

2023

International Patient Advocacy Group Meeting



CARE AND COMBINATION THERAPIES

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SMA Standard of Care Guidelines: revised 2018

**Diagnosis and management of spinal muscular atrophy; Part 1:
Recommendations for diagnosis, rehabilitation, orthopedic and
nutritional care**

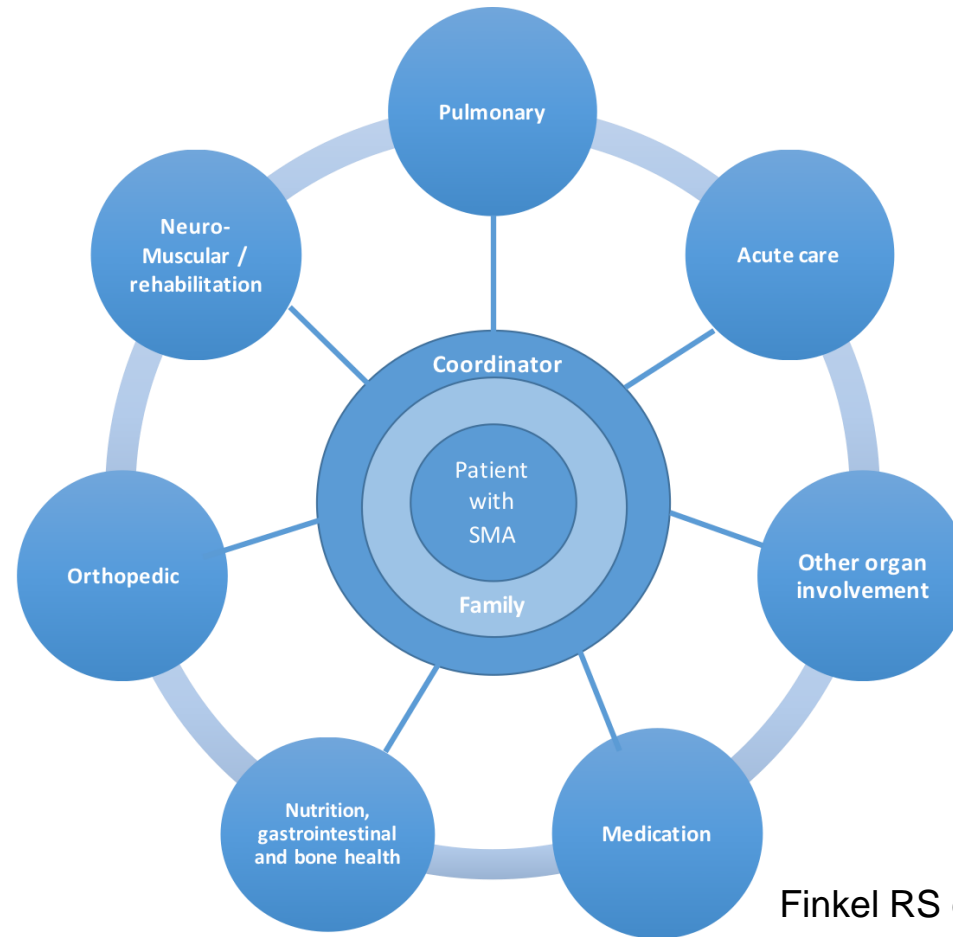
Neuromuscular Disorders 28: 103-115, 2018

**Diagnosis and management of spinal muscular atrophy; Part 2:
Pulmonary care and acute care; medications, supplements and
immunizations; other organ systems; and ethics**

Neuromuscular Disorders 28:197-207, 2018

**Updated SMA Diagnosis and SMA Treatment considerations are
in final preparations for publication.**

Multidisciplinary Coordinated Care



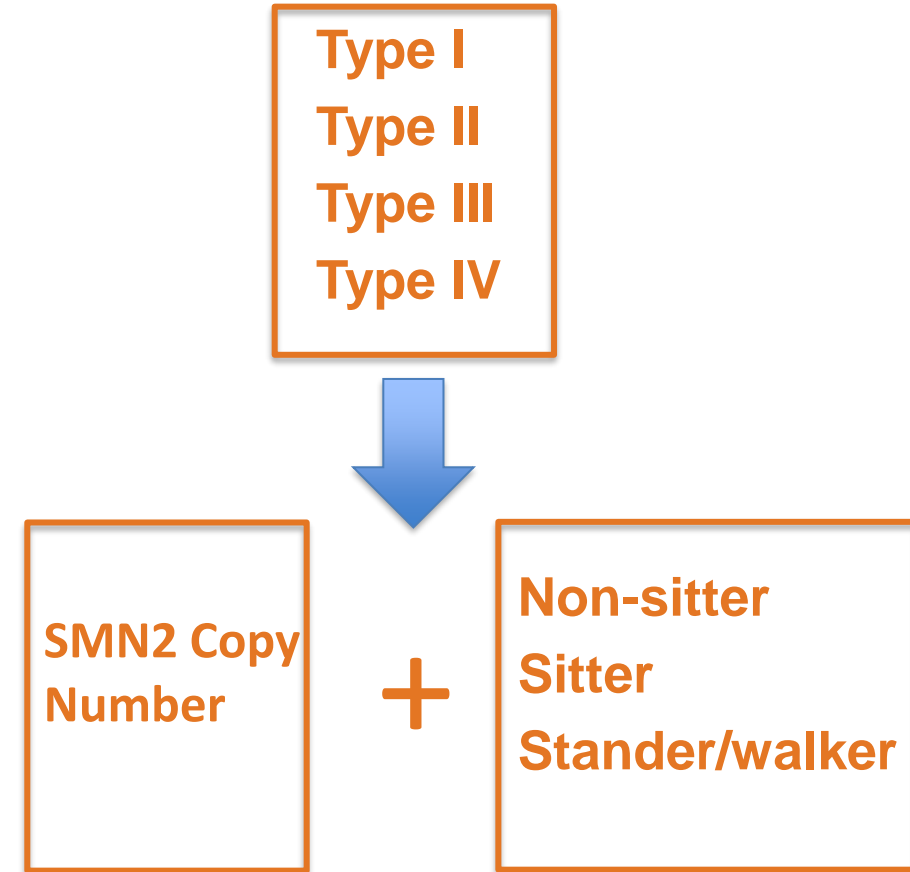
Finkel RS et al, NMD 28:197-207, 2018

New Treatments and Care

- **Standard of Care - critically important to optimize function**
 - Breathing
 - Close monitoring
 - Coughing support and clearing secretions
 - Breathing support during sleep as needed
 - Nutrition
 - Growing and gaining weight is key to optimizing motor function and strength
 - Monitoring swallow
 - Physical and Occupational Therapy
 - Optimize function and impact of new treatments

