



STATE OF SMA

2022 REPORT



ACKNOWLEDGMENTS

Cure SMA is thankful to all individuals with spinal muscular atrophy (SMA) and their families who have generously shared their data. Their willingness to share details about how SMA impacts their families and daily lives allows us to advance the understanding of this disease and lays the foundation for continued progress on behalf of our community.

Cure SMA is grateful for the support and funding provided by the Cure SMA Real World Evidence Collaboration (RWEC) and the Cure SMA Industry Collaboration (SMA-IC) for research initiatives.

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

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. Funding for the development of the State of SMA was provided by the Cure SMA RWEC. Members of the RWEC include Biogen, Novartis Gene Therapies, Genentech/Roche, and SMA Europe.

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 SMA therapeutics to more effectively address a range of scientific, clinical, and regulatory challenges. Current members include Cure SMA, Biogen, Scholar Rock, Novartis Gene Therapies, Biohaven Pharmaceuticals, Epirium Bio, Genentech/Roche, and SMA Europe. Funding for the research included within the State of SMA Report was provided by the 2022 SMA-IC; members include Cure SMA, Biogen, Genentech/Roche, Scholar Rock, Novartis Gene Therapies, Biohaven Pharmaceuticals, Epirium Bio, and SMA Europe.

Cure SMA Care Center Network

Since 2018, Cure SMA has partnered with hospitals across the U.S. with the goal to improve healthcare for people with SMA. Every Care Center Network site submits consented patient information and data to the Cure SMA Clinical Data Registry. This data is then analyzed to drive healthcare improvements.

The SMA Care Center Network includes the following sites:

ADULT & PEDIATRIC CENTERS

Boston Children's Hospital, Boston, MA
 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
 The Children's Hospital of Philadelphia, Philadelphia, PA
 The University of Michigan, Ann Arbor, MI
 University of California, Los Angeles (UCLA), Los Angeles, CA
 University of Miami, Miami, FL
 University of New Mexico, Albuquerque, NM
 University of Rochester Medical Center, Rochester, NY
 University of Utah, Program for Inherited Neuro Disorders, SLC, UT
 Washington University/St. Louis Children's Hospital, St. Louis, MO

ADULT CENTERS

Baylor College of Medicine, Houston, TX
 Northwestern University, Evanston, IL
 Stanford Health, Palo Alto, CA
 The Ohio State University, Wexner Medical Center, Columbus, OH

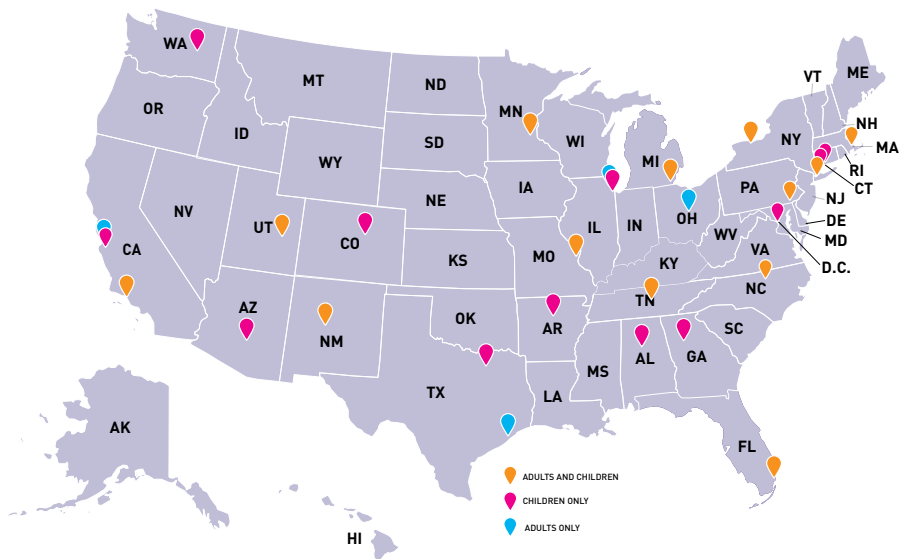
PEDIATRIC CENTERS

Advocate Children's Hospital, Park Ridge, IL
 Arkansas Children's Hospital, Little Rock, AR
 Children's Healthcare of Atlanta, Atlanta, GA
 Children's Hospital Colorado, Aurora, CO
 Children's National Medical Center, Washington, D.C.
 Children's of Alabama, Birmingham, AL
 Phoenix Children's Hospital, Phoenix, AZ
 Seattle Children's Hospital, Seattle, WA
 Stanford Children's Health, Palo Alto, CA
 University of Texas Southwestern/Children's Health, Dallas, TX
 Vanderbilt University Medical Center, Nashville, TN
 Yale Pediatric Neuromuscular Clinic, New Haven, CT

CARE CENTER NETWORK

Mission

To provide the best care, including offering new therapies, and to gather and disseminate new knowledge to advance the SMA standard of care for pediatric and adult persons with SMA.



Additional Acknowledgments

Funding for the Cure SMA Care Center Network has been provided in part by the Erin Trainor Memorial Fund, the Tyler William Orr Memorial Fund, and the Oscar G. and Elsa S. Mayer Family Foundation.

DEAR CURE SMA COMMUNITY,

We are pleased to share with you the second annual State of SMA report. The goal of the SMA report is to share highlights and trends using data 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 from 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 20 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.

In the past year we have witnessed many successes in SMA. SMA newborn screening is now available in 48 states, covering almost all children born in the U.S. being screened for SMA. Additionally, we estimate that approximately 70% of people with SMA have received an FDA approved treatment for SMA. The number of clinical trials is at the highest level ever. The SMA Care Center Network has expanded to 29 centers across the U.S. We are excited about what next year will bring for SMA.

Many thanks to those who contribute to the Cure SMA databases. This report would not be possible without you. Participating in our surveys and registries enables us to capture your voice and understand your unique journey. Every participant counts and lends insight into further understanding the changing landscape of SMA. This work celebrates you.

Thank you for your commitment to Cure SMA.

Sincerely,



Lisa Belter, MPH
Vice President, Data Analytics



Sarah Whitmire, MS
Director, Data Analytics



Mary Schroth, MD, FAAP, FCCP
Chief Medical Officer

ABOUT THIS REPORT

This report is based on internal data from Cure SMA data sources and output from the SMA model, which Cure SMA created to estimate demographic and clinical characteristics of individuals with SMA in the U.S..

Both the patient-reported data and the clinician-reported data are presented in this report. In some of our analyses, we have combined the data sources. Even though data comes from multiple sources and perspectives, previous analyses have shown high reliability between the patient-reported and clinician reported data.¹

The data in this report includes individuals who are:

- Diagnosed (both self-reported and/or clinically confirmed) with 5q SMA
- Included in one or more of our databases as of December 31, 2022
- Residents of the U.S.

Please note that all the analyses within this report are descriptively showing what we see in the data, but they do not adjust for factors that may bias the results. Caution should be taken when interpreting the results.

Here are a few terms that you will see as you read this report:

CARE CENTER NETWORK:

SMA Care Centers across the U.S. who partner with Cure SMA to provide patient consented information and data to the Clinical Data Registry with the goal to improve healthcare for people with SMA.

CLINICAL CHARACTERISTICS:

The description of SMA-specific attributes.

CLINICIAN REPORTED DATA:

Data that is gathered from clinician reported medical records about a patient seeking care, commonly through medical records, case report forms, or surveys.

ELECTRONIC CASE REPORT FORM (eCRF):

Digital questionnaire used to collect data.

ELECTRONIC MEDICAL RECORD (EMR):

Digital version of a patient's healthcare chart.²

INCIDENCE OF SMA:

The number of individuals born with spinal muscular atrophy out of all births. In other publications, you may see this referred to as "birth prevalence".

INSTITUTIONAL REVIEW BOARD (IRB):

A group that has been formally designated to review and monitor biomedical research involving human subjects. The IRB has the authority to approve, modify, or disapprove research.³

MORTALITY RATE PER YEAR:

The frequency of the occurrence of death within a subgroup of individuals within a one-year period.

PATIENT-REPORTED DATA:

Data that is gathered directly from a patient, commonly through online surveys and questionnaires.

PREVALENCE OF SMA:

The number of individuals that are currently living with SMA.

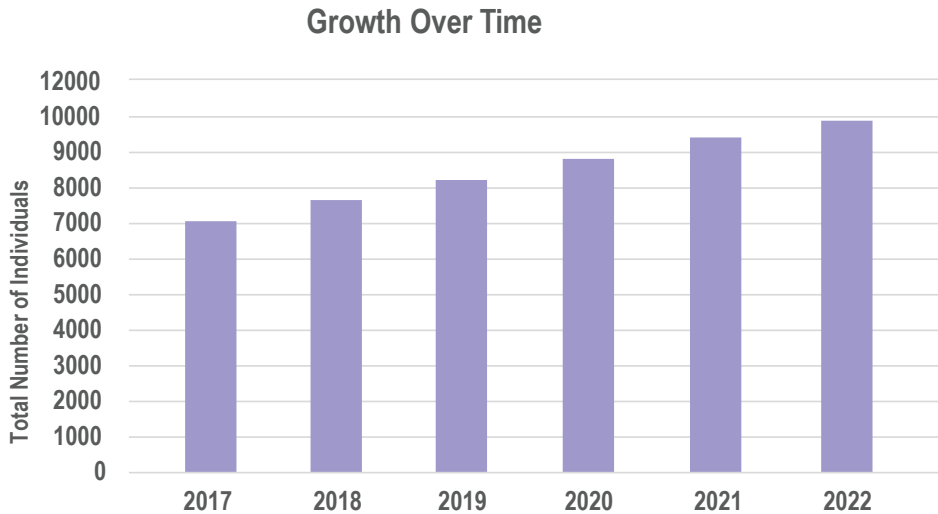
References:

1. Belter L, Whitmire S, Curry M, Schroth M. Comparing Spinal Muscular Atrophy (SMA) outcomes between a patient-reported membership database and a clinical data registry. Poster presented at the American Academy of Neurology in Boston MA in April 2023.
2. What Is An EMR? Everything You Need To Know – Forbes Advisor
3. Institutional Review Boards (IRBs) and Protection of Human Subjects in Clinical Trials | FDA

CURE SMA DATABASES

Cure SMA Membership Database

The Cure SMA membership database constitutes one of the largest patient-reported data repositories for people living with SMA 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 use de-identified patient data from the membership database and receive Institutional Review Board (IRB) approval prior to project start.



DATA TYPE:
Patient and caregiver- provided data

YEARS:
1996-Present

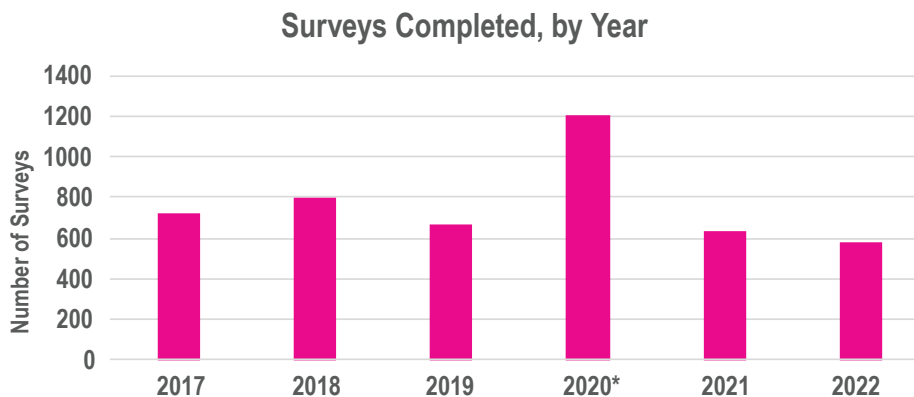
SIZE:
>9,700 individuals

GEOGRAPHIC SPAN:
International

CORE DATA FIELDS:
Demographics, diagnosis date, SMA type, number of SMN2 copies, and deceased date (if applicable)

Community Update Survey (CUS)

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



DATA TYPE:
Survey

YEARS:
2017-2022

SIZE:
2,436

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 CDR is an Institutional Review Board (IRB) governed database for individuals with SMA comprised of electronic medical records (EMR) sourced data from Care Center Network sites and clinician-entered electronic case report forms (eCRFs) to gather additional information that is not easily found in the EMR. The registry was launched in October 2018. As some of the new Care Center Network sites are being integrated into the CDR, this report contains data from 20 of the 29 sites.

