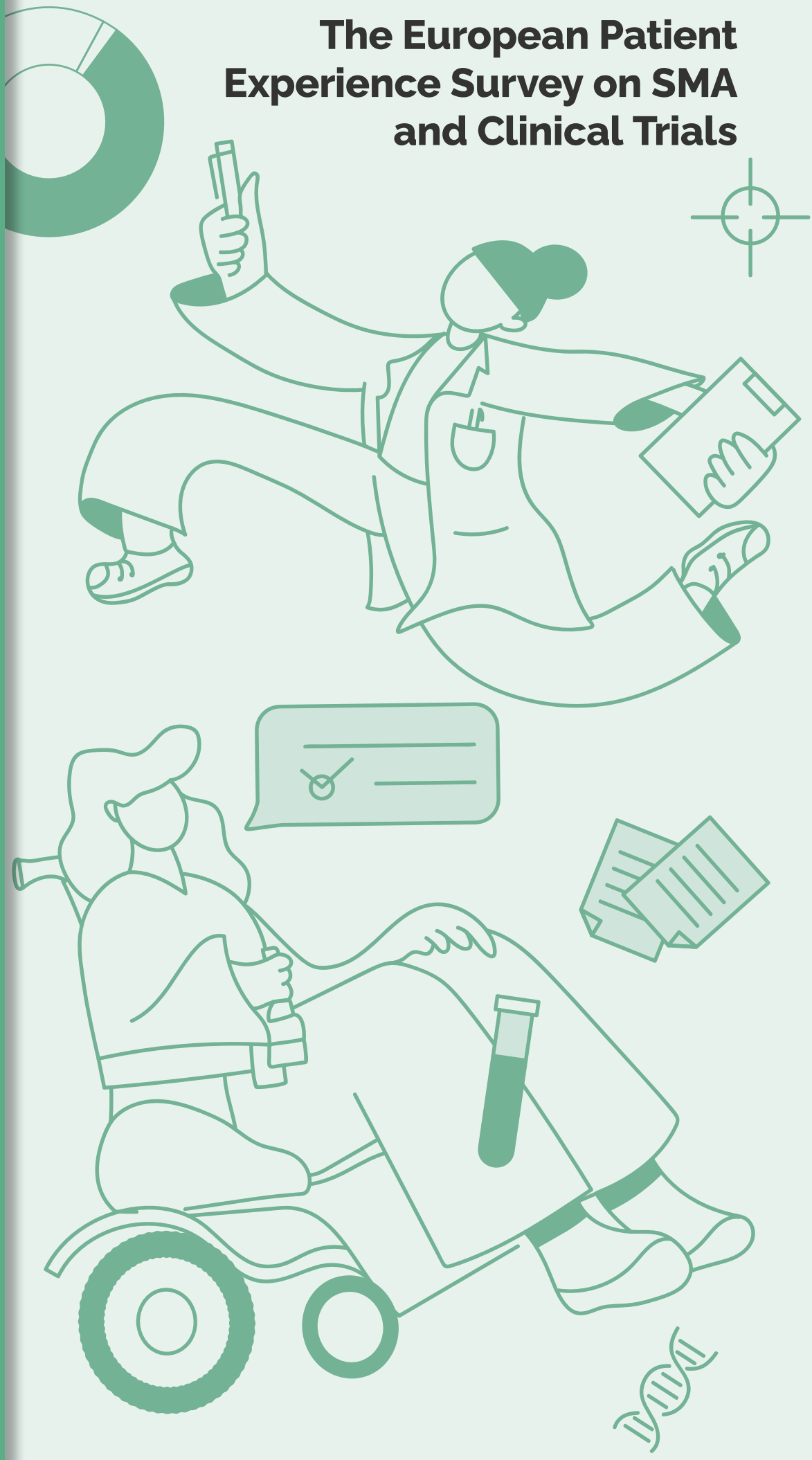
SMA EUROPE

One Goal Series

Together We Prioritise

The European Patient Experience Survey on SMA and Clinical Trials



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Acknowledgements

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SMA Europe extends special thanks to all its volunteers, including members of the Adults Committee, Treatment Committee, and SMA Europe Delegates, whose contributions were vital to the success of the project, from helping to define the survey's scope and design to piloting, translating, and disseminating it for maximum reach and participation.

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SMA Europe

SMA Europe is a non-profit umbrella organisation of spinal muscular atrophy (SMA) patient organisations from across Europe. Together, through greater understanding, we work towards creating a better world for all those living with SMA.

United, at European level and in collaboration with all stakeholders, we achieve our vision of creating a better world for all those living with SMA. This is our reason for being, above all else. It infuses everything we do and is what we invite others to help us achieve.

SMA Europe works to bring effective treatments and optimal care to everyone affected by SMA.

Research

We accelerate breakthrough research in SMA through our biennial call for research proposals and our scientific congresses.

Advocacy

We use evidence-based advocacy and represent the voice of patients in decisions that affect them.

Awareness & Outreach

We campaign to raise awareness for SMA and promote the interests of our community.

We always put the voice of those affected by SMA at the heart of everything we do by:

Empowering our member organisations to advocate and campaign for them at a national level; and

Influencing healthcare, pharmaceutical, and regulatory decision-makers to involve them at an international level.

Only through true representation of the SMA community – the unique wants, experiences and aspirations of the people behind the condition – will their voices be heard and needs be met.

The EUPESMA Survey Series

Our European Patient Experience Survey (EUPESMA) Series is designed to map the experiences and expectations of people living with SMA and to ascertain their needs and wants. With this evidence, SMA Europe advocates for equitable access to optimal treatment and care in Europe.

Why do we need Pan-European patient experience surveys?

Access to treatment and care solutions remains fragmented and unequal. **Community-generated data gives a credible, collective voice to advocate** for fairer policies and equal access for all.

Europe-wide results show where care and treatment work well and where gaps remain, helping to **understand expectations, design solutions** that respond to real needs, and **generate tangible impact.**

People living with SMA have diverse experiences and needs. Community surveys ensure that every voice is heard, because each single one of them is equally important.

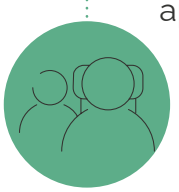
By gathering data directly from individuals and families living with SMA, **surveys translate lived experience** into reliable evidence that reflects everyday realities.

EUPESMA Survey on SMA and Clinical Trials

The EUPESMA Survey on SMA and Clinical Trials aimed to understand the experiences and expectations of people living with SMA as it relates to clinical trial participation.

The survey was open to people living with SMA (16 years old or older), and parents and caregivers of people living with SMA, including both people who had participated in clinical trials before and people who had not.

The survey was designed in close collaboration with people living with SMA and their caregivers for accuracy and appropriateness.



The EUPESMA Survey was approved by the Ethics' Review Board at Tilburg University. SMA Europe member organisations disseminated the survey in their communities.

The data was collected between December 2023 and February 2024.

