BEST PRACTICES FOR CLINICAL RESEARCH COORDINATORS IN SPINAL MUSCULAR ATROPHY (SMA)

RECOMMENDATIONS TO SUPPORT THE EFFECTIVE CONDUCT OF CLINICAL TRIALS IN SMA

cure SMA

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Authorship & Acknowledgements

The Cure SMA Industry Collaboration (SMA-IC) was established in 2016 to leverage the experience, expertise, and resources of pharmaceutical and biotechnology companies, as well as other nonprofit organizations involved in the development of spinal muscular atrophy (SMA) therapeutics to more effectively address a range of scientific, clinical, and regulatory challenges. Current members include Cure SMA, Scholar Rock, Biogen, Novartis, Biohaven Pharmaceuticals, Genentech/Roche, Alcyone Therapeutics, NMD Pharma, and SMA Europe. Funding for this project was provided by members of the 2018 -– 2021 and 2023 SMA-IC which included Astellas Pharmaceuticals, Biogen, Biohaven Pharmaceuticals, Cytokinetics Inc., Epirium Bio, Genentech/Roche Pharmaceuticals, Novartis Gene Therapies, Novartis Pharmaceuticals, and Scholar Rock, Inc.

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Table of Contents

Introduction

Within the last decade, the treatment landscape for spinal muscular atrophy (SMA) has changed dramatically. With multiple FDA-approved therapies and more experimental treatments in clinical trials, patients have access to evidence-based treatments for a devastating disease that – until late 2016 – was managed solely via supportive and palliative care measures.

To better meet the needs of trial sponsors and the SMA patient community in the context of this evolving landscape, Cure SMA has launched a Clinical Trial Readiness Program with resources to support clinical trial site readiness throughout the United States (www.curesma.org/clinical-trial-readiness), including this toolkit.[1] These activities have been undertaken with the understanding that while clinical trials in general are extensive undertakings requiring significant preparation, time, and expense, clinical trials in SMA present unique challenges. In SMA trials, it is important to consider:

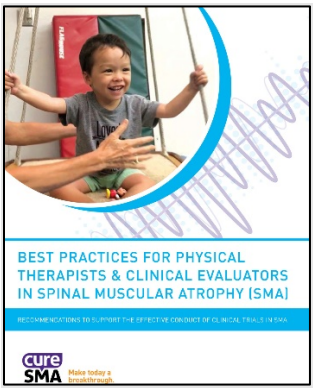
- the evolving natural history of SMA as the standard of care evolves and additional therapies become available;
- the multiple outcome measures that can be used to evaluate clinically meaningful changes, depending on SMA type; and
- the day-to-day burden that SMA places on patients and families, which can make their participation in clinical trials especially challenging.

Recognizing the central role that clinical research coordinators (CRCs) play in clinical trials, Cure SMA developed this set of best practices to help CRCs — especially those new to SMA trials — understand and navigate the challenges they may encounter. The recommendations were developed based on significant input from experienced SMA trial coordinators, parents of children involved in trials, and published resources.[2] They should be viewed as a guide but not an authoritative resource, recognizing that guidance from clinical trial sponsors, institutional review boards, and regulatory authorities takes precedence when planning for, conducting, and closing trials.

[1] For more details on the Cure SMA Clinical Trial Readiness Program refer to the Peterson et al. (2020) publication entitled: "The SMA Clinical Trial Readiness Program: creation and evaluation of a program to enhance SMA trial readiness in the United States" published in the Orphanet Journal of Rare Diseases (doi: 10.1186/s13023-020-01387-8).

[2] To develop these best practices, Cure SMA reviewed published literature and resources on trial coordination and conducted a series of semi-structured interviews with experienced clinical research coordinators and parents whose children had participated in SMA trials.

Additional Resources in This Series

Toolkits on SMA, Clinical Research Coordination, and Clinical Evaluation		
Toolkits can be downloaded at: www.curesma.org/clinical-trial-readiness.		
		
Basics of SMA and the Effective Clinical Trial Conduct	Best Practices for Clinical Research Coordinators in SMA	Best Practices for Physical Therapists & Clinical Evaluators in SMA
Webinars And Workshops		
Webinars and workshops relevant to the SMA clinical research community are available on the Cure SMA Clinical Trial Readiness Program YouTube playlist.		
Evaluations And Checklists		
For educational readiness evaluation checklists that help sites and physical therapists assess their readiness for clinical trials, email clinicaltrialreadiness@curesma.org.		
Information on External Training Resources		
	Cure SMA has compiled reference guides for external resources on SMA, genetic diseases, and clinical research topics, which are also available on the Clinical Trial Readiness Program hub at www.curesma.org/clinical-trial-readiness	

Section 1: The Role and Responsibilities of Clinical Research Coordinators

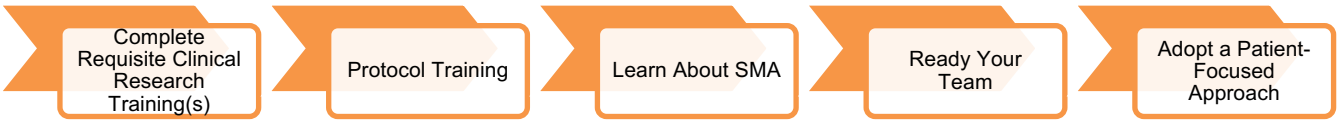
Clinical research coordinators (CRCs), also known as Study Coordinators (SCs), are central to the effective conduct of clinical trials. They play an especially critical role in spinal muscular atrophy (SMA) trials because the disease's complexity creates the need for involvement of large, multidisciplinary research teams and increased support for patients and families. With the evolving SMA therapeutic pipeline, clinical research landscape, and treatment landscape, effective trial coordination has never been more crucial. CRCs' interactions with research participants and their families can have a powerful impact on these individuals' experiences throughout the trial process, and can be a determining factor in how effective sites are at recruitment, enrollment, and retention.

CRCs work under principal investigators (PIs) to conduct trials using good clinical practices (GCP), and act as the primary communication liaison between trial participants, investigators, hospital staff and research support units, and the study sponsor. They have a diverse set of responsibilities that may include:

- Submitting documents to the Institutional review board (IRB)
- Negotiating and managing contracts and budgets
- Managing regulatory documents and trial documentation
- Recruiting, screening, and obtaining informed consent (often in partnership with principal investigators)
- Ensuring that protocol-related procedures are scheduled, carried out within allotted timeframes ,and recorded according to good clinical practices, while keeping research participants' safety and well-being at the forefront
- Managing participant follow-up
- Maintaining study-related records and data and reporting adverse events
- Ensuring integrity and ethics in the study and site conduct
- Ensuring compliance with research protocols and assisting with quality assurance audits
- Creating a space were patients feel welcomed and comfortable

The responsibilities of coordinators have expanded with the increasing complexity of modern clinical trials, and they have become indispensable to clinical research teams (Fisher, 2006).

Section 2: Preparing for an SMA Trial



Requisite Clinical Research Training and Protocol Training

Before CRCs become actively involved in trials, completion of certain trainings is essential for effective support of appropriate, ethical conduct of research.

- *Foundational training* includes trainings required for participation in clinical research. For links to training checklists, please see Appendix Table A1. Topics typically covered in foundational trainings include the following:
    - Human subjects research training
    - Research administration
    - Research with minors
    - Good clinical practice
    - Informed consent
    - HIPAA for clinicians & non-clinicians with research responsibilities
    - FDA regulated research
    - Bloodborne pathogens and infection control training
    - Conflicts of interest
    - Animal research

- *Training to meet institutional and sponsor requirements* may also be required for CRCs.

