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ORIGINAL RESEARCH

Effects of the COVID-19 Pandemic on SMA Screening and Care: Physician and Community Insights

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ABSTRACT

Objective: As part of efforts to reduce diagnostic delays and enhance clinical trials, Cure SMA evaluated the effects of COVID-19 on SMA care and clinical trial conduct.

Introduction: Spinal muscular atrophy (SMA) is an autosomal recessive neuromuscular disease characterized by progressive, potentially debilitating muscle weakness and atrophy. Uninterrupted access to early diagnosis, disease-modifying treatment, and care for SMA is vital to avoiding irreversible motor neuron death and achieving optimal patient outcomes.

Methods: Two surveys were conducted: a provider survey and a community survey. The Provider Impact Survey, distributed from November 24, 2020, through March 8, 2021, assessed COVID-19's effects on referrals for evaluation of suspected SMA, cancellations and delays of SMA-related care, and clinical trials. The Community Impact Survey was fielded in three waves between April 7, 2020 and July 19, 2021, in tandem with Cure SMA COVID-19 support programs.

Results: A total of 48 completed provider surveys (22 from care sites, 26 from care-and-trial sites) reflected decreases in referrals for suspected SMA, increases in appointment cancellations and delays, and patient reluctance to attend in-person visits due to COVID-19. One-third of care-and-trial sites reported trial recruitment delays, and one-quarter reported pausing trial enrollment. Results of the Community Impact Survey, completed by 2047 individuals, showed similar disruptions, with 55% reporting changes or limitations in accessing essential SMA-related services.

Conclusions: This research evaluates the pandemic's interruption of SMA care and research. These insights can help mitigate and increase preparedness for future disruptive events. Expanded use of virtual tools including telehealth and remote monitoring may enhance continuity and access. However, additional research is required to evaluate their effectiveness. While this research was specific to SMA, its findings may have relevance for other patient communities.

Keywords: Appointment wait times; COVID-19 pandemic; Diagnosis; Newborn screening; Referrals; SMA; Spinal muscular atrophy; Triage

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Key Summary Points

Why carry out this study?

The progressive, irreversible nature of spinal muscular atrophy (SMA) makes early diagnosis and uninterrupted care essential for optimal outcomes, particularly for the most severe form of the disease (Type 1).

Healthcare providers and SMA-affected individuals and their caregivers were surveyed to understand the effects of the COVID-19 pandemic on the continuity of clinical care and clinical trial conduct.

Respondents were asked which factors impacted SMA-related services that required in-person visits, such as trial recruitment, diagnosis confirmation, treatment administration, and physical therapy.

What was learned from the study?

Delays and cancellations of in-person SMA care and research appointments were common during the COVID-19 pandemic and were initiated by both healthcare providers and patients/caregivers to prevent viral exposure.

It is critically important that SMA healthcare providers and researchers develop contingency plans to avoid future disruptions in healthcare and clinical trial conduct.

Along with scheduling and logistical flexibility, priority should be placed on the development of remote clinical outcome assessments; local or mobile blood sample collection sites; remote physical therapy sessions; digital monitoring devices; and safe, on-schedule continuation of treatment administration.

INTRODUCTION

On May 5, 2023, the World Health Organization (WHO) announced that the COVID-19 pandemic no longer qualifies as a global health emergency [1]. WHO made this announcement more than three years after the organization first declared that COVID-19 infection had reached global pandemic status. The pandemic caused extraordinary disruptions to healthcare systems worldwide, including in the United States (US), where the President declared a national emergency on March 13, 2020 [2]. As the number of COVID-19 infections skyrocketed, healthcare providers struggled to meet COVID-related and non-COVID related patient needs under the strain of supply and staff shortages, overwhelming demand for medical care, and the ongoing threat of infection [3, 4]. The same pressures affected clinical trial staff, who grappled with balancing the need for protocol consistency against the risk of exposing trial participants to COVID-19 infection [5, 6]. On March 18, 2020, the Centers for Medicare and Medicaid Services issued, with the support of the American Medical Association and the American College of Surgeons, "Non-emergent, Elective Medical Services and Treatment Recommendations" [1]. These guidelines encouraged delaying or triaging through virtual care all but those healthcare concerns for which "lack of in-person treatment or service would result in patient harm." A week later, the FDA published, "Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency: Guidance for Industry, Investigators, and Institutional Review Boards" [7]. Many individuals and their caregivers delayed healthcare appointments due to concerns about COVID-19 exposure. To compensate for the reduction in in-person care, healthcare providers and clinical researchers expanded the use of digital tools and telemedicine [8, 9].

Delays in healthcare can have profound consequences for individuals living with serious but treatable diseases for which early intervention and/or consistent treatment are critical to achieving optimal health outcomes. Spinal

muscular atrophy (SMA) is one such disease. It is an autosomal recessive neuromuscular disease characterized by progressive muscle weakness and atrophy [10–16]. SMA affects an estimated one in 11,000 infants in the US each year and about 8 million Americans are genetic carriers [17]. Without disease-modifying therapy, SMA progressively diminishes an individual's strength, energy, muscle function, and ability to independently perform activities of daily living. SMA has traditionally been classified into four primary clinical phenotypes (Types 1–4) based upon age of symptom onset and motor milestone achievement, with SMA Type 1 being the most common and severe [16, 18–20]. More recently—because new drug treatments have changed the progression of the disease—optimizing motor function ability following treatment has become a greater focus [21].