DATA TYPE:
Electronic medical records and electronic case report form

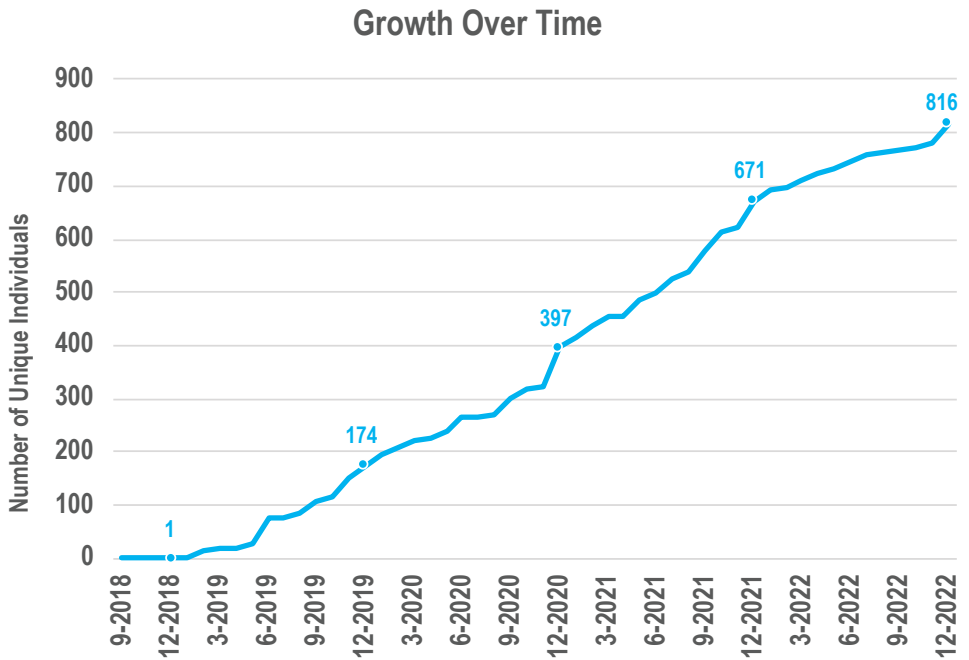
YEARS:
2018-Present

SIZE:
>800 individuals

GEOGRAPHIC SPAN:
U.S.*

CORE DATA FIELDS:
Demographics, genetic information, motor function, diagnoses, medications, procedures, laboratory studies, vitals signs, etc.

**Data from a few international patients who receive care in the U.S. are included in this registry.*



Newborn Screening Registry Database (NBSR)

The NBSR 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.

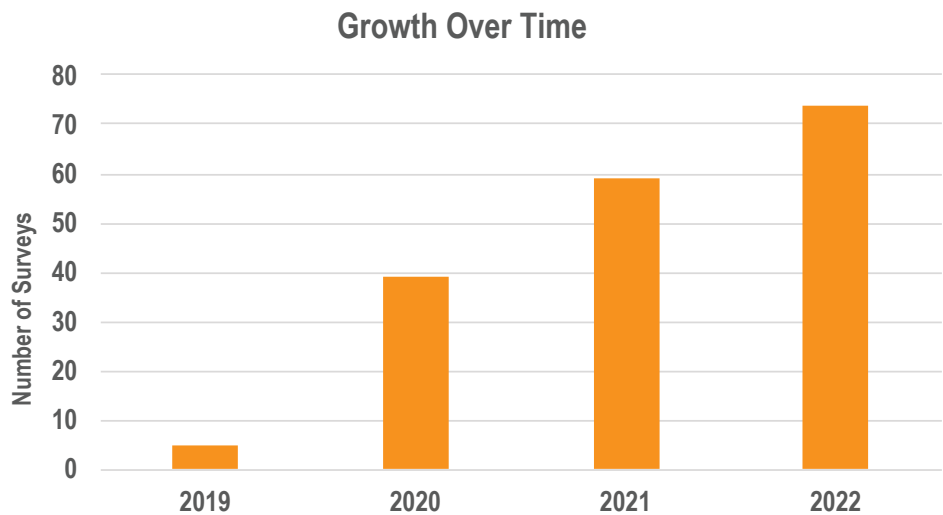
DATA TYPE:
Survey

YEARS:
2019-Present

SIZE:
>70 individuals

GEOGRAPHIC SPAN:
U.S.

CORE DATA FIELDS:
Demographics, SMN2 copy number, diagnosis date, treatment, treatment date, motor function milestones



SMA MODEL

The “SMA Model” is not a database, but a model that was created by Cure SMA to estimate characteristics of the population with SMA in the U.S.

Results from the model are based on internal and external real world inputs, and the following assumptions were made:

- SMA incidence of 1 in 11,000¹
- SMA subtype incidence of 60% for Type 1, 30% for Type 2, and 10% for Type 3/4¹
- Median age of survival of 4 years, 40 years, and 78 years for SMA Type 1, Type 2, and Type 3, respectively²
- Race and ethnicity estimates adjusted based on SMA carrier rates described by Sugarman et al.³; and the 2010 U.S. Census⁴

We anticipate that the availability of multiple effective SMA treatments, the increase in newborn screening, changes in survival, and a better understanding of the incidence of SMA will have an impact on the model’s output.

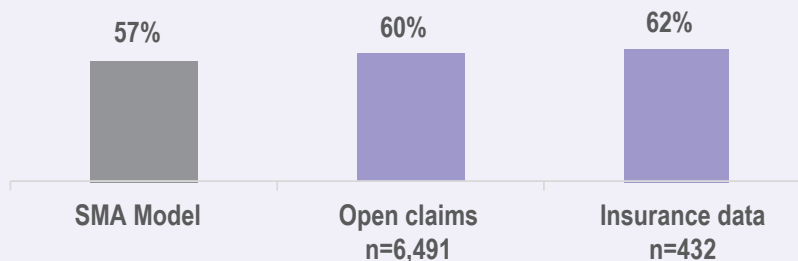
Is it time to update our model?

In 2022, we sought to understand if the results of our model aligned with two very large medical and pharmacy claims datasets

1. Open claims - Aggregated data sourced from pharmacies, EMR, clearinghouses, etc.
2. Insurance data - Adjudicated claims that were sourced directly from a large insurance provider

Findings:

- There was a higher proportion of adults in the claims data (60-62%) than the SMA model output (57%)



This suggests that the survival rates in our model may be too low; however, additional work needs to be done to understand how representative the claims datasets are of the larger SMA community.

- The SMA model results for distribution of sex assigned at birth were aligned with the claims data

As a result, Cure SMA is currently working to update our model inputs with available data. Stay tuned!

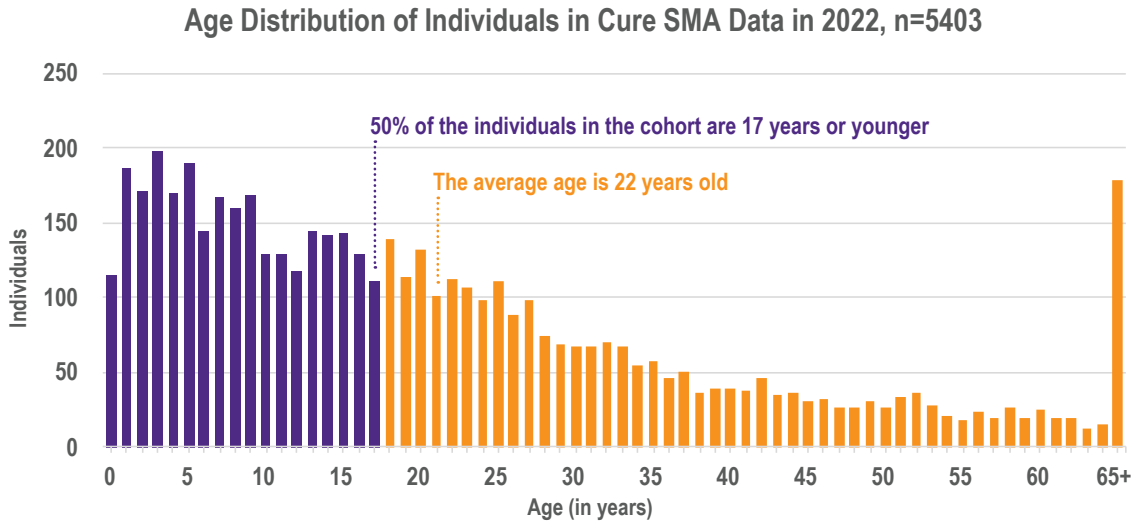
1. Verhaart IEC, Robertson A, Wilson IJ, Aartsma-Rus A, Cameron S, Jones CC, Cook SF, Lochmüller H. Prevalence, incidence and carrier frequency of 5q-linked spinal muscular atrophy - a literature review. *Orphanet J Rare Dis.* 2017 Jul 4;12(1):124.
2. Based on Cure SMA internal assumptions
3. Sugarman EA, Nagan N, Zhu H, Akmaev VR, Zhou Z, Rohlfis 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/PST045219>

DEMOGRAPHICS AND CLINICAL CHARACTERISTICS

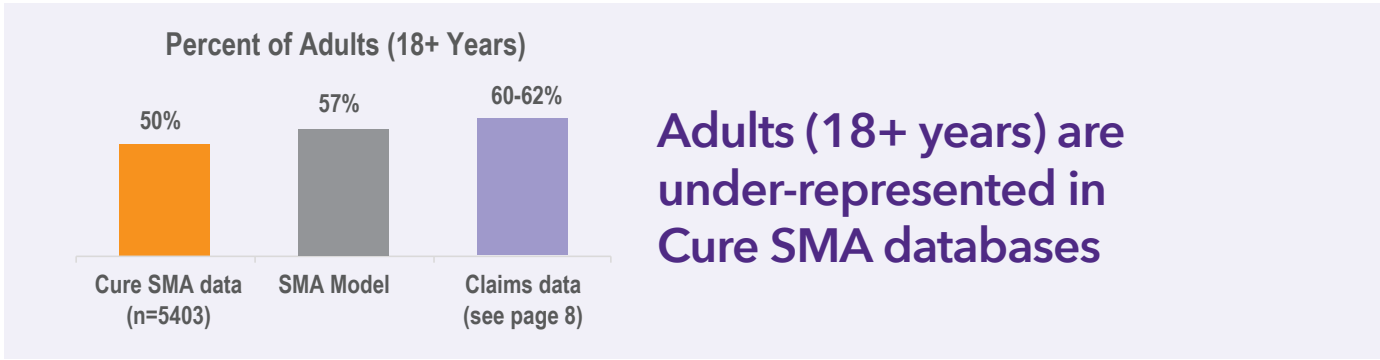
Cure SMA seeks to understand the broad diversity of the SMA community in the U.S. Recent projects have included:

- Analyzing demographic characteristics of individuals with SMA that were found in 3 large claims and EMR databases
- Survey to better understand the demographics of the SMA community

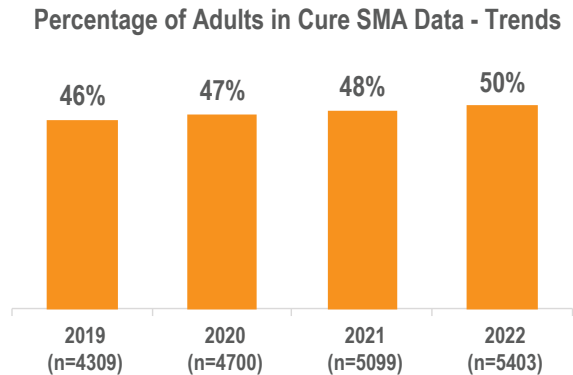
AGE



Average Age: 22 years | Standard Deviation: 18 years | Median Age: 17 years



However, steady progress has been made to improve the adult representation in our data over the last few years

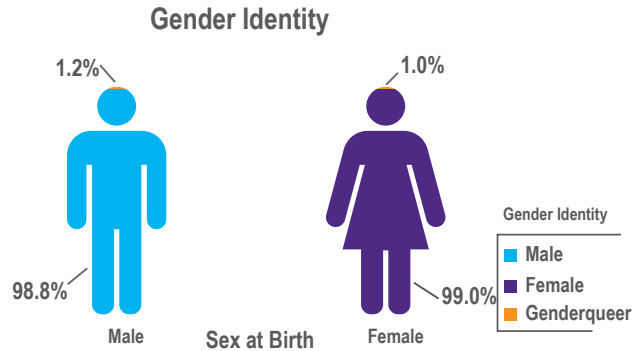
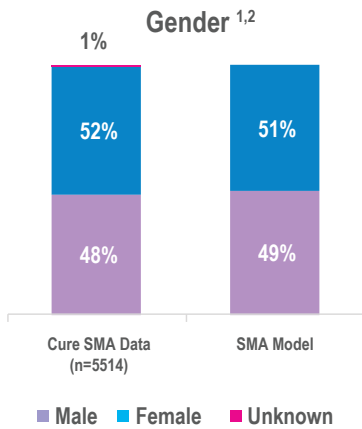


Cure SMA Data Sources: Membership data, CUS, CDR, and NBSR data combined. Individuals participating in multiple sources were de-duplicated.