- *Additional training* may include professional certifications, such as those from the Society of Clinical Research Associates (SOCRA) and the Association of Clinical Research Professionals (ACRP). Several handbooks are available that address coordinator roles, responsibilities, and training resources in depth (see Appendix Table A2). In addition, online references from academic institutions may be helpful, including libraries of online templates, recommendation documents, as well as training presentations and checklists (see Appendix Table A4).

- *Protocol-specific training* should also be completed, as required by the trial sponsor.

Learn About SMA

Becoming familiar with SMA is essential for success in SMA trials. Understanding the disease, its cause and natural history, and how it may impact affected individuals and families will empower coordinators to more quickly anticipate issues that may arise during trials. This understanding can also help coordinators develop greater empathy for patients and families, which parents say can increase trust and comfort on the part of trial participants and parents. For more background on SMA, coordinators are encouraged to refer to Cure SMA's Clinical Trial Readiness Toolkit on the Cure SMA Clinical Trial Readiness webpage and the references listed in Appendix Table A3 (Cure SMA, 2019). For an interactive learning opportunity, coordinators may also find Cure SMA's SMArt Moves disease awareness campaign materials helpful.

SMA Resource Spotlight: SMArt Moves

SMArt Moves is a disease awareness and educational campaign to empower parents, pediatricians and other healthcare professionals to swiftly recognize and diagnose the early signs of motor delays. The SMArt Moves website includes a plethora of resources – including videos of SMA affected infants and a checklist.

Ready Your Team

Multidisciplinary supportive care is required for patients with SMA (Mercuri, 2022). Your research team may include your PI, neurologists, Physical Therapists (PTs), pulmonologists, electrophysiologists, and hospital staff. The CRC is responsible for preparing the research team for prospective trial participant visits and coordination throughout the course of the clinical trial. Considerations should be made to ensure that the research team is well-coordinated, efficient, and able to achieve a patient-centric approach to the clinical trial.

When working with a new protocol, review the protocol from the standpoints of both the site and trial participants. The CRC must be organized and in communication with the research team through-out the pre-screening, screening, and research visits to ensure internal coordination. The CRC must understand what exams, labs, and assessments will be done and which staff need to be involved and to what capacity for each visit. The scheduling of these procedures should be done well in advance so that staff has proper notification.

CRCs will usually be the point person for the patient, and is taked to directing questions and concerns to the correct person on the research team. It may be helpful for the CRC to create an internal checklist to ensure that each member of your research team is in tune with the needs of the patient and their families.

Adoption of a Collaborative, Patient-Focused Approach

A collaborative, patient-focused approach is increasingly emphasized in health care and drug development. When the patient is not at the heart of all research activities, the outcome and success of the clinical trials are often compromised (Sharma, 2015; Hand, 2018). A patient-focused approach emphasizes the needs of the patient, involves assessing trial design and operations from a patient's perspective, and can include integrating SMA patient community input directly into the clinical trial design. This type of approach may improve the patient experience and increase the success of clinical trials, and should be applied to all aspects of trial operations (Sharma, 2015; Hand, 2018; PhRMA, n.d.).

A Parent's Perspective

Q: If you were to enroll in another clinical trial, what would you want your research team to know?

A: I want to know that if we have a problem, they will take care of it, and that they have anticipated things on our behalf – to feel just a little bit like a VIP when we're in the hospital.

- Father of two children with SMA

A patient-focused approach is especially important in SMA because of the stress and uncertainty that trial participants and families may face. Trial participants and families may face a host of challenges depending on the age of the trial participant, the treatment(s) taken, and family circumstances. These could include:

- *Uncertainty and fear connected with receiving a diagnosis of SMA.* Participants may be unsure of what the diagnosis will mean for themselves and their families, and fearful about challenges it may create in their lives.
- *Stress caused by clinical trial requirements.* Clinical trials can require significant commitments including travel; time away from home, work, and school; and research visits that can feel intense and tiring.
- *Daily challenges in managing care and coping with the burden of disease.* Trial participants and families may encounter multi-dimensional management, complications, and the need for emergency care and hospitalizations due to complications (Qian et al., 2015; Cruz et al., 2018).
- *Frustrations with limitations caused by the disease.* Affected individuals as well as parents and caregivers may be trying to juggle not only treatment and care for children, but also their careers and other responsibilities.

To be patient-focused throughout the trial process, experienced coordinators and families recommend:

- *Actively listening and responding to participants, parents, and caregivers.* Families, caregivers, and research participants need to feel heard, supported, and engaged. They need to know there

is someone who will listen to their questions, concerns, and struggles during the trial process so they are not alone.

- *If possible, shadowing participants and families during clinical visits*. Shadowing participants and families provides direct perspective on their experiences. This will also allow CRCs to learn about study procedures and what is required during particular visits.
- *Proactively streamlining as many aspects of trial participation as possible.* As appropriate and allowable by the protocol, coordinate communication, research visit schedules, and travel to be sensitive to patient and family needs.
- *Being aware that families, caregivers, and the patients themselves may want to be very involved in care and in the trial process.* Consider ways to more directly involve families and patients (noting that after 7 years of age children typically get to decide and give assent to participate in a trial). Patients and families are often open to questions and happy to help educate the research staff on matters pertaining to their care and that of their loved one.
- *Working with research team colleagues to encourage adoption of a patient-focused approach by the whole team.* Communicating the needs and interests of trial participants and families to promote strong coordination across the team.

For an overview of key insights from the 2022 Cure SMA Patient-Led Listening Session held with FDA g on how SMA impacts patients and families and current unmet needs, please see Appendix Table A6. To learn more about related issues and challenges in SMA clinical trials and rare disease trials more generally, please see Appendix Table A3 and Appendix Table A4.

Considerations for Study Start-up

Many challenges and delays can occur as sites prepare to engage in clinical trials. Common challenges experienced by sites include IRB approval delays, allocating time for required team training, and extended legal/budget reviews, negotiations, and executions, and site infrastructure as well as bandwidth limitations (Atassi et al., 2013; UCLA CTSI, 2016). CRC's are regarded as a central point of communication and can be critical in helping to mitigate study start-up challenges.

- *Be organized and proactive* to avoid preventable delays in accomplishing key tasks. Start the process of developing checklists and project target deadlines to track progress.
- *Be familiar with the process and key personnel* needed to review, negotiate, and approve relevant documentation.
- *Maintain clear and transparent communication* with all stakeholders engaged in the study start-up process (e, g., research team, CROs, sponsors, IRB centers, etc.) to manage expectations.
- Leverage past site experiences, templates, and knowledge to shorten star-up activities timelines.

KEY POINTS: PREPARING FOR A TRIAL

- Before becoming involved in clinical trials, it is important for CRCs to complete appropriate training, including general as well as protocol-specific training. They are also encouraged to learn about SMA.
- CRCs are encouraged to adopt a patient-focused approach.
- CRCs can help extend the patient-focused mindset to other members of the research and care teams.
- Develop a strategy to mitigate common bottlenecks and challenges encountered during study start-up.

Section 3: Recruitment, Screening, and the Informed Consent Process

Recruitment for SMA Trials

As the primary liaison between sites and study participants, CRCs play a central role in recruitment of patients for clinical trials. CRCs are often the initial point of contact for potential participants, and may be responsible for obtaining informed consent, screening, and follow-up with participants over time.