Impact of SMA Treatments

- **Changing outcomes**
- **Changing SMA classification - Type**
 - Used to describe severity and predict outcome
 - Determined by age of symptom onset and maximum motor function achieved
- **Current important descriptions**
 - SMN2 copy number
 - Age of SMA symptom onset
 - Age at first treatment
 - Symptoms if present, at time of first treatment
 - Maximum motor function achieved



SMA Disease Modifying Treatments

	Nusinersen (Spinraza®)	Onasemnogene abeparvovec-xiox (Zolgensma®)	Risdiplam (Evrysdi®)
US Approval Date	December 23, 2016	May 24, 2019	August 7, 2020, Updated May 30, 2022
Approved age	All	Less than 2 years old	All
Description	Antisense oligonucleotide	Single stranded <i>SMN1</i> DNA via adeno-associated virus (AAV9) vector	Small molecule
Mechanism	<i>SMN2</i> mRNA splicing modifier	Functional replacement with <i>SMN1</i> DNA episome	<i>SMN2</i> mRNA splicing modifier
How given	Intrathecal bolus	Intravenous over 60 minutes	Enteral liquid (oral or feeding tube)
How often	4 loading doses over 2 months, then every 4 months	One time only	Daily
Body distribution	Cerebral Spinal Fluid	Blood stream – systemic	Enteral - systemic

State of SMA: 2022 Report



Content Highlights:

Demographic and Clinical Characteristics
Patient Journey – Diagnosis
Newborn Screening
Treatments and Care

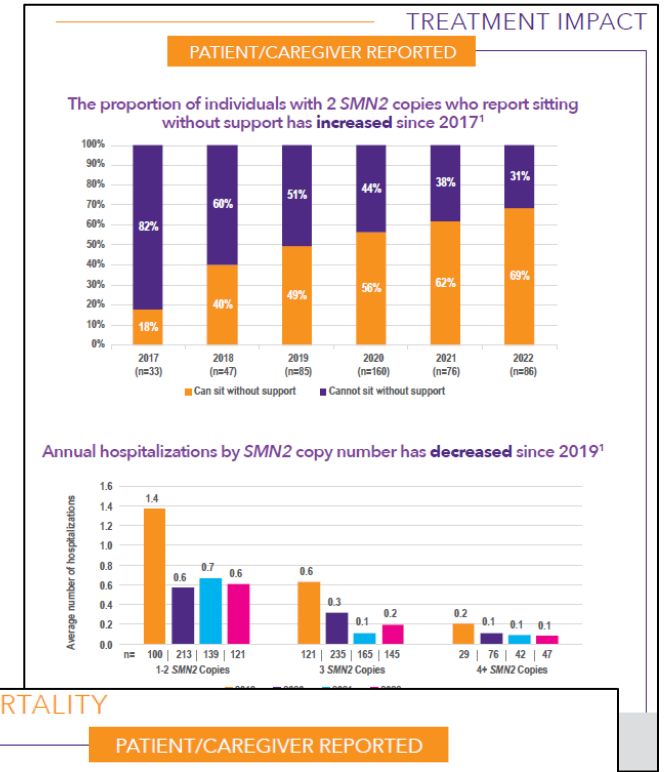
Data Sources:

Membership Database
 patient/caregiver reported data

Community Update Survey
 patient/caregiver survey

Clinical Data Registry
 data from electronic medical records
 and linked case report forms

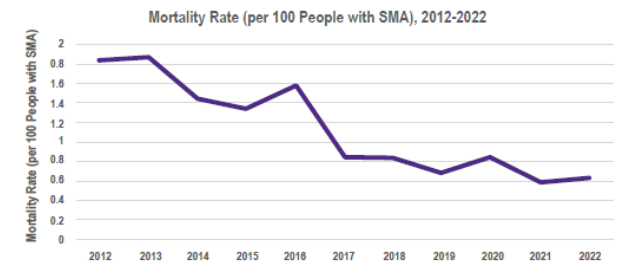
Newborn Screening Registry
 parent/caregiver survey



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 with SMA to **0.63 per 100** individuals with SMA.



Treatment Utilization: Pediatric Compared to Adult

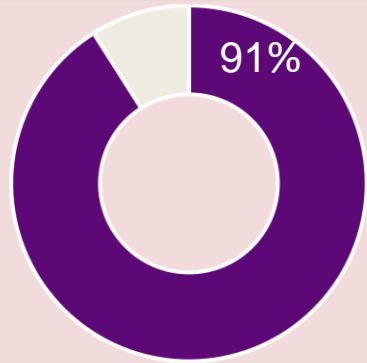
Community Reported Treatment by Age – 2022 Survey

80.7%

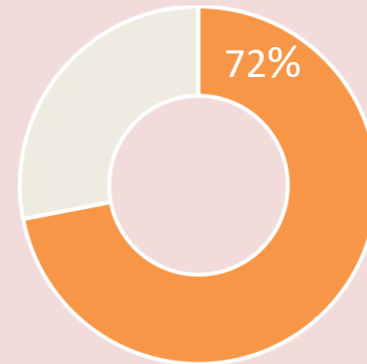
of individuals in the Community Update Survey have a reported SMA treatment (current or historical)

n=483

PEDIATRICS
Under 18 years



ADULTS
18 years or older



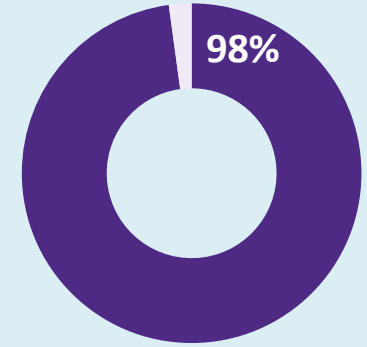
Clinician Reported Treatment by Age – SMA Registry