Prior to the advent of drug treatments, SMA was the leading genetic cause of death in children under two years of age [22]. Since 2016, the FDA has approved three disease-modifying treatments for SMA, including an antisense oligonucleotide, a *SMN1* gene-replacement therapy, and an *SMN2* splicing modifier [23–25]. SMA was added to the Recommended Uniform Screening Panel in 2018, and, as of February of 2023, 99% of all infants born in the US are being screened for SMA [26]. These developments have enabled many individuals with SMA to receive early diagnosis and treatment. Clinical trial results and real-world evidence continue to demonstrate the positive impact of treatment on disease progression, health outcomes, and life expectancy, as well as the benefit of early intervention, particularly for infants born with Type 1 SMA. As such, it has become critically important to prioritize timely SMA diagnosis and treatment [26–33].

Shortly after the onset of the pandemic in spring 2020, providers reported reductions in pediatric well-visits and developmental screening and surveillance [27, 28]. This observation generated concerns within Cure SMA regarding potential delays in the recognition of SMA symptomatology, diagnosis, and treatment initiation. During the pandemic, SMA community members had to balance concerns about COVID-19 exposure with the need to access key healthcare services for management of SMA, such as treatment administration and monitoring, physical therapy, and in-home care [29–31]. While telehealth visits can support continuity of care in some settings, many SMA-related services—such as diagnosis confirmation, drug administration, and physical therapy—still require in-person interaction [29, 32–36].

For individuals with SMA, appointment delays and/or cancellations may have serious consequences in the form of psychological stress and worse health outcomes [30, 37–40]. Cure SMA, an advocacy organization for the SMA community, maintains the largest database of SMA-affected individuals globally [41]. Cure SMA has a portfolio of initiatives aimed at reducing diagnostic delays and optimizing clinical trial management for SMA-affected individuals [10]. In this study, we sought to determine whether the COVID-19 pandemic caused delays in SMA diagnosis, care, and treatment access. Understanding the causes of these delays will help clinicians and researchers better prepare to utilize remote methods to avoid future interruption of services. To achieve these aims, Cure SMA surveyed healthcare professionals at SMA care and clinical trial sites, as well as individuals living with SMA and their caregivers.

METHODS

A healthcare provider survey—the "Provider Impact Survey"—was developed to assess COVID-19's effects on incoming referral frequency for the evaluation of suspected SMA; treatment initiation rates for symptomatic, newly diagnosed individuals as well as those identified via newborn screening (in applicable states); treatment completion rates for SMA-affected individuals who had received care prior to the pandemic; potential barriers to access to specialty services; and SMA clinical trials.

The Provider Impact Survey was hosted on a web-based survey platform (Alchemer) and deemed exempt from IRB review by WIRB-Copernicus Group Institutional Review Board (WCG IRB). The Provider Impact Survey

(Appendix A) was distributed to 351 healthcare providers at known SMA treatment and clinical trial sites within the US who had opted in to receive communications from Cure SMA via emails sent from the Alchemer survey platform. Participants received a US$60 gift card as compensation for their time. The survey was open from November 24, 2020 through March 8, 2021. Data were collected and analyzed by Cure SMA and its consultant partner, Faegre Drinker Biddle & Reath LLP. The findings presented are descriptive in nature and no statistical testing was performed.

Separately, the "Community Impact Survey" was distributed in three waves to affected adults and caregivers residing in the US, in conjunction with a Cure SMA form for affected individuals and families requesting a COVID-19 support package (Appendix B). Survey participants did not receive any monetary compensation for filling out the survey within the request form; however, each care package contained different items, and individuals were eligible to receive all three care packages if they completed each request form. The Community Impact Survey focused on the effects of COVID-19 on community members' daily lives and SMA care access. No vaccination data were collected because COVID-19 vaccines were not available when the survey was launched. Support packages were publicized to the Cure SMA community via email, website postings, and social media. The first survey launched on April 7, 2020 and closed on November 18, 2020. The second survey launched on July 29, 2020, and the third survey launched on November 18, 2020. Both the second and third survey remained open at data cut on July 16, 2021. Due to the overlapping time periods and methods of distribution, respondents may have completed surveys in various orders and on the same day (i.e., November 18, 2020); therefore, analysis of trends over time regarding the impact of COVID-19 on the community are not presented here. All responses were compiled via the Blackbaud Luminate Online platform. If individuals completed multiple surveys, the most recent survey was used for reporting aggregate results. The only exception was for questions related to COVID-19 exposure; in this instance, the data represent any answer of "yes" given in any survey to diagnosis, symptoms, exposure, or hospitalization due to COVID-19 (in other words, if an individual answered yes in any survey, that was counted, but only once for that individual). WCG IRB provided a post-survey IRB review exemption determination, allowing for the publication of research findings. However, all individual data are considered confidential, with only aggregate results shared. This survey was also conducted in accordance with the Helsinki Declaration of 1964 and its later amendments.