Translations were available in 14 European languages: Czech, Dutch, English, French, German, Greek, Italian, Polish, Romanian, Russian, Serbian, Spanish, Swedish, and Ukrainian.

We received a total of 895 survey responses from 51 countries around the world [1].

[1] **Methodological note:** All responses to our survey questions were optional and participants could skip any question. The data and percentages reported in this document reflect the proportion of people who responded to each question.

Why a focus on clinical trials?

Since 2017, three pharmacological treatments for SMA have been approved by the European Medicines Agency (EMA) after being tested for safety and effectiveness in clinical trials.

Clinical trials remain key for the SMA community, ensuring that new and improved medicines for SMA continue to be developed. Indeed, today, existing medicines are still being tested to observe their effectiveness over time and in diverse groups of people living with SMA. In addition, improved versions of existing medicines, new SMN protein enhancers, along with new therapies targeting muscles and other areas (e.g., neuromuscular junctions) are also being developed, bringing hope for further positive impacts on the condition.

The success of a clinical trials depends on a variety of factors, including the recruitment of people living with SMA who meet the established criteria for the study, and are willing to participate to all procedures throughout the duration of the trial. While clinical trial participants may expose themselves to some risks, they may also have early access to therapies that may not reach the market for many years.

What are clinical trials?
Did you know?

Clinical trials are research studies conducted to evaluate the safety, effectiveness, and potential side effects of medical products, devices, or interventions in individuals with specific conditions. Before a medicine or treatment can be marketed, regulatory agencies like the European Medicines Agency in Europe, the Food and Drugs Administration in the USA, or other national bodies, require substantial evidence from these trials to ensure that the benefits of the drug outweigh its risks. The conduct of clinical trials must also be approved by these regulatory bodies to ensure that they meet ethical and scientific standards.

Typically, clinical trials proceed through phases: phase 1 (testing safety and dosage), phase 2 (evaluating efficacy and side effects), phase 3 (confirming effectiveness and monitoring long-term safety), and phase 4 (post-market surveillance to track long-term effects).

Conducting clinical trials in rare diseases like SMA, however, can present specific challenges due to the small size of the population living with the disease, the urgent need for treatments, a limited understanding of disease pathophysiology (the physiological processes that cause or result from a disease), and challenges in recruiting control groups. Rare disease clinical trials can therefore require adaptive designs to improve the efficiency of the study. For example, these studies may rely on populations that are more heterogeneous than in a typical trial. Historical data or prior knowledge may be used as control groups to replace or supplement control groups. Real-time adjustments to the clinical trial design may also be adopted based on the data collected during the study. Rare disease clinical trials might therefore have to rely on smaller numbers of participants or broaden inclusion criteria to accelerate recruitment time and optimise product development to help bring treatments to approving authorities faster.

Understanding how to best facilitate and improve clinical trial participation for people living with SMA is therefore vital to ensure that medicines for SMA can continue to:

- be developed and tested for safety and effectiveness,
- reach the market and, consequently, people living with SMA.

Seeking direct input from people living with SMA is crucial to clinical trial success, and a good practice that needs to be routinely integrated in the process of clinical trial design.

For instance, designing patient-friendly clinical trials can help improve feasibility for participants, making it easier to enrol and participate in all phases and procedures of the study. Similarly, conducting clinical trials for substances that address patient-relevant issues can help ensure interest in the medicine and adherence to the therapy once the new drug is on the market.

The EUPESMA 2023 Survey on SMA and Clinical Trials sought to provide insight into clinical trial participation experiences, challenges to participation, and future wishes in relation to clinical trials to shed light on patient perspectives that can inform the design of future clinical trial and enhance their success.

"Clinical trials bridge research and care. Their impact relies on how they are designed and conducted."

Clinical Trials in SMA
Did you know?

Following the identification of the SMN1 gene in 1995, efforts focused on developing disease-modifying treatments. In 2011, the first clinical trial began for nusinersen (Spinraza®), an intrathecal medicine that enhances SMN protein production. Spinraza® became the first medicine approved in the European Union for SMA in 2017. Meanwhile, a gene therapy delivering a functional copy of the SMN1 gene (onasemnogene abeparvovec-xioi, Zolgensma®) was developed and underwent clinical testing, receiving approval in 2019. Finally, in 2021, another disease-modifying treatment, Risdiplam (Evrysdi®), an SMN protein enhancer administered orally, was approved.

Current clinical trials focus on advancements in gene therapy and SMN protein enhancers, muscle-targeted therapies, and other therapeutic approaches, such as targeting neuromuscular junctions to improve communication between motor neurons and muscle cells.

For further information, please visit:
sma-europe.eu/clinical-trials-for-sma

Who participated in this survey?

Countries
of residence

SMA as a spectrum: towards a new disease description for SMA

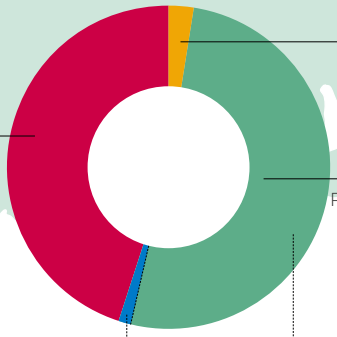
What characteristics best describe SMA? How do we identify them in a changing disease landscape?

SMA is a widely heterogeneous disease that impacts individuals in different ways and to different degrees. Traditionally, SMA has been treated as a disease that could be classified in rigid groups, SMA types, based on symptom onset and the motor functions achieved by an individual. However, this categorisation fails to account for the significant variability in both the symptoms and the progression of the disease among individuals living with SMA within each type.

The diversity of experiences of people living with SMA has become even more significant now that better care and disease-modifying therapies are available. Early diagnosis and newborn screening can help identify the condition even before the first visible symptoms appear, and SMA medicines have transformed the natural history of the disease, that is how the condition was known to progress overtime in the absence of treatment. In addition, it has become increasingly clear that the impact of SMA goes beyond motor function and further factors play a critical role in the condition.

SMA Europe is working on a new, encompassing description of SMA that better captures the lived reality of the condition as one that includes multiple domains and presents along a complex spectrum different for each individual. Our hope is that this new description will help surpass the outdated classification, which is still often used to limit access to SMA treatment and care.