Challenges for Recruitment in SMA Trials

Timely and efficient recruitment is vital, and recruitment for a progressive rare disease such as SMA can pose unique challenges:

- *The rarity of SMA can make it difficult to connect with and recruit patients for trials.* SMA affects approximately one in 10,000-11,000 newborns (Sugarman, 2012; Verhaart, 2017). This can make it more difficult to identify and recruit individuals for trials.

- *Parents and affected individuals may still be working through the diagnosis when they seek out trials and dealing with a complex array of emotions and life changes.* The emotional toll may make initial interactions feel more challenging and heighten the need for empathy and compassion.

- *SMA pediatric and neonate patients in particular are very heterogeneous.* Individual variations in anatomy, metabolism, disease presentation and progression, and possible secondary health problems can potentially confound clinical trial results and may further limit an already small pool of eligible patients (Grimsrud et al., 2015; Stevenson, 2015; Cruz et al., 2018; Baer, n.d.; Center for Drug Evaluation and Research, 2017).

- *Because patients are geographically dispersed, patients may travel long distances for trials.* In a disease that can take a significant physical and emotional toll and make even “the littlest of tasks monumental,” traveling to participate in a clinical trial can become an almost insurmountable burden (Cruz et. al, 2018).

Ongoing changes in the regulatory and treatment landscapes are affecting the SMA clinical trial landscape. The 2016 approval of SPINRAZA (nusinersen), 2018 approval of Zolgensma, and 2020 approval of Evrysdi (risdiplam) have significantly changed the treatment landscape. Additionally, as newborn screening ghas now been implemented in all 50 states, studies are shifting toward enrollment at or near birth to enroll pre-symptomatic patients. Beyond this, coordinators and their sites may also find themselves discussing research options with pre-natal patients.

SMA Resource Spotlight: Care Series Booklets

The booklets aim to help the SMA community understand key concepts and services to promote informed decision making about treatment and care. Topics covered under the booklet series includes *Understanding SMA, Learning About Clinical Trials, Living Unlimited: Adults, and more*! Access the booklet series here on the Cure SMA website.

Facilitating Recruitment & Connecting with the Patient Community

To mitigate potential challenges, coordinators will find it helpful to have well thought-out plans for communicating trial opportunities to potential participants. Utilizing advertising platforms, communication strategies, and consideration of patient barriers (e.g., travel challenges) can support efficient recruitment (Augustine, Adams, & Mink, 2013; International Rare Diseases Research Consortium (IRDiRC), 2016; Tweet, 2011). Specific strategies and tactics are presented in the table below.

Strategies to Facilitate Recruitment	
Share Trial Information on Your Site's Website	After obtaining IRB-approval, share trial contact information on your website to ensure visitors have access to current information.
Connect with Regional Clinics	Spread the word about the trial(s) for which you are recruiting to the patient and clinical community, including other clinics that may be able to refer patients for trials.
Partner with Patient Groups	Patient advocacy groups that maintain SMA patient contact registries may be particularly helpful for connecting interested individuals with particular trials, as well as for increasing recruitment (Association of Clinical Research Professionals (ACRP), n.d; Simbec-Orion, 2022).
Be Active on Social Media	Social media is a powerful communication tool that parents and caregivers may turn to for trial information (SMA Europe & TREAT-NMD, 2016; Murphy, 2016). It can provide a direct and cost-efficient platform for increasing awareness of clinical trials and informing potential participants of eligibility requirements (Krischer et al., 2017; Shpillber, 2017). CRCs and sites should also be aware of potential drawbacks of social media.[3]

[3] There is a continuing discussion on the benefits of utilizing social media to engage prospective participants and on ethical considerations connected with utilization of social media (Krischer et al., 2017; Gelinas et al., 2017). Additionally, information

Regardless of how you communicate about trials, be conscious of appropriate review and approval processes and be prepared to respond to questions from prospective trial participants.

KEY POINTS: RECRUITMENT

- SMA trials pose unique challenges for recruitment because of the rarity, heterogeneity, and burden of the disease. CRCs will benefit from understanding these challenges upfront, so they can proactively work to mitigate them.
- Ensuring that information on trials at your site is accessible to the patient community is very important. Creating visibility with clinics that may be able to refer patients to your site, working with patient advocacy groups, and using social media are all avenues that may help to support recruitment.
- Always be prepared to promptly respond to prospective trial participants to support effective and timely recruitment and avoid missing enrollment windows.

Institutional Review Board (IRB) Submissions

The Clinical Research Coordinator may be responsible for submitting documents to the Institutional Review Board related to:

- The research protocol
- Investigator's brochure
- Sample consent document
- Any materials on the study that prospective study subjects will receive
- Documentation of the risks and benefits of the research
- Information on the composition of the subject population and inclusion/exclusion criteria used for selection

The following recommendations regarding IRB submissions may assist with more streamlined and successful IRB approvals (Nesom, 2019):

shared by patients on social media may lead to unrealistic expectations about interventions (SMA Europe & TREAT-NMD, 2016). CRCs, PIs, and study sites may therefore need to be prepared to address potential misconceptions and to caution participants, parents, and caregivers about relying on unofficial results or feedback from other participants on social media.

- The whole study must be described in detail in the IRB application in narrative form so that the procedures and the trial participants' experience can be easily understood from an outsider's perspective.

- You must show the IRB that a thorough process has been developed for obtaining consent from participants during the recruitment stage.

The majority of the IRB's role occurs when the research is being initiated. However, the site must send periodic reports to the IRB once the participants are enrolled and the clinical trial is underway (Rodriguez, 2021). This open line of communication between the clinical investigator and the IRB is important. The IRB must be inormed of any changes in the research activity, including the completion of the study as well as any unexpected events. The IRB will also typically require long-term follow-up and data gatherine, even after participants have finished the trial.

Screening Prospective Trial Participants

Before a research participant can enter a clinical trial, they must undergo a screening process to determine if they are eligible to participate. An IRB-approved study protocol is used to ascertain eligibility.

Pre-Screening

Prospective study participants can learn about clinical trials in a variety of ways: they may be referred by health care professionals within or outside of your institution or learn about your study through their networks. Pre-screening assesses if prospective participants meet inclusion criteria for a trial and whether a full screening visit is appropriate. Since relationships with prospective study participants begin at the point of first contact, this initial interaction can be significant in determining whether the prospective study participant enrolls in the trial. Kindness, attention, and ability to listen and provide clear responses to inquiries are essential. This is particularly important since this can be a vulnerable and emotional time.

As part of the pre-screening process, CRCs may need to:

- *Assess certain specific attributes of trial eligibility*, which may include age, SMA type, respiratory status (O2 saturation)/respiratory support/hours on BiPAP, and ability to perform or not perform specific motor milestones (sit or stand, walk, etc.).
- *Collect additional information related to*:
    - Contact information, and information about the best form of contact for follow-up questions and information about the study, including the informed consent form (ICF)
    - General health and current treatment they may be undergoing
    - Past participation in other research studies
    - Medical records (in preparation for the screening visit)

To prepare for pre-screening:

- *Be prepared to answer questions about a study at all times*. Consider creating a quick fact sheet or script with key information about ongoing trials, including information potential participants will need to decide whether to proceed.
- *Create a checklist to ensure you collect all necessary information*.

