

# **Embracing The Voices of Persons Affected by Spinal Cord Injury: A Roadmap to Addressing Unmet Needs in Spinal Cord Injury Care Through Patient-Focused Drug Development**

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## **Acknowledgment**

This paper was created through a collaborative effort between the Spinal Cord Outcomes Partnership Endeavor (SCOPE) and the North American Spinal Cord Injury Consortium (NASCI). The content within reflects conversations, research, and ideas from:

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This work was funded by the Spinal Cord Outcomes Partnership Endeavor.

## **Section #1: Introduction & Methodology**

### **Introduction**

People living with spinal cord injuries<sup>1</sup> (SCI) often experience significant, long-term impairments with restoration of neurological deficits and function remaining limited. Data show that the estimate of the annual incidence of traumatic SCI (tSCI) is approximately 54 cases per one million people in the United States, or about 18,000 new cases each year. The estimated number of people with tSCI living in the United States is approximately 309,000 persons, with a range from 259,000 to 394,000 persons.<sup>2</sup> Despite decades of effort to provide therapeutic interventions and effective care for this population, there continue to be substantial unmet needs.

As of 2025, there are limited clinical benefits achieved using current approaches in SCI care, and no effective strategies exist as of yet to repair SCI.<sup>3</sup> Unmet needs are many and diverse, including but not limited to a need for treatments to improve autonomic dysfunction, bladder and bowel control, sexual function, and function in limbs and extremities. It is critical to engage people living with SCI at all stages of the research process, and people living with SCI have indicated that they want their voices to be heard in discussions regarding how to address and overcome these shortcomings in existing approaches to treatment. According to the results of a 2019 survey of people living with SCI and care partners<sup>4</sup>, 90% of people living with SCI and their families want to be involved in the setting of research priorities. In the same survey, 83% of respondents reported that people living with SCI and their families are left out of the research process until the point when researchers seek clinical trial participants.<sup>5</sup>

The U.S. Food and Drug Administration's (FDA) Patient-Focused Drug Development (PFDD) program represents a unique opportunity for key stakeholders in the therapeutic development ecosystem, including regulators, medical product developers (MPD), and researchers to hear directly from persons with SCI and their care partners as to their lived experience with the condition. PFDD is a systematic approach aimed at ensuring that patients'<sup>6</sup> experiences, perspectives, needs, and priorities are captured and meaningfully incorporated into drug development and evaluation. According to the FDA, the primary goal of PFDD is to "better incorporate the patient voice in drug

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<sup>1</sup> While many of the issues raised in this paper may also be relevant to people living with non-traumatic spinal cord injury (ntSCI), this paper focuses primarily on traumatic spinal cord injury (tSCI). This reflects the scope of the epidemiological data cited, the focus of the expert interviews conducted, and the areas of emphasis in patient preference studies reviewed. Future work may explore whether and how a PFDD effort might incorporate the perspectives and priorities of those living with ntSCI.

<sup>2</sup> [https://sites.uab.edu/nscisc/?utm\\_medium=golink&utm\\_source=golink](https://sites.uab.edu/nscisc/?utm_medium=golink&utm_source=golink)

<sup>3</sup> <https://academic.oup.com/proteincell/article/14/9/635/7033459>

<sup>4</sup> The authors acknowledge that there is no universal consensus on terminology for individuals who provide care—variously referred to as care partners, caregivers, caretakers, or similar terms. For consistency, we use "care partner" throughout this paper.

<sup>5</sup> <https://nasciconsortium.org/wp-content/uploads/2019/04/Final-report-SCI-2020-panel-and-survey-results-NASCIC.pdf>

<sup>6</sup> While "patient" is neither the preferred nor, in many cases, the appropriate term, the word patient is the standard terminology used in FDA PFDD efforts. The authors recognize that it is not the preferred term, and throughout this paper, we limit the use of the term as much as possible.

development and evaluation.”<sup>7</sup> This goal also includes better incorporating patient voices in the development of devices and biologics.

The principal initiative of the FDA’s program is PFDD meetings. PFDD meetings are focused on a specific disease or condition, led by the FDA or by an external group with FDA attendance, to systematically obtain perspectives of people affected by SCI (PaSCI) on the severity of a condition, its impact on daily life, and their assessments of available treatment options. Since the PFDD program’s launch in 2012, patient advocates and coalitions have participated in more than 100 meetings to provide patient-centered input for their specific conditions. For example, during the 2017 externally-led PFDD meeting for Spinal Muscular Atrophy (SMA), patient input helped the FDA and stakeholders in attendance, including medical product developers and researchers, better understand the experiences that characterize living with the disease and the risks that this clinical population would accept in exchange for identified treatment benefits, contributing to the eventual approval of two new therapies for SMA.<sup>8</sup>

This paper aims to provide guidance for the SCI community, including people living with SCI<sup>1</sup>, care partners, medical product developers, researchers, and medical practitioners, in informing the development of an effective and well-represented SCI PFDD approach. The guidance within addresses key issues, such as:

- How to leverage existing literature and patient preference data—and identify gaps in these resources—to develop the agenda for an SCI PFDD meeting. If needed, this process may include commissioning a new preference survey of people living with SCI to inform discussions that focus on priorities researchers, medical product developers, and regulators can realistically address given the current state of the science.
- Special considerations for organizing a PFDD meeting that allows for representative participation by PaSCI.
- Organizational and financial considerations in planning an EL-PFDD meeting.
- PFDD’s potential to identify the outcomes that matter to persons with SCI and their care partners for medical product developers to target with therapies.