RESULTS

Provider Impact Survey recruitment yielded 48 complete unique responses (Table 1). Of these, 22 came from sites that provide patient care ("care sites") and 26 were received from sites that provide SMA patient care and reported participation in one or more sponsor-initiated SMA clinical trials ("care-and-trial sites"). Provider surveys reflected a range of specialty areas, with the majority being pediatric neurologists and neuromuscular specialists (Table 1). Most practiced in academic settings and were from urban centers.

Cure SMA obtained 3110 completed surveys from 2047 unique individuals for the Community Impact Survey (Table 1). Individuals with SMA and their caregivers who responded to the Community Impact Survey reflected a range of ages of SMA-affected individuals, with the most common age group being those under 5 years. The most common SMA type represented was Type 2.

Frequency of Referral for Newborn Screening and Suspected SMA

Between September 2019 and February 2020, 47.1% of care-and-trial respondents indicated newborn screening referrals were received once quarterly, while 23.1% of care sites received referrals of this type about twice a year (Table 2). These rates were likely influenced by the fact that, at the time of the survey, only 11.8% of care-and-trial site respondents indicated that

Table 1 Characteristics of survey respondents

Attribute	Care-and-trial sites ($n = 26$)	Care sites ($n = 22$)	Total
Provider survey respondents ($n = 48$)			
Participant specialty[a]			
Adult neurology	7.7% (2)	4.5% (1)	6.3% (3)
Developmental pediatrics	0% (0)	4.5% (1)	2.1% (1)
Genetic counseling	3.8% (1)	0% (0)	2.1% (1)
Neurology	7.7% (2)	4.5% (1)	6.3% (3)
Neuromuscular specialist	53.8% (14)	45.5% (10)	50.0% (24)
Nursing	3.8% (1)	13.6% (3)	8.3% (4)
Pediatric pulmonary	3.8% (1)	13.6% (3)	8.3% (4)
Pediatric neurology	65.4% (17)	50.0% (11)	58.3% (28)
Physical therapy	0% (0)	9.1% (2)	4.2% (2)
Other	3.8% (1)	9.1% (2)	6.3% (3)
Years in practice			
0–5 years	15.4% (4)	9.1% (2)	12.5% (6)
6–10 years	42.3% (11)	22.7% (5)	33.3% (16)
11–15 years	11.5% (3)	22.7% (5)	12.5% (6)
16–20 years	0% (0)	9.1% (2)	4.2% (2)
21–30 years	19.2% (5)	18.2% (4)	18.8% (9)
Over 30 years	11.5% (3)	18.2% (4)	14.6% (7)
Practice type			
Multi-specialty group	11.5% (3)	18.2% (4)	14.6% (7)
Direct hospital employee/contractor	19.2% (5)	31.8% (7)	25.0% (12)
Academic faculty practice	61.5% (16)	45.5% (10)	54.2% (26)
Other	7.7% (2)	4.5% (1)	6.3% (3)
Practice location[b]			
Urban	88.5% (23)	63.6% (14)	77.1% (37)
Rural	7.7% (2)	13.6% (3)	10.4% (5)
Suburban	3.8% (1)	22.7% (5)	12.5% (6)
Total # of SMA affected patients at practice			
1 to 5	0% (0)	13.6% (3)	6.3% (3)
6 to 10	0% (0)	9.1% (3)	6.3% (3)
11 to 20	11.5% (3)	13.6% (5)	16.7% (8)
20 to 30	23.1% (6)	22.7% (2)	16.7% (8)

Table 1 continued

Attribute	Care-and-trial sites ($n = 26$)	Care sites ($n = 22$)	Total
> 30	65.4% (17)	40.9% (9)	54.2% (26)
SMA NBS referrals to site[c]			
Yes	65.4% (17)	59.1% (13)	62.5% (30)
No	23.1% (6)	27.3% (6)	25.0% (12)
N/A—SMA not on state NBS panel	11.5% (3)	13.6% (3)	12.5% (6)
Community impact survey[d] respondents (n = 2047)			
Current age of affected individual[e]			
< = 5 years old			28.8% (589)
6–10 years old			15.2% (311)
11–17 years old			16.2% (331)
18–25 years old			13.0% (266)
> = 26 years old			26.9% (550)
SMA type[f]			
Type 1			29.5% (603)
Type 2			47.6% (974)
Type 3			21.5% (441)
Type 4			1.4% (29)

[a]Respondents were given the option to select all that apply. Pediatric neurology refers to training and specialization in the neurologic care of children; adult neurology refers to training and specialization in the neurologic care of individuals 18 years of age and older; neurology refers to training and specialization in the neurologic care of individuals of any age or developmental stage

[b]Practice location refers to the population density and proximity to a metropolitan area of the community where care was provided, with urban being the most densely populated and within a major metropolitan area, suburban being of medium population density and near a major metropolitan area, and rural being of low population density and distant from a major metropolitan area

[c]NBS = newborn screening

[d]The first Community Impact Survey launched with the COVID-19 Support Package request on April 7, 2020 and closed on November 18, 2020 with 1642 unique responses. The second Community Impact Survey launched with the Medical Support Bracelet request on July 29, 2020 and remained open at data cut (July 16, 2021) with 442 unique responses. The third Community Impact Survey launched with the COVID-19 PPE Package request on November 18, 2020 and remained open at data cut (July 16, 2021) with 1026 unique responses