Preparing for the Screening Visit

After the pre-screen is complete and eligibility to continue to screening has been confirmed, screening visit preparation begins. CRCs are encouraged to:

- *Prepare template communications ahead of time with the materials and information that potential participants need to proceed so that this can be sent promptly after pre-screening. (See callout box below.)*

Information to Send Prospective Trial Participants Prior to the Screening Visit

- ✓ Informed consent form (ICF)
- ✓ Relevant information about the screening visit, such as:
  - — The date, time, and duration of the visit
  - — Who will provide the ICF
  - — Staff who will be involved in the visit
  - — The main procedures involved (medical exam, physical therapy assessment, labs, EMG studies, parent/patient reported surveys etc.)
- ✓ What the parents or patients will need to bring, as appropriate, such as:
  - — Information to verify eligibility, such as genetic testing results and other pertinent medical records
  - — Patient equipment (batteries, food pumps, AMBU bags in case of emergencies, particularly for type 1 patients)
  - — Meals or snacks to last the time of the visit
- ✓ Relevant CRC and site contact information
- ✓ Encouragement to list questions that arise as they review trial information – especially about the ICF – to encourage careful focus on the information and that they can bring these questions to the screening visit to discuss with the PI

- *Create an internal checklist to prepare the site team for the visit and ensure everyone is attuned to the needs of the patient and their family.* Strategies similar to those discussed in the forthcoming section on preparing for a research visit may be helpful.
- *Send this information to prospective participants promptly after pre-screening and as far in advance of the screening visit as possible.* Sending information out promptly will allow for more

thorough review of informed consent and information about the purpose of the study, study procedures, time commitment including number of study visits, risks and possible benefits, and compensation, etc.

During the Screening Visit

During the screening visit, the prospective participant is introduced to the study staff, and the ICF is reviewed with the study principal investigator and/or clinical research coordinator. The purpose of this visit is to collect more information about the eligibility of the research participant, including medical history and overall health. Typically, the participant may undergo several evaluations including neurological exams, physical therapy evaluations, electromyography, x-rays, and labs to name a few. The results of all evaluations will help to determine a participant's eligibility to enter the clinical trial. It may take more than one visit (particularly with the SMA type 1 patients) to complete the screening process and to determine if patient will be eligible for enrollment into an investigational study. Beyond the steps recommended above, CRCs are encouraged to do the following to help to streamline screening, and make patient and family experiences more positive:

- *Demonstrate a patient-focused approach by identifying steps you might be able to take to make the day go more smoothly for the patient and their family.* There may be some simple things you can do to ensure a more positive experience. For instance, if siblings are along for the visit, consider having toys available for them to play with during the day.

- *Ensure strong communication and coordination with and between participants (patients and families) and the site's research and care teams throughout the course of the day.*

The Informed Consent Process

Because SMA is most commonly diagnosed in children it is possible that parents will provide consent for their child to participate in the trial. Past clinical trials in rare diseases have found that due to the increased burden associated with the diagnostic journey and subsequent management of a rare disease, the informed consent process can be challenging. Some parents indicate that they do not recall giving consent for their children to participate in clinical trials when initially approached (Costello et al., 2007). This reinforces the importance of approaching the informed consent process as a continuing dialogue with parents and patients throughout the clinical trial experience (Steinhillber, 2015; Joseph, Craig, & Caldwell, 2013). Additionally, informed consent forms may be difficult for families to understand, leading to a need for especially clear communication. Some strategies suggested for improving the pediatric informed consent process include:

- *Having a physician present when consent from parents is obtained or having the physician obtain consent from the parents themselves*, to help parents develop trust, which is essential to increasing the chances of obtaining consent (Steinhillber, 2015).

- *Attending to practical considerations, such as ensuring that there is ample time for review of the ICF in advance of screening* and printing multiple copies of the ICF for the research visit, so that parents and participants can more easily follow along when it is reviewed.
- *Assessing the understanding of the parent or child (if old enough to provide assent), by asking questions about critical details of the study outlined on the ICF.*
- *Being intentional and flexible about how each conversation about informed consent is approached,* as the circumstances of each patient and family will be different, as will their ability to understand and absorb information will differ (Steinhillber, 2015; Joseph, Craig, & Caldwell, 2013).

For a summary on how to effectively prepare and conduct screening visits, see Appendix Table A5.

KEY POINTS: SCREENING AND INFORMED CONSENT

- Initial interactions with prospective trial participants can play a significant role in determining whether participants pursue enrollment. Kindness, attention, and ability to listen and provide answers are essential.
- Carefully preparing for both pre-screening and screening conversations will help these go more smoothly and ensure that the site and participant obtain all necessary information.
- The informed consent process is often viewed as a continuing dialogue requiring thoughtful conversation, as each person's ability to understand and absorb information differs.
- Parents of children with SMA may be overwhelmed and coping with their child's diagnosis of a progressive debilitating disease which may influence their ability to give informed consent. Informed consent cannot be obtained unless the signing parent and/or research participant has demonstrated a solid understanding of the trial, study procedures and expected risks and benefits. CRCs should be mindful of the ethical issues this can raise and ensure that informed consent is an ongoing dialogue throughout the clinical trial experience.

Spotlight: Cure SMA Clinical Trial Experience Survey

- Cure SMA conducted a survey in 2019 to understand participant perspectives on SMA clinical trial management and patient-centric management practices (Peterson et al., 2022). Understanding the clinical trial experiences and attitudes of SMA trial participants can aid significantly in optimizing the design and management of the clinical trials, and can also improve the success of recruitment and retention, especially with regards to diseases as life-altering as SMA.
- 70 unique survey responses were submitted by SMA-affected adults or the caregivers of children that had participated or were actively participating in an SMA clinical trials.
- The study findings indicated overall positive experiences with SMA clinical trials management and showed the following with regards to the trial participants' attitudes:
    - Top motivators:
        - Clinical benefit
        - Investigational drug access
        - Opportunity to help others
    - Top concerns:
        - Safety
        - Risk vs. benefit justification
        - Pain accompanying tests
    - Top benefits of trial participation:
        - Hope for a better future
        - Helping others
        - Relationships with the study team
- Survey findings showed that participant gender, age and race were significant predictors of their attitudes. Additionally, respondent type, knowledge of SMA, distance to the trial site, and treatment era also impacted patients' attitudes.
- The top recommendation for improving study management was to provide ample information to the prospective and current trial participants to ensure their understanding of the clinical trial study.
- CRCs can have a particularly unique and impactful relationship with patients and their families that can determine if they feel comfortable in participating in the clinical trial and that their specific needs are met. The understanding, responsiveness, and trustworthiness of CRCs were all qualities that were indicated as important to trial participants.
- When designing and conducting SMA clinical trials and in interactions with potential participants during all stages including recruitment, the factors that were found to motivate and discourage participation in SMA clinical trials should be taken into consideration.

Section 4: Research Visits

SMA clinical trial participation requires strong commitments from patients, families, and caregivers. Research visits can disrupt participants' routines, who may need to travel significant distances to research sites. Long days in the clinic may feel draining for patients and families. For adult patients, trial participation can disrupt careers and daily routines (Cruz et al., 2018). As a result, a streamlined approach to patient engagement in the context of research visits can be especially helpful.

Planning Research Visits

Organizing clinical trials that decrease the burden of travel, visit intensity or frequency, and decrease disruption to the participant's life may help patients and promote retention in clinical trials (DeWard et al., 2014; United BioSource, 2017). The following tips may improve patient and site experiences.

At the Outset of the Trial

- *Ensure thorough knowledge of the trial protocol.* Know what exams, labs, and assessments will be done and which staff need to be involved for each visit. Schedule procedures and notify staff well in advance of visits. When working with a new protocol, review the protocol from the standpoints of both the site and trial participants. Anticipate potential roadblocks, and how you will address these.