1. Age was calculated as of December 31st of the calendar year being reported.
2. All graphics include individuals that were alive for the full year being reported.

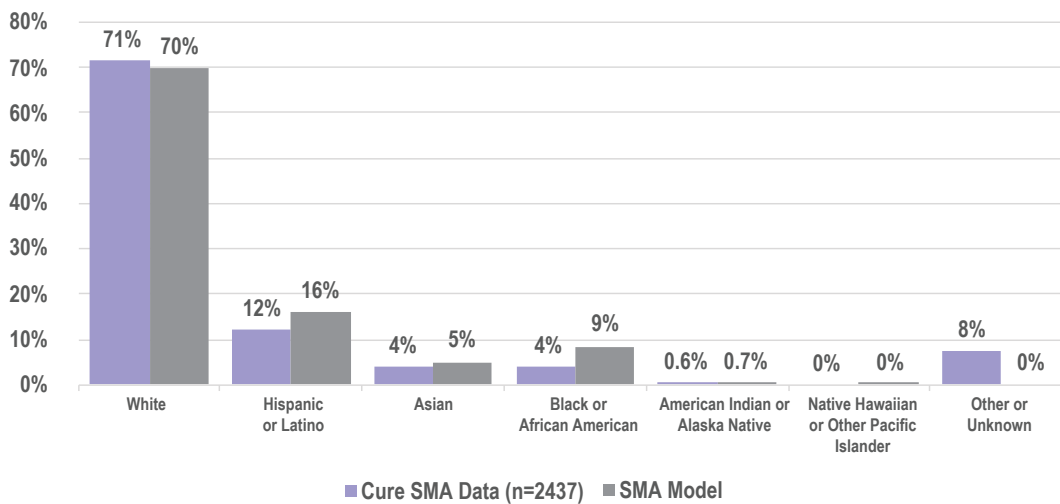
GENDER / GENDER IDENTITY

PATIENT/CAREGIVER REPORTED



RACE/ETHNICITY CATEGORIES

Combined Race/Ethnicity Categories in 2022²



Absolute Percent Change of Representativeness of the Cure SMA Databases from 2019 to 2022:

▼ -2.4% |
 ▲ +1.2% |
 ▲ +0.2% |
 ▲ +0.3% |
 ▲ +0.1% |
 = 0.0% |
 ▲ +0.6%

Cure SMA Data Sources: Membership data, CUS, CDR, and NBSR data combined. Individuals participating in multiple sources were de-duplicated.

Analysis Notes:

- All graphics include individuals that were alive for the full year being reported.
- 1 – administrative gender is collected in the CDR
- 2 – if gender or race/ethnicity was provided for the same individual in multiple databases, the self-reported data was prioritized

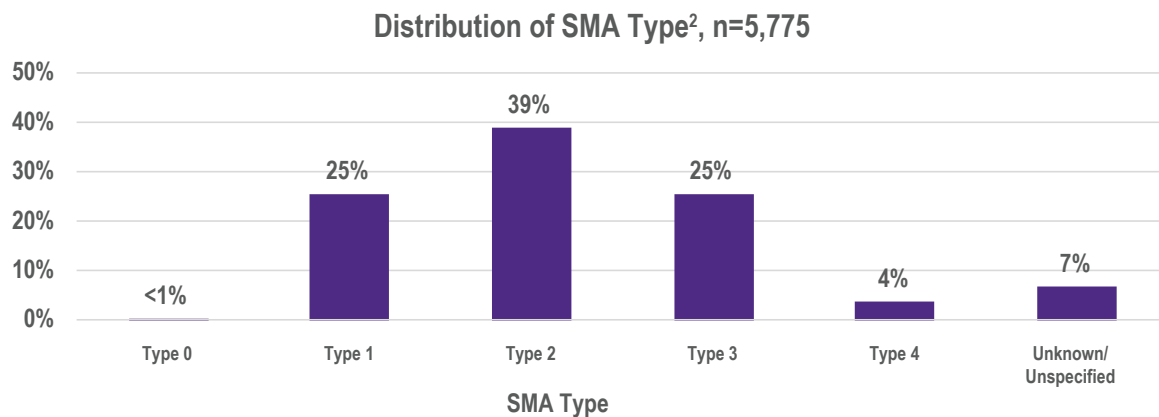
PREVALENCE OF SMA

The number of people currently living with SMA in the U.S.

Cure SMA is updating the SMA Model, which estimated the number of individuals currently living in the U.S. with SMA was 9,000, but we anticipate that number is increasing based on trends in our data¹

SMA TYPE:

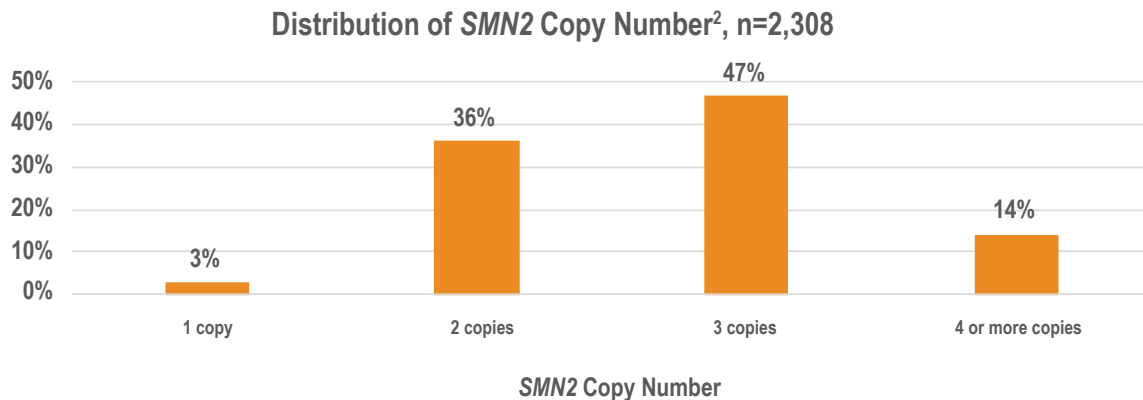
Historically, SMA was characterized by a classification system for describing age of symptom onset and maximum motor function achieved. This classification divides SMA into five types: Types 0, 1, 2, 3, and 4.



The majority of individuals in Cure SMA data sources have Type 2 SMA.

SMN2 COPY NUMBER:

SMN2 is an inefficient variant of the SMN1 gene. This means that SMN2 cannot fully make up for the mutated SMN1 gene. The number of SMN2 genes can vary from person to person, and individuals with more SMN2 copies usually have a less severe form of SMA than those with fewer copies. However, there are exceptions.



The majority of individuals in Cure SMA data sources have 3 copies of SMN2.

Cure SMA Data Sources: Membership data, CUS, CDR, and NBSR data combined. Individuals participating in multiple sources were de-duplicated.

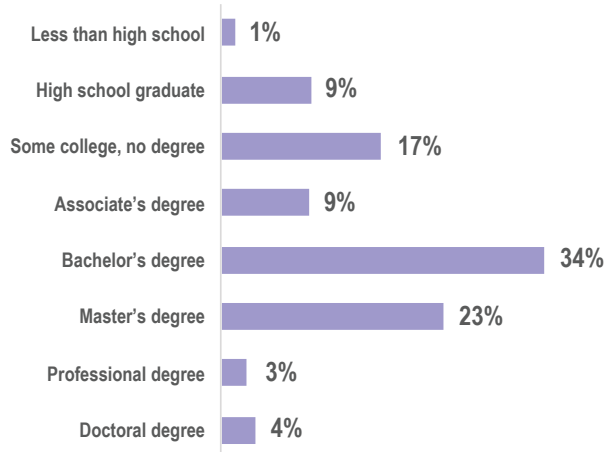
Analysis Notes:

- 1 - Based on the Cure SMA "SMA Model"
- 2 - If SMA type or SMN2 copy number were reported in multiple data sources, the clinician-reported data was prioritized

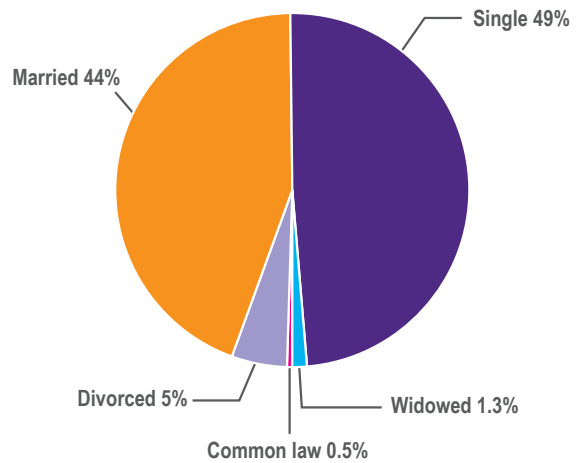
SOCIOECONOMIC CHARACTERISTICS: ADULTS WITH SMA¹

PATIENT/CAREGIVER REPORTED

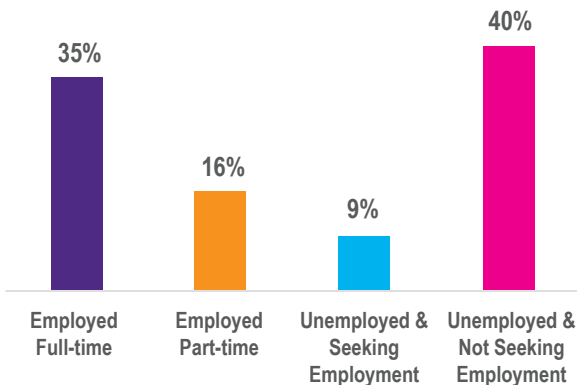
Highest Level of Education Obtained, n=577



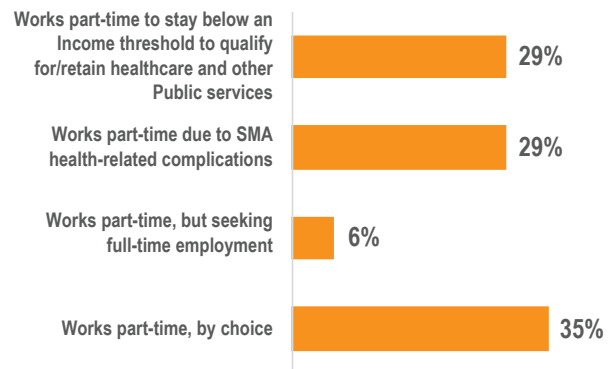
Marital Status, n=829



Employment (18 Years and Older), n=175²



Reasons for Working Part-Time, n=34²



Household Income, n=522



Cure SMA Data Sources: Membership data and CUS

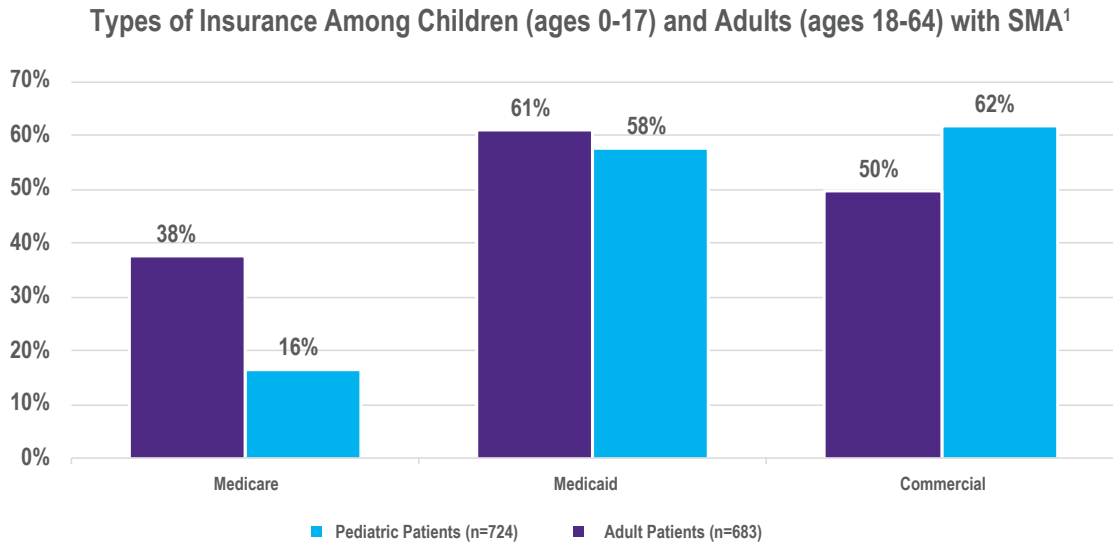
Analysis Notes:

- All graphics include individuals that were alive for the full year being reported.
- 1 – adults ages 18 and older
- 2 – Data from 2022 CUS

INSURANCE

PATIENT/CAREGIVER REPORTED

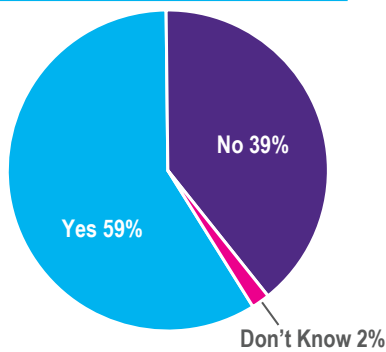
SMA care is expensive and includes many out-of-pocket costs for outpatient medical care, hospitalizations, and medications. Most children with SMA are enrolled in government-funded insurance programs.