## **Methodology**

This paper adopts a multifaceted approach to provide guidance for the SCI community in shaping an effective and comprehensive SCI PFDD strategy.

Semi-structured qualitative interviews (N=8) were conducted with recognized experts from a variety of relevant fields, including SCI researchers and practitioners, regulatory specialists, and medical product developers. Below are the individuals interviewed for this paper:

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<sup>7</sup> <https://www.fda.gov/drugs/development-approval-process-drugs/cder-patient-focused-drug-development>

<sup>8</sup> <https://www.curesma.org/sma-industry-collaboration-releases-spinal-muscular-atrophy-voice-of-the-patient-vop-report/>

- Kim Anderson-Erisman, Director of the Northeast Ohio Regional SCI Model System based at the MetroHealth Rehabilitation Institute.
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- James Valentine, Director, Hyman, Phelps & McNamara PC.

In addition to the expert interviews, this paper is informed by a targeted literature review of SCI patient preference studies and the results of surveys administered to people living with SCI and their care partners. Further, this paper is informed by existing FDA guidance and literature related to PFDD.

## **Section #2: Unmet Needs in Spinal Cord Injury Treatment and Care**

The SCI clinical population is a prime candidate to host an externally-led PFDD meeting based on guidance released by the agency. The FDA states that PFDD meetings target disease areas and conditions that have in common several key characteristics:

- An identified need for patient input.
- A disease area [or condition] that is chronic, symptomatic, or affects functioning and activities of daily living.
- A disease area [or condition] for which aspects of the disease are not formally captured in clinical trials.
- A disease area [or condition] for which there are currently no therapies or very few therapies, or the available therapies do not directly affect how a patient feels, functions, or survives.
- Disease areas [or conditions] that have a severe impact on identifiable subpopulations (such as children or the elderly).<sup>9</sup>

As demonstrated in the subsections below, SCI is a catastrophic diagnosis where people affected typically endure lifelong complications impacting multiple body functions that create challenges in everyday living, and it shares the characteristics defining a condition suitable for a PFDD meeting.

### **Background on Spinal Cord Injuries in the United States**

SCI is “a serious medical condition, which often results in severe morbidity and permanent disability. It occurs when the axons of nerves running through the spinal

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<sup>9</sup> <https://www.fda.gov/media/160223/download?attachment>

cord are disrupted, leading to loss of motor and sensory function below the level of injury. Injury is usually the result of major trauma, and primary injury is often irreversible.<sup>10</sup> SCI is particularly devastating from a health and economic standpoint. The average age of injury for people with tSCI is 44 years old, and many people are injured before turning 30 years old. People living with SCI often face numerous complications, leaving those affected at greater risk of morbidity and mortality. As a result, SCI is particularly costly, with an estimated lifetime economic burden per individual ranging from \$1.5 million to \$6 million depending on the severity of injury and age at injury.<sup>2</sup>

Vehicle crashes are the leading cause of traumatic injury, closely followed by falls. Commonly, individuals injured in vehicle crashes are younger and suffer more severe SCI, while individuals injured in falls tend to be older with milder injuries (with exceptions for situations like a work-related fall from a high ladder). Acts of violence (mainly gunshot wounds) and sports/recreation activities are also common causes.<sup>2 11</sup>

Temporally, SCIs are commonly divided into three phases: acute, subacute, and chronic. They are also sometimes temporally divided into the acute (<48 hours), subacute (48 hours to 14 days), intermediate (14 days to 6 months), and chronic (>6 months) phases.<sup>12</sup> The exact division and duration of phases can vary in research and practice. Acute injury generally describes the phase immediately after injury, during which time there is some neuro recovery; chronic injury is the last, longer-term stage where neuro recovery has plateaued; and subacute/intermediate describes the bridge stages between acute and chronic.<sup>13</sup> For this paper, we use the classifications from the 2020 NASCIC survey discussed below<sup>5</sup>: individuals in the acute phase refer to those within one-week post-injury, chronic refers to individuals that are 6 months or longer post-injury, and subacute are those individuals that fall in between these benchmarks.

Currently, there are few available treatment options for neurorestoration and recovery of function for people who are living with SCI. Existing clinical interventions for SCI “focus on neuroprotection including early surgical decompression and stabilization, augmentation of spinal cord perfusion, and plasticity inducing interventions such as neurological rehabilitation training in the sub-acute and the chronic phases.”<sup>14</sup> The clinical benefit achieved using existing approaches is limited, and while there are clinical trials underway at time of this paper, there are currently no FDA-approved interventions to repair SCI. As such, people living with SCI often experience long-term dysfunction and lifelong disability.

## **Unmet Needs in SCI Treatment and Care**

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<sup>10</sup> <https://pubmed.ncbi.nlm.nih.gov/32809556/>

<sup>11</sup> <https://www.nscisc.uab.edu/Public/Recent%20Trends%20in%20Causes%20of%20SCI%20-%202023.pdf>

<sup>12</sup> <https://pubmed.ncbi.nlm.nih.gov/28447605/>

<sup>13</sup> <https://www.ncbi.nlm.nih.gov/books/NBK560721/>

<sup>14</sup> <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10501188/>

There are considerable unmet needs in SCI treatment and care in the United States. Below is a table of findings citing prevalent unmet needs from the perspective of people living with SCI, using data from the NASCIC Report of the SCI 2020 Panel and Consumer Survey. This survey included individuals with SCI of varying causes, injury levels, and time since injury.<sup>5</sup>

<b>Survey Result<sup>5</sup></b>
90% of people living with SCI and their families want to be involved in setting research priorities.
83% of respondents reported that people living with SCI and their families are left out of the research process until researchers are looking for clinical trial participants.
58% of respondents reported current research focuses too much on acute injuries [within 1-week post-injury].
70% of respondents reported chronic injuries [6 months or longer post-injury] are under studied in research.
90% of respondents reported funders should do more to direct researchers to design treatments that reflect the needs of people living with SCI and their families.
91% of respondents reported widely available treatments that restore small amounts of function that positively improve daily life now are highly desirable.
98% of respondents reported restoring bladder, bowel, and sexual function are still important.