Profiles



45%
Father, mother, or legal guardian of the person with SMA.
n = 389

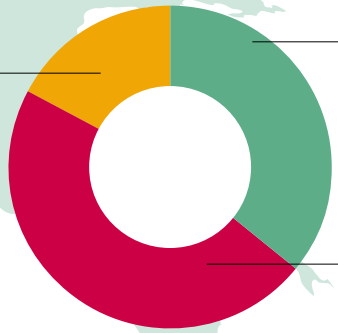
2.6%
Another person
n = 22

52.4%
Person with SMA themselves
n = 447

1.5%
Completing the survey with assistance
n = 13

50.9%
People completing independently
n = 434

Mobility status

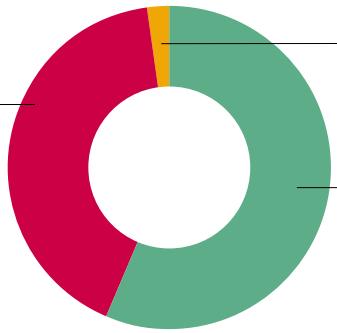


36.1%
Non-sitters
n = 237

16.8%
Walkers
n = 110

47.1%
Sitters
n = 309

Sex

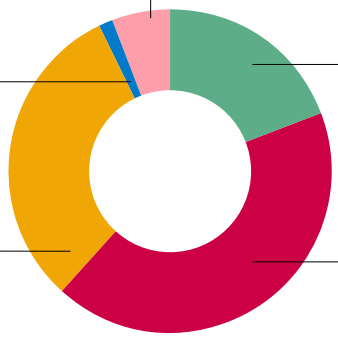


41%
Male
n = 318

2%
Prefer not to say
n = 15

57%
Female
n = 435

SMA Types



2,9%
Others
n =26

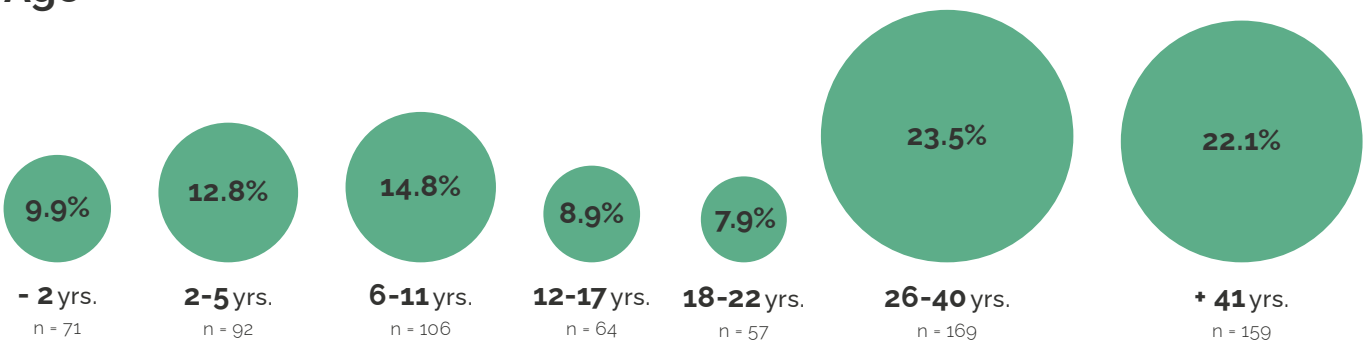
1,4%
Type IV
n = 10

19,7%
Type I
n = 139

31,9%
Type III
n = 225

43,3%
Type II
n = 306

Age



9.9%
- 2 yrs.
n = 71

12.8%
2-5 yrs.
n = 92

14.8%
6-11 yrs.
n = 106

8.9%
12-17 yrs.
n = 64

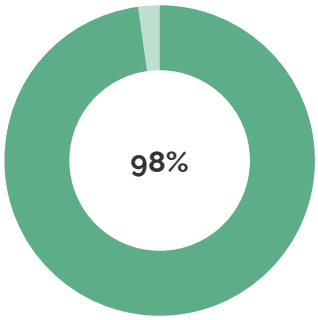
7.9%
18-22 yrs.
n = 57

23.5%
26-40 yrs.
n = 169

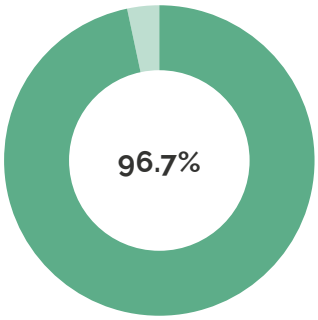
22.1%
+ 41 yrs.
n = 159

Is there a pending need for new clinical trials in SMA?

SMA is a rather unique case in the rare disease arena in that three disease-modifying therapies have been approved and on the market. In addition, new compounds are also currently being tested. Even in this landscape, our data shows that survey participants think that there still is a need for new clinical trials in SMA and for new SMA medicines.



Say there is a need for new clinical trials
n=629



Say there is a need for new SMA medicines
n=623

What should future clinical trials in SMA focus on?

When asked what clinical trials in SMA should focus on in the future, the most frequently chosen areas of preference were (n=644):

71.3%
New treatments for SMA

70.2%
Muscle treatments

62.7%
Regenerative medicine

55.1%
Improving breathing

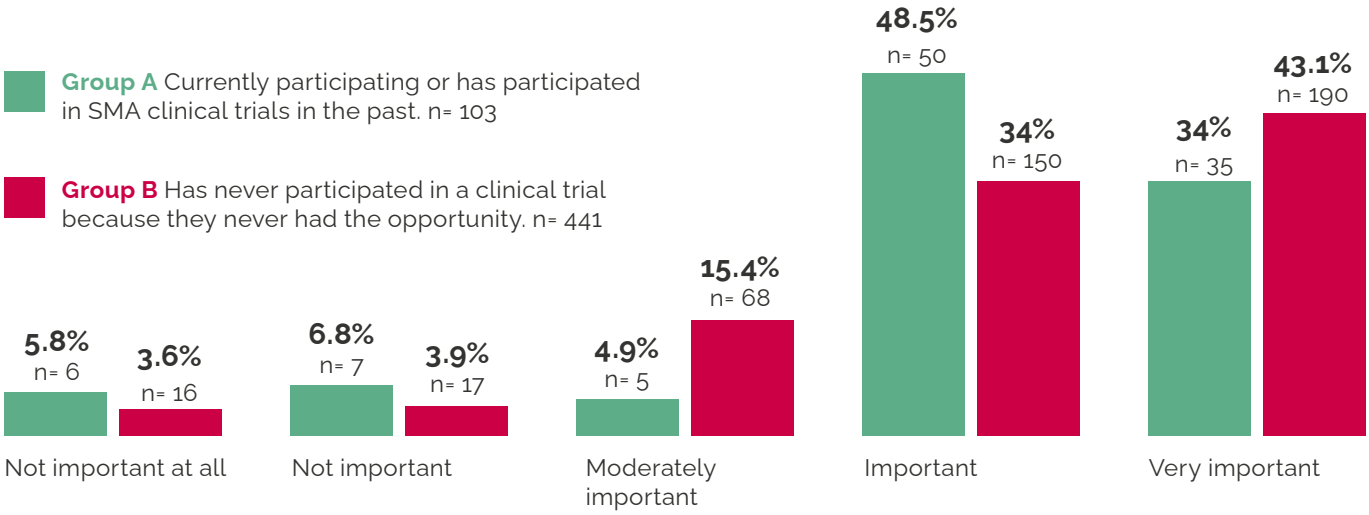
53.8%
Improving versions of existing treatments

What are the expectations regarding clinical trials' design?