- *Create customized pre-visit and visit checklists to ensure all the appropriate preparations are addressed and the protocol is followed.* While studies or sponsors may provide starting checklists, it is important to tailor these to ensure that no steps – especially those that are site-specific – are missed.

- *Develop contingency plans.* Things can come up throughout the course of trials that impact your plans. Patients may arrive late, research team schedules may be disrupted, and coordinators may find themselves home sick the day before a patient's visit. Prepare for these contingencies. A positive culture can also help a research team adapt to unanticipated changes.

Scheduling Research Visits

- *Make patients and caregivers aware of the time commitments up front to avoid misunderstandings or unrealistic expectations.* It is important that trial expectations and visit schedules are well-understood before consent is signed. Balancing participant and family needs with protocol requirements can be difficult for the most experienced CRCs.

- *Structure visits to accommodate participant preferences, as feasible and allowable under the protocol*, by:

- Asking participants (and caregivers) about scheduling preferences and constraints
- If feasible, conducting assessments and tests over multiple days and avoiding scheduling research and care visits on the same day to reduce fatigue
- Scheduling PT appointments involving evaluation with primary outcome measures when participants are at their prime (often in the morning); PT evaluations are a major component of research visits and maintaining reliability of outcome measure assessments is integral to clinical trial success
- Maintaining consistency across visits to decrease the burden of trial participation

- *Implement internal processes and tools to streamline scheduling*, such as:

  - Making it standard practice to enter visit schedules into the research calendar immediately after consent is obtained, so visits are booked with more advance notice and research staff (neurologists, PTs, pulmonologists, electrophysiologists, hospital staff) are notified as soon as possible. This also ensures that patients are scheduled on a “first come, first served” basis when possible, if permitted by patient’s health status.
  - As the study progresses, scheduling future visits while the families are at the site to increase efficiency and reduce the need for follow-up communication.
  - Developing strong communication skills and platforms within the research team, between different departments, and with external personnel to efficiently coordinate patient visits and obtain and prepare resources (M. Gibbons, personal communication, May 14, 2018).

Best Practices for Scheduling and Preparing for PT Clinical Evaluations

When scheduling and preparing for PT evaluations, experienced PTs who have worked on SMA clinical trials recommend the following:

- ✓ Scheduling Clinical Evaluations
  - Schedule evaluations when participants are at their prime (often in the morning)
  - Ensure the participants are well-nourished
  - Consider having patients who travel long distances arrive a day prior to the evaluation to decrease fatigue
  - If feasible, keep the environment (e.g. location, time of day, and equipment) consistent throughout their participation in the trial
- ✓ Preparing for Clinical Evaluations
  - Make sure equipment is clean and functional
  - Minimize distractions in the environment
  - Ensure participants bring appropriate clothing and footwear
  - Minimize factors that can negatively impact the participants mental and emotional state (e.g. participants can feel agitated after blood draws)

Challenges can sometimes arise when scheduling visits and may affect the consistency of the environment and the reliability of the evaluation. It is important for CRCs to communicate and coordinate effectively with PTs to address the variability and minimize the impact on the participant's performance.

More information on outcome measures assessments and clinical evaluations can be found in the Cure SMA Best Practices for Physical Therapists and Clinical Evaluators in Spinal Muscular Atrophy (SMA) on the Cure SMA Clinical Trial Readiness webpage (Cure SMA, 2019).

Pre-Visit Preparation

- *A few days ahead of the research visit, confirm that participants are prepared and offer tips for the visit day.* You may want to confirm that all travel and accommodations are in order, and encourage the patients and families to make sure that they are well-rested and are well-nourished (Pruss et al., 2010; Stevenson, 2015; Swoboda et al., 2007).

- *Confer with research team members the day before the visit to confirm appointment times, objectives, and patient information.* Sending reminders of visits and times when each PI/Co-I or technician will see the patient is also recommended as it helps staff prepare for their day. Reminders may also include information about the clinical trial, the research patient, and relevant information on the health of the patient.

- *Do a walk-through the day before the visit to confirm that everything is in order.* Checking that equipment is working, printing and prefilling paperwork, checking the expiration dates of drugs, and preparing lab kits can help the visit go smoothly.

In addition, CRCs may ask experienced patients about scheduling approaches that have worked for them and implement these approaches. Overall, ongoing and clear communication with research participants, the study team, and all inter-dependent research units is essential to effective trial operations.

KEY POINTS: RESEARCH VISITS

- CRCs are encouraged to take a thoughtful approach to scheduling and structuring clinical trial visits to reduce the burden of trial participation on patients and promote retention.
- Confirming plans with the research team and conducting a walk-through the day before a research visit can help visits to go smoothly.
- Checklists can be invaluable tools in preparing for patients' research visits. They can help CRCs ensure adherence to the protocol, that patient needs are met, and that visits proceed smoothly.
- Considering contingency plans (e.g., in the event that a patient's arrival is delayed) may help a coordinator be prepared for unexpected disruptions to the visit, so that the visit can still proceed successfully.

Section 5. Retaining Patients: The Importance of Attentiveness, Empathy, and Compassion

Once patients enroll in a study, retention becomes an important consideration. Due to the relatively small size of the SMA population, participant retention can be especially vital to trial success; however, several factors may hinder retention. Although this is changing with the evolving treatment landscape, some patients may become unable to continue with the trial for health-related reasons, or may not survive. Other times, patients may find participation overwhelming and difficult to manage. Many of the recommendations presented in the preceding section may promote retention: reducing the burden of trial participation by proactively ensuring that their patients' needs are met during the trial; ensuring well-coordinated research visits; and helping patients to feel supported during the clinical trial by establishing trust, being flexible and adaptable to the family's schedule when scheduling visits, and cultivating open, active, and honest communication.

A Parent's Perspective

"[Our coordinator] just went above and beyond to make us comfortable and the kids comfortable. That's what stands out about the first visit… [he] was the kind of person who was very relatable, he was approachable, he sympathized with our frustrations, and if he would fix something he would."

– A father of two children with SMA

The value of attentiveness, empathy, and compassion cannot be understated. Families invest time and energy in trials, and may appreciate extra support. Parents of children who participated in SMA clinical trials have emphasized that CRCs who go "above and beyond," can make an incredible difference. The smallest things can make a huge difference: parents have expressed gratitude for coordinators who demonstrate warmth and concern for patients and their families, take the time to learn about their lives, and find ways to make things just a little easier – whether by having toys available for siblings who come along for visits, or being available for questions when they are away from the sites and seeing local physicians. When CRCs make themselves available to patients in person, by email, and phone, this can also help patients feel supported.

Finally, coordinators should be mindful that as patients or their caregivers deal with the challenges of their illness or those of a complex trial, they might voice their frustrations to the coordinators. Not taking these frustrations personally, and continuing to be compassionate may help coordinators continue to be effective in their role even in the face of these challenges. As one mother of three children with SMA put it, *"Parents can be overwhelming…We might have a gazillion questions and seem overwhelming…but we're just trying to do what is best for our kids."*

KEY POINTS: RETENTION

- CRCs can help to reduce the burden of trial participation by proactively ensuring that their patients' needs are met during the trial.
- CRCs are encouraged to establish open, active lines of communication with SMA patients and families participating in a trial, and more generally to adopt a patient-focused approach to improve the participant's clinical trial experience.