There were 1,825 respondents to the survey above, comprised of the following demographics:

- 85.1% people living with SCI, 11.2% family members, 3.8% care partners.
- 65.2% male, 34.8% female.
- 9.2% ages 18-30, 22.2% age 31-45, 39.5% ages 46-60, 29.2% age 61 or older.
- 15% cervical 1-4, 31.1% cervical 5-8, 16.2% thoracic 1-6, 12.1% lumbar 1-5, 1.1% sacral 1-5.
- 1.6% less than 1 year post injury (YPI), 21.4% 1-5 YPI, 19.3% 6-10 YPI, 13.7% 11-15 YPI, 9.7% 16-20 YPI, 34.2% 21 + YPI.

These survey findings informed several steps by NASCIC to address the lack of involvement of people with lived experience as advocates in research, as well as the willingness of researchers to engage SCI research advocates. NASCIC formed a working group that represented a diverse team of people with lived experience, clinicians, and researchers to create the SCI Research Advocacy Course.<sup>15</sup> The course is an online curriculum that provides people with lived experience the opportunity to better understand SCI research, research processes, and opportunities to get involved in lay terms. Researchers and clinicians, in turn, are provided with the opportunity to learn more about the lived experience of people living with SCI. NASCIC has also created a form of ‘matchmaking’ where people living with SCI who want to be advocates in research can connect with researchers and clinicians who want to have SCI research advocates involved in their work.

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<sup>15</sup> <https://nascic.org/courses/nascic-scirac-english/>

Using available information and data, we can also point to specific progress made since the survey's publication that address identified needs outlined in the survey results above. For example, the SCI field has seen progress since 2019 in response to the following two statements in the table: "Current research focuses too much on acute injuries [within 1-week post-injury]" and "Chronic injuries [6 months or longer post-injury] are under studied in research." Analytical tools available on SCITrialsFinder.net show that of the 279 SCI trials from 2013 to 2018, 27% recruited participants with acute SCI, 30% recruited participants in the subacute phase, and 43% recruited participants with chronic SCI. In contrast, of the 634 trials from 2019 to 2024, 24% recruited participants with acute SCI, 30% recruited participants in the subacute phase, and 46% recruited participants with chronic SCI. These data demonstrate that there has been a slight positive shift in trials that are inclusive of participants with chronic injuries.

A well-executed PFDD-meeting can inform strategies for responding to the issues in SCI care described above.

### **Key Past SCI Patient-Centered Studies**

Over the past two decades, a growing body of research has examined the recovery goals, treatment preferences, and lived experiences of people with SCI. This section highlights four particularly influential and illustrative studies that have helped shape the field:

- 1) "Targeting Recovery: Priorities of the Spinal Cord Injured Population" by Kim Anderson, PhD, 2004
- 2) "Recovery Insights Following Spinal Cord Injury: A Consumer's Perspective" by Gretchen A. Ferber, MD, MFA and Kim Anderson, PhD, 2025.
- 3) "Functional recovery priorities and community rehab service preferences" by Lam et al., 2022.
- 4) "Functional Priorities in Persons with Spinal Cord Injury: Using Discrete Choice Experiments to Determine Preferences" by Lo et al., 2016.

Together, these studies offer critical insights that should directly inform the design and focus of any future SCI PFDD initiative.

*Anderson, 2004*<sup>16</sup>

Anderson's 2004 study, "Targeting Recovery: Priorities of the Spinal Cord Injured Population," was one of the first to systematically document the recovery goals of people living with SCI. Using surveys disseminated online and by mail, the study found that for people with tetraplegia, regaining hand and arm function was the most frequently cited priority (48.7%), while people with paraplegia most commonly prioritized sexual function and bowel/bladder control. Across both groups, the restoration of bladder/bowel and sexual function consistently ranked among the top two preferences.

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<sup>16</sup> <https://www.liebertpub.com/doi/10.1089/neu.2004.21.1371>

The study helped catalyze broader efforts to incorporate the lived experience of people with SCI into outcome selection and research design. While modest in scale, it remains a foundational work and is frequently cited in subsequent literature. Anderson also acknowledged several limitations, including potential underrepresentation of respiratory function, and highlighted the need for more comprehensive and representative research.

*Ferber & Anderson, 2025<sup>17</sup>*

In their 2025 article, “Recovery Insights Following Spinal Cord Injury: A Consumer’s Perspective,” Ferber and Anderson present the most comprehensive synthesis to date of the priorities of people living with SCI. Reviewing 68 peer-reviewed studies representing over 11,000 individuals with SCI, the authors examine what people with SCI say matters most to them across differences in injury level, completeness, time since injury, demographic characteristics, and cultural context.

The review identifies three interrelated domains of priorities: functional recovery, management of secondary complications, and preferences for interventions. Across these areas, motor function, bladder and bowel control, and sexual function consistently rank among the most important goals. Ferber and Anderson emphasize that secondary complications and functional priorities are deeply intertwined. For example, improving bladder or bowel control can reduce pain, decrease infections, and increase independence, producing cascading benefits across daily life.