[e]Current age reflects the current age at the time of survey submission

[f]SMA type was self- or caregiver-reported

Table 2 Pre-pandemic frequency of newborn screening or suspected SMA referrals

Pre-pandemic referral frequency (Sept. 2019–Feb. 2020)	SMA newborn screening referral[a]		Referral for suspected SMA	
	Care-and-trial sites ($n = 17$) % (n)	Care sites ($n = 13$) % (n)	Care-and-trial sites ($n = 26$) % (n)	Care sites ($n = 22$) % (n)
Once weekly	0% (0)	0% (0)	3.8% (1)	0% (0)
Once monthly	29.4% (5)	15.4% (2)	46.2% (2)	31.8% (7)
Once quarterly	47.1% (8)	15.4% (2)	34.6% (9)	40.9% (9)
About twice a year	5.9% (1)	23.1% (3)	3.8% (1)	18.2% (4)
About once a year	5.9% (1)	15.4% (2)	11.5% (3)	9.1% (2)
Not applicable; SMA was not included within my state's newborn screening panel during the specified time	11.8% (2)	30.8% (4)	n/a	n/a

[a]Sample size reflects number of respondents practicing in states for which SMA was included within newborn screening panel at time of survey completion

their state newborn screening panel did not yet include SMA, whereas 30.8% of care site respondents reported that SMA was not yet included in their state's newborn screening panel. Rates of referral for suspected SMA prior to the pandemic were more similar between care-and-trial and care sites; 80.8% of care-and-trail sites reported receiving referrals for suspected SMA either once monthly or once quarterly, and 72.7% of care sites reported receiving once monthly or once quarterly suspected SMA referrals (Table 2).

When asked to compare SMA newborn screening referral frequency during the pandemic with that of pre-pandemic frequency, none of the provider respondents from care-and-trial sites reported decreases; 17.6% indicated that they had increased and 82.4% indicated that no change had occurred (Fig. 1). Among care site respondents, 7.7% indicated that referrals based on newborn screening for SMA had decreased during the pandemic, 23.1% indicated that referrals had increased, and 69.2% indicated that no change had occurred (Fig. 1). The majority of both SMA care-and-trial and care site respondents reported no change in the frequency of referrals to evaluate cases of suspected SMA (Fig. 2). However, 11.5% of care-and-trial sites and 27.3% of care sites reported a decreased frequency of referrals for evaluation of suspected SMA diagnosis. Also, 11.5% care-and-trial sites and 4.5% care sites reported an increase in the number of referrals (Fig. 2).

Community-Reported Concerns about COVID-19

The majority of Community Impact Survey respondents (75%) reported no known exposure to COVID-19 (Fig. 3). Despite these low levels of reported exposures, SMA community respondents reported concerns about the pandemic's effects on their care and lives. These concerns included being diagnosed with COVID-19 (47.4%), a shortage of medical supplies and treatment (68.0%), and unemployment (10.9%) (Fig. 4).

Disruptions to SMA-Related Care

Both the provider and community surveys reflect high rates of cancellations and/or delays