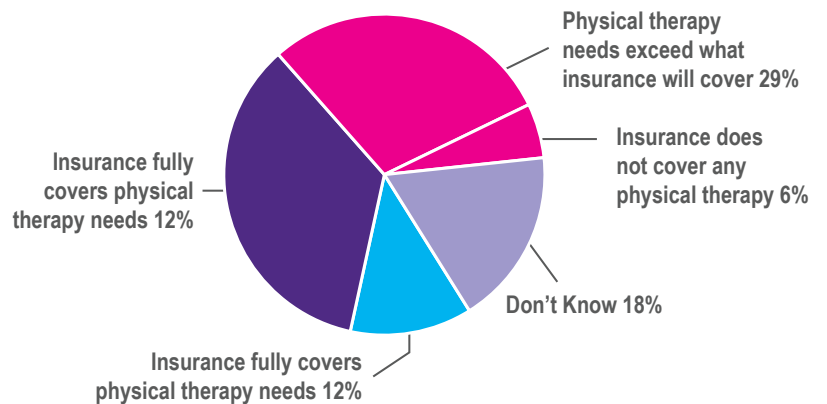
INSURANCE COVERAGE

Barriers to access insurance coverage for specialized care and treatments exist for some individuals with SMA.

59% of individuals treated with an SMA therapy have received an insurance denial related to SMA treatment coverage, n=327



35% of individuals have physical therapy needs that exceed their health insurance coverage, n=382



Cure SMA Data Sources: Membership and CUS data

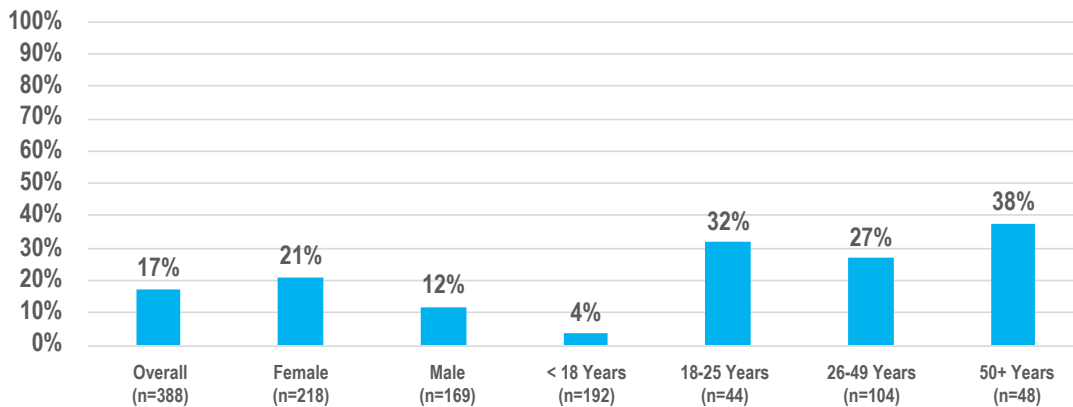
Analysis Notes:

- All graphics include individuals that were alive for the full year being reported.
- 1 – Insurance categories are not mutually exclusive

PATIENT/CAREGIVER REPORTED

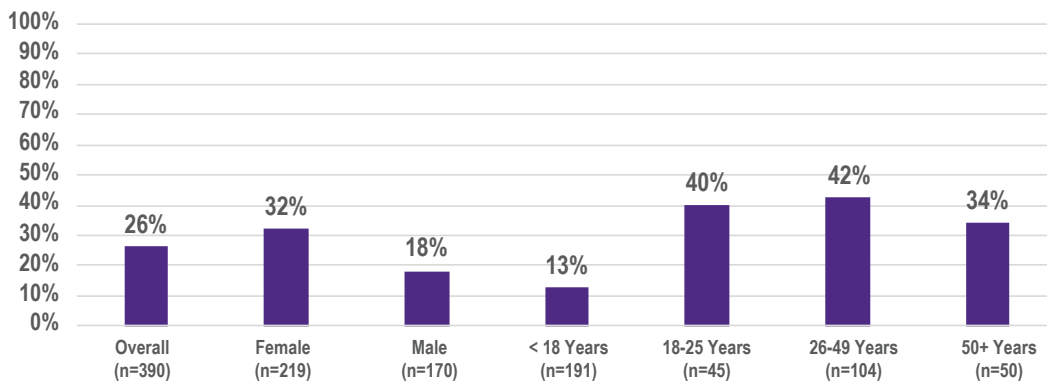
A qualitative study by Cure SMA found that individuals with SMA reported their mental health, including anxiety and depression, to be severely impacted by SMA¹

Depression Diagnoses Among Individuals with SMA, by Gender and Age Categories



Among those individuals diagnosed with depression, 58% were treated for depression in the last year.

Anxiety Diagnoses Among Individuals with SMA, by Gender and Age Categories



Among those individuals diagnosed with anxiety, 57% were treated for anxiety in the last year.

If you are experiencing anxiety or depression, please contact your healthcare provider. You are not alone.

Cure SMA Data Sources: CUS data

Analysis Notes:

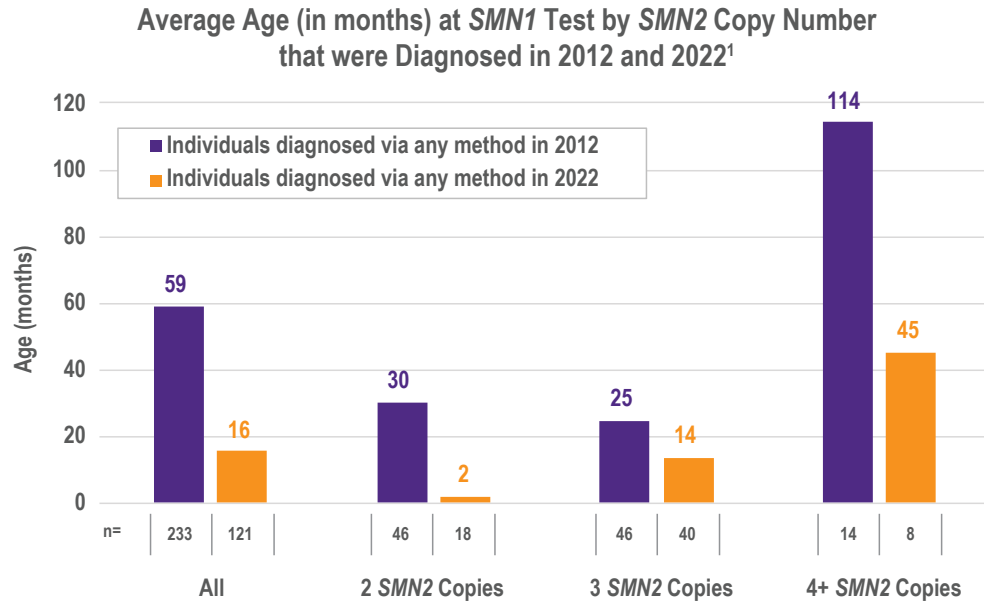
1 - Mazzella A, Curry M, Belter L, Cruz R, Jarecki J. "I have SMA, SMA doesn't have me": a qualitative snapshot into the challenges, successes, and quality of life of adolescents and young adults with SMA. *Orphanet J Rare Dis.* 2021;16(1):96.

PATIENT JOURNEY

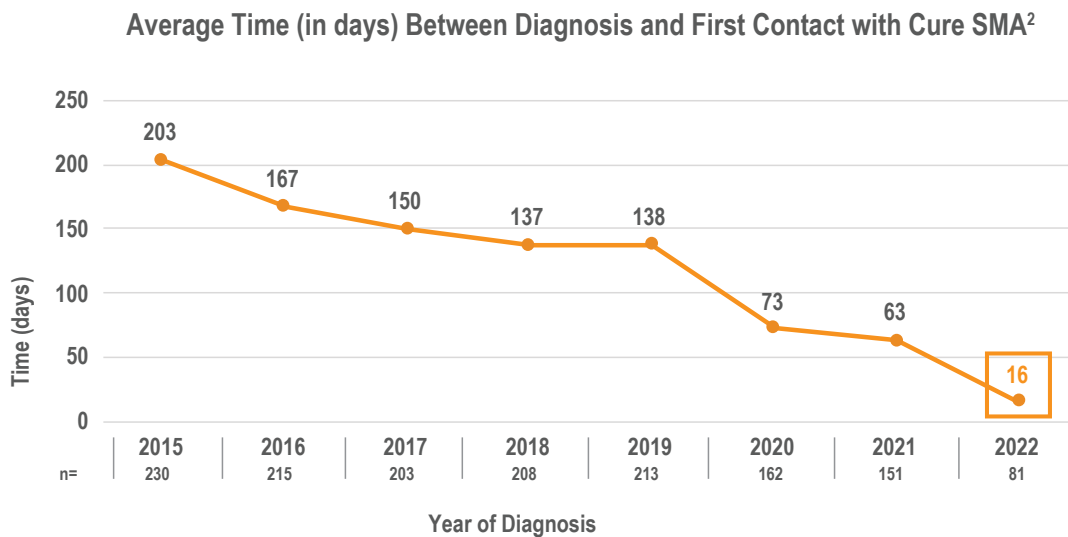


The patient journey encompasses experiences from diagnosis to treatment and ongoing management

The average age at diagnosis of SMA has decreased in the past 10 years



In addition, the time between diagnosis and first contact with Cure SMA has decreased from over six months to approximately two weeks



Cure SMA Data Sources: Membership data, CUS, CDR, and NBSR data combined. Individuals participating in multiple sources were de-duplicated.

Analysis Notes:

- 1 - The minimum and maximum values were removed from each group
- 2 - The minimum and maximum values were removed for each year