Relatedly, the authors demonstrate that individuals’ recovery priorities inform how they assess the risks and benefits of potential interventions. People with SCI weigh risks and benefits in relation to the functions they most want to regain, and are often willing to accept significant burdens, such as invasive procedures or potential side effects, when an intervention aligns with those goals. This decision-making process reflects more than clinical logic; it reflects personal context, including time since injury, age, injury characteristics, and risk tolerance. Across interventions such as neuroprostheses, assistive technologies, surgical reconstruction, and clinical trials, people with SCI consistently express the desire for greater autonomy and for a voice in shaping their care.

Yet, despite the robust evidence base that exists, Ferber and Anderson argue that the field has failed to act on the priorities that people with SCI have long made clear. Sexual function, for example, is routinely ranked as a high priority but remains understudied. Further, the authors critique how studies rarely include racially and socioeconomically diverse participants or examine how structural factors shape recovery goals. Likewise, they note that terms like “meaningful recovery” appear frequently in regulatory and research settings but are seldom defined using input from people with SCI themselves.

Ferber and Anderson conclude by arguing that further surveying of the priorities of people living with SCI is unnecessary. In their view, the priorities are known. What is

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<sup>17</sup> <https://www.sciencedirect.com/science/article/pii/S104796512400069X?via%3Dihub>

needed now is alignment between the perspectives of people with SCI and the choices made by researchers, clinicians, product developers, and regulators. Their review provides a detailed roadmap for achieving that alignment and should serve as a foundational reference for any future PFDD initiative focused on SCI.

*Lo et al., 2016*<sup>18</sup>

The 2016 study, "Functional Priorities in Persons with Spinal Cord Injury: Using Discrete Choice Experiments To Determine Preferences," was conducted by Lo C et al. to determine the priorities of individuals with SCI to guide future research. However, unlike the Anderson study discussed above and Lam et al. study referenced below that used a priority ranking system, this study used a discrete-choice experiment (DCE) to determine the preference of five high-priority areas of functional recovery: arm/hand use, walking, bladder/bowel control, sexual function, and relief of pain.

The researchers used a DCE because "although ranking methodology provides a valid order for priorities, the relative difference in weights between the prioritized health functions could have been either very small or very large." DCEs, on the other hand, allow participants to choose from various scenarios in which they weigh their preference for one type of functional recovery against the loss or lack of improvement in another area.

The survey sampled 151 SCI-affected individuals from the United States and Australia, of which 79 had paraplegia and 72 had tetraplegia. The participants in Australia were found through support group newsletters and organization websites, while the American participants were recruited by emailing information "via the Miami Project research volunteer registry." All participants completed a survey consisting of 20 discrete-choice scenarios and demographic and injury-related questions. Most participants completed the survey online.

The researchers found that arm/hand function was the most preferred function and the least likely to be traded off. The second most highly favored was bladder/bowel function, and sexual function was the most likely to be traded off, making it the least preferred function. There were no major differences in preference between tetraplegics and paraplegics other than tetraplegics preferred situations that involved limiting chronic pain, and paraplegics preferred to retain hand/arm function or gain walking ability. The researchers also found that individuals living with an SCI for over three years were more likely to prioritize eliminating chronic pain. No other preferences were different between the two groups. In line with the other two studies, Lo C et al. also found that arm/hand function and bladder/bowel function were the two highest priority areas of functional recovery.

*Lam et al., 2022*<sup>19</sup>

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<sup>18</sup> <https://www.liebertpub.com/doi/10.1089/neu.2016.4423>

<sup>19</sup> <https://www.frontiersin.org/journals/neurology/articles/10.3389/fneur.2022.941256/full>

The 2022 study, "Functional Recovery Priorities and Community Rehab Service Preferences," by Lam CY et al., surveyed SCI-affected individuals from China to determine what type of functional recovery they prioritize the most. Additionally, the survey included questions regarding the respondent's attitudes toward community rehabilitation services and advanced technology and research. Much like in Anderson's study, the researchers were interested in learning about the functional recovery priorities of individuals living with SCIs to make rehabilitation practices, public health initiatives, and medical studies more responsive to patients' priorities.

A collection of non-governmental organizations distributed the survey to individuals with traumatic and non-traumatic SCI injury as well as their care partners. The survey received 87 responses, with 74 from SCI-affected individuals and 13 from care partners. Like in Anderson's 2004 work, the survey grouped areas of functional recovery known to have a substantial impact on SCI patient quality of life into seven categories: arm/hand function, upper body/trunk strength and balance, bladder/bowel function, sexual function, elimination of chronic pain, normal sensation, and walking movement. The survey asked patients to rank the seven areas in order of importance to them. They also answered questions about SCI community rehabilitation services and "their willingness to try advanced technology in rehabilitation, and their expectations of the effects of advanced technology and research on their quality of life in the coming ten years."

The survey results closely resembled many of the findings from Anderson's study, with a few notable differences. For tetraplegic individuals, respondents ranked recovery of hand/arm function as the highest priority, with a median ranking of 2 out of 7. Upper body/trunk strength, balance, and bladder/bowel function followed with a median ranking of 3. Sexual function was last, with a median ranking of 7. In the case of paraplegic individuals, the highest priority was gain of bladder/bowel function with a median ranking of 2, followed by walking movement with a median ranking of 3. Arm/hand function and sexual function were the lowest priority, with both having median rankings of 5. The opinion of primary care partners was similar to tetraplegic individuals, with them ranking arm/hand function the highest alongside upper trunk/body strength and balance, and bladder/bowel function being ranked the second highest. Once again, gain of sexual function was ranked the lowest priority.