96.7%

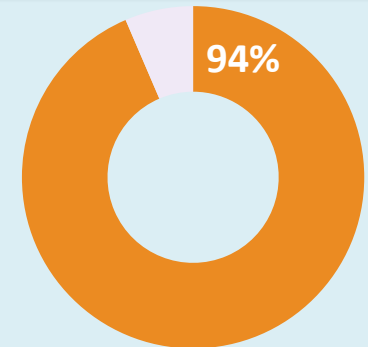
of individuals in the CDR have a reported SMA treatment (current or historical)

n=900

PEDIATRICS
Under 18 years



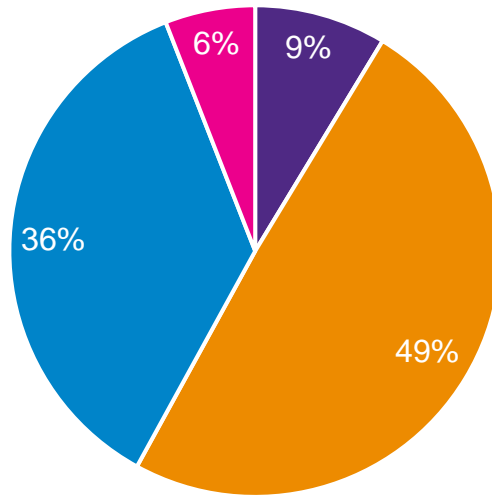
ADULTS
18 years or older



Treatment Utilization: 2022 Community Update Survey

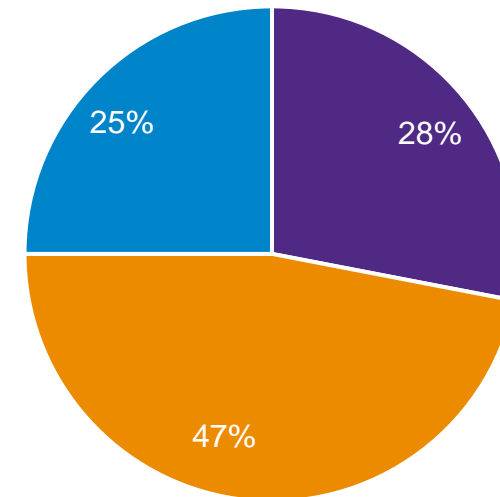
PATIENT/CAREGIVER REPORTED

Children with SMA
<18 years of age
(n=219)



■ 0 Treatment ■ 1 Treatment ■ 2 Treatments ■ 3 Treatments

Adults with SMA
≥18 years of age
(n=264)