Expectations on open label extensions

Another important aspect to consider when participating in a clinical trial is whether an open label extension will be granted at the end of the trial, that is, if you can continue to receive the substance being tested after the clinical trial ends and the substance has been proven safe and effective.

We asked participants in groups A and B how it important it was to them that an open label extension was granted at the end of a clinical trial. In both groups A and B, most participants reported it was "important" or "very important".



What is an open label extension?

Did you know?

The Declaration of Helsinki on the Ethical Principles for Medical Research Involving Human Participants states that:
"In advance of a clinical trial, post-trial provisions must be arranged by sponsors and researchers to be provided by themselves, healthcare systems, or governments for all participants who still need an intervention identified as beneficial and reasonably safe in the trial."

In other words, clinical trial participants should be presented with the option to continue receiving the intervention or substance being tested after the trial ends, provided that no harm has been identified.

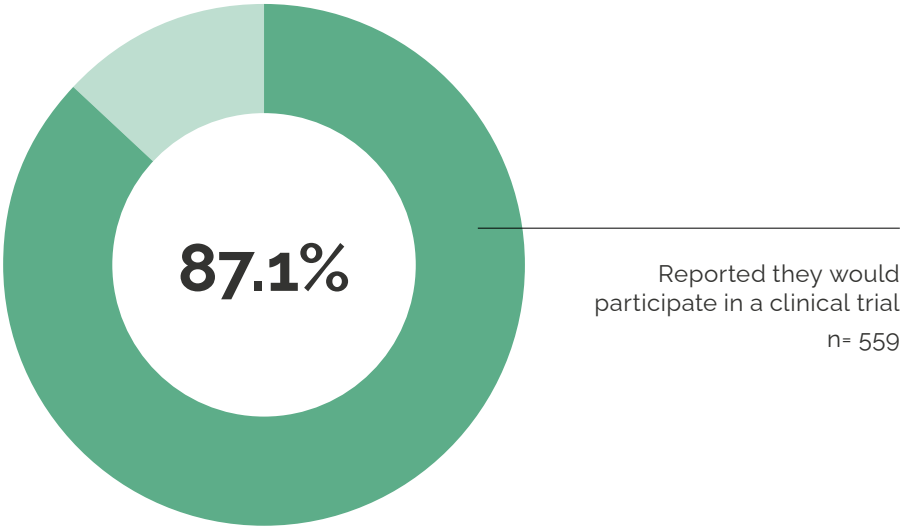
Open label extensions are post-clinical trial provisions that allow study participants to continue to receive the tested substance after the clinical trial has ended and while it is under the process of being approved by regulatory authorities, for instance the European Medicine's Agency.

Open label extensions are often advantageous for researchers and trial sponsors as well, because, if embedded in the clinical trial design, they allow to continue to collect additional data on the efficacy, tolerability, and safety of the drug.

Even so, an open label extension is not always guaranteed, and clinical trial participants should pay close attention to this aspect when signing up for a clinical trial.

Are people living with SMA willing to participate in clinical trials?

People living with SMA are willing to participate in clinical trials



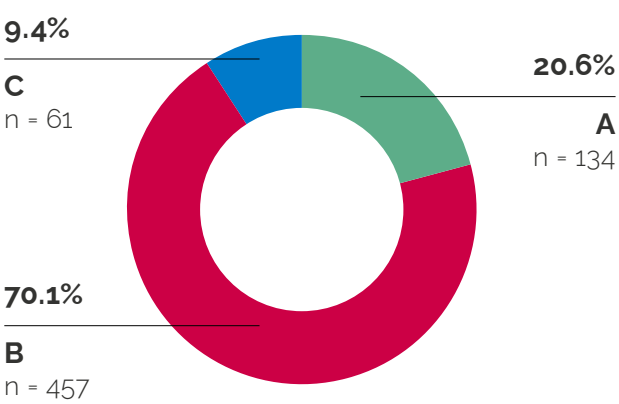
Participation in SMA Clinical Trials

From here on, we will refer to this following groups when presenting our survey data:

Group A
Currently participating or has participated in SMA clinical trials in the past

Group B
Has never participated in a clinical trial because they never had the opportunity

Group C
Has never participated because they did not want to



The following sections explore how we could ensure that people living with SMA continue to be interested in clinical trials, but also how clinical trials could be designed in patient-centric ways to facilitate participation. This is crucial because clinical trials remain a key instrument to improving current medicines and making sure new and complementary medicines can continue to be developed.

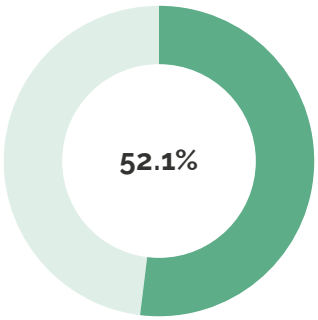
What was it like to participate in a clinical trial?

Only a small percentage of our survey participants (20,6%, n=134), had previously participated or was currently participating in a clinical trial for SMA.

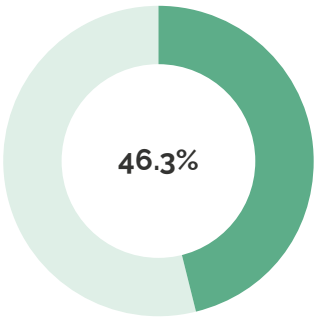
Most clinical trial participants had participated in one clinical trial (81,5%), and only a small percentage had participated in two trials (12,3%) or more (6,2%).

Clinical trial participants had participated in trials that had started between 2000 and 2023, with 73,6% of trial participants having started their trial after the year 2020 with, 44,2% of trials still running and 55,8% already closed.

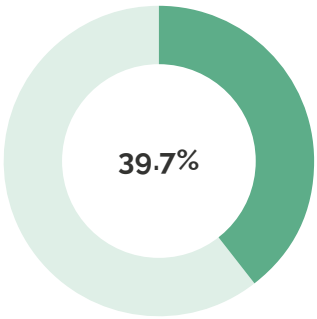
Why did clinical trial participants decide to participate in a clinical trial?