Other noteworthy results were that only 14.9% of respondents thought their current community rehabilitation services were adequate, while 57.5% thought they were inadequate. Additionally, the outlook on the likelihood of advanced technology improving their quality of life in the next ten years varied greatly between paraplegics and tetraplegics, with 29.2% of people with tetraplegia responding that they thought a significant breakthrough was unlikely compared to 3.8% of people with paraplegia.

The main limitation of this study was that the surveyed population was comprised entirely of individuals from Chinese ethnic/cultural backgrounds, making results difficult to generalize in relation to other SCI populations because of cultural and economic differences.

## **SCI Outcome Measures**

## *Common SCI Outcome Measures*

The availability of validated and sensitive outcome measures is crucial to ensuring patient-centered progress in SCI treatment and care. In interviews with SCI outcome measure experts for this paper, various measures used in both clinical trials and clinical practice were discussed. Common SCI outcome measures referenced by interviewees include:

- Various aspects of the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI), including upper extremity motor scores, lower extremity motor scores, light touch of a pinprick sensory scores, zone of partial preservation, and neurorestorative or neuro-recovery outcomes.
- Motor levels, particularly in the cervical region.
- ASIA Impairment Scale (AIS) Conversion.
- Graded Redefined Assessment of Strength Sensibility and Prehension (GRASSP)
- Capabilities of Upper Extremity Test (CUE-T).
- Grasp-Release Test
- 6-minute walk (6MWT), 10-meter walk (10MWT), and other walking measures.
- Quality of life measures, including the Satisfaction With Life Scale (SWLS).
- Spinal Cord Independence Measure (SCIM).

The list above is not comprehensive of all SCI outcome measures used in practice. Several comprehensive resources are linked in the footnotes below.<sup>20 21 22</sup>

## *Common Shortcomings of Existing Outcome Measures*

There are numerous shortcomings in the existing outcome measures used in SCI treatment and care. Below is an overview of the prevalent shortcomings identified in our conversations with experts. The shortcomings identified below reflect the opinions of the experts interviewed for this paper and are not an exhaustive list. For a more comprehensive discussion of the shortcomings of existing outcome measures, see Bolliger et al., 2018 and Jones et al., 2018.

### *Limited Impacts on Daily Living:*

While some outcome measures demonstrate statistical or clinical significance, their direct impact on daily activities is not always clear.<sup>23</sup> Researchers can identify statistically significant changes in outcome measures, but there are many factors that could influence these scores. For example, experts indicated that using common outcome measures such as upper extremity motor scores, sensory changes, and others may reveal statistically significant changes for researchers without making a meaningful difference in activities of daily living for people living with SCI.

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<sup>20</sup> <https://scireproject.com/outcome-measures/>

<sup>21</sup> <https://commondataelements.ninds.nih.gov/Spinal%20Cord%20Injury>

<sup>22</sup> <https://www.sralab.org/rehabilitation-measures>

<sup>23</sup> <https://pubmed.ncbi.nlm.nih.gov/25510192/>

A commonly referenced example illustrating this point during interviews for this paper was the movement of a pinky (the little finger) for people living with SCI who lost function in their arms and hands. Regaining movement of a pinky for these individuals may be clinically significant but likely does not meaningfully improve their day-to-day lives. Yet, at the same time, regaining movement in a pinky can be the first step toward considerable progress in the early development of new devices and interventions.

*Outcome measures are not sensitive enough:*

For an impairment-based example, motor scores of the International Standards for Neurological Classification of SCI (ISNCSCI) only measure “key muscles,” such as biceps and muscles in the wrist, so the measure may not pick up improvements in non-key muscles unless specifically tested.

Further, people living with SCI will adapt to their condition. As a result, when relying on patient-reported outcomes (PROs) examining how difficult a task is in usual environments, the baseline can be remarkably high, which makes it challenging to measure neurorestorative impact. Moreover, as discussed above, while outcome measures can detect differences, those differences may not always correlate well with what a patient considers a meaningful improvement.

*Lack of one “perfect outcome measure”:*

There is no perfect outcome measure, so the decision to implement a variety of measures to evaluate different aspects of the SCI experience is often made in practice, which can become burdensome for patients.

Researchers can respond to this issue in part through goal attainment scaling (GAS). GAS is a method of scoring the extent to which a patient’s individual goals are achieved in the course of intervention.<sup>24</sup> In effect, each patient has their own personalized outcome, but scored in a standardized way to allow statistical analysis.

*Use of Medical Jargon in PROs:*

Legacy outcome measures can rely heavily on medical jargon, confusing patients and care partners.

## **Special Considerations for SCI Clinical Trial Design**

Clinical trials involving individuals with SCI necessitate careful consideration of unique factors and potential obstacles. Outlined below is a non-exhaustive list of issues based on our discussions with experts and common barriers encountered in designing clinical trials for this population:

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<sup>24</sup> <https://www.sralab.org/sites/default/files/2017-06/Tools-GAS-Practical-Guide.pdf>

- Recruiting individuals from diverse racial, ethnic, and economic backgrounds.
- Differing levels of bowel function, bladder function, degree of pain, spasticity, and upper and lower extremity function.
- Awareness of trials.
- Limited window of eligibility for studies, as many trials are in the subacute phase.
- Financial burdens on patients.
  - Transportation barriers.
  - The need for physical accommodations for people living with SCI.
  - Unpaid caregiver costs.
- Narrow exclusion criteria that are too restrictive to recruit a representative pool of participants.
- A lack of objective biomarkers in SCI research.