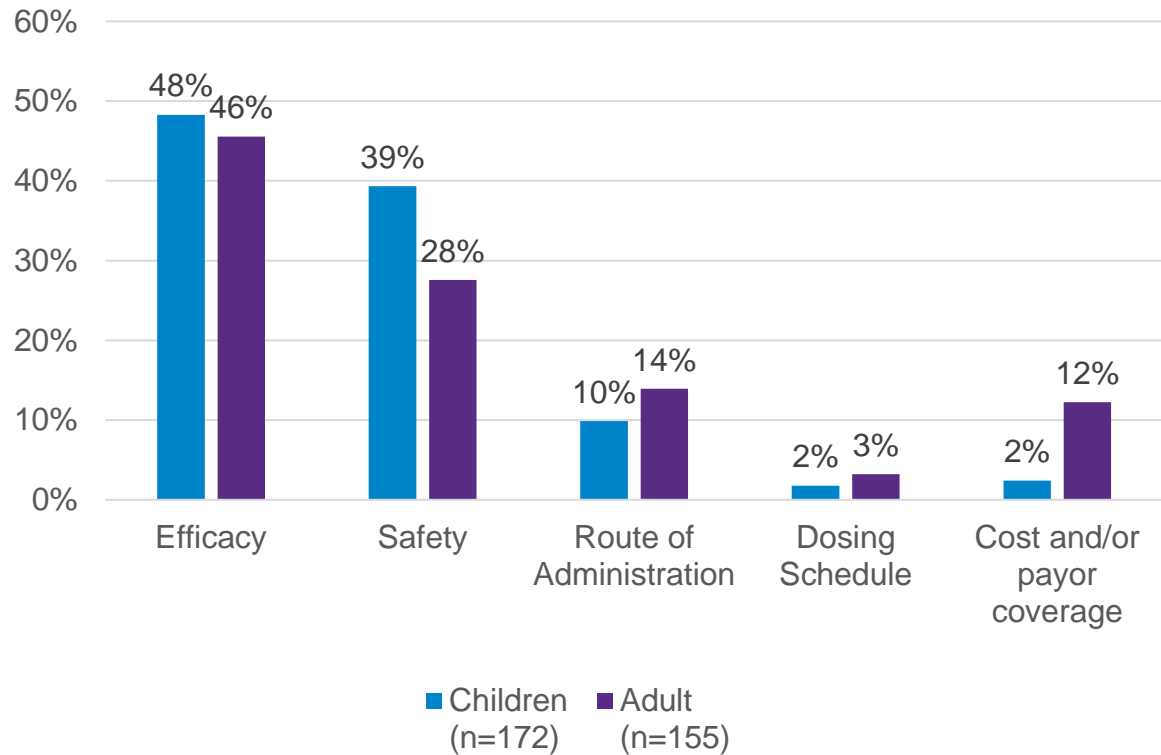


■ 0 Treatment ■ 1 Treatment ■ 2 Treatments

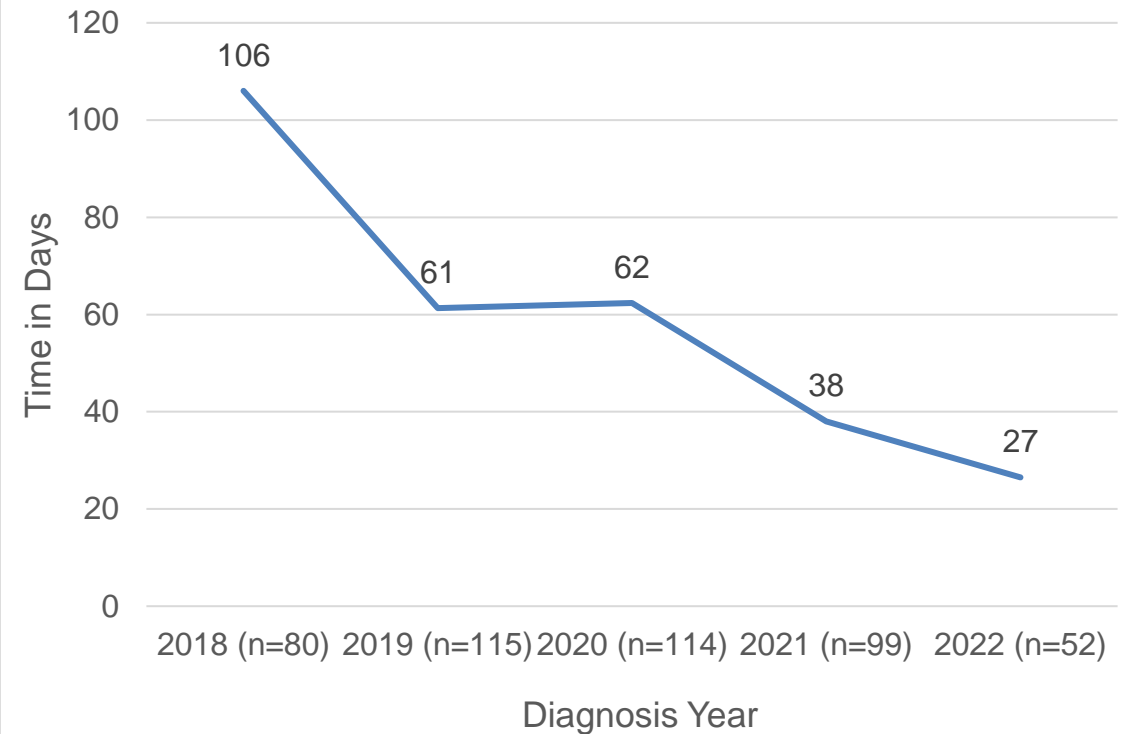
Treatment Utilization

PATIENT/CAREGIVER REPORTED

Important Factors when Choosing an SMA Treatment



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



Combination Treatment Definitions

- **Single Treatment**

- Has received one specific SMA FDA approved drug/therapeutic treatment

- **Concurrent Treatments**

- Has received two or more SMA FDA approved treatments at the same time

- Includes any prior treatment with gene replacement therapy

- **Sequential Treatments**

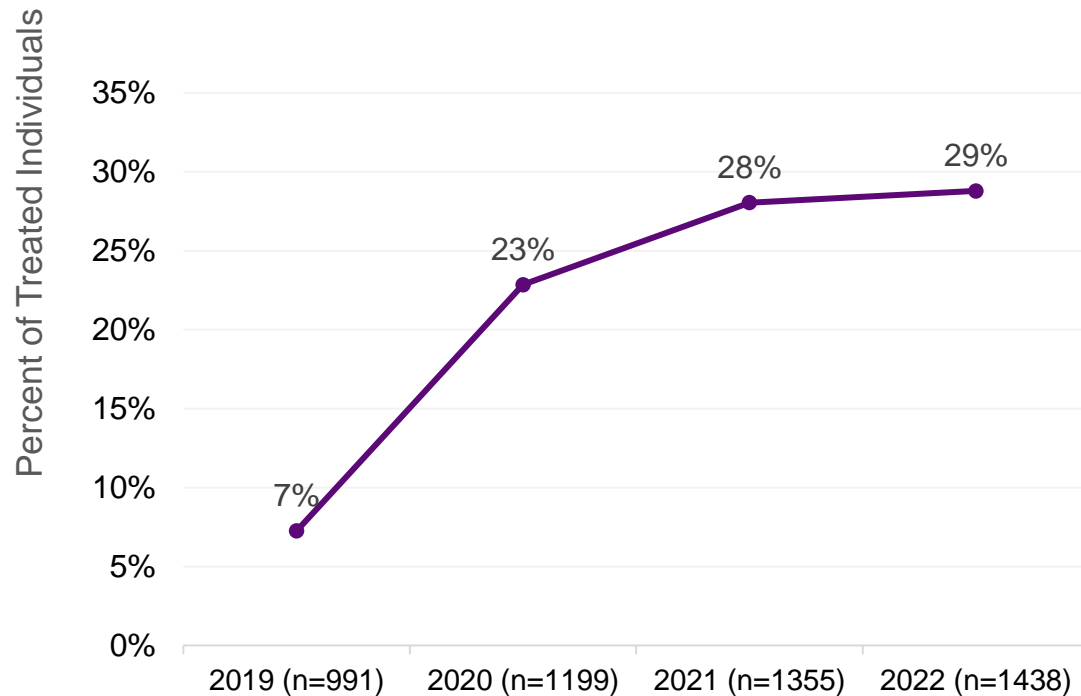
- One SMA FDA approved treatment is discontinued and then SMA FDA approved treatment is started

- Includes secondary treatment with SMA gene replacement therapy

Combination Treatments

Combined data

Percent of Treated Individuals that Utilized Multiple Therapies – Trends¹



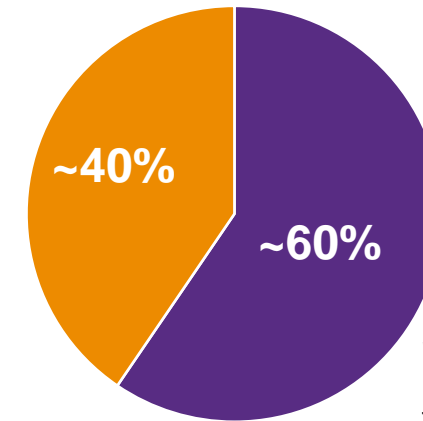
Combined data

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

Concurrent Treatment

~ 40% of individuals indicated the start date of one treatment was before the end date of another treatment.

Note: this includes all individuals who initiated a treatment after receiving Zolgensma.



Sequential Treatment

~ 60% of individuals indicated that one treatment's end date was before the next treatment's start date.

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.