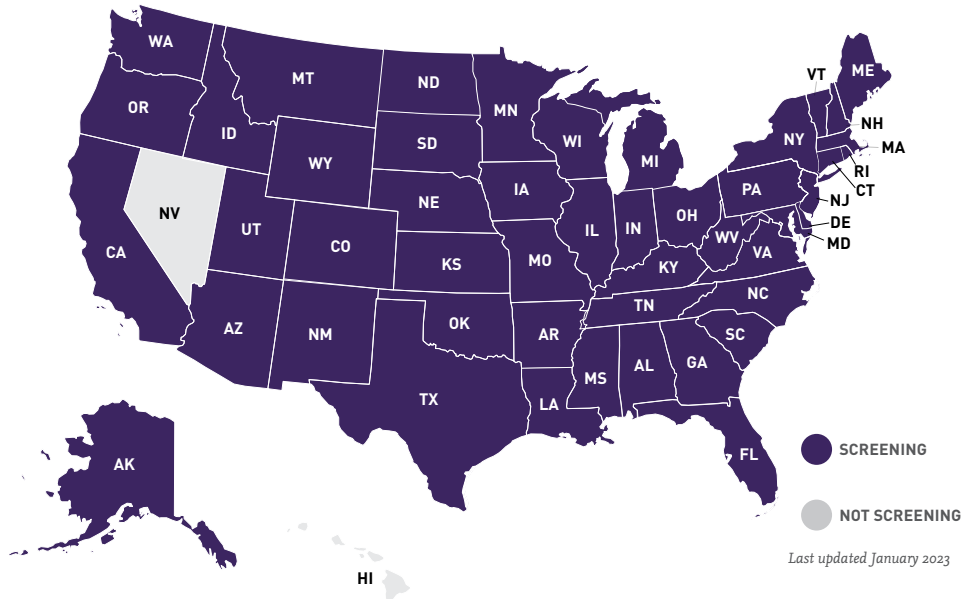
NEWBORN SCREENING



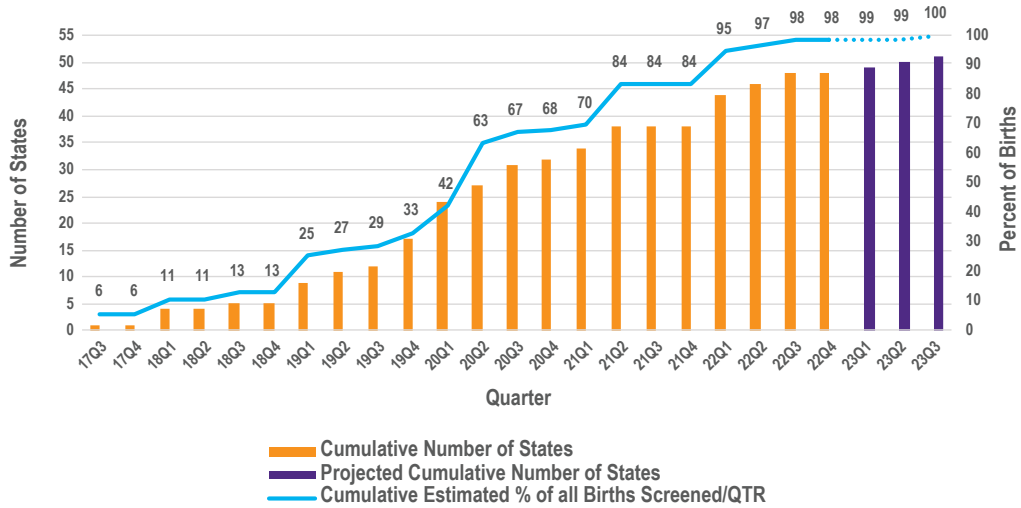
The follow pages focus on characteristics and outcomes of individuals with SMA identified by newborn screening in the U.S.

NEWBORN SCREENING: STATUS AT THE END OF 2022

48 states were screening for SMA, which covered approximately 98% of newborns in the U.S.



Quarterly Growth: Number of States and Washington, D.C. Screening for SMA and Percent of Infant Births Screened in the U.S.^{1,2}



- 1 – SMA information per Cure SMA State NBS implementation tracking
- 2 – 2020 CDC birth rate

NEWBORN SCREENING: INCIDENCE OF SMA

Incidence: The number of people that were diagnosed with SMA per year in the U.S.

DATA FROM U.S. PUBLIC HEALTH STATE LABS

Cure SMA has asked each state that has implemented SMA newborn screening for data on the number of individuals screened and the number of individuals that screened positive for SMA. This data will provide a better understanding of the number of individuals diagnosed with SMA in the U.S. each year (incidence rate).

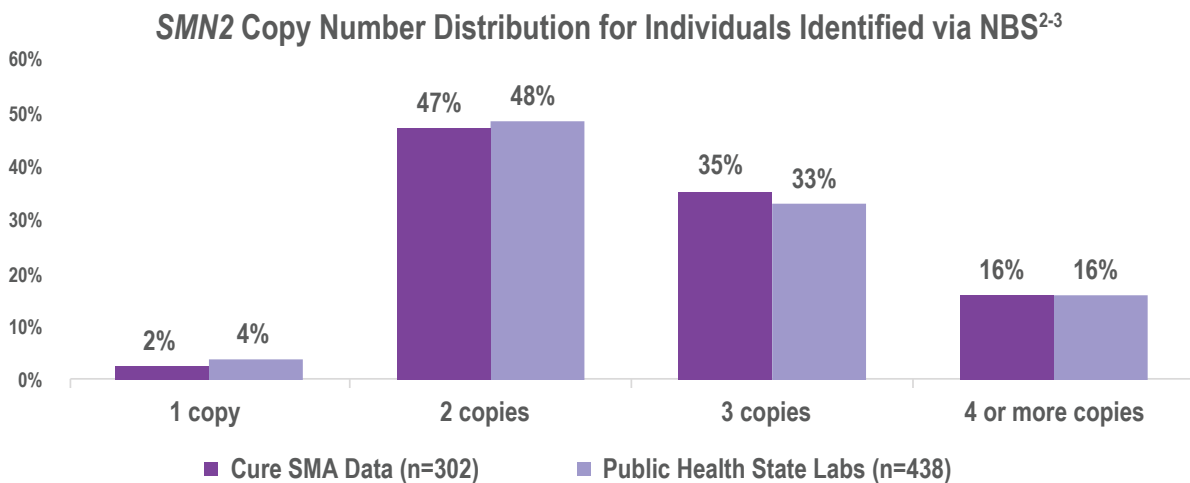
As of December 2022, data from 42 states showed:

- More than 8 million infants have been screened for SMA to date
- An estimated 513 infants screened positive and SMA diagnosis confirmed
- The preliminary estimated incidence of SMA is approximately 1 in 15,000 births¹

Previous estimates put the incidence of SMA at 1 in 11,000 births; However, based on additional data gathered to date, we estimate that the incidence is now closer to 1 in 15,000¹ births and may continue to evolve over time.

DISTRIBUTION OF SMN2 COPY NUMBER

Cure SMA data are consistent with what the public health state labs are reporting.



The data suggests that nearly half of individuals that are born with SMA have 2 copies of SMN2.

Cure SMA Data Sources: Membership data, CUS, CDR, and NBSR data combined. Individuals participating in multiple sources were de-duplicated.

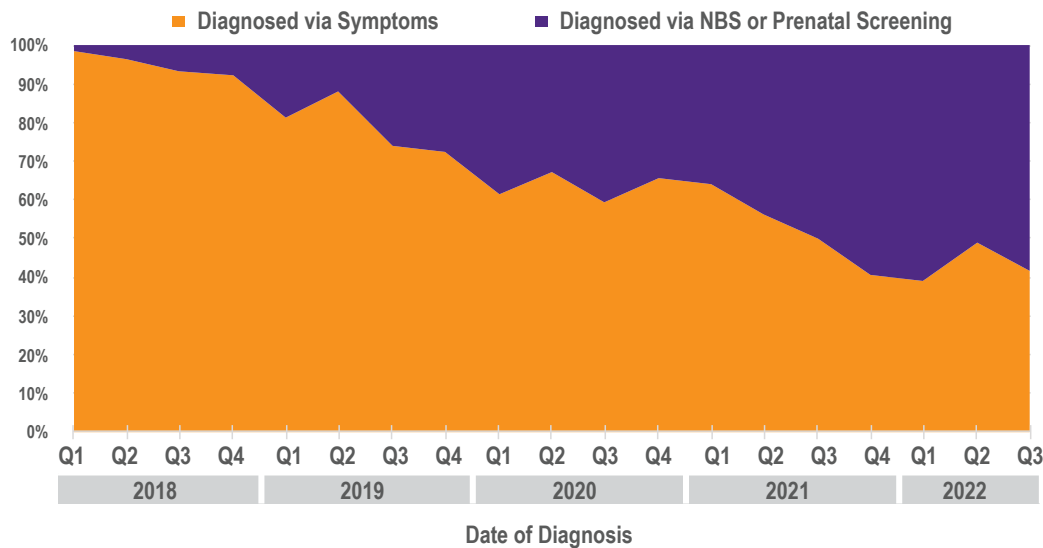
Analysis Notes:

- 1 - Data based on state lab screening rates as of December 31, 2022. These numbers are estimates.
- 2 - If SMN2 copy number were reported in multiple data source, the clinician-reported data was prioritized
- 3 - Data includes all individuals identified via newborn screening in 2022 or earlier.

NEWBORN SCREENING: DIAGNOSIS

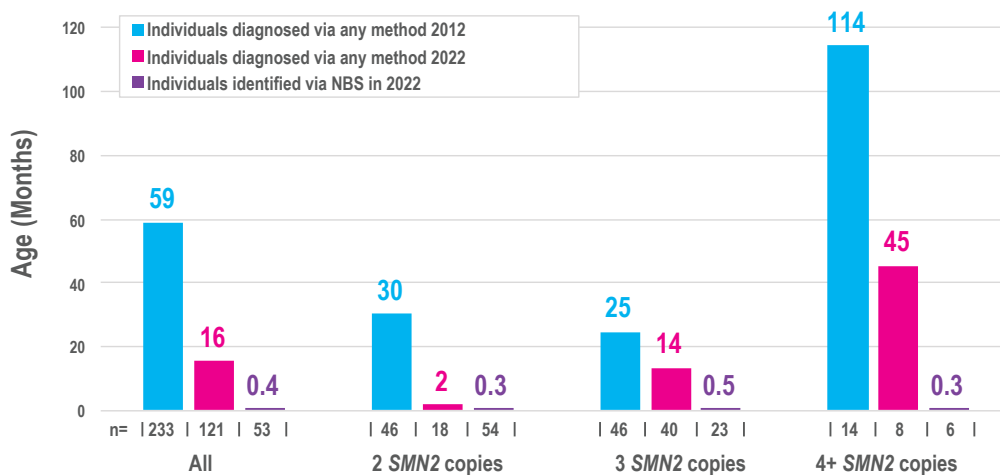
Increased newborn screening has been accompanied by a decreasing frequency of symptomatic diagnoses, but there is still a high number of symptomatic diagnoses due to birth prior to their state's implementation of a newborn screening program or cases being reported as false negatives.

Diagnosis Method, by Date of Diagnosis^{1,2}



Newborn screening has allowed for earlier diagnosis, regardless of *SMN2* copy number.

Average Age (Months) at *SMN1* Test by *SMN2* Copy Number that were Diagnosed in 2012 and 2022^{1,3}



Cure SMA Data Sources: Membership data, CUS, CDR, and NBSR data combined. Individuals participating in multiple sources were de-duplicated.

Analysis Notes:

- 1 - If diagnosis date was reported in multiple data source, the clinician-reported data was prioritized
- 2 - Samples ranged from n=24 to n=73; Q4 of 2022 was not reported due to low sample size
- 3 - The minimum and maximum values were removed from each group

NEWBORN SCREENING: CARE

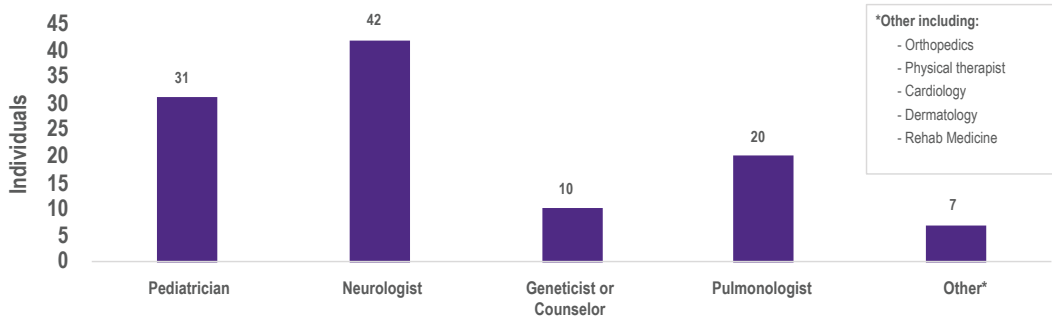
INDIVIDUALS IDENTIFIED BY NBS ONLY

Age at NBS Survey:
 Mean: 7.5 months
 Median: 4.8 months
 Range: 3 days – 6 years

The following analyses are all parent/caregiver reported and are restricted to individuals over three months old at the time of survey.

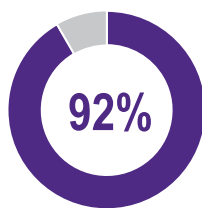
Most parents and caregivers reported that the care team consisted of a neurologist and/or a pediatrician. Physical therapy, occupational therapy, and feeding therapy are more frequently used by individuals with one or two copies of *SMN2*.

PARENT/CAREGIVER REPORTED

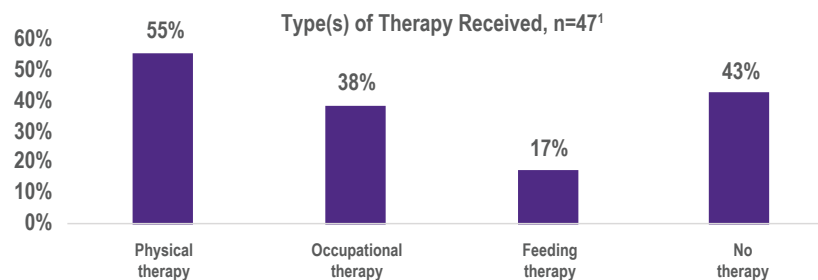
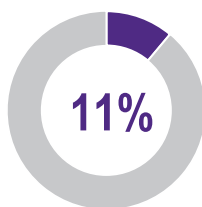


USE OF PHYSICAL, OCCUPATIONAL, AND/OR FEEDING THERAPY

Individuals with 1-2 Copies of *SMN2*, n=24



Individuals with 3+ Copies of *SMN2*, n=18



Cure SMA Data Sources: NBSR only - Data includes all individuals identified via newborn screening in 2022 or earlier.