## **Section #3: Patient-Focused Drug Development Meetings**

### **Patient-Focused Drug Development (PFDD) Background**

During the first five years of the FDA's PFDD program, the FDA organized and led 24 disease-specific meetings. Since 2017, to allow for more meetings, the meetings have instead been externally organized with FDA attendance. The FDA has attended over 80 externally-led (EL) meetings since this change.<sup>25</sup>

In their materials, the FDA identifies several potential key outcomes from disease-specific PFDD meetings. These outcomes include:

- Clinical trial endpoints and relevant Clinical Outcome Assessment (COA)-related concepts to assess.
- What patients consider unmet needs for therapies, and what risks they would potentially be willing to tolerate with a therapy.
- What patients consider a meaningful treatment benefit, etc.<sup>26</sup>

### **PFDD Success Stories: Three Examples**

Since the program's launch in 2012, there are many examples of the impact that meetings have had on patient communities that demonstrate the potential of a successful SCI PFDD. Below are three examples:

#### *Sickle Cell Disease (SCD)*<sup>27</sup>

**Disease Background:** SCD is a group of disorders that causes red blood cells to contort into a sickle shape. The cells die early, leaving a shortage of healthy red blood cells (sickle cell anemia), and can block blood flow, causing pain (sickle cell crisis).

**Before PFDD:** For decades, SCD had one approved agent – a repurposed cancer drug. 30% of SCD clinical trials failed to complete enrollment, and a focus on pain as the primary symptom led to excessive corporate and regulator attention on pain medication options, dosing schedules, pain scores, opioid stigma, etc.

**After PFDD:** In the five years following the SCD PFDD meeting, the FDA approved three SCD-specific agents. One of the new agents, Voxelotor (Oxbryta), aims to improve red blood cell function, a distinction from other approved agents that primarily target pain. The meeting also “led to agreement on clinical and surrogate endpoints for accelerated approval and a confirmatory study.”<sup>28</sup>

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<sup>25</sup> <https://www.fda.gov/industry/prescription-drug-user-fee-amendments/externally-led-patient-focused-drug-development-meetings>

<sup>26</sup> <https://www.fda.gov/media/160223/download?attachment>

<sup>27</sup> <https://www.fda.gov/industry/prescription-drug-user-fee-amendments/public-meeting-sickle-cell-disease-patient-focused-drug-development>

<sup>28</sup> <https://www.sciencedirect.com/science/article/pii/S1551714420302391>

## *Epidermolysis Bullosa (EB)*<sup>29</sup>

**Disease Background:** EB is a genetic skin fragility disorder due to defective structural proteins in the skin. Wounds are caused by trivial trauma and friction.

**Before PFDD:** Prior to the 2018 PFDD meeting for EB, trials for the condition were directed by the FDA to yield “clinically meaningful” treatment effects based on FDA burn wound guidelines despite different mechanisms of EB wound injury and healing.

**After PFDD:** In response to the 2018 EB PFDD meeting, the FDA released EB disease-specific guidance that allowed for disease-specific endpoints relating to incremental healing and analgesic effects.

## *Spinal Muscular Atrophy (SMA)*<sup>8</sup>

**Disease Background:** SMA refers to a group of hereditary diseases that can damage and kill specialized nerve cells in the brain and spinal cord (motor neurons). SMA is characterized by weakness and wasting in muscles used for movement.<sup>30</sup>

**Before PFDD:** Before the 2017 SMA EL-PFDD meeting, there was only one FDA-approved treatment for people living with SMA, Spinraza, approved less than six months prior to the meeting.

**After PFDD:** Patient input helped the FDA and stakeholders in attendance better understand the risks that this patient population would accept in exchange for identified treatment benefits, contributing to the eventual approval of two new treatments for SMA: the first ever FDA-approved gene therapy, Luxturna, in 2017, and the approval of the first-ever systemically-administered somatic gene replacement therapy, Zolgensma, in 2019.

## **How PFDD Can Help Improve Outcomes for People Living with SCI.**

People living with SCI, as shown through survey data and patient preference studies, face many unmet needs. Additionally, as described above, there are several shortcomings in the existing outcome measures used in SCI treatment and care. Interviews with experts and guidance from the FDA suggest several ways that a PFDD can inform strategies for improving outcomes for people with SCI and build on the learnings of past research:

- 1) Identifying the effects of SCI that matter most to people living with SCI and care providers.

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<sup>29</sup> <https://www.fda.gov/media/128419/download>

<sup>30</sup> <https://www.ninds.nih.gov/health-information/disorders/spinal-muscular-atrophy>

- 2) Developing a better understanding of patient perspectives on participating in clinical trials and on interventions aimed at improving function, managing complications, and enhancing quality of life.
- 3) Improving stakeholder understanding of benefit-risk assessments for SCI populations.
- 4) Achieving stakeholder alignment on the patient-preferred language used in SCI diagnosis, treatment, and care.
- 5) Selecting/identifying validated measures for body systems important to people living with SCI to construct endpoint(s) for functional improvement.
- 6) Identifying gaps in existing outcome measures that may lead to modifications to existing measures or recommended development of new measures.

