BASED ON AGE OF ONSET AND MAXIMUM MOTOR FUNCTION ACHIEVED)

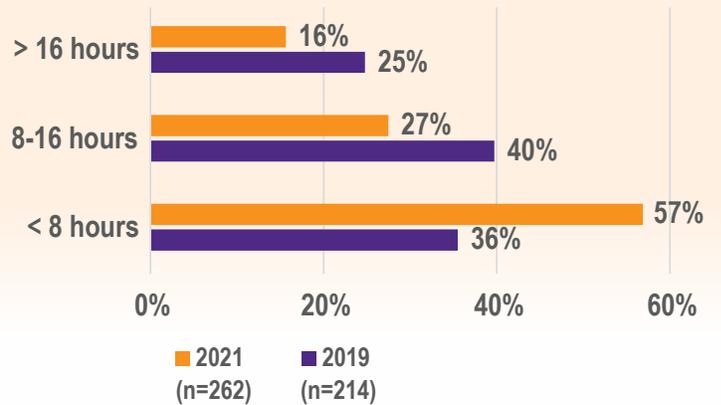
Percent of individuals with an “unknown” SMA type in the Cure SMA Membership Database



The average number of hospitalizations per person has decreased for all major SMA types since 2018<sup>1</sup>



For those requiring it, time on breathing support has decreased from 2019 to 2021<sup>2</sup>



### Membership Data

1. Year is year of Community Update Survey
2. Data collected from the 2019 & 2021 Community Update Survey

THE MORTALITY RATE OF SMA IN 2021 WAS APPROXIMATELY ONE-THIRD OF WHAT IT WAS IN 2009, HAVING DECREASED FROM **1.56 PER 100** INDIVIDUALS TO **0.55 PER 100** INDIVIDUALS WITH SMA.

Annual Mortality Rate (per 100 people with SMA), 2009 - 2021