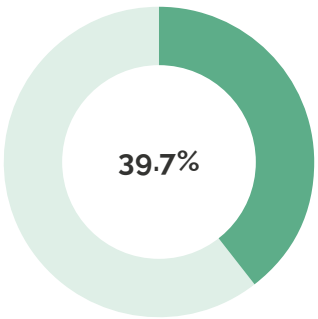
Stop disease progression
n= 63



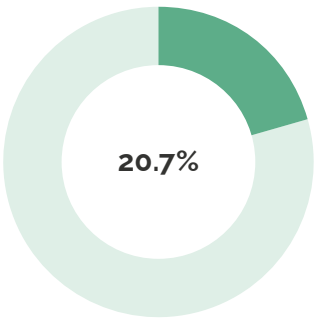
Early access to medicine
n= 56



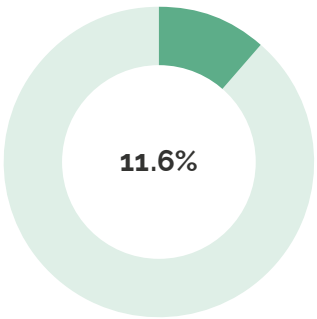
Only way to access treatment
n= 48



Enhancing current treatment
n= 48



Access to specialised care
n= 25

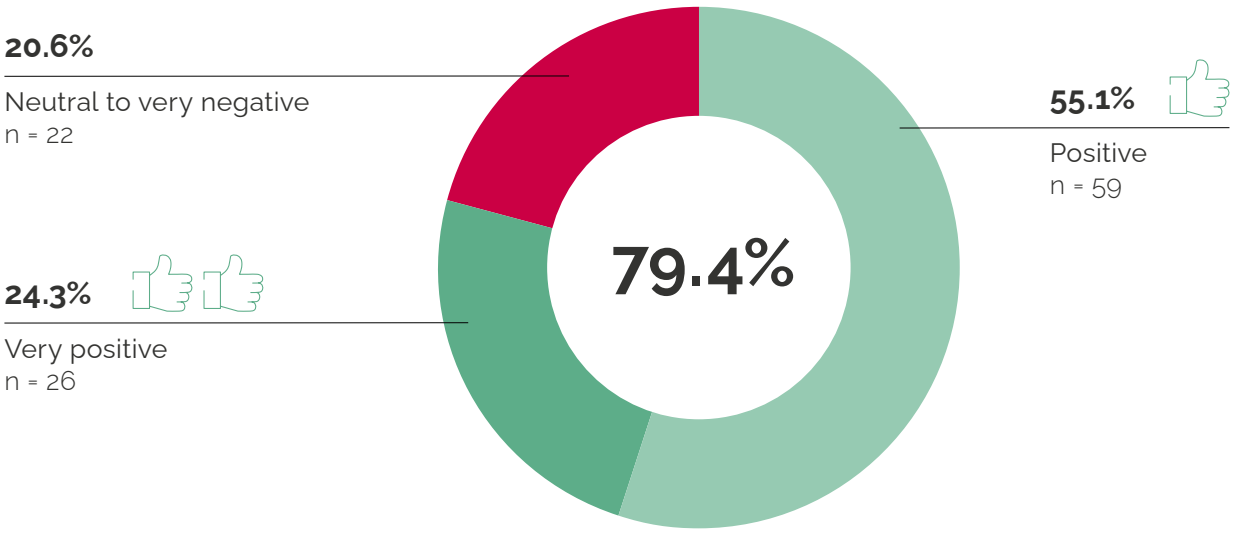


Other
(Including helping research)
n= 14

What was their experience like?

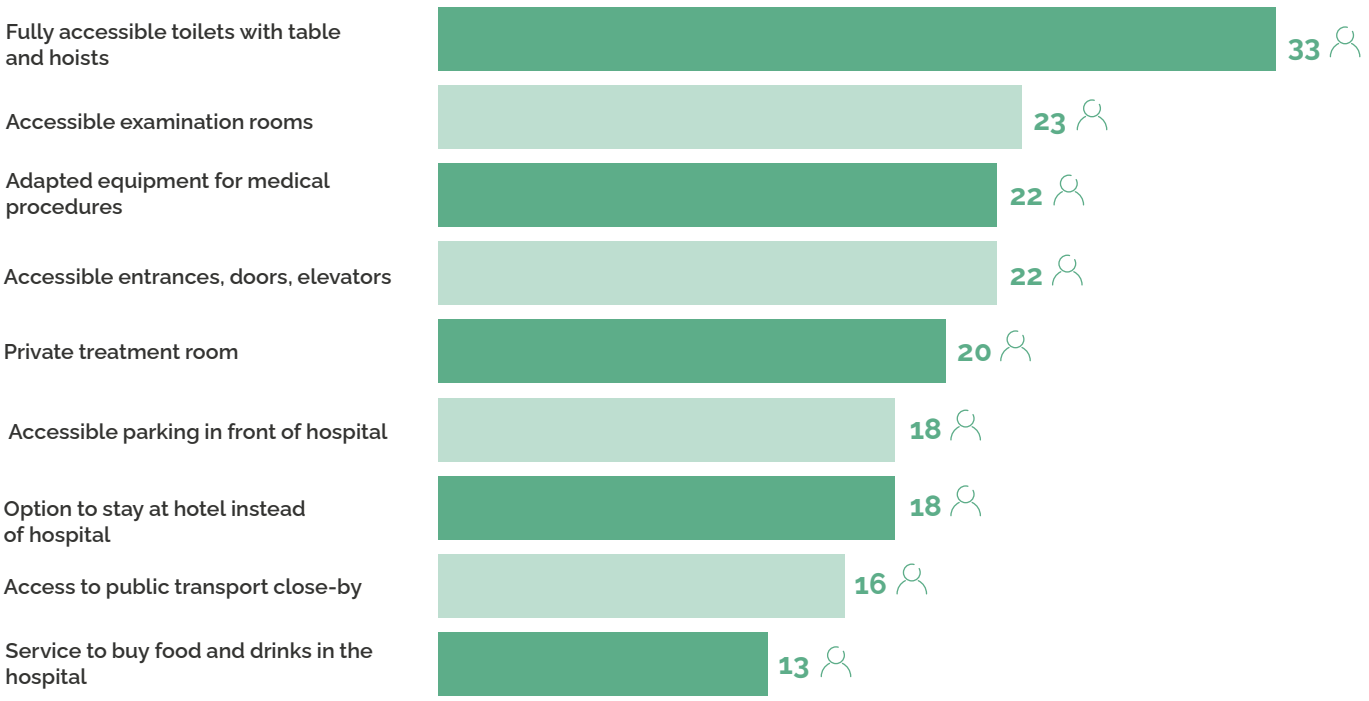
Overall, 79,4% of our survey participants found their experience participating in a clinical trial positive (55,1%) or very positive (24,3%).

Still, some identified areas of potential improvement and unmet needs that could be address when designing new clinical trials with a patient-centric approach in the future.