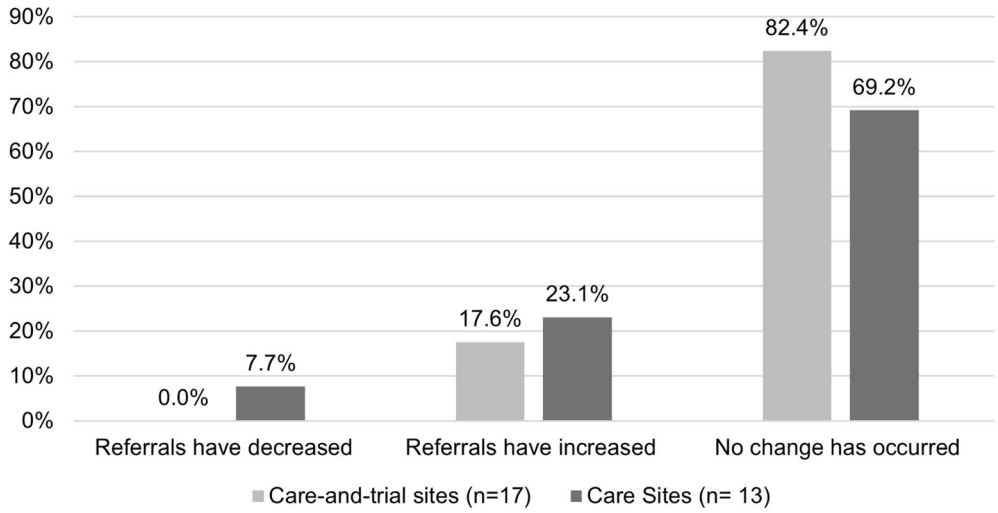

Fig. 1 Change in SMA newborn screening referral frequency since pandemic onset

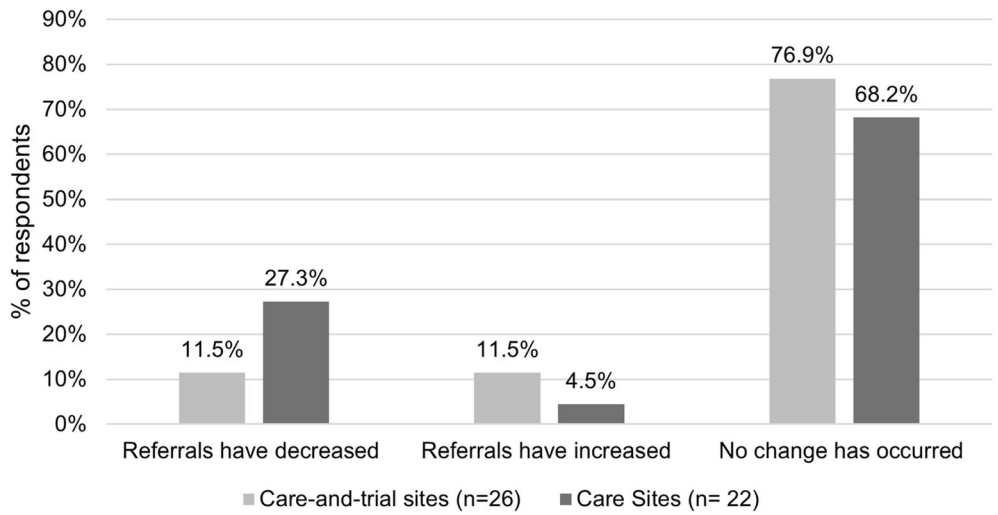

Fig. 2 Change in suspected SMA referral frequency since pandemic onset

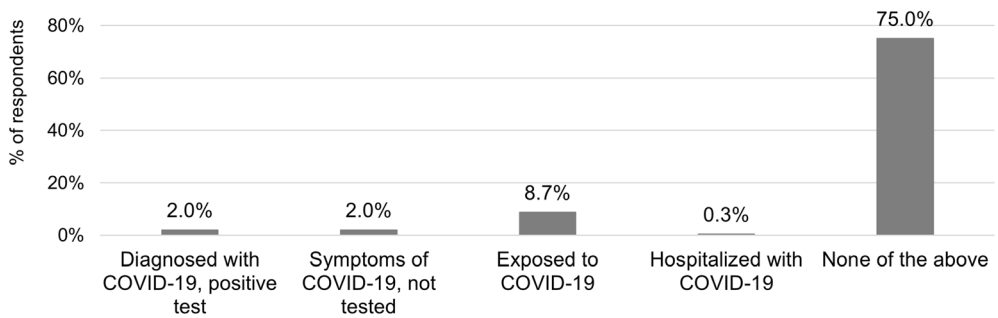

Fig. 3 COVID-19 diagnoses and exposures in the SMA community. *$n = 2047$; respondents had the option to "select all that apply" from the provided responses

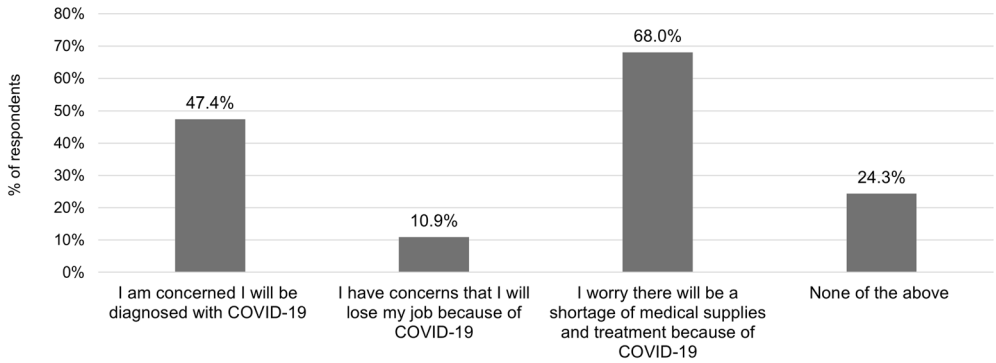

Fig. 4 SMA community concerns regarding COVID-19's effects on health and daily life. *$n = 1216$; respondents had the option to 'select all that apply' for the provided responses. Question was not included on the first survey distribution

of SMA-related appointments (Table 3). Results from both surveys indicate that SMA-related services such as physical therapy were the most likely to have been disrupted, with 80.8% of care-and-trial site respondents, 72.7% of care site respondents, and 42.9% of community respondents reporting delays or cancellations of these services during the survey period (Table 3). Provider and community survey results reflect relatively few cancellations for SMA-related drug treatment administration appointments: 26.9% of care-and-trial site, 27.3% of care site, and 22.6% of community respondents reported cancelling or delaying appointments for SMA drug treatment over the course of the survey period (Table 3).

The provider surveys offer additional perspective on reasons for cancellations and delays: 95.2% of care-and-trial site and 86.4% of care site respondents reported that concerns about COVID-19 exposure caused patients and/or their family members to delay or cancel an appointment at any time during the pandemic (Table 3). However, cancellations due to exposure concerns fell over time, with 65.4% and 63.6% of care-and-trials sites and care, respectively, reporting cancellations during the month prior to the end of the survey. Likewise, 69.2% of care-and-trial site respondents and 59.1% of care site respondents reported cancelling or delaying appointments for SMA-related care at any point due to the pandemic, whereas this rate had decreased to 26.9% and 4.5%, respectively, in the month prior to survey completion (Table 3). Care-and-trial site respondents reported that the most common reasons for SMA care appointments to be cancelled or delayed were because the hospital (72.2%) or the provider (72.2%) deemed the appointment non-emergent (Table 4). Care site respondents reported that the most common causes of cancellations and delays were providers deeming appointments non-emergent (61.5%) and state executive orders (61.5%).