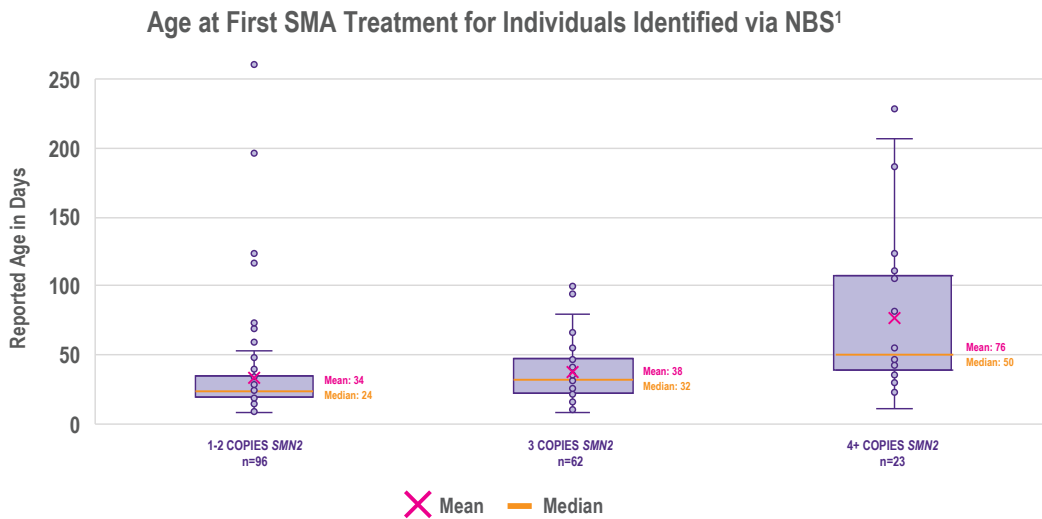
Analysis Notes:

- Data includes all individuals identified via newborn screening in 2022 or earlier
- 1 – Parent/caregiver can select multiple therapy options. Note 1 survey that was missing a response was excluded.

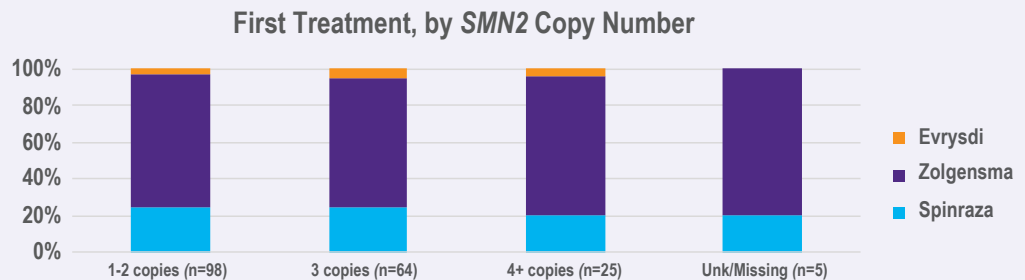
INDIVIDUALS IDENTIFIED BY NBS ONLY

AGE AT FIRST UTILIZATION OF FDA APPROVED SMA TREATMENT

Newborn screening allows for earlier diagnosis, which impacts the timing of intervention. In general, individuals identified by newborn screening had a shorter time to first treatment, especially for infants with lower number of SMN2 copies. At least 50% of the individuals with one to two copies of SMN2 in the NBS registry reported receiving treatment within 24 days after birth (median).



98% of newborn screened individuals had received treatment as of 12/31/2022. Zolgensma® was commonly seen as the first SMA treatment across SMN2 copy categories.



The median age at first treatment ranged from 16 days (Evrysdi®) to 29 days (Zolgensma®); however, there was variability across treatments.

Age at First FDA Approved Treatment, by Treatment Name

TREATMENT	N	MEAN AGE	MEDIAN AGE
Evrysdi	7	21 days	16 days
Spinraza	46	35 days	23 days
Zolgensma	139	48 days	29 days

Cure SMA Data Sources: Membership data, CUS, CDR, and NBSR data combined. Individuals participating in multiple sources were de-duplicated.

- If conflicting treatment start dates were reported in multiple data source, the clinician-reported data was prioritized. Individuals were removed if their treatment start date was prior to their birth date or if any treatment start dates were unknown.
- 1 - The minimum and maximum values were removed from each group.

NEWBORN SCREENING: IMPACT

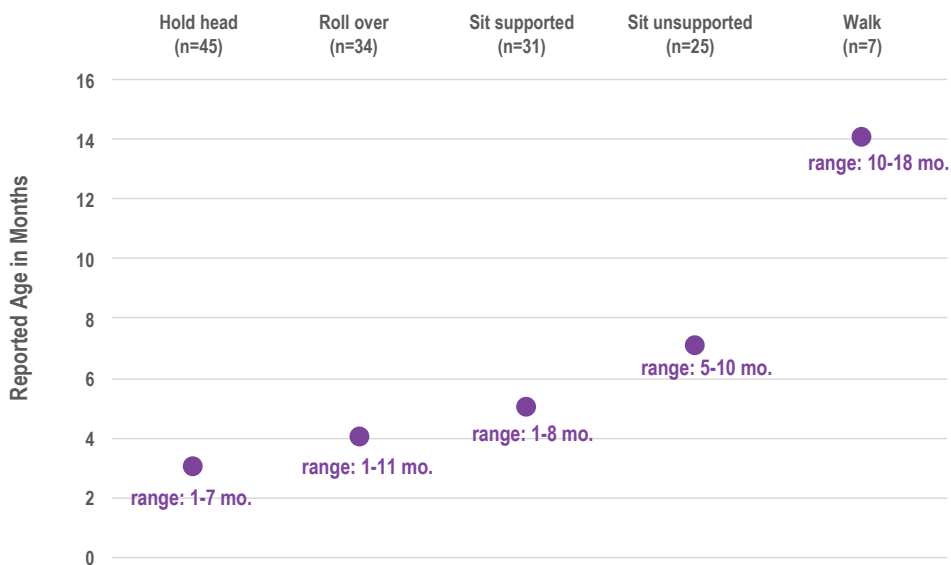
INDIVIDUALS IDENTIFIED BY NBS ONLY

DEVELOPMENTAL MILESTONE ACHIEVEMENTS

Parents and caregivers of children with SMA have reported that their child had achieved motor milestones atypical for their *SMN2* copy number based on previous natural history studies¹.

PARENT/CAREGIVER REPORTED

Reported Median Age at Milestone Achievement:



Distribution of *SMN2* Copy Number by Milestone Achievement

Legend:

- 1-2 copies *SMN2*
- 3+ copies *SMN2*
- Unknown



Cure SMA Data Sources: NBSR only - Data includes all individuals identified via newborn screening in 2022 or earlier

- This analysis is treatment agnostic
- 1 - Kolb SJ, Kissel JT. Spinal muscular atrophy. *Neurol Clin.* 2015; 33(4): 831-846.

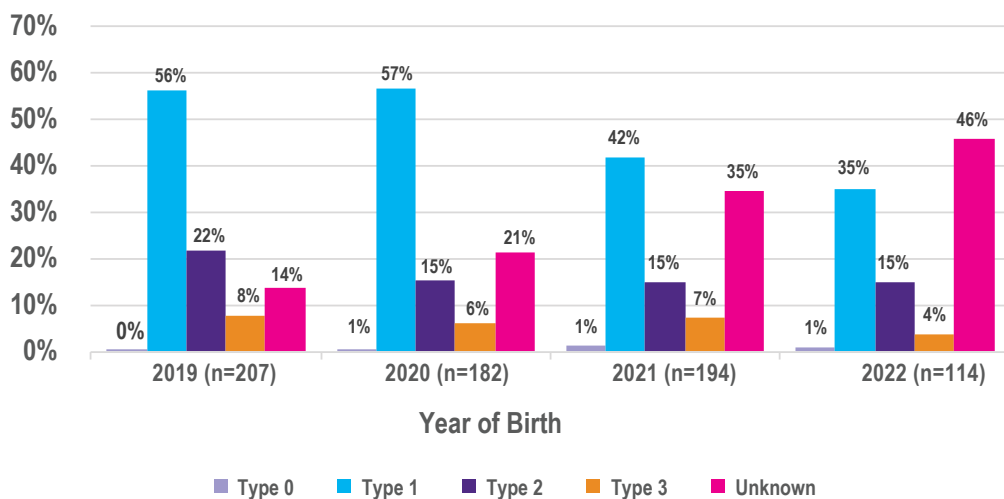
NEWBORN SCREENING: IMPACT

Describing SMA: an evolution

Due to newborn screening and availability of SMA disease modifying treatments, characterizing SMA is changing. The classification using SMA type is based on age symptoms started and highest level of motor function development achieved. Due to early treatment, symptom onset may be delayed and symptoms may be milder.

The percent of individuals born each year with an unknown SMA Type has increased in our data from 14% in 2019 to 46% in 2022.

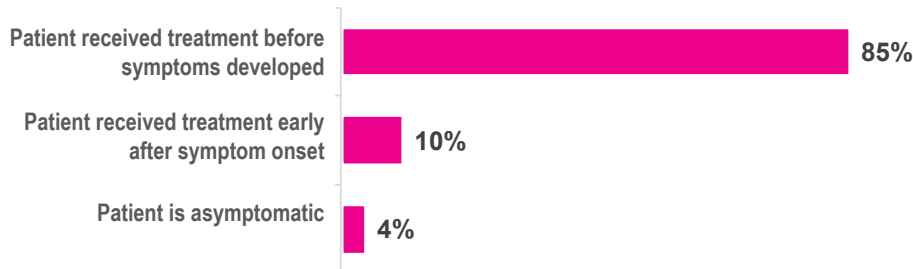
Trends in SMA Type Distribution, by Year of Birth¹



Care Center Network clinicians reported that SMA Type was marked as “Unknown” due to **treatment being administered** prior to symptom development for most patients with an unknown SMA Type.

CLINICIAN-REPORTED

Reasons for An Unknown SMA Type, n=48²



Cure SMA Data Sources: Membership data, CUS, CDR, and NBSR data combined. Individuals participating in multiple sources were de-duplicated.

Analysis Notes:

- 1 – If SMA type was reported in multiple data source, the clinician-reported data was prioritized
- 2 – CDR data only

TREATMENT AND CARE

The SMA treatment pipeline continues to advance. Currently, there are three FDA approved treatments for SMA:

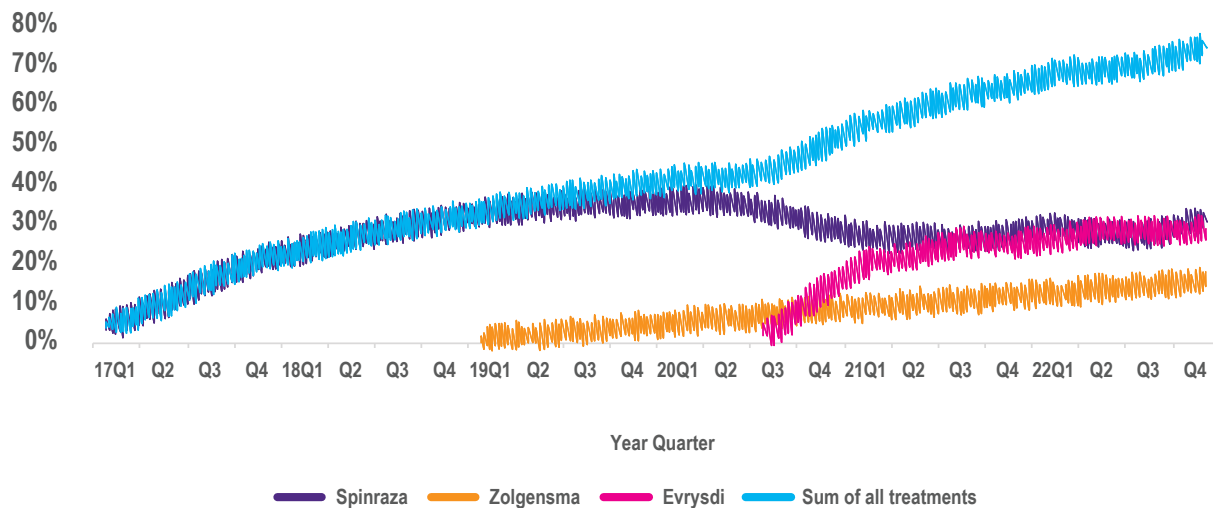
Treatment	Approval Date	Age Eligibility	SMA Type Eligibility
Spinraza® (nusinersen)	12/23/2016	All ages	All SMA types
Zolgensma® (onasemnogene abeparvovec-xioi)	5/24/2019	Individuals < two years old	All SMA types
Evrysdi® (risdiplam)	8/7/2020	All ages	All SMA types

There are multiple clinical trials that continue to evaluate new therapies. To learn more, please visit:

<https://www.curesma.org/cure-sma-clinical-trials/>

Approximately 65-75% of individuals with SMA in the U.S. had received an FDA approved treatment in Q4 2022¹⁻³

Percent of Patients Currently on SMA Treatment in the U.S.