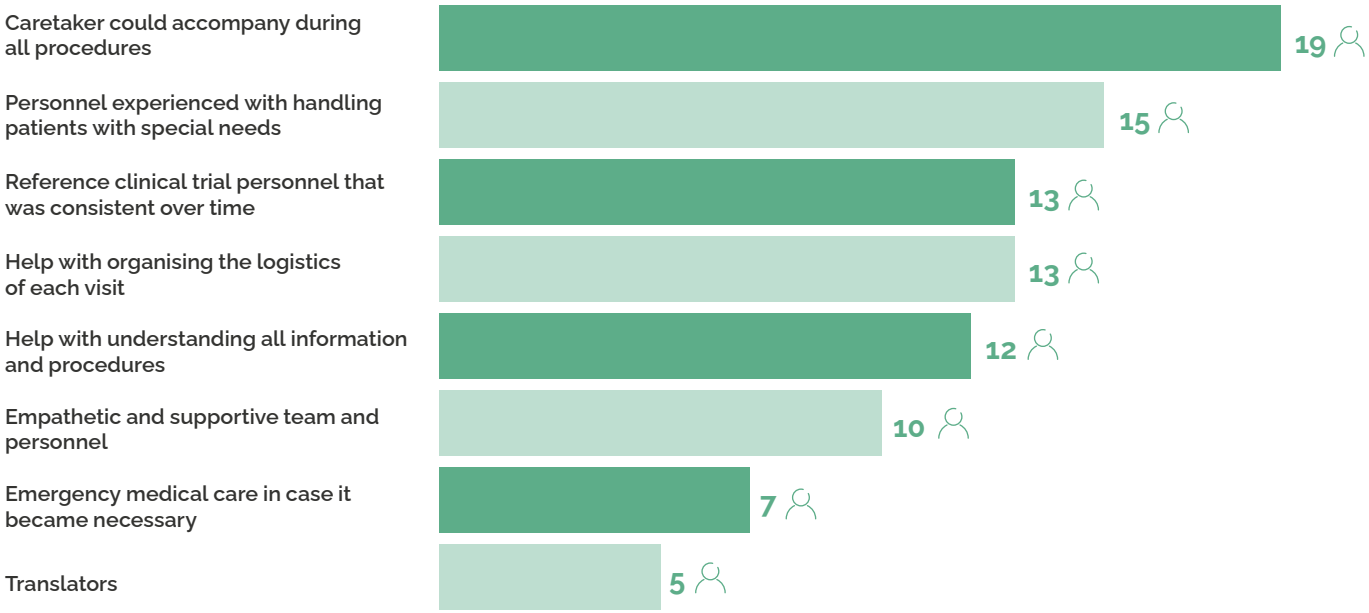
Missing infrastructure

While the majority of group A participants found their experience with the clinical trial hospital infrastructure positive or very positive (74,3%, n=81 of 109 responding), some clinical trial participants (n= 73) reported missing essentials such as fully accessible toilets or examination rooms, adapted equipment for medical procedures, and more.



Missing services

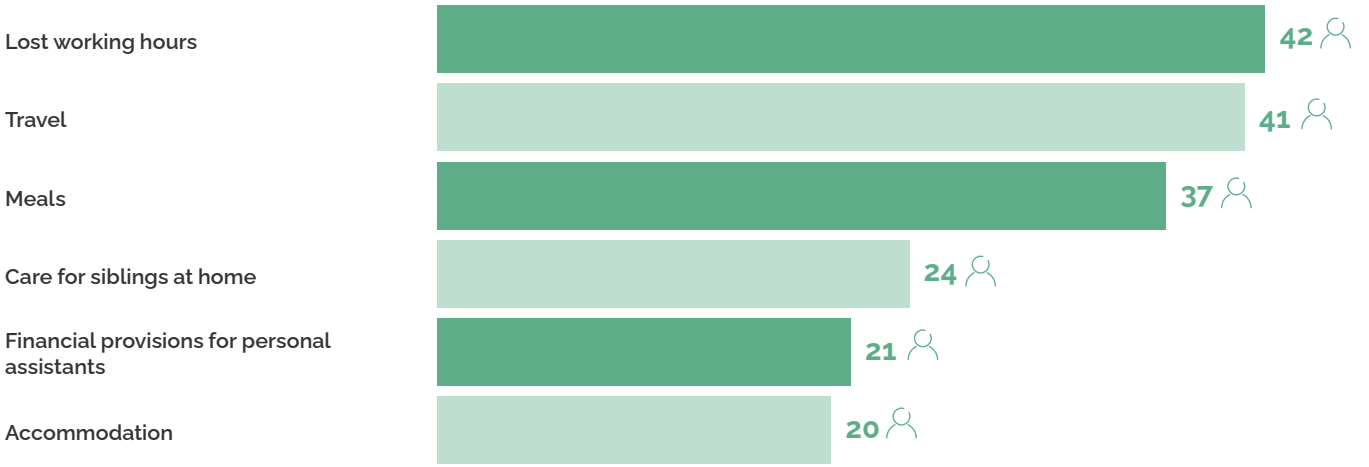
Similarly, 85% (n= 92) of participants responding to this question had a positive or very positive experience with the services offered at the clinical trial site. Yet, some participants (n=53) reported that they would have needed essential services that were not available to them. This included having a caregiver accompanying the patient during all procedures, dealing with personnel experienced with handling patients with special needs, or having a consistent reference person throughout the duration of the trial.



Missing cost coverages

The majority of Group A answering this question (n=110) reported their experiences with the coverage of costs and expenses to be neutral (40%, n=44) or positive (42%, n= 46).

Of 85 participants answering this question, some reported that some of the following expenses were not reimbursed, including compensation for missed working hours, travel and meals.



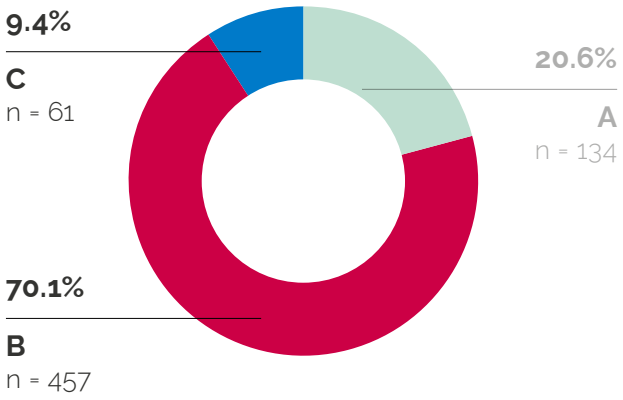
Number of people reporting missing of infrastructure, services, and cost coverage.

What about those who never participated in a clinical trial?

Our survey respondents who had never participated in a clinical trial were divided into two groups based on why they never participated to a clinical trial:

Group B, who never participated because they did not have the opportunity, and

Group C, who never participated because they did not want to.