Section 6: Considerations Related to Patient Care: Standards of Care, Supportive Care, and Care Coordination

The Coordinator in the Context of the Care Team

Beyond being part of the research team, CRCs frequently communicate with and between members of the care team. SMA is a complicated condition requiring extensive care involving multiple specialties and potentially multiple sites (IRDiRC, 2016). Beyond scheduling visits, coordinators need to be aware of other times when they will need to take action**.** For example, a coordinator may need to obtain records related to an adverse event from other clinics or hospitals (e.g. hospitalization, records of vaccines, concomitant medications taken or supporting information for a serious adverse event); proactive communication and follow-up can be important in obtaining the needed records. Patients may also have questions when they are away from the sites and are seeing local physicians. As the patient's primary point of contact for the trial, it can be helpful for CRCs to be readily accessible. A key aspect of the coordinator's role is to direct participants (or parents) to the right individuals on the care team to address their questions or needs.

Considerations for Standard of Care and Supportive Care

While CRCs will not be directly responsible for decisions regarding standard of care or supportive care in the context of the trial, these are two important issues with implications for clinical trials. Adherence to a standard of care can aid in discerning the effects of the intervention versus the health support in rare disease trials, and improve patient outcomes (Kinnett, Dowling & Mendell, 2016; Finkel, 2016; Finkel, Bishop, & Nelson, 2016). Trial sites may be expected to implement and monitor the SMA standard of care. However, embedding supportive care and standard of care into clinical trial protocols can prevent some participants from meeting inclusion criteria, especially since care is not universally available (SMA Europe & TREAT-NMD, 2016; Finkel, Bishop, & Nelson, 2016). Thus, this topic may come up in the context of discussions pertaining to eligibility or in questions from patients.

Effectively delivering supportive care (e.g., ventilator and nutritional support) in the context of a trial can also aid in reducing variability among SMA patients. If a clinical trial protocol includes required supportive care, participants should be made aware at enrollment that participants would be expected to receive such support to continue in the trial. However, patients (or parents) always have the right to decline supportive care interventions and to elect a palliative care approach. CRCs and trial staff are encouraged to have a continuing dialogue regarding these issues with the patient/parent throughout the trial (SMA Europe & TREAT-NMD, 2016; Finkel, Bishop, & Nelson, 2016). Again, while a CRC may not be the person to ultimately address all of these issues or questions, a coordinator can play an important role by connecting patients to the right individuals for these discussions.

KEY POINTS: CONSIDERATIONS RELATED TO PATIENT CARE

- Be prepared for the operational complexities that come with coordinating across specialties, care-sites, and trial sites may help CRCs to be more effective in their roles in SMA trials.
- CRCs are encouraged to engage in proactive communication and follow-up with external physicians and external care sites to obtain medical records efficiently to obtain records of adverse events.
- Adherence to the standard of care can aid in discerning confounding factors and improve outcomes for patients. CRCs may find it helpful to understand SMA standards of care and to consider how, in their role, they can help support adherence to the standards of care.
- CRCs are encouraged to understand whether a trial protocol has supportive care requirements and to be prepared to have a continuing dialogue with patients and caregivers on these requirements and implications for trial participation, but CRCs will need to respect the decisions of parents or patients to elect either a proactive or palliative care approach.

Conclusion

Clinical trial coordinators play an essential role in clinical trials, especially in SMA. Through close collaboration with their team, effective execution of responsibilities, and adoption of a patient-focused approach, coordinators can help trials to run more smoothly.

Over time, CRCs may find that they want to extend the approaches described in this document to the broader SMA community, and engage in professional workshops and conferences. Such engagement may enable coordinators to continue to learn about challenges and strategies to improve trial site readiness and enhance the patient's experience in clinical trials. Coordinators may also discover opportunities for learning methods and practices for the care and management of SMA patients from experienced SMA physicians and caregivers and even the patients themselves.

Finally, given the opportunity, CRCs in SMA trials can help contribute to the success of SMA trials by being active collaborators in trial design and feedback processes.

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Appendix

The tables below provide information on additional resources that may be helpful for clinical research coordinators.

Table A1 is a compiled list of trainings offered for CRCs. Some links to access these trainings can be found below. CRCs are encouraged to peruse this list and partake in trainings they find relevant and beneficial. In addition, there are CRC training checklists links below to serve as a template in the training of new CRCs.

Table A2 highlights a few key overview references that CRCs may find helpful. It contains both books specifically related to CRCs, as well as a variety of broader online resources for CRCs.

Table A3 provides information that will help CRCs familiarize themselves with SMA, including the perspectives of affected individuals and their caregivers on the disease, and information on standard of care.

Table A4 includes information about numerous external references. The goal is to provide CRCs with tools and resources to help with especially critical tasks and activities. The tools that are listed and referenced within the following table are provided for general reference and have been obtained from a variety of sources, as indicated below.

Table A5 includes a tips and trick sheet on how CRCs can thoughtfully approach preparing for and conducting screening visits while adopting a patient-focused approach. This is followed by a quick tip one-pager on creating tools and templates to assist with screening prospective study patients.

A6 provides an overview of key insights from the 2022 Cure SMA Patient-Led Listening Session held with FDA to help CRCs understand how SMA impacts patients and families.

None of the materials referenced here nor this set of best practices supersede information provided or required by your facility or trial sponsors.

Table A1: Available Training Checklists

	Title	Resource Description	Resource Link
Available Training Checklists	UCSF Suggested Training for Clinical Research Coordinators	This is a list of courses, with brief descriptions, of suggested trainings for Clinical Research Coordinators at UCSF. Course slides and some additional reference materials are also available on the site.	https://hub.ucsf.edu/research-coordinator
	UCD Coordinator Training Checklist	This is a checklist form for coordinator training from the University of California-Davis Medical Center.	http://www.ucdmc.ucdavis.edu/clinicaltrials/documents/coordinator_training_checklist.pdf

Table A2: Key Overview Resources Relevant to Clinical Trials

	Title	Resource Description	Resource Link
Books	Responsible Research: A Guide for Coordinators (2006)	A thirteen-chapter guide to all aspects of the CRC position, with both practical and ethical emphasis. Topics discussed include ethics and human subject's protection, responsible conduct, the informed consent process, pediatric informed consent and assent, study implementation and start-up, recruitment and retention of research subjects, documentation, quality assurance in clinical trials, communication, education and training, and future trends in professionalization.	https://www.amazon.com/Responsible-Research-Coordinators-Carol-Fedor/dp/1901346684
	CRC Guide to Coordinating Clinical Research (2004)	A well-known and comprehensive set of training tools and reference guides for novice and experienced coordinators. Topics covered include CRC roles and responsibilities, regulations and GCP, study preparation, work with study subjects, informed consent, case report forms and EDC, and study closure, among other topics.	https://www.amazon.com/Guide-Coordinating-Clinical-Research-Second-ebook/dp/B00EZTPW3M
Online	ACRP Resources Database	The Association of Clinical Research Professionals (ACRP) website Resource Center contains a multitude of free tools and templates. Cure SMA has highlighted a few templates specifically from ACRP below (see table), but CRCs are encouraged to peruse the entire resource center.	https://acrpnet.org/
	ACRP Core Competency Guide for CRCs	Published in 2017, this ACRP resource is a comprehensive guide for CRCs. It is available for free download.	https://www.acrpnet.org/core-competency-guidelines-clinical-research-coordinators-crcs/
	SOCRA ONLINE Educational Offerings	SOCRA's online courses are "intended to provide access to training and continuing education that will promote quality clinical research, protect the welfare of research participants and improve global health."	https://www.socra.org/conferences-and-

	for Clinical Research Education		education/online-courses/
	SMA Trial Readiness Toolkit	The CRC toolkit is part of a larger toolkit created by Cure SMA intended for new SMA clinical trial sites. It has content on every aspect of the clinical trial process and how it pertains to SMA, as well as a detailed description of SMA. Cure SMA encourages CRCs to peruse the entire toolkit for more information, as well as the Cure SMA website for parent- and family-friendly materials.	https://www.curesma.org/clinical-trial-readiness/
	Best Practices for Physical Therapists & Clinical Evaluators in Spinal Muscular Atrophy (SMA)	Cure SMA and physical therapists with experience in SMA clinical trials developed this toolkit, which discusses the roles and responsibilities clinical evaluators and comprehensive information on outcome measures used in SMA clinical trials.	https://www.curesma.org/clinical-trial-readiness/