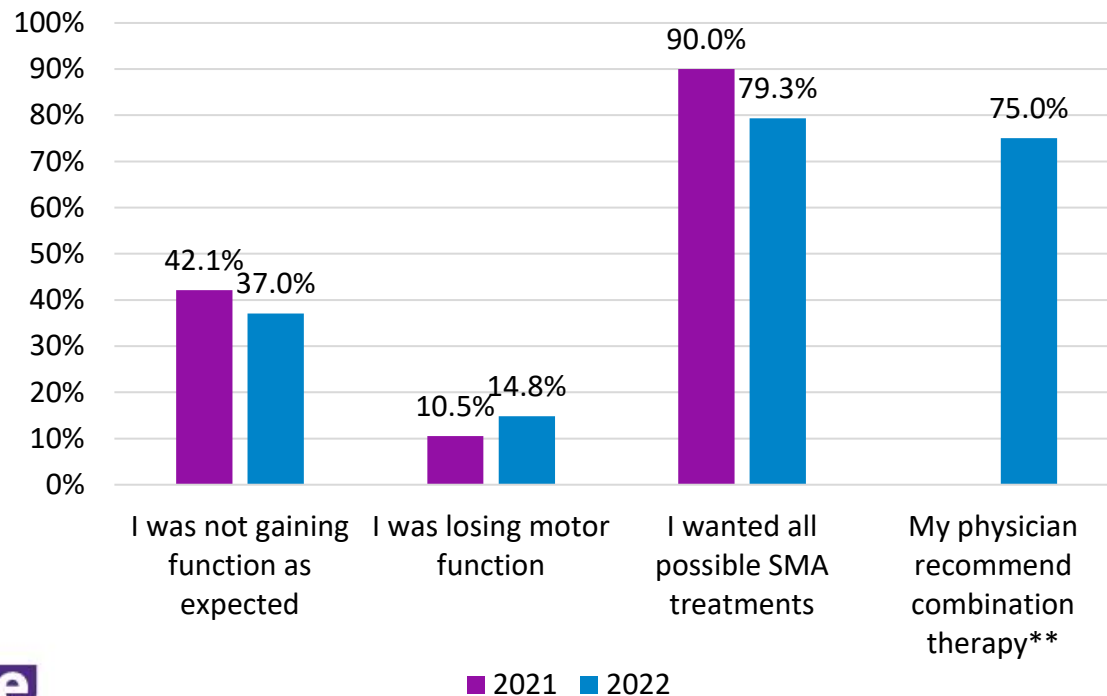
Combination Therapy and Decision-Making

Community Feedback

- 142 individuals completed a survey for both 2021 & 2022.
- 40.1% (57/142) and 49.3% (70/142) were treated with more than one therapy in 2021 and 2022, respectively.

Patient/Caregiver-reported

Reasons for Being Treated with Combination Therapy by Survey Year (select all that apply)

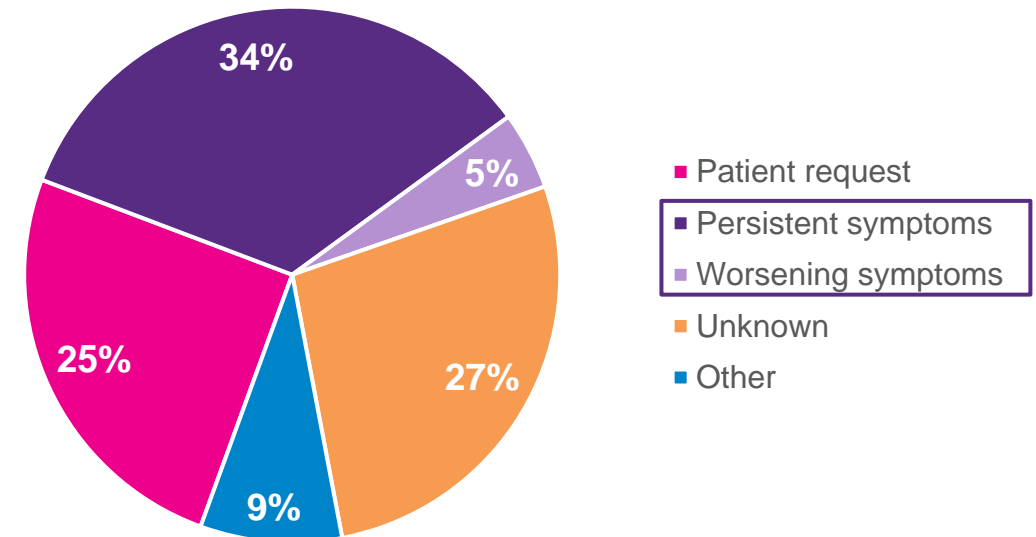


**Physician recommending combination therapy was not an option in the 2021 CUS

Healthcare Provider Feedback

Clinician-reported

Primary Reason an Additional Treatment was Added to the Treatment Regimen, n=234*

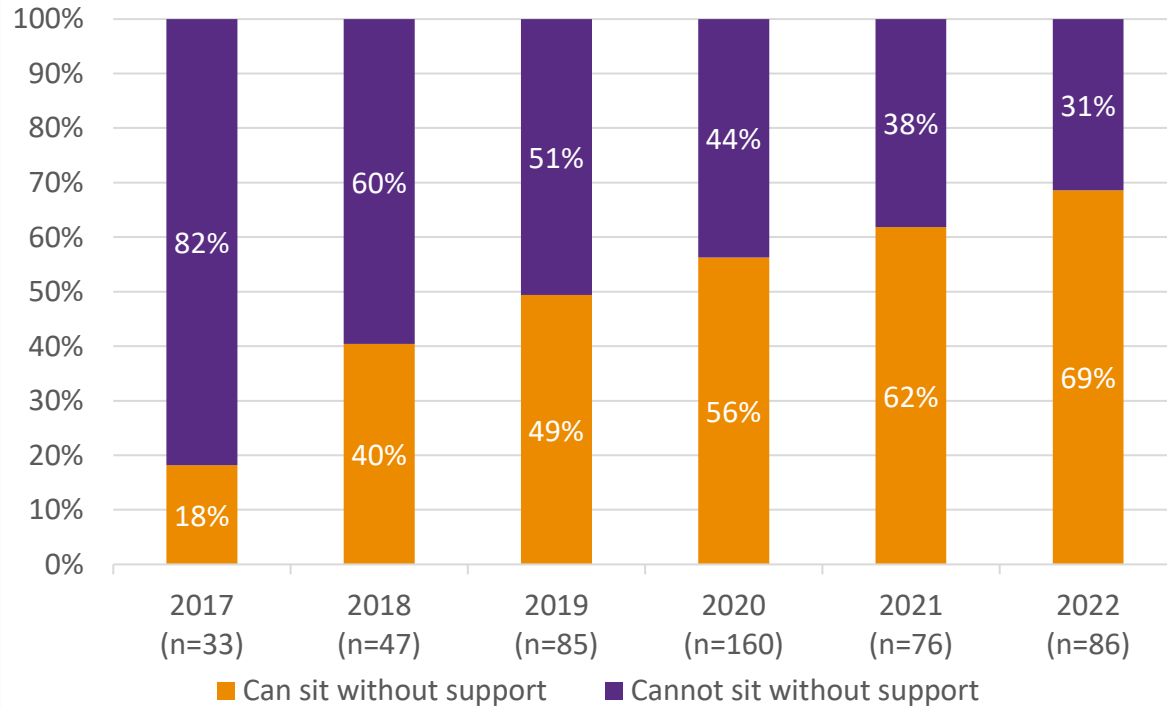


- Treatments do not have to be concurrently used
- May include a small proportion of individuals that received a drug through clinical trial