Use of Telehealth in SMA-Related Care

Nearly all sites reported utilization of telehealth within their practices. In general, care-and-trial sites were more likely to report having used telehealth than care sites: this was true for March through June 2020 and the month prior to survey completion (Fig. 5). Reported use of telehealth declined over the year-long period covered by the survey.

Effects of COVID-19 on SMA Clinical Trials

Care-and-trial site respondents reported noteworthy effects of COVID-19 on clinical trials. Slightly more than one-quarter of trial sites (25.9%) reported having paused enrollment, and one-third indicated that recruitment was noticeably delayed (data not shown). About 73.1% of respondents indicated an increase in cancelled or rescheduled visits by trial participants, with 80.8% of sites indicating exposure concerns as a reason participants canceled visits (data not shown). The most frequently reported

Table 3 Causes and frequency of SMA-related appointment cancellations and/or delays during pandemic

Type of appointment cancellation or delay	Provider impact survey[a]				Community impact survey[b] ($n = 2047$) % (n)
	At any time during pandemic		Month prior to survey completion		
	Care-and-trial sites ($n = 26$) % (n)	Care sites ($n = 22$) % (n)	Care-and-trial sites ($n = 26$) % (n)	Care sites ($n = 22$) % (n)	
Clinic/facility cancelled or delayed appointment for SMA-related care	69.2% (18)	59.1% (13)	26.9% (7)	4.5% (1)	42.5% (870)
Clinic/facility cancelled or delayed appointment for SMA drug treatment	26.9% (7)	27.3% (6)	11.5% (3)	9.1% (2)	22.6% (463)
Clinic/facility cancelled or delayed appointment for an SMA-related service (e.g., physical therapy)	80.8% (21)	72.7% (16)	38.5% (10)	18.2% (4)	42.9% (878)
Patient and/or family cancelled or delayed SMA-related appointments due to exposure concerns	95.2% (25)	86.4% (19)	65.4% (17)	63.6% (14)	n/a
Changes or limitations in accessing essential SMA-related services (e.g., physical therapy, in-home health care)	n/a	n/a	n/a	n/a	55.3% (1131)
It was a personal choice to cancel or delay any SMA-related appointment for care or treatment	n/a	n/a	n/a	n/a	34.7% (711)
None of the above	n/a	n/a	n/a	n/a	27.8% (569)

[a]The Provider Impact Survey was launched on November 24, 2020 and closed on March 8, 2021

[b]The first Community Impact Survey launched on April 7, 2020 and closed on November 18, 2020 with 1642 unique responses. The second Community Impact Survey launched on July 29, 2020 and remained open at data cut (July 16, 2021) with 442 unique responses. The third Community Impact Survey launched on November 18, 2020 and remained open at data cut (July 16, 2021) with 1026 unique responses

reason for delaying clinical trial visits was a determination by site administration that appointments were non-emergent, a cause of delays or cancellations reported by 46.2% of trial sites (Table 4). Provider determinations that appointments were non-emergent, and changes to trial protocols or informed consent documents, were also each reported as causes of appointment delays or cancellations by 30.8% of sites. Additionally, 42.3% of clinical trial sites reported cessation of pulmonary function testing, and 15.4% had ceased use of certain motor function scales (data not shown). These evidence-based assessments are integral to the evaluation of SMA disease progression and treatment response in clinical and research settings [42].

Finally, care-and-trial sites employed numerous strategies for mitigating the effects of the pandemic on clinical studies, with varying degrees of success (Fig. 6). Telemedicine and prioritization of assessments were most often ranked "very helpful" (by 66.7% and 72.7% of trial sites, respectively), whereas increased stipends and additional concierge services were most often ranked "least helpful" (by 64.3% and 43.8% of trial sites, respectively).

Table 4 Reasons for SMA appointment cancellations and/or delays, as reported by care-and-trial sites and care sites

	Types of appointment cancellations/delays							
	Appointment for SMA care[a]		Appointment for SMA treatment[a]		Appointment for SMA-related services[a]		Clinical trial	
	Care-and-trial sites ($n = 18$) % (n)	Care sites ($n = 13$) % (n)	Care-and-trial sites ($n = 7$) % (n)	Care sites ($n = 6$) % (n)	Care-and-trial sites ($n = 21$) % (n)	Care sites ($n = 16$) % (n)	Care-and-trial sites ($n = 26$) % (n)	Care sites ($n = 22$) % (n)
Executive orders by state on dental, medical and surgical procedures	61.1% (11)	61.5% (8)	28.6% (2)	66.7% (4)	47.6% (10)	62.5% (10)	26.9% (7)	–
Executive orders by city on dental, medical and surgical procedures	44.4% (8)	30.8% (4)	0% (0)	33.3% (2)	33.3% (7)	25.0% (4)	26.9% (7)	–
Hospital and/or clinic administration deemed appointment non-emergent	72.2% (13)	53.8% (7)	28.6% (2)	50.0% (3)	81.0% (17)	68.8% (11)	46.2% (12)	–
Provider deemed appointment non-emergent	72.2% (13)	61.5% (8)	28.6% (2)	33.3% (2)	61.9% (13)	56.3% (9)	30.8% (8)	–
Delays due to exposure of clinic staff to COVID-19	5.6% (1)	0% (0)	28.6% (2)	0% (0)	4.8% (1)	0% (0)	3.8% (1)	–
Delays due to clinic staff testing positive for COVID-19	11.1% (2)	0% (0)	14.3% (1)	0% (0)	4.8% (1)	6.3% (1)	3.8% (1)	–
Changes in the clinical trials protocol or informed consent	–	–	–	–	–	–	30.8% (8)	–