Data Sources: Internal modeled estimates derived from quarterly earnings reports from Biogen, Roche, and Novartis.

- These are estimates and may over or under represent treatment utilization.
- 1 - This model does not account for concurrent treatment use
- 2 - Anyone treated with Zolgensma® was categorized as “currently on treatment” for all quarters following treatment
- 3 - Data here is presented by standard calendar quarters: January, February, and March (Q1) April, May, and June (Q2) July, August, and September (Q3) October, November, and December (Q4)

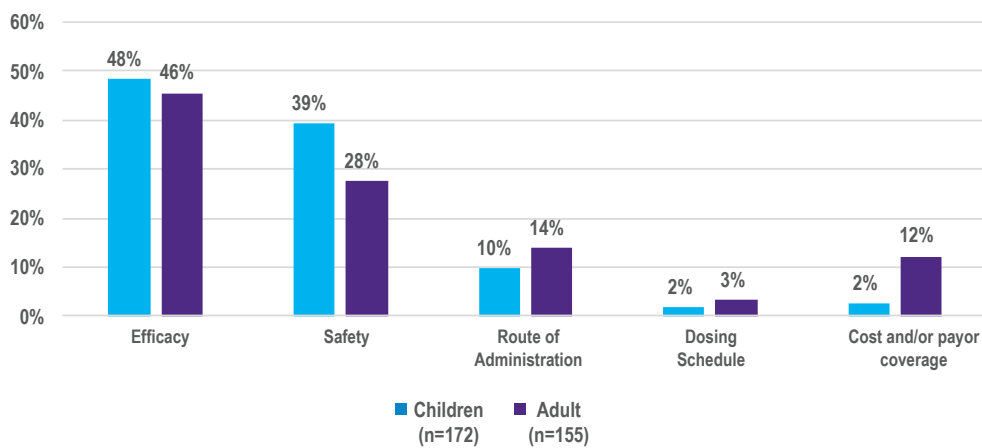
TREATMENT: OBSERVATIONS IN OUR DATA

90.6% of individuals in the Cure SMA databases have received at least one FDA approved treatment for SMA^{1,2}

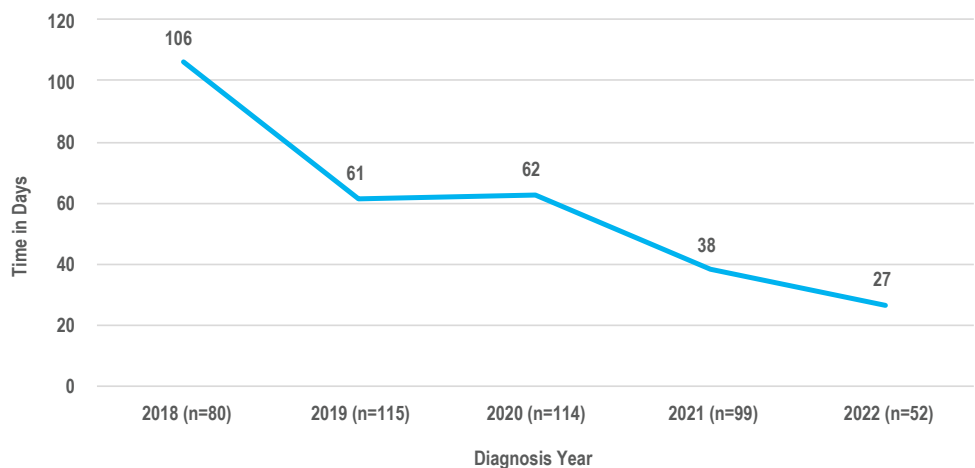
Efficacy and safety were reported as the most important factors when choosing an SMA treatment according to individuals and caregivers

PARENT/CAREGIVER REPORTED

Important Factors when Choosing an SMA Treatment



Average Time between Diagnosis and First FDA Approved Treatment, by Diagnosis Year¹



In general, the time it takes to receive a treatment after being diagnosed with SMA has decreased each year, and the average was less than 1 month for individuals diagnosed in 2022.

Cure SMA Data Sources: Membership data, CUS, CDR, and NBSR data combined. Individuals participating in multiple sources were de-duplicated.

Analysis Notes:

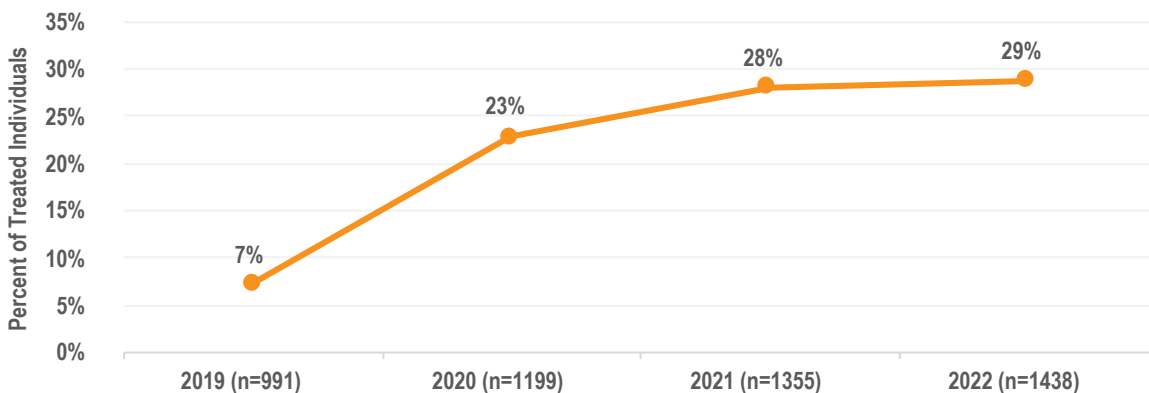
- 1 – Based on data from n=2,256 with treatment status information available and no evidence of investigational therapy use.
- 2 – Treatment was defined as any evidence of utilization of an FDA approved therapy at the time of analysis.
- 3 – Analysis included individuals where the date of diagnosis occurred on or before date of first treatment.

TREATMENT: _____

OBSERVATIONS IN OUR DATA

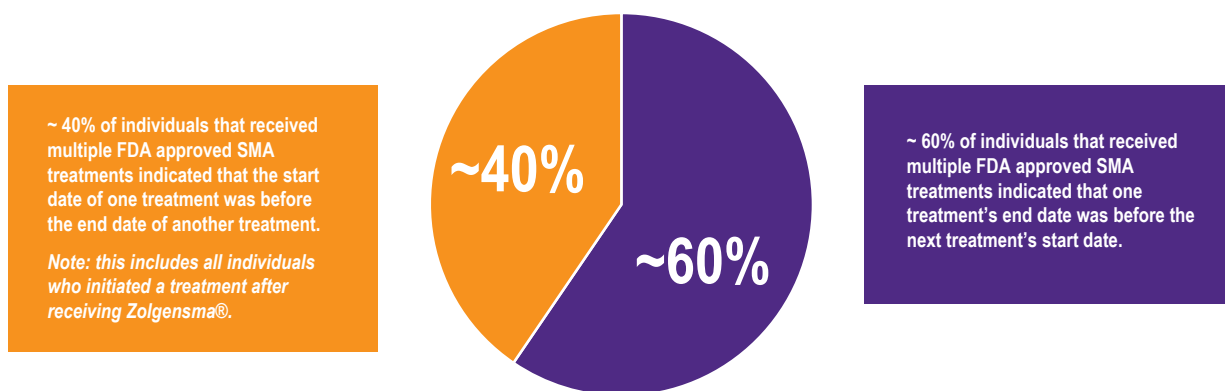
Approximately 30% of treated individuals have received two or more FDA approved SMA treatments and the use of multiple SMA treatments has risen since 2019.

Percent of Treated Individuals that Utilized Multiple Therapies – Trends¹



Approximately 40% of patients on multiple FDA approved treatments received overlapping treatments (>1 day) and 60% received treatments in a sequential manner.

Treatment Patterns for Patients who Received Multiple Treatments, n=378²



1. Cure SMA Data Sources: Membership data, CUS, CDR, and NBSR data combined. Individuals participating in multiple sources were de-duplicated.

- Based on data from individuals with treatment status information, a reported start date for each medication reported, and no evidence of a non-FDA approved therapy. Each year is cumulative.

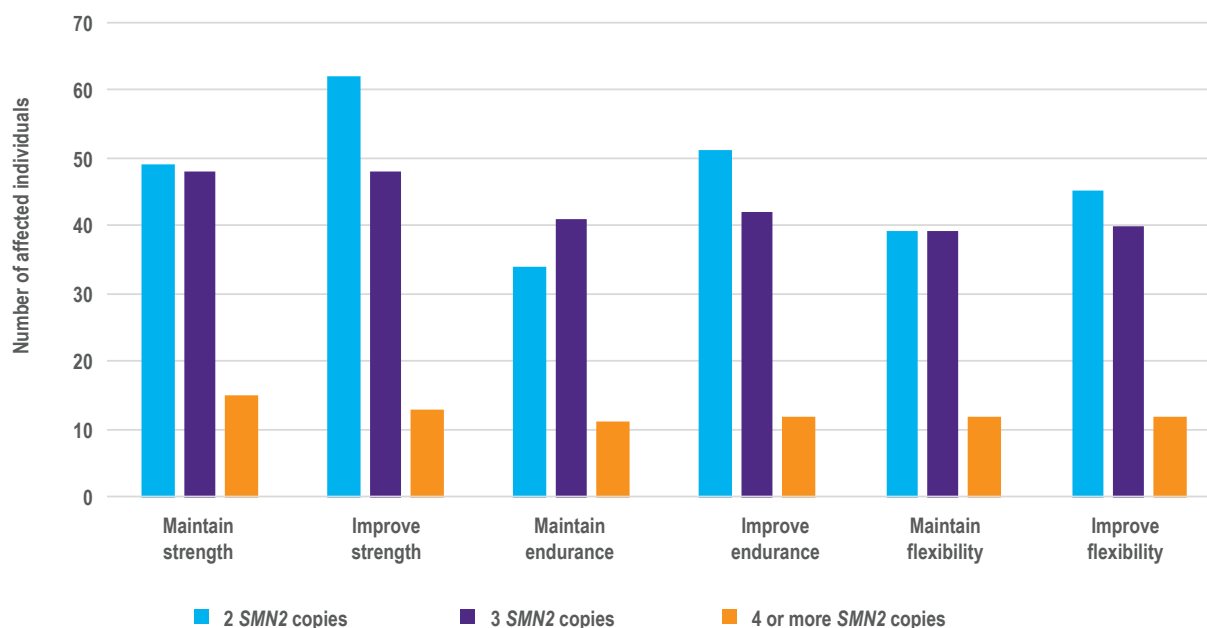
2. Cure SMA Data Sources: Membership data, CUS, and CDR data combined. Individuals within the NBSR only were not included as the NBSR does not collect treatment end dates. Individuals participating in multiple sources were de-duplicated.

- Based on data from n=378 individuals with treatment status information, a reported start, a reported end date (if status was noted as discontinued), and no evidence of a non-FDA approved therapy. Overlap was defined as greater than 1 day.
- Treatment end date is clinician or caregiver reported.