Treatment Impact

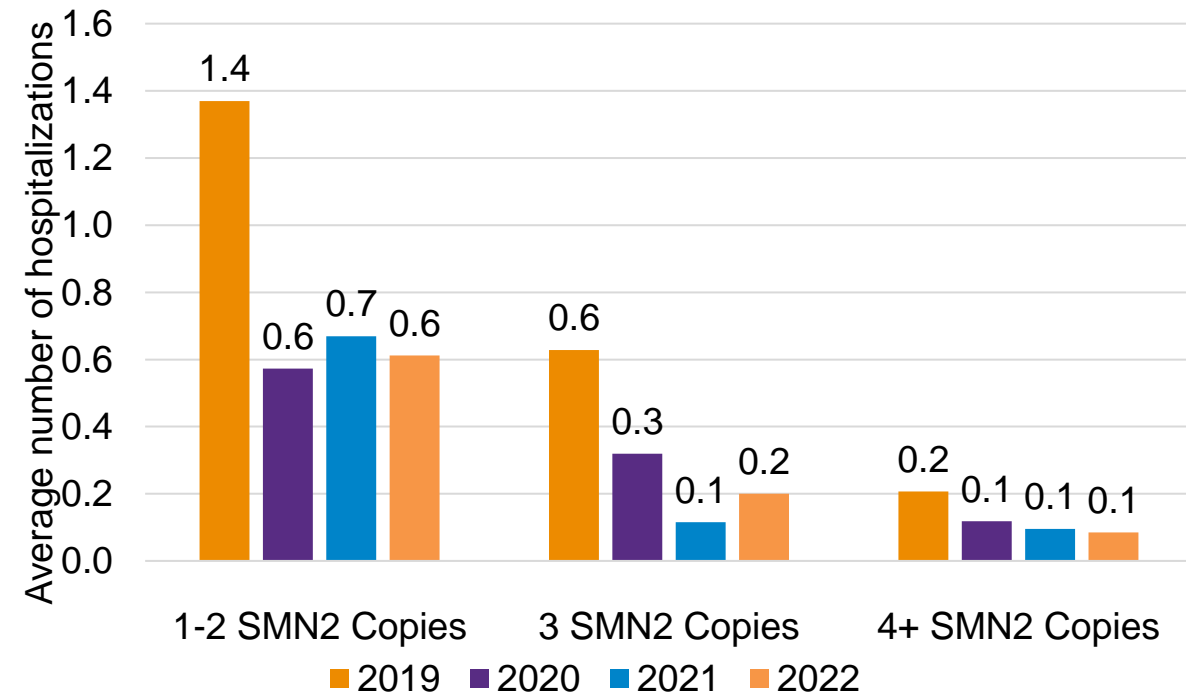
Patient/Caregiver-reported

Proportion of individuals with 2 *SMN2* copies who report sitting without support since 2017¹