### **Key Stakeholders in a Well-Represented SCI PFDD Approach**

Stakeholder collaboration is essential in organizing an EL-PFDD meeting. There are six key stakeholder groups to involve, each with well-defined roles:

- 1) People living with SCI and care partners
- 2) Patient Advocacy Organizations (PAO)
- 3) Medical Product Developers
- 4) Practitioners
- 5) Researchers
- 6) The FDA

#### *People with SCI and Care Partners*

Individuals who share their experiences and perspectives during PFDD meetings are limited to people with SCI and their care partners (spouses, parents, family members, and friends). The meetings aim to hear from people who have direct lived experience with the condition, not researchers (other than to share scientific background as discussed below), advocates without lived experience, medical product developers, or others. When recruiting people living with SCI and care partners to participate, organizers should take steps to ensure that participants represent a diverse group of people with lived experience. Participants should represent diverse social, ethnic, racial, geographic, gender, and economic backgrounds and have a diversity of attitudes toward their conditions, including people who are risk-averse, risk-tolerant, risk-seeking, etc.

#### *Patient Advocacy Organizations (PAO)*

PAOs are responsible for organizing EL-PFDD meetings. Typically, the process is led by one PAO but with the support of other similar organizations. The leading PAO (or PAOs if it is a coalition) is the decision-maker in planning and organizing the PFDD meeting.

It is crucial that the PAO leading the efforts builds consensus with other major PAOs in the same disease area prior to initiating the PFDD meeting process with the FDA. The leading PAO should utilize best practices in consensus building, including the use of practices like multi-voting, nominal group technique, Delphi technique, consensus development conference, and others. PFDD meetings should accurately represent the patient community involved, a feat that can only be achieved if the major groups representing the same patient populations are aligned. Previously, the FDA has declined to accept requests for EL-PFDD meetings because the PAO leading the effort did not attempt to build consensus with other PAOs representing the same patient population.

Below is a list of leading PAOs in the SCI community based on interviews with SCI experts. This list is not exhaustive, and there may be other SCI PAOs who can provide valuable input toward PFDD meeting efforts:

- North American Spinal Cord Injury Consortium (NASCI)
- Unite 2 Fight Paralysis
- United Spinal Association
- Paralyzed Veterans Association
- The Christopher & Dana Reeve Foundation

### *Medical Product Developers (MPDs)*

MPDs can help fund a PFDD meeting, provide key input on where they view the opportunities for medical product development in SCI, provide real-life experience on the obstacles posed by regulatory agencies, and speak to the state of the treatment pipeline. MPDs cannot have decision-making authority in the planning and organizing process of a PFDD meeting.

MPDs are also a key audience of EL-PFDD meetings, as learnings from the meetings will influence their future actions in therapeutic research and development.

### *Practitioners and Researchers*

Condition experts are present during a PFDD meeting to share scientific background before discussion but do not share input on PaSCI preferences and experiences. Clinical researchers and academics (who are not part of the PAO leading the effort) should not have decision-making authority in the planning and organizing process of a PFDD meeting. However, researchers, particularly outcome experts, could play a significant role in deciding on the scope of the PFDD meeting during the pre-planning stages. For example, in the case of SCI, outcome experts can speak to whether there are robust, existing measures to evaluate functions prioritized by people living with SCI in patient preference studies.

## *The FDA*

The FDA has several roles during an EL-PFDD meeting. At the official start of the process, the Agency approves requests to have an EL-PFDD meeting with FDA attendance. During the planning stage, the FDA has PFDD staff liaisons who can provide input on planning efforts. Agency representatives attend the meetings and later make regulatory decisions influenced by the learnings from the PFDD process.

### **Special Considerations for Organizing an SCI PFDD Meeting**

There are key considerations that organizers of an SCI EL-PFDD meeting should address in developing a strategy for this specific patient community. Regulatory and SCI experts interviewed for this paper highlighted several considerations, including defining the scope and agenda of a SCI PFDD meeting, practical adaptations for this patient community, ensuring an accurate representation of the SCI patient population, and others.

#### *Defining the Scope and Agenda of a SCI PFDD Meeting*

Several experts interviewed for this paper shared concerns that one PFDD meeting meant to represent the entire SCI community could be too broad. SCI is not one-size-fits-all; the type and location of injury, injury severity, chronicity of injury, and more all influence the experiences and preferences of individuals living with SCI. Given this diversity, a real risk in the planning process is organizing a meeting that fails to capture important nuances or leaves participants feeling their perspectives were overlooked. These concerns helped shape this paper's emphasis on careful agenda design and inclusive planning.

At the same time, input from experts with direct experience in the FDA's PFDD process strongly suggests that the agency is likely to grant only one EL-PFDD meeting per disease or condition. This means the SCI community must plan for a single, comprehensive meeting that reflects the full spectrum of lived experiences across the SCI population.

To accomplish this, we recommend a strategy that maintains a broad meeting scope while using available tools—such as community surveys, expert interviews, and working groups—to help prioritize which topics to spotlight during the meeting. For example, agenda development could be guided by preference data that identifies the most pressing concerns across subpopulations, ensuring the meeting gives voice to individuals with different types, levels, and stages of injury, as well as people with a wide range of functional goals and day-to-day challenges.

Rather than narrowing the meeting scope and risking the exclusion of individuals whose experiences fall outside that initial frame, these preparatory efforts would allow organizers to thoughtfully structure the meeting to promote inclusive representation and meaningful dialogue. This could include organizing testimony and discussion

panels by body system, injury stage, or other relevant categories while maintaining a unified meeting framework.

Ultimately, the goal is to design a meeting that is both comprehensive and representative—broad in scope but structured in a way that captures the diverse and nuanced perspectives of people living with SCI. Doing so will maximize the value of the PFDD meeting for people living with SCI and for key audiences such as researchers, regulators, and medical product developers.