Wanting to, but not having the opportunity to participate

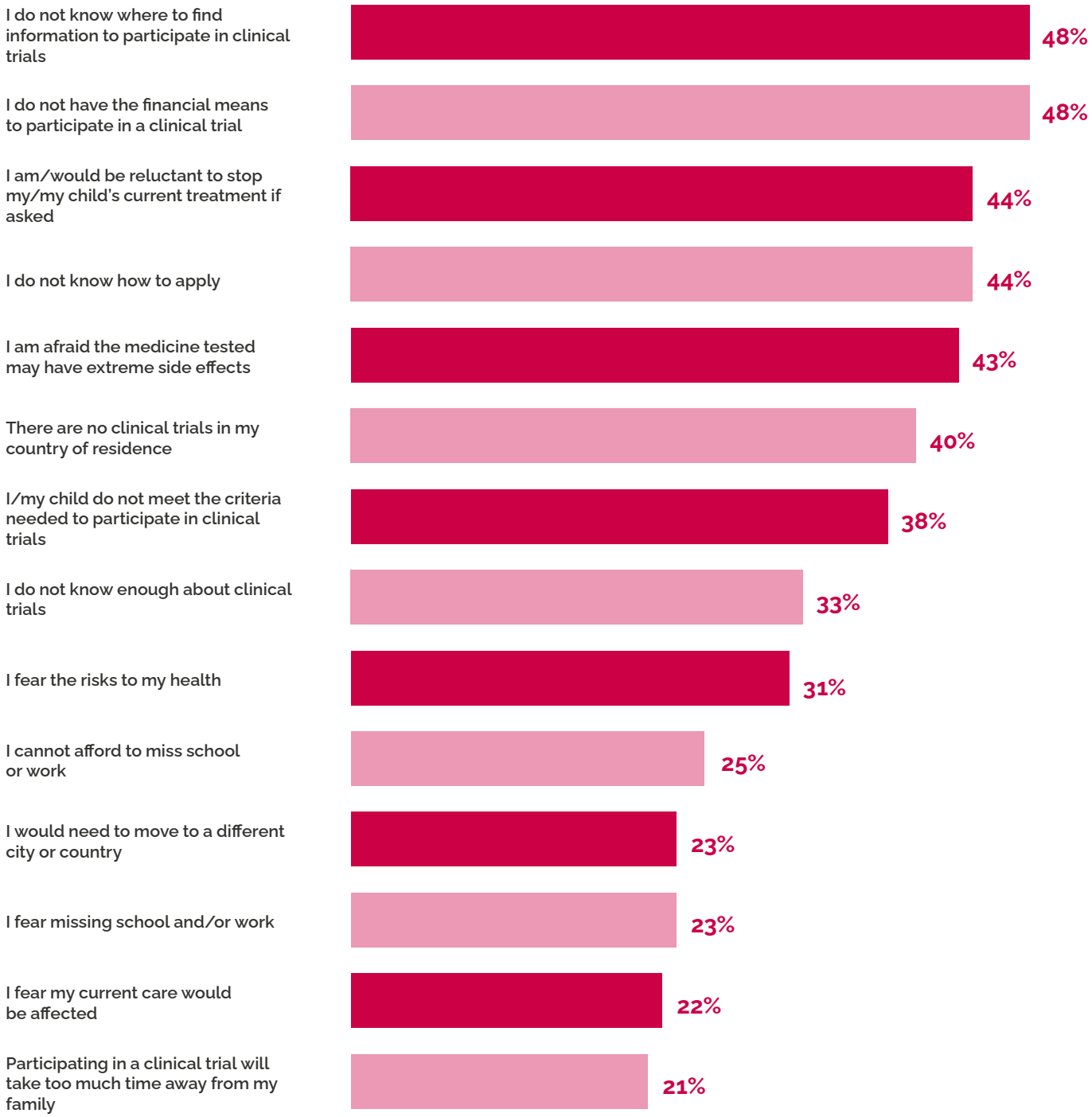
Group B, who reported never participating in a clinical trial because they did not have the opportunity to do so, represented the largest group of our total survey respondents (70,1%, n = 457).

But why were they not able to participate?
The top two reasons for not participating mentioned by our Group B participants have to do with a lack of information about clinical trials and how to apply to participate in one. Importantly, this obstacle to clinical trial participation has the potential to be overcome with better and more systematic information to the patient community.

The third most-mentioned reason has to do with the absence of clinical trials in the participant's country, closely followed by not meeting the clinical trial criteria. These challenges may prove more complex. Clinical trials need to be conducted in well-established and trusted clinical trial sites; however, measures could be in place to support participants in traveling to sites outside their home countries, including support with finances, logistics, and family support. Inclusion and exclusion criteria that establish who can participate in a clinical trial are vital to the scientific soundness of the clinical trial, and participant groups that are too heterogeneous may impact identifying clear trends in the effect of substances being tested. At the same time, it is important that these criteria are expanded to improve representation throughout the SMA continuum to test efficacy in different sub-groups.

Group B reported the following reasons

Results with percentage of participants in Group B with 20% or above.



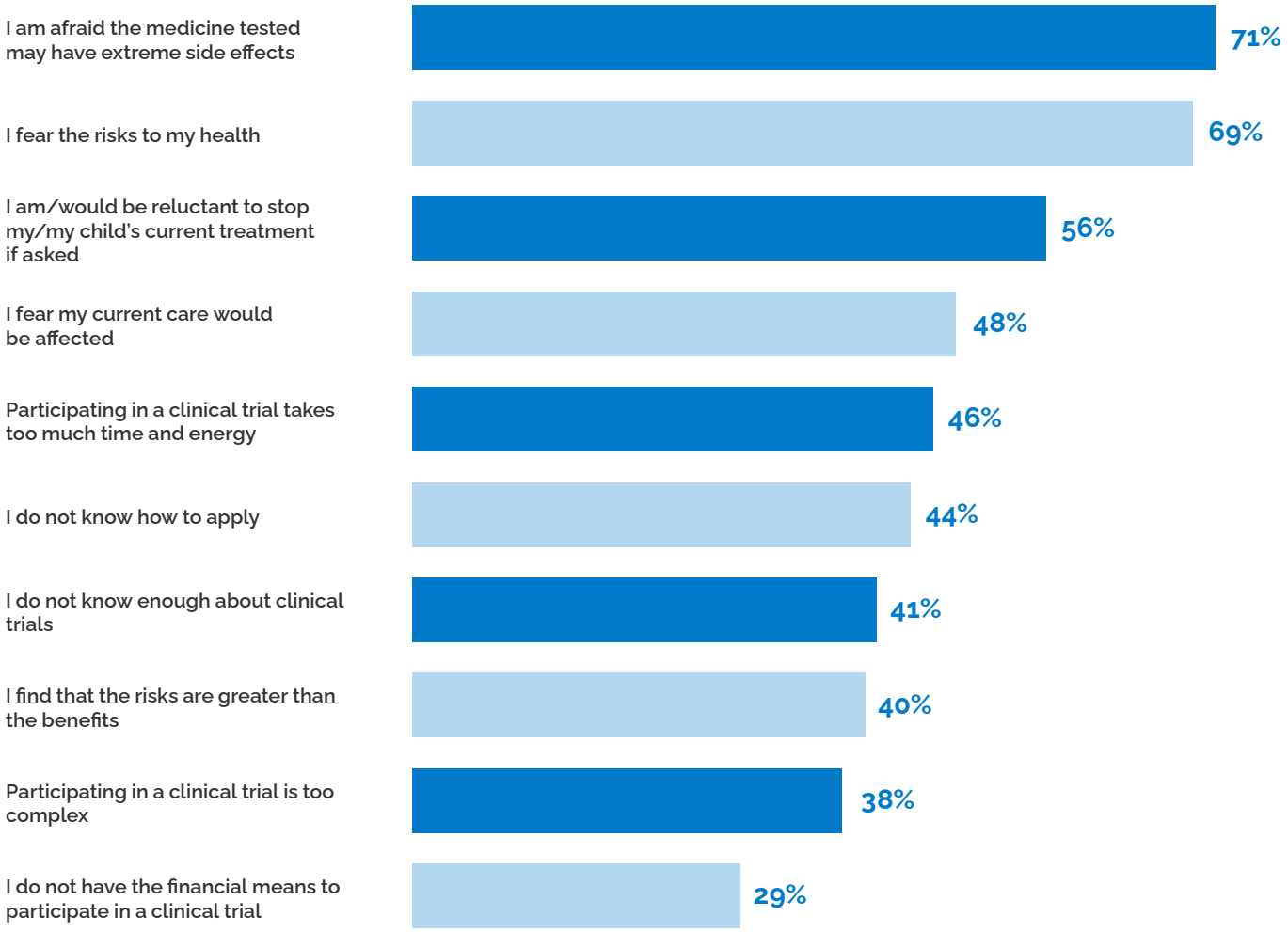
Not participating because of not wanting to