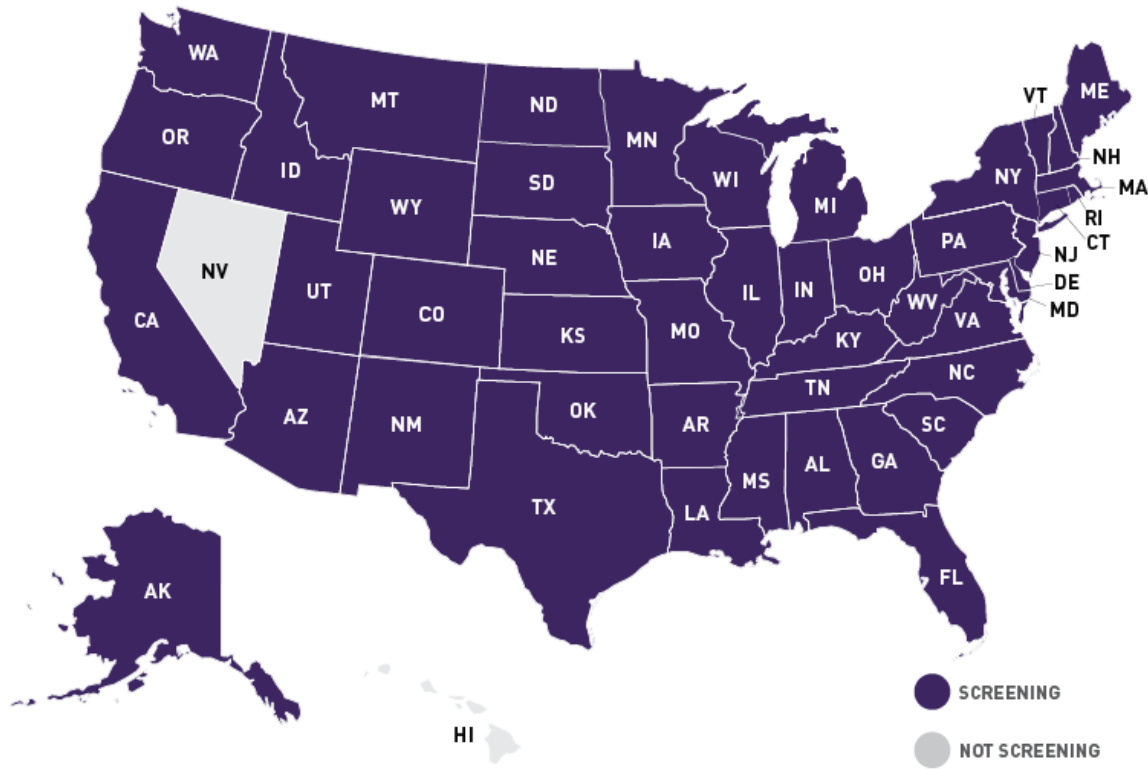
Patient/Caregiver-reported

Annual hospitalizations by *SMN2* copy number¹



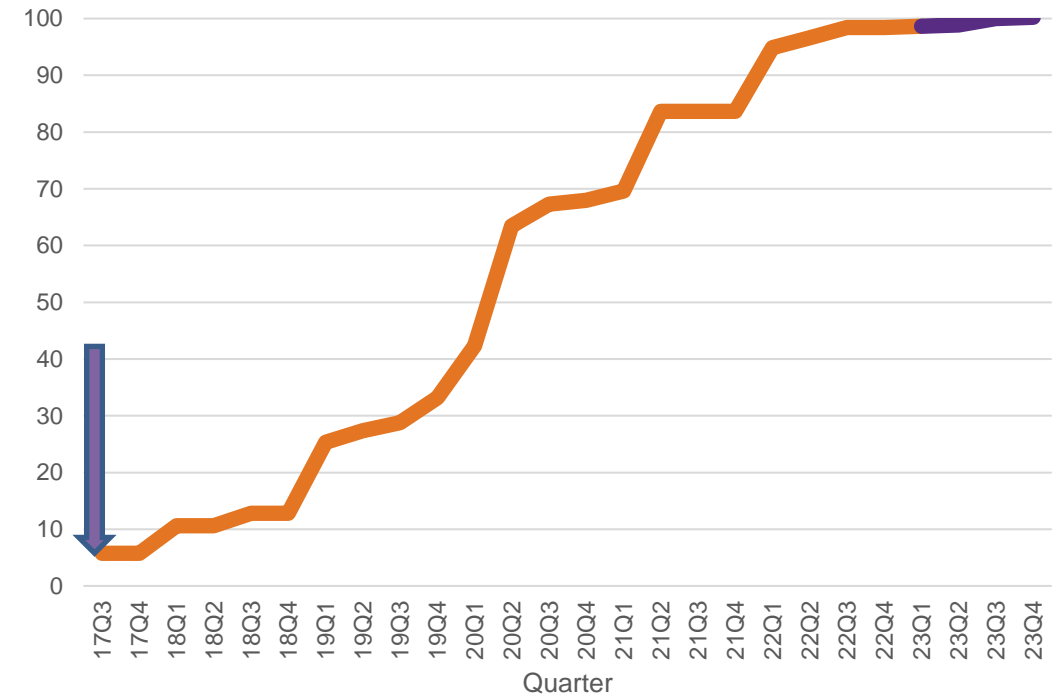
SMA Newborn Screening – 99%!

48 States Currently Screen for SMA



Last updated January 2023

% Births Screened for SMA in the US

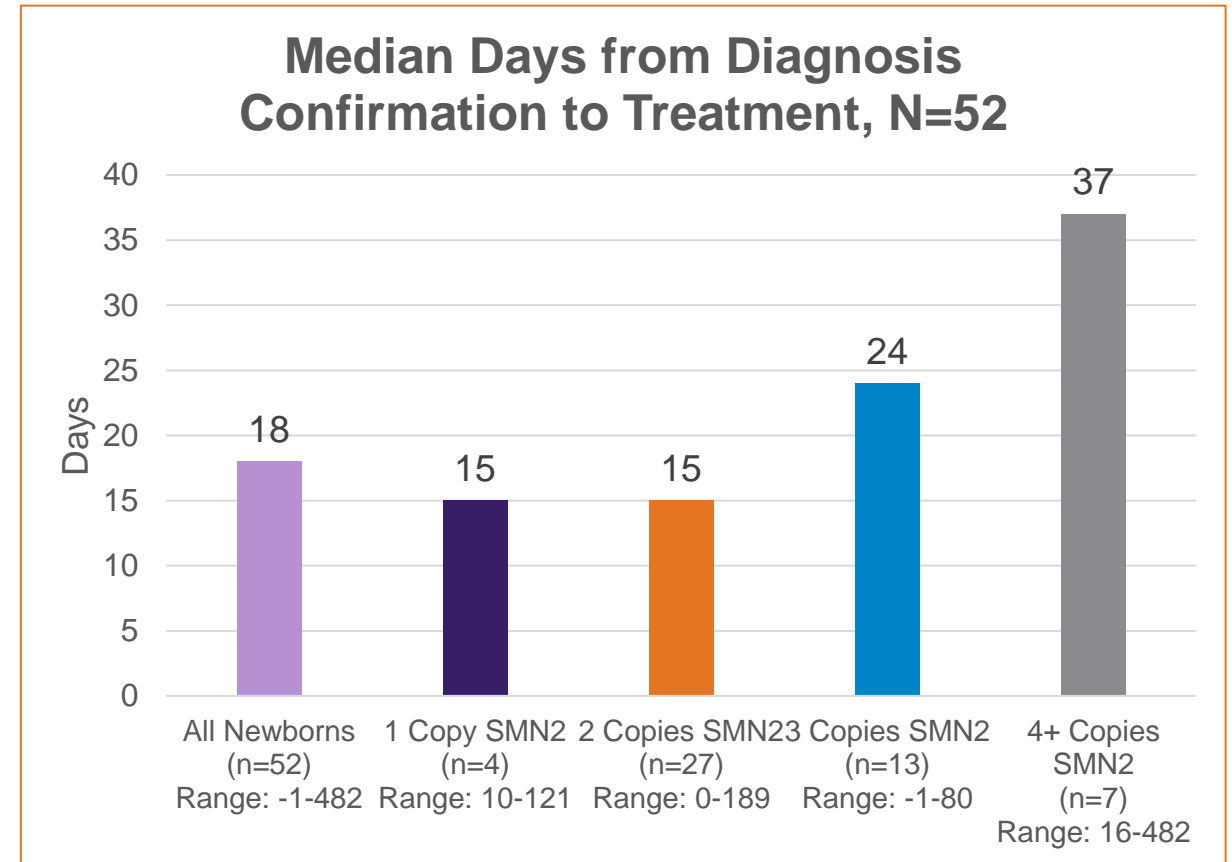
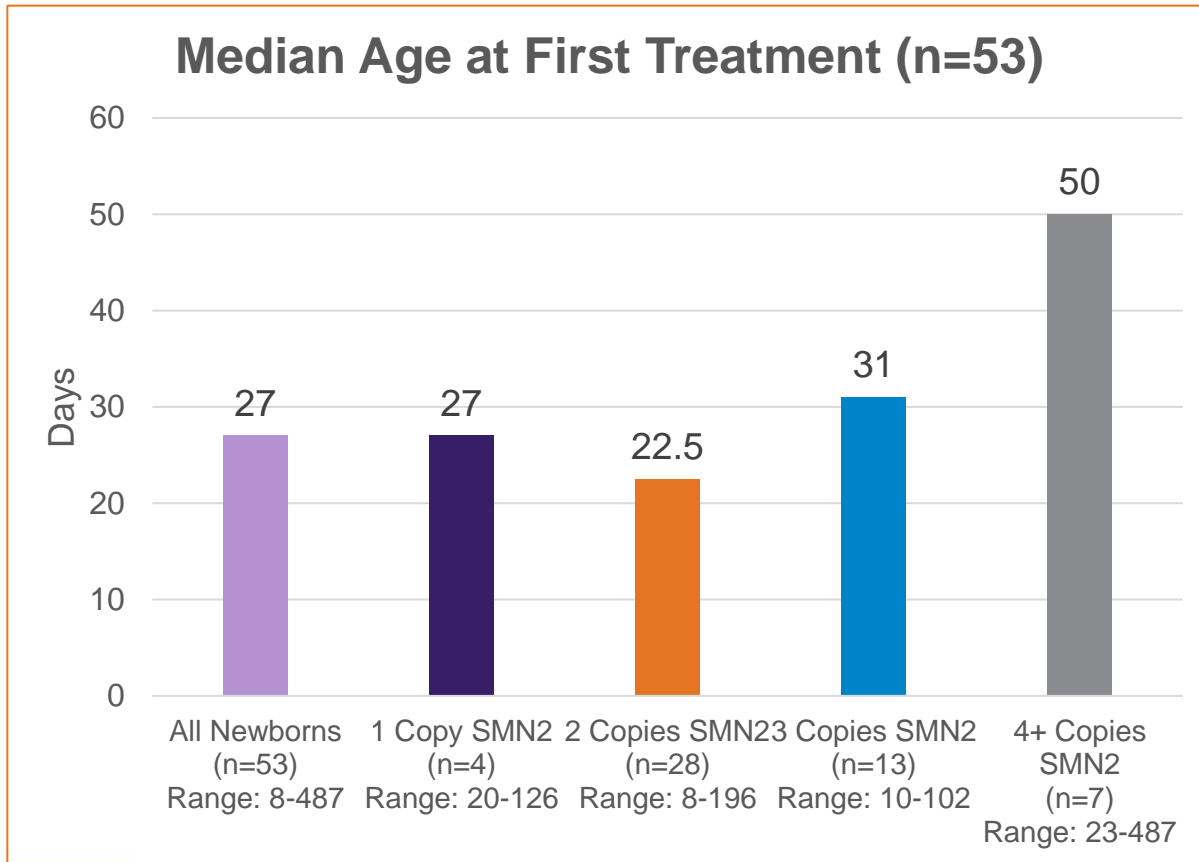