Table A3: Resources for Further Reading on SMA

	Title	Resource Description	Resource Link
SMA	Voice of the Patient Report: A summary report resulting from an Externally Led Patient-Focused Drug Development Meeting Reflecting the U.S. Food and Drug Administration (FDA)Patient-Focused Drug Development Initiative	This document is a report of the Cure SMA's April 2017 Externally Led Patient-Focused Drug Development (PFDD) Meeting with FDA. The report details SMA patient, parent, and caregiver perspectives on disease burden, treatments, and clinical trials for SMA patients. The report was developed as a resource for the FDA and drug development community to help "researchers, clinicians, payers and other related organizations, to provide a better understanding of the needs, hopes and goals of [the SMA] community."	https://www.curesma.org/wp-content/uploads/2018/01/SMA-VoP-for-publication-1-22-2018.pdf
	Briefing Document to the Clinical Trial Readiness in Spinal Muscular Atrophy (SMA) SMA Europe, TREAT-NMD and European Medicines Agency Meeting	This briefing document, prepared by SMA Europe and TREAT-NMD, discusses challenges of care in different SMA types and considerations to keep in mind when conducting and coordinating a clinical trial with each SMA type. The document also outlines ongoing discussions regarding standard of care and supportive care and ethical issues/ concerns associated with them.	http://www.ema.europa.eu/docs/en_GB/document_library/Other/2016/12/WC500217553.pdf
	Publications on Standard of Care	Published in two parts, these publications address standard of care for SMA, including updates to standard of care recommendations published in 2007. — Mercuri E, Finkel RS, Muntoni F, et al. Diagnosis and management of spinal muscular atrophy: Part 1: Recommendations for diagnosis, rehabilitation, orthopedic and nutritional care. Neuromuscul Disord. 2018;28(2):103-115. — Finkel RS, Mercuri E, Meyer OH, et al. Diagnosis and management of spinal muscular atrophy: Part 2: Pulmonary and acute care; medications, supplements and immunizations; other organ systems; and ethics. Neuromuscul Disord. 2018;28(3):197-207.	Part 1: https://www.ncbi.nlm.nih.gov/pubmed/29290580 Part 2: https://www.ncbi.nlm.nih.gov/pubmed/29305137
	SMA-Europe Workshop Report: Opportunities and Challenges in Developing Clinical Trials for Spinal Muscular Atrophy in Europe	This workshop report briefing document, prepared by SMA Europe and TREAT-NMD, discusses recommendations for improving clinical trials in SMA.	https://ojrd.biomedcentral.com/track/pdf/10.1186/1750-1172-8-44?site=ojrd.biomedcentral.com

Table A4: Further Reading on Specific Activities Involved in Clinical Trials

	Title	Resource Description	Resource Link
Recruitment and Retention	Recruitment & Retention Planning: Getting Started	NINDS has assembled several resources to help clinical research sites with recruitment and retention activities.	https://www.ninds.nih.gov/Funding/Apply-Funding/Application-Support-Library/Recruitment-Retention-Planning-Getting-Started
	Participant Retention Practices in Longitudinal Clinical Research Studies with High Retention Rates	This peer-reviewed open access article details patient retention strategies and recommended practices based on an evaluation of 19 longitudinal clinical research studies with high retention rates.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5319074/
	Recruitment & Retention Toolbox	The Trial Innovation Network has assembled numerous resources for recruiting and retaining patients. The Trial Innovation Network is a collaborative initiative under the National Center for Advancing Translational Science's (NCATS) Clinical and Translation Science Awards Program (CTSA) that aims to "innovatively address critical roadblocks in clinical research."	https://trialinnovationnetwork.org/recruitment-retention-toolkit/
	Clinical Trials for Rare Diseases-Finding and Keeping Patients	This article reviews the challenges and issues associated with recruiting participants and retaining participants into a clinical trial. This article also highlights how a patient-focused approach can aid in retaining participants in a rare disease clinical trial.	https://www.bhdsyndrome.org/forum/bhd-research-blog/clinical-trials-for-rare-diseases-finding-and-keeping-patients/
	5 Operational Considerations for Rare Disease Trials	This article raises five key operational challenges that may arise within rare disease research, and offers suggestions for addressing these challenges.	https://premier-research.com/perspectives-5-operational-considerations-rare-disease-trials/
	Small Population Clinical Trials Task Force Workshop Report and Recommendations	This report analyzes different methods of performing clinical trials and addresses challenges in recruitment and retention of participants, especially for rare diseases. The article outlines some possible solutions to these challenges and encourages patient interaction throughout the clinical trial process.	http://www.irdirc.org/wp-content/uploads/2017/12/SPCT_Report.pdf
	Practical Aspects of Recruitment and Retention in Clinical Trials of Rare Genetic Diseases: The Phenylketonuria (PKU) Experience	This article describes various platforms and considerations that can help in the retention and recruitment of participants in rare disease clinical trials.	https://link.springer.com/article/10.1007%2Fs10897-013-9642-y

	Experience with Direct-to-Patient Recruitment for Enrollment into a Clinical Trial in a Rare Disease: A Web-Based Study	This is a study that compared a traditional IRB approved site recruitment process with a web-based recruiting method. Although the web-based approach recruited fewer patients than the traditional IRB method, it resulted in a significantly higher ratio of eligible patients.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5350442/
	Social Media Aided in Recruiting for Clinical Trial in Rare Disease	This article discusses the use of social media as a recruitment tool for a study on the rare disease short chain acyl CoA dehydrogenase deficiency (SCAD). The article also highlights some advantages of using social media as a recruiting tool in comparison to other established methods.	https://www.healio.com/hematology-oncology/practice-management/news/online/%7B6ddd9104-4636-46f7-b22e-29e2dffd0d13%7D/social-media-aided-in-recruiting-for-clinical-trial-in-rare-disease
	Using Social Media as a Research Recruitment Tool: Ethical Issues and Recommendations	This article analyzes ethical considerations around social media as a recruitment tool.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5324729/
	Informed Consent Checklist (1998)	HHS also has published an Informed Consent Checklist (1998).	https://www.hhs.gov/ohrp/regulations-and-policy/guidance/checklists/index.html
	10 Lessons Learned in Recruitment for Pediatric Trials	This document focuses on pediatric clinical trials. It provides suggestions for dealing with the challenges associated with pediatric trials such as consent and interacting with the participants and their parents.	https://forteresearch.com/news/10-lessons-learned-in-recruitment-for-pediatric-trials/
	Clinical Trials in Children	This article outlines in detail the different aspects of designing, conducting and coordinating a clinical trial. It also describes the ethical concerns and considerations for coordinating a pediatric clinical trial and interacting with the participants and their parent's/care givers when obtaining consent.	https://forteresearch.com/news/10-lessons-learned-in-recruitment-for-pediatric-trials/
Networking	Clinical Research Coordinators eForum	The ACRP has a CRC eforum where CRCs can share SOPs, resources, and tips.	http://community.acrpnet.org/communities/community-home/digestviewer?CommunityKey=a99b18d8-fe55-4ea0-a064-551ac5fcb5f0#_ga=2.1566769.146407219.1523455913-1851954241.1522246115