A smaller group, **Group C**, in our survey reported never having participated in a clinical trial because they did not want to (9,4%, n = 61).

Fears about risks and extreme side effects rank among the top reasons for not wanting to participate in clinical trials. These reasons are followed by concerns that current treatment would need to be suspended or that current care would be affected by clinical trial participation.

Group C reported the following reasons

Results with percentage of participants in Group B with 20% or above.



Conclusions

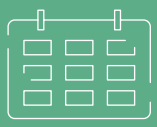
The EUPESMA Survey on SMA and Clinical Trials provides patient experience data for patient advocates as well as stakeholders in the pharmaceutical industry, regulatory realm, and policy sector about current experiences, challenges, and future wishes in clinical trial participation among people living with SMA in Europe.

Our survey participants...

Overwhelmingly **reported a pending need for new medicines and new clinical trials** for SMA.

Expressed a **preference for new trials** that would focus both on new treatments and improved versions of existing treatments for SMA.

Would want new studies to focus on **muscle treatments**, **regenerative medicine**, and **improving breathing.**



Consider **open label extension provisions** as an **important and very important** factor for deciding to participate in a clinical trial.

Are willing to participate in clinical trials, but many never had this opportunity before.

Had **positive experiences** in participating in clinical trials, yet much is still to be improved to make clinical trials more patient-friendly, including better infrastructure, services, and cost coverage.

Had many reasons for wanting to participate in clinical trials, the top-reasons being to **stop disease progression, gain early access to medicine,** and because it was the only way to access treatment.

Listed different reasons for not participating in a clinical trial. For those seeking opportunities to participate in clinical trials, the main reasons had to do with a **lack of information** on clinical trials and enrolment. For those who do not want to participate, the reasons focused on **fears about risks** involved in clinical trial participation.

List of acronyms and abbreviations

Adaptive Trial Design: Flexible clinical trial model allowing protocol modifications based on ongoing results.

Adult Committee of SMA Europe: SMA Europe volunteer group contributing to the projects and initiatives of the organisation, composed of adults living with SMA.

ATMP: Advanced Therapy Medicinal Product (innovative therapies such as gene and cell therapies).

Cure SMA: U.S.-based nonprofit organisation dedicated to improving the lives of individuals with Spinal Muscular Atrophy.

Declaration of Helsinki: Ethical principles for medical research involving human subjects.

DNA: Deoxyribonucleic Acid (the hereditary material that carries genes, which contains the instructions essential for growth, development, functioning, and reproduction).

Disease-modifying therapy (DMT): A treatment that targets the underlying causes of a disease to slow or alter its natural course and improve patient outcomes.

EMA: European Medicines Agency.

Ethical Approval: Permission from an ethics committee to conduct a study.

ERB: Ethics Review Board (for EUPESMA: Tilburg University Ethics Review Board).

EU: European Union.

EUPESMA: European Patient Experience Survey on SMA.

Evrysdi® (risdiplam): Oral SMN protein enhancer; approved in 2021.

FDA: Food and Drug Administration (United States).

Gene Therapy: Treatment that introduces or modifies genetic material to produce a therapeutic effect.

Group A: People currently participating in or who have participated in SMA clinical trials.

Group B: People who never participated in a clinical trial because they lacked the opportunity.

Group C: People who never participated because they did not want to.

Heterogeneous Population: Diverse participant group in clinical trials, common in rare disease research.

Historical Control Group: Use of prior data as a control instead of a randomised control group.

mRNA: Messenger RNA (a molecule that carries genetic instructions from DNA to the cell's protein-making machinery).

NMJ: Neuromuscular Junction (The connection between a motor neuron and a muscle fiber; targeted in new SMA therapies).

n: A statistical abbreviation representing the "number" or count of respondents for a particular answer.

OLE: Open Label Extension. Continued treatment phase after a clinical trial ends, allowing ongoing access to a tested drug.

Pan-European: Covering multiple European countries.

Phase 1: Testing safety and dosage of a new drug, normally in a small group of healthy volunteers.

Phase 2: Evaluating efficacy and side effects in patients.

Phase 3: Confirming effectiveness and monitoring long-term safety in a larger patient population.

Phase 4: Post-market surveillance after a drug's approval.

% (Percentage): Indicates proportion or share in survey results.

≈ (Approximately): Indicates rounded or approximate numbers.

®: Registered Trademark (indicates that a name or logo is officially registered as a trademark with the relevant authority).

Post-Market Surveillance: Continuous monitoring of a drug's safety and effectiveness after release.

QoL: Quality of Life (implied measure used in SMA Europe studies).

RCT: Randomised Controlled Trial (standard type of clinical research).

Regulatory Authority: Official body (like EMA or FDA) overseeing and approving clinical trials.

SMA: Spinal Muscular Atrophy.

SMA Delegates: Representatives from SMA Europe's member organisations.

SMA Europe: Spinal Muscular Atrophy Europe (the umbrella organisation of SMA patient associations in Europe).

SMN: Survival Motor Neuron (protein critical for motor neuron health).

SMN1: Survival Motor Neuron 1 gene (defective in SMA).

SMN2: Survival Motor Neuron 2 gene (backup gene partially compensating SMN1 deficiency).

SMN Protein Enhancer: A therapy increasing the production of the SMN protein.

Spinraza® (nusinersen): First disease-modifying treatment for SMA, approved in 2017; an SMN protein enhancer administered intrathecally.

Treatment Committee: SMA Europe group composed by expert patient advocates focusing on therapy-related matters.

U.S.: United States of America.

yrs: Abbreviation for "years" (used in the "Age" demographic chart).

Zolgensma® (onasemnogene abeparvovec-xioi): Gene therapy delivering a functional SMN1 gene; approved in 2019.

SMA EUROPE

Additional information

For any questions, or more detailed data, you can send a request to SMA Europe

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