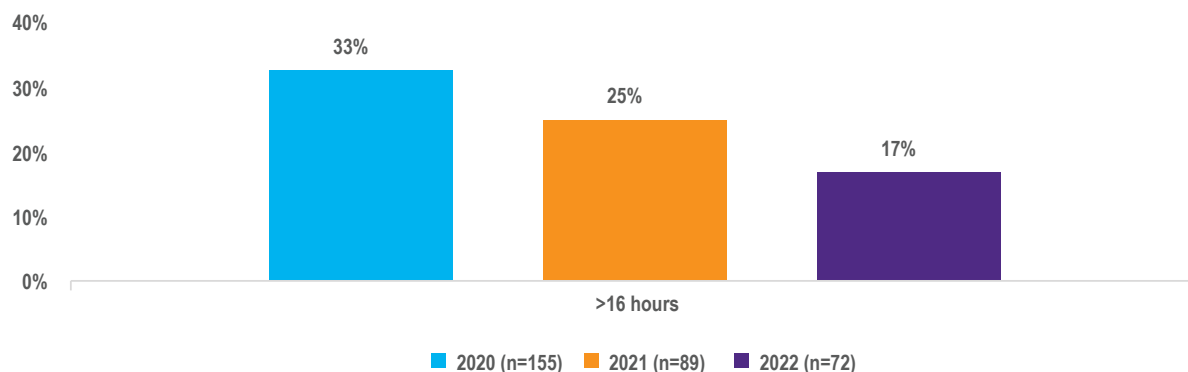
PATIENT/CAREGIVER REPORTED

On average, individuals affected with SMA have 1.9 hours of physical therapy a week.¹

Goals of Physical Therapy by SMN2 Copy Number



The proportion of individuals with 2 SMN2 copies requiring 16 hours or more of breathing support has **decreased** from 2020 to 2022.



Cure SMA Data Sources: CUS

Analysis Notes:

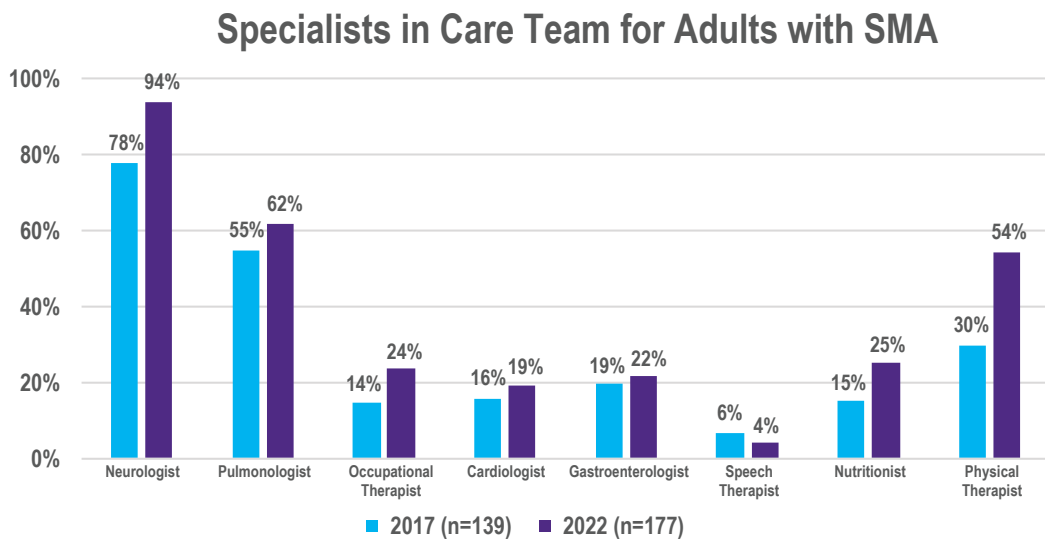
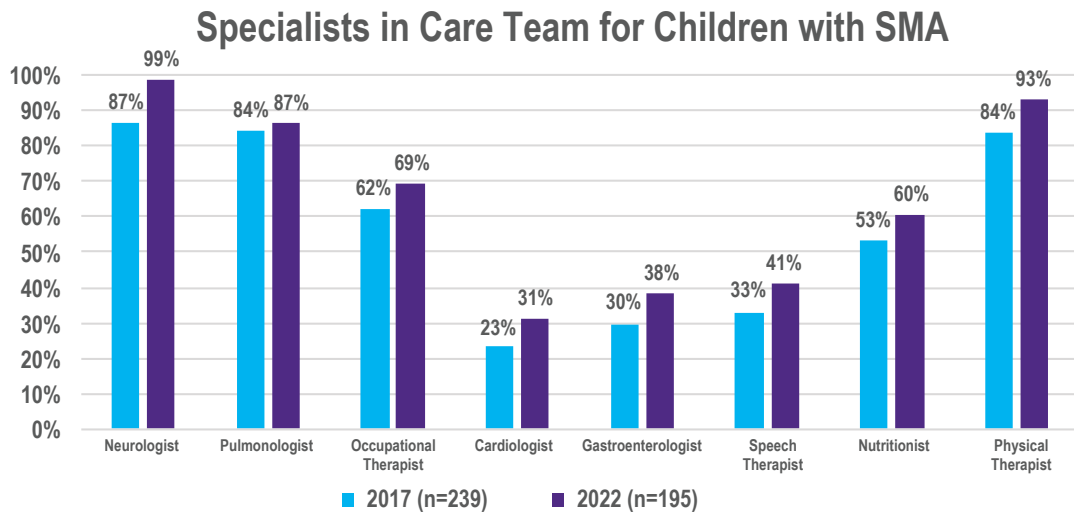
¹ n=238, respondents could choose more than one goal for physical therapy

PATIENT CARE

PATIENT/CAREGIVER REPORTED

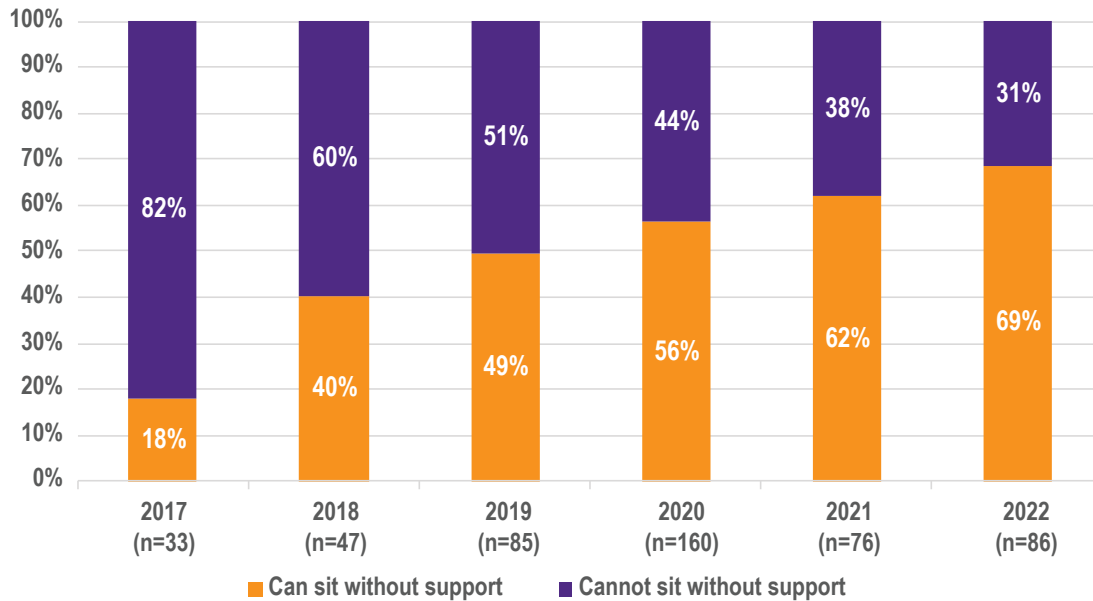
In 2022, 97% of children with SMA and 80% of adults with SMA reported having an in-person appointment with a physician or specialist for SMA related care.

There has been an increase in multidisciplinary care in children and adults with SMA when comparing specialists in a care team between 2017 & 2012.

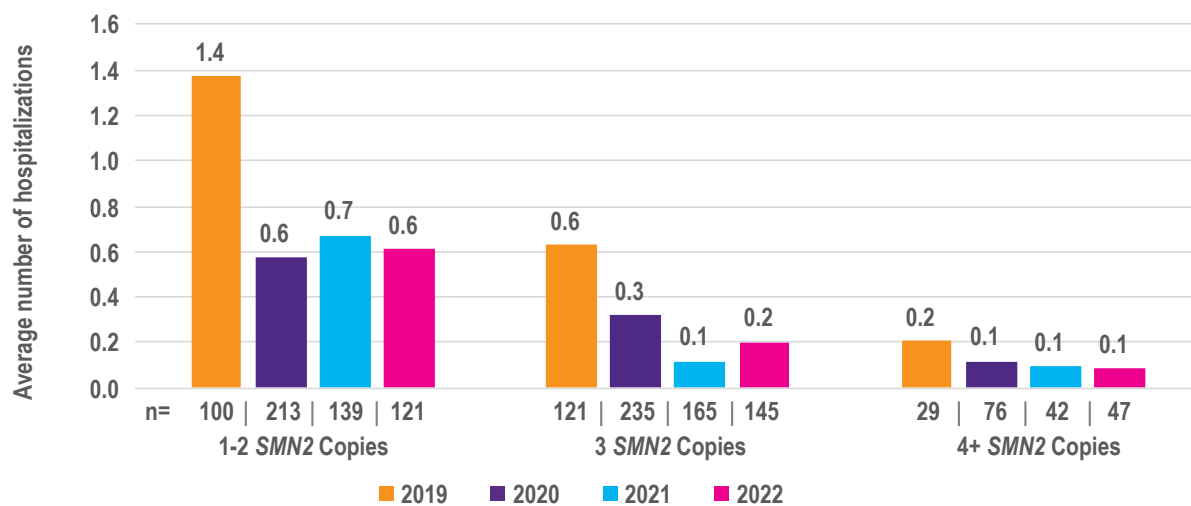


PATIENT/CAREGIVER REPORTED

The proportion of individuals with 2 *SMN2* copies who report sitting without support has **increased** since 2017¹



Annual hospitalizations by *SMN2* copy number has **decreased** since 2019¹



Cure SMA Data Sources: CUS

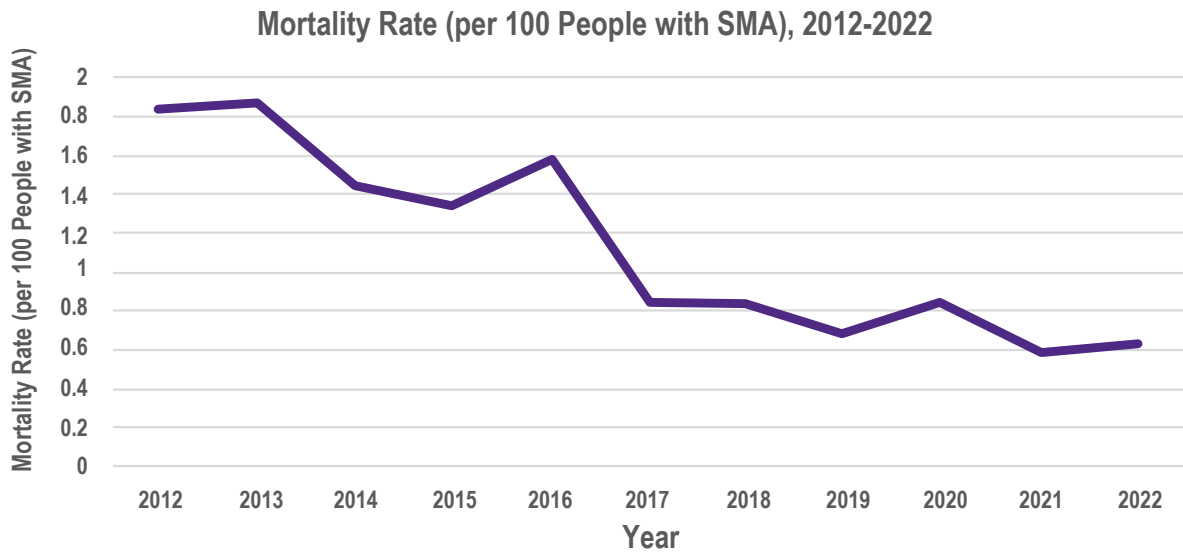
Analysis Notes:

- 1 – Based on year of CUS. Individuals included in analysis were > 9 months of age at time of survey.

TREATMENT IMPACT: MORTALITY

PATIENT/CAREGIVER REPORTED

The mortality rate of SMA in 2022 was approximately one-third of what it was in 2012, having decreased from **1.84 per 100** individuals to **0.63 per 100** individuals with SMA.



Cure SMA Data Sources: Membership Data

There has been significant progress made in the SMA community but **we will not stop until we have a cure.**

For more information, visit www.curesma.org.