### *Practical Adaptations and Considerations When Organizing an SCI PFDD Meeting*

When planning a PFDD meeting for SCI patient populations, organizers may face unique barriers distinctive from other communities where patients do not experience the same severity of physical disability. Organizers should be cognizant of these considerations and include adaptations in their planning. Considerations include:

- Transportation to an in-person meeting can be more burdensome for individuals with SCI, who may use wheelchairs and other related equipment, than for individuals without mobility limitations who participated in other disease-specific PFDD meetings. Similarly, transportation is likely to pose a greater financial burden compared to individuals without physical impairments.
- The environment of an in-person meeting must be easily accessible for those with mobility impairments and accommodating for those with care partners.
- Acknowledgment and consideration in the planning process of participants' differing levels of bowel function, bladder function, degree of pain, spasticity, and upper and lower extremity function.
- Unpaid caregiver costs.

In recent years, since the COVID-19 pandemic, many EL-PFDD meetings have been held remotely. Organizing a remote SCI meeting could address some of the potential issues outlined above, but this format may present new challenges. For instance, inconsistent internet access, varying levels of technological proficiency, and difficulty replicating informal networking and social engagement can all limit participants' ability to fully benefit from a virtual event. Therefore, whether the meeting is held in person or online, organizers should intentionally design and implement plans to alleviate as many barriers to participation as possible.

### *Ensuring Diverse and Accurate Representation of the SCI Patient Population*

It is essential that lived-experience participants of an SCI PFDD meeting are an accurate representation of the diverse SCI community. The lived experience panels, in particular, should represent a diverse assortment of perspectives. As discussed above, organizers should consider chronicity and severity of injury in their planning and take steps to recruit individuals with diverse risk-benefit profiles, including people who are risk-averse, risk-tolerant, risk-seeking, etc.

In addition, to accurately represent the patient population, attendees must be racially, ethnically, socioeconomically, and gender diverse. Experiences, perspectives, and health outcomes can differ for people of different backgrounds. Historically, there has been considerable variability in rehabilitation outcomes within the population of spinal cord-injured individuals across racial and socioeconomic groups.<sup>31</sup> White, more affluent individuals are also more often represented in SCI research and clinical studies than others, and geographic differences often limit the participation of people from areas of the country without major SCI centers. Organizers should be deliberate in their planning to recruit a diverse, representative group of participants.

If organizers choose to commission patient preference surveys to inform their decision on the scope of a meeting, they should address the same issues as above related to diverse and accurate representation.

## Implementation Challenges and Recommended Next Steps

### *Implementation Challenges*

There are several potential implementation challenges to be aware of during the planning process. The following table outlines implementation challenges, descriptions, and potential solutions:

<b>Implementation Challenge</b>	<b>Description / Key Question</b>	<b>Potential Solution(s)</b>
Organizing an EL-PFDD meeting is a significant financial commitment.	The estimated costs of organizing a meeting are significant, with experts interviewed for this paper suggesting costs of ~ \$150,000 to organize an externally-led meeting.	Past meetings have been sponsored by medical product developers with ties to the specific patient community.
Staying organized during planning.	SCI PFDD leaders need to be highly organized. There are many moving parts to consider in planning.	There are a few best practices to help maintain organization during planning, including: <ul style="list-style-type: none"> <li>• Following the model of prior PFDD meetings.</li> <li>• Having one person from the leading organization take charge of project management.</li> </ul>

<sup>31</sup> <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3746335/>

		<ul style="list-style-type: none"> <li>• If budget allows, retaining outside firms with experience planning PFDD meetings.</li> </ul>
Stakeholder Communication	There is a lack of existing communication between key stakeholders: medical product developers, government, academia, patient advocacy, and people living with SCI.	The Spinal Cord Outcomes Partnership Endeavor (SCOPE) can assist in coalition building. SCOPE membership includes key stakeholders, such as key opinion leaders from academia, government representatives, medical product developers, and PAOs. The SCOPE PFDD subcommittee also has representation from all stakeholder groups, including people living with SCI.

*Recommended Next Steps*

Based on the information laid out above, informed by SCI literature, published FDA guidance, and interviews with experts, this paper recommends the following next steps toward planning an SCI PFDD meeting:

- 1) **Align Stakeholders:** Major SCI stakeholders align and form a collaborative coalition led by people living with SCI, with representation from care partners, leading patient advocacy organizations, researchers, clinicians, and medical product developers. This group should work together to guide the planning process, elevate lived experience, and ensure transparency and trust across stakeholder groups.
- 2) **Define Meeting Priorities:** Draw on existing patient preference data—and commission new surveys if needed—to identify the most pressing unmet needs, areas of functional impact, and treatment goals from the perspective of people living with SCI. These priorities should also be evaluated in light of scientific feasibility and the current state of therapeutic development.
- 3) **Plan Inclusively:** Design the meeting to reflect the full diversity of the SCI community. This includes ensuring representation across racial, ethnic, geographic, socioeconomic, and functional backgrounds. Organizers should also address practical barriers to participation such as technology access, caregiving needs, and mobility accommodations to ensure all participants can fully engage.

- 4) **Engage Regulators and Industry:** Proactively involve the FDA at the outset of the planning process to align expectations and receive guidance on format and content. Simultaneously, engage medical product developers to promote alignment between patient-identified priorities and areas of innovation, and to help ensure the meeting yields actionable insights that drive future investment in SCI-focused therapies and technologies.