[a]Respondents of the Provider Impact Survey were asked to identify the cause of reported appointment cancellations or delays. Sample size reflects number of respondents that previously reported the type of appointment cancellations/delays occurred at any time within their clinic as a result of the pandemic

DISCUSSION

These combined survey results provide new perspectives on how COVID-19 has affected SMA diagnosis, care, and research. Appointment cancellations and delays were common, occurred for several reasons, and were initiated by both providers and patients and their caregivers. Community concern about potential exposure to COVID-19 was a driving factor of appointment cancellations and delays. Early in the pandemic, limited access to testing

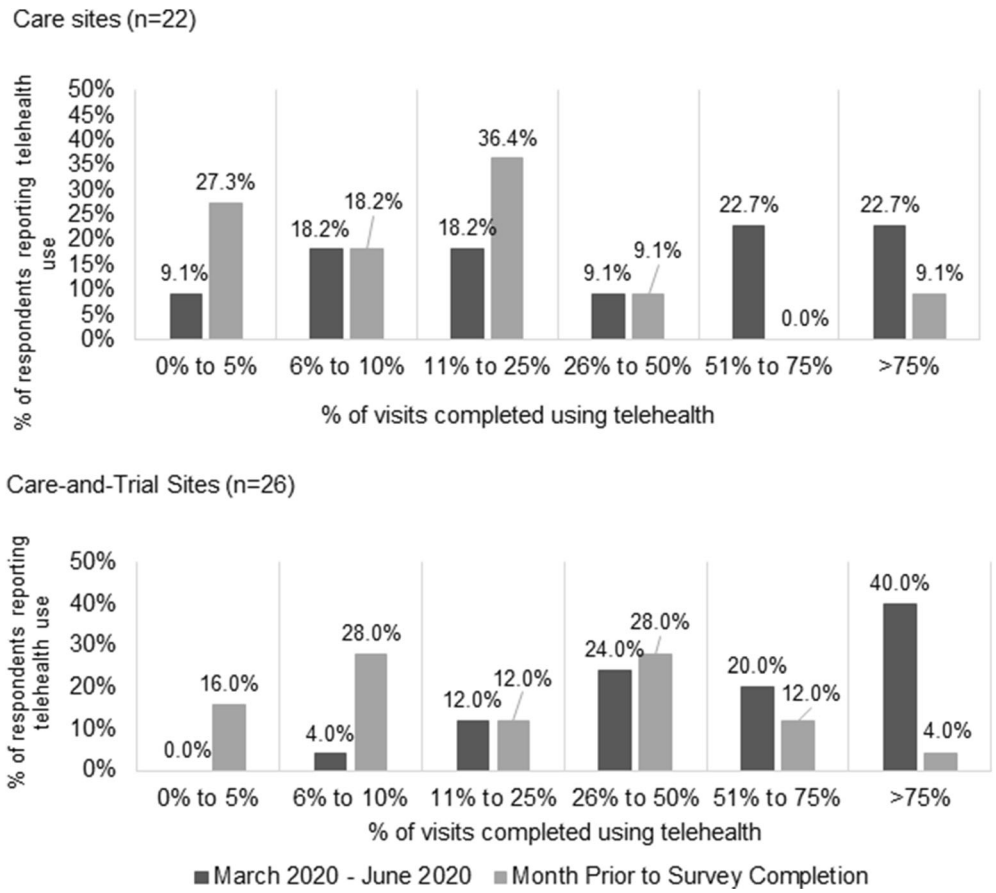

Fig. 5 Percentage of clinic visits completed using telehealth. Respondents reported percent of clinic visits completed using telehealth during the first 4 months of the pandemic (March 2020–June 2020), and the month prior to survey participation. The Provider Impact Survey was launched on November 24, 2020 and closed on March 8, 2021. Types of telemedicine services offered within practice for SMA care sites and care-and-trial sites at time of survey completion, respectively, were live video conferencing (100%, 100%), real-time telephone visit (86.4%, 76.0%), remote patient monitoring (4.5%, 0%), and store and forward asynchronous video (9.1%, 12.0%)