States not screening: Nevada and Hawaii

SMA Newborn Screening Registry: Time to SMA Treatment

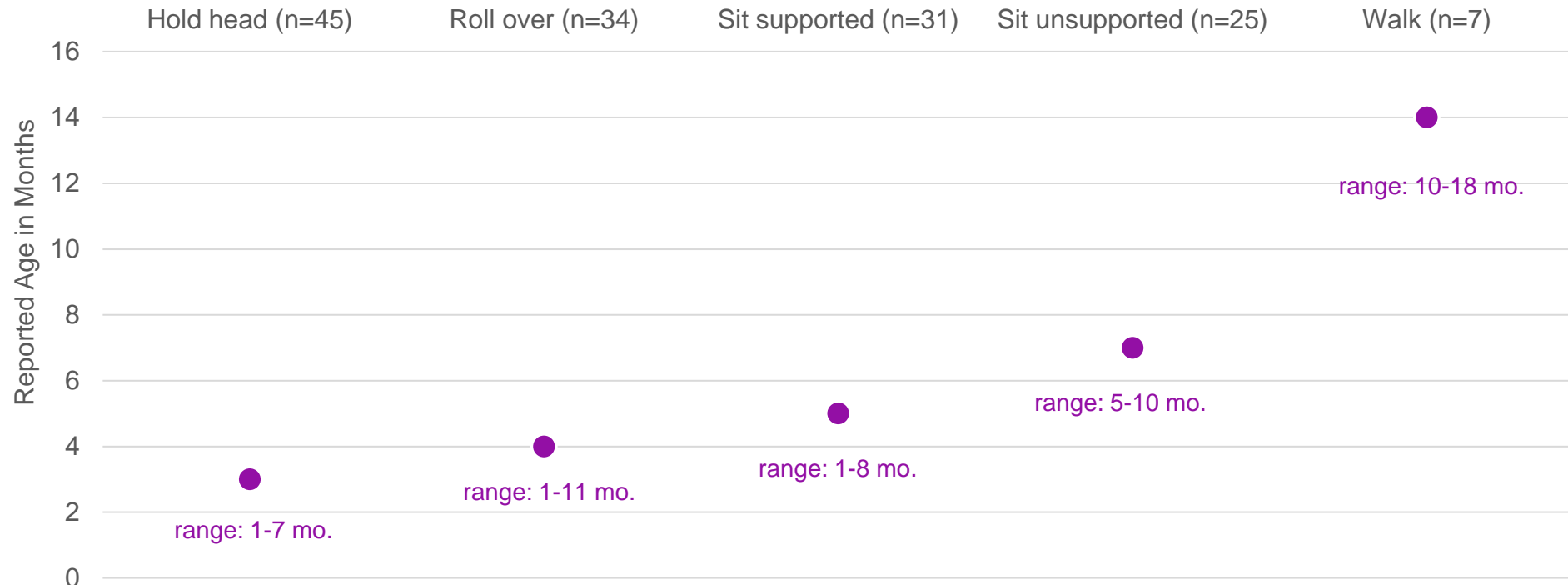
Patient/Caregiver-reported

Reported age at diagnosis confirmation: Median: 7 days (Range: 1 – 40 days)



Impact of SMA Newborn Screening

PARENT/CAREGIVER REPORTED



Distribution of SMN2 Copy Number

Legend:

1-2 copies SMN2

3+ copies SMN2

Unknown



Standard of Care - Back to Basics

- **Standard of Care - critically important to optimize function**
 - Breathing
 - Nutrition
 - Musculoskeletal care
 - Physical and Occupational Therapy
 - Orthopedic care
- **Treatments are disease modifying – not cures**
- **Specialist care**
 - Monitor side effects
 - Document response to treatment and changes over time - Learning together