Table A5: Resources for Screening Prospective Trial Patients

Tips and Tricks for Screening Prospective Trial Participants

Regardless of the source and type of contact, relationships with study participants begin at the first point of contact. Prospective study participants' experiences during pre-screening and screening can have lasting impressions and heavily influence decisions about enrollment. Kindness, attention, and ability to listen and provide answers at this time are essential. This is particularly important since—at least for pediatric patients—these contacts are often made shortly after diagnosis, which can be a highly vulnerable and emotional time. Taking a thoughtful approach to preparing for screening and adopting a patient-focused approach that prioritizes the prospective trial participant's needs (and those of his or her family) can go a long way in easing this process for your team and for trial participants.

Pre-Screening

Preparing Yourself

- *Know your study protocol (or studies)!* Always be prepared to answer questions about studies that you are coordinating. Consider creating a fact sheet with key information that you can quickly reference.
- *Create a checklist of the information that you need to obtain* during pre-screening to make sure that you collect all relevant information and avoid unnecessary follow-up.
- *Create response templates with information about your study or studies* that you can quickly personalize, so that you are ready to respond to prospective patients in a timely manner.

Interacting with Prospective Participants

- *Be kind and attentive*. Prospective participants (or parents) will likely be processing a lot of information and emotion when they contact you.
- *Be mindful about your choice of words.* Speak so that you can be easily understood.
- *Gently ask questions to confirm understanding* and ensure that the participants (or parents) have the information they need.
- *Ensure that you ask the necessary questions to make sure that the prospective participant meets the inclusion criteria* (e.g., age, confirmed diagnosis, is pre/post symptomatic) to avoid unnecessary screen fails.
- *Alert the patient of the type of information and records that he or she must bring to the visit,* and follow-up with this information via email.

Screening

Preparing Yourself

- *Prepare template communications with all information and material that potential participants need for screening (including the ICF)*, so this can be customized and sent out promptly after pre-screening.
- *Create a schedule and a checklist for preparing your team for the visit*.
- *Implement task management strategies that help you stay on track* with communication and follow up with your team and with prospective participants.

Preparing Your Site

- *Once a visit date has been set, alert the team and enter it into all relevant calendars.* Obtain necessary document/registration/grant numbers, etc., to ensure access and a seamless visit.
- *Check in with your team the day before the visit* to confirm schedules and objectives and ensure that everyone is attuned to the needs of the patient and his or her family.
- *Complete CRFs headers and obtain the required information ahead of time, if possible,* to be ready for the clinician.
- *On the visit day, be attentive to team coordination* to help the visit go smoothly.

Interacting with Prospective Participants

- *Send visit information promptly after pre-screening and as far before screening as possible* to allow for thorough review.
- *Ensure that participants know what to bring to the screening visit (e.g., key documentation).*
- *Encourage participants to list questions that arise* as trial information is reviewed and to bring these to the screening visit for discussion.

Creating Tools and Templates to Assist with Screening

Each study is unique, so it is not possible to create one-size-fits-all tools and templates for trials. This said, certain activities and considerations apply to all clinical trials. Keeping the following in mind may help you to develop more effective tools and templates for clinical trials.

Tools and Templates to Create

For Communicating with Prospective Participants

- *A fact sheet (or sheets) with key information about the study (or studies)* that you are conducting.
- *If helpful—especially if you are new to clinical research—a script that outlines how you plan to handle conversations with prospective participants.*
- *A checklist of information that you need to obtain during pre-screening* to make sure that you collect all relevant information and avoid unnecessary follow-up.
- *Template communications (e.g., follow-up emails)* with materials and information that you need to send to prospective participants after pre-screening, such as the following:
  - Informed consent form (ICF)
  - Relevant information about the screening visit, such as the date, time, duration, who will be involved, who will provide the ICF, and the procedures involved
  - What to bring, such as information to verify eligibility (e.g., medical records), patient equipment, meals or snacks
  - Encouragement to create a list of any questions about the trial and to bring these questions to the visit
  - Relevant CRC and site contact information

For Task Management and Team Coordination

- *A checklist of actions to prepare your team for screening visits.*
- *Tools that will help you to stay organized and to follow up quickly,* such as task management trackers to help you follow what needs to be done when, and whether it has been done, and team calendars to make scheduling easier.

Questions to Ask When Creating Tools and Templates

Completeness

- Do the materials I've created cover all of the information and actions that they need to cover?

Clarity

- Are the materials I've created clear and easy to follow? (If you're unsure, ask your research participants!)
- Will prospective participants with no prior research experience be able to understand the information that I'm sharing? If not, what can I do to address their questions?

Consistency with Trial Protocol

- Is everything that I've created consistent with the trial protocol?

Need for Review and Approval

- Will anything I've created need to be reviewed and approved by others, such as the principal investigator I'm working with?
- If so, when and how will I obtain the necessary approvals?

Access to the Tools and Templates

- Where will I keep my tools and templates? Will I be able to find them quickly and easily?
- In the case that I'm out of the office or unavailable, will my colleagues know where to find them?

A6: Overview of 2022 Cure SMA Patient-Led Listening Session with FDA: The Shifting Landscape of Spinal Muscular Atrophy (SMA) and Unmet Needs Across the SMA Population

There has been a significant shift in the SMA treatment landscape in recent years as three SMN-upregulating therapeutics have been approved by the FDA. To better understand the current unmet needs, burden of disease, and perspectives of patients with SMA and their families, Cure SMA held a patient-led listening session with the US FDA on August 4, 2022. The attendees of this session included six patient advocates, FDA representatives from the Center for Drug Evaluation and Research (CDER) and Biologics Evaluation and Research (CBER), and representatives from Cure SMA.

The patients described the limitations that the disease has placed on their lives, and emphasized that they would like to see therapeutics developed that target muscle gain and strength. The patients also expressed gratitude for the existing FDA-approved SMA treatments that have improved their quality of life and reduced the burden of disease.

During the session, a need for combination/add-on therapies was stressed. Some patients have experienced motor function gain through the use of SMN-dependent therapies, but noted that there has not been a gain in the strength of muscles required for vocalizing, swallowing, and smiling. Other patients commented on the need for combination/add-on therapies to reduce disease progression and facilitate additional motor function gain. The ultimate hope for patients is that they perform normal daily activities with more independence.

Patients and their families also noted some concerns that they have with participating clinical trials including a reluctance to pause their current therapeutic regimen to participate in a trial that has a placebo arm. They also noted that travel can be a barrier to participating. Additionally, some were concerned with potential long-term side effects of the treatments, and suggested post-marketing surveillance to monitor these effects.

More information on the session can be found at https://www.curesma.org/patient-led-listening-session-with-fda2022/, and a meeting summary is available at https://www.curesma.org/wp-content/uploads/2022/10/FDA-Patient-Led-Listening-Session-Summary-FOR-FDA.pdf.

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