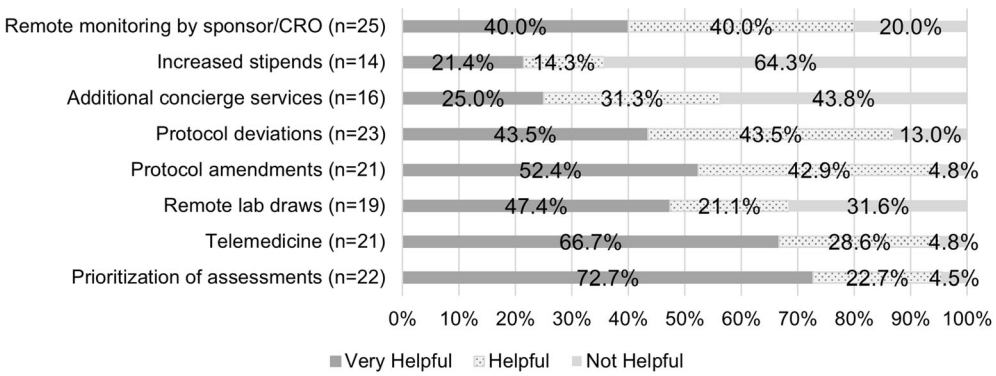

Fig. 6 Strategies for mitigating impact on clinical studies

combined with limited knowledge of COVID-19 symptoms, transmission mode, and management may have increased respondents' reluctance to risk COVID-19 exposure compared to later in the pandemic, when testing and information about COVID-19 were more accessible. The reluctance by the SMA community to pursue their in-person appointments was likely compounded by decisions made by clinics and facilities to cancel or delay appointments. To mitigate disruptions to patient care, many clinical sites used telemedicine in their practices. A larger proportion of care-and-trial sites than care sites reported using telehealth during both the early period of the pandemic (March through June 2020) and the month prior to survey completion. Reported use of telehealth declined over the year-long period covered by the survey (Fig. 5).

Although many care-and-trial and care sites were able to successfully adopt and scale telemedicine and digital tools during the COVID-19 pandemic, the rapid shift from in-person to remote care limited the opportunity for iterative testing and the evaluation of tools and processes that might have otherwise been used to ensure care quality [43, 44]. For this reason, several neuromuscular disease research groups have recently published "roadmaps" outlining processes for developing and testing disease-specific assessment protocols and tools that enable remote care and for patients with neuromuscular diseases like SMA [43–45]. Furthermore, SMA researchers and clinicians concur that remote care and treatment plans should include refinement and validation of:

1. Clinical outcome assessments, including assessments administered through telemedicine by a clinician and assessments made through patient reported outcome measures, for both motor and respiratory functions [29, 43, 46].
2. Local sites for the collection of blood samples, or mobile collection at patients' homes [34, 44, 46].
3. A plan for how to maintain the treatment administration schedule whenever possible while preserving patient safety [29, 30, 47].
4. Remote physical therapy sessions [43, 48].
5. Digital devices to monitor variables such as respiratory function, muscle strength and function, sleep, and physical activity [9, 44].
6. For clinical trials, the development of additional remote protocols to enable digital recruitment, enrollment, and informed consent [7, 9, 46].

These assessments, tools, and adaptations should be patient-centric and customized according to factors like disease severity [35, 43], comorbidities [34, 49], patient age [9, 44, 48, 50], access to the internet [43, 44], and the coadministration of drugs like corticosteroids that are necessary but lower immunity [29, 34, 36]. Additionally, strategies like use of prioritized assessments and protocol flexibility (both encouraged by the FDA during the pandemic) may help ensure trial continuity [34].

This study has several limitations. Sampling bias is a concern due to recruitment methods and the voluntary nature of all surveys. Both surveys were distributed to individuals who had opted in to receive communications from Cure SMA, are therefore likely to be more engaged with SMA than the average healthcare provider or patient, and may not be representative of the broader SMA provider and patient communities. As such, inferences about the meaning of these findings for populations beyond our survey samples should be approached with caution. If, for instance, survey respondents were more proactive about ensuring early diagnosis and care continuity than the clinical and patient communities generally, our survey may underestimate the effects of COVID-19 on SMA care and research. Apart from these issues, lack of specificity about time periods in Community Impact Survey questions may have introduced potential for variability in responses. Finally, Community Impact Survey respondents could identify as living with SMA Types 1–4, but were not given the option of identifying as "presymptomatic." This may have caused the survey to exclude or misclassify respondents, skewing the survey results.

CONCLUSION

The research findings presented here illustrate disruptions to SMA care and research created by the ongoing COVID-19 pandemic, including delays in diagnosis, interruption of SMA treatment and services, and limitations on participation in clinical trials. Collectively, these data provide an important "call to action" for SMA providers, care centers, clinical trial sites, patients, and families to collaborate in leveraging innovative approaches and implementing flexible strategies for managing any future healthcare system crisis. The pandemic created an opportunity to learn if tools that enable decentralized care, such as telehealth and remote monitoring, work well for the SMA community. As it is likely that the use of some tools may become less prevalent once the pandemic subsides, it is important for the SMA community to be deliberate in evaluating and advocating for optimal care delivery models. If developed properly, remote strategies have the potential not only to make SMA care and research more adaptable in times of crisis but also to ease the patient burden of care and clinical trial participation under normal conditions.

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Compliance with Ethics Guidelines. Prior to distribution, WIRB-Copernicus Group Institutional Review Board (WCG IRB) that the Provider Impact Survey was exempt from full IRB review and granted a consent waiver to allow for the publication of research findings. All respondents were informed via the Cure SMA privacy policy that findings may be published. All individual data was considered confidential, and only aggregate results are shared in the manuscript. This survey was conducted in accordance with the Helsinki Declaration of 1964 and its later amendments.

Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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