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Stem Cell Clinical Trials for Spinal Cord Injury: Readiness, Reluctance, Redefinition

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Abstract A wealth of scientific and clinical research has focused on the use of stem cells as a potential therapy for spinal cord injury (SCI), culminating most recently in the initiation of clinical trials. However, with the urgency that scientists and clinicians have undertaken to move forward with novel therapies for this devastating injury, the perspectives of stakeholders who live with a SCI have been left behind. Translational research in this rapidly growing field therefore overlooks a critically important viewpoint. We address this concern with a qualitative study of the perspectives on experimental stem cell treatments from individuals who have actually suffered a spinal cord injury. Using focus groups and interviews, we engaged individuals with thoracic and cervical SCIs at sub-acute and chronic stages post-injury. We found four major themes that inform the progression of stem cell research to clinical trials: '*readiness*', '*the here and now*', '*wait and see*', and '*informed hope*'. Taken together, the data suggest a profound difference related to target timing of stem cell clinical trials and the perspectives about timing from those who are the end-beneficiaries of therapy. To bridge this gap, we conclude with a number of considerations for the timing disparity of trials and recommendations for improving informed consent.

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Introduction

Significant efforts within the biomedical sciences are being made to develop therapeutic strategies for stem cell transplantation for spinal cord injury (SCI) [1–3]. However, this research and its enthusiastic translation into human trials are being conducted with little information about the values and priorities of the end-beneficiaries themselves—those directly affected by SCI—to guide it. With approximately 130,000 newly affected individuals around the world each year [4], the relative absence of data about their views on emerging therapies is a major gap in the translational trajectory [5]. We and others have argued that for the science to be applied for maximum health good, it is critical to identify and address the considerations of all stakeholders—scientists, clinicians, people with SCI, and family members—along the full continuum from injury to recovery or adaptation, and to anticipate associated ethical challenges of emerging interventions at the earliest stages of research [6, 7].

A small number of researchers to date have tackled this social science challenge. In one report published in 2003, Estores suggested that the input of stakeholders is vital to the development of studies about SCI, as is their participation in focus groups and in other qualitative research designed to understand consequences, priorities and preferences over time [8]. In the same year, Anderson reported on results of a study in which she engaged stakeholders directly in her research [9]. As a scientist with 20 years of experience living with a cervical SCI, she delivered key

data on the highest priorities for functional recovery after SCI and quality of life. Anderson demonstrated, for example, that regaining arm and hand function is most important to people with tetraplegia, and sexual function is the highest priority for people with paraplegia. Improvement of bladder and bowel function is of shared importance to both injury groups. Taken together, their results demonstrate that the perspectives of individuals living with SCI can inform a scientific community largely fixated on improving lower extremity function, and that the recovery of the ability to walk is not necessarily the main goal.

In 2008, Grunwell et al. conducted interviews with a parallel stakeholder group—clinical and scientific members of the stem cell community [7]. Their findings highlighted the importance of ethical considerations around stem cell research for diseases of the central nervous system broadly, and specifically around issues of cross-species cell transplantation, the evidence needed to justify movement of research to preclinical trials, enrollment of vulnerable populations including children, and public trust. More recently, Kwon et al. (2009) surveyed a larger sector of this community about the preclinical scientific evidence needed on stem cell therapies before translation to human trials [10]. They reported that behavioral recovery in locomotor performance is the most important indicator of meaningful clinical efficacy. In addition, many respondents in their study expressed that the demonstration of stem cell efficacy in large-animal or primate models is necessary before proceeding to preclinical trials in humans. Overall, the shared hope of the researchers was for a rational, collaborative and realistic pre-clinical research framework for bringing effective treatments to persons with SCI.

Scarce reports such as these exist against a backdrop of an increasing number of stem cell clinical studies that are ongoing or on the horizon for SCI. Much attention has been directed recently to the first North American FDA-approved clinical trial by Geron Corporation (Geron, Menlo Park, CA), for example, assessing the safety and tolerability of human embryonic stem cells derived from oligodendrocyte progenitor cells in patients with complete thoracic paraplegia [11]. Other clinical trials involve individuals with sub-acute or chronic SCI who have received transplantations of various cell substrates, including antilogous bone marrow derived cells [12–18], autologous olfactory mucosal grafts [19], and autologous olfactory ensheathing cells [20]. These studies generally all focus on the safety and feasibility a stem cell therapy of interest, as efficacy is essentially impossible to determine from the small, non-randomized participant groups on which they are based. They are also occurring alongside other clinical trials with stem cells for neurologic disorders such as stroke [21].

In this project, we sought the direct input of individuals with SCI about early clinical stem cell transplantation trials. Our goal was to deliver evidence-based recommendations for SCI trials of stem cell therapies that would meet the challenges identified by these individuals. Our findings here are part of a larger scale study that includes the full range of stakeholders: persons with SCI, their network of family and friends, and health care professionals. Based on our clinical experience and the peer-reviewed literature [22] in this wider context of the research, we hypothesized that individuals with the most severe functional impairments, i.e., cervical injuries, would be most eager to participate in stem cell trials.

Methods

Recruitment

Participants with traumatic SCI were recruited between August 2009 and September 2010 through a provincial Canadian database housed at the sole SCI referral center for a population of approximately 4 million people. The sample was drawn from four patient groups based on two major criteria: (1) Level of SCI in reference to the last pre-injury level of function—We included individuals who had suffered a cervical SCI with a neurological level of C4, C5, C6, or C7, or a thoracic SCI with a neurologic level of T4 to T12. (2) Time post-injury—Individuals who had suffered a spinal cord injury within one to seven months of the study were entered into the sub-acute arm of the study. These individuals were in the time window where the greatest neurologic recovery was still potentially occurring. Those with injuries more than 18 months prior to the study were entered into the chronic arm, based on the premise that their neurologic impairment was established and stable. Individuals within 8 to 18 months were not eligible for participation in this study as they tend to be in a plateau post-injury phase during which neurologic recovery might be occurring, but at a much slower rate than during the first 6–7 months. In essence, we sought the perspectives from two distinct groups—one in which neurologic recovery is likely to still be actively occurring, and the other in which neurologic recovery has ceased.

Eligible participants were sent a letter of invitation, a consent form, and an information FAQ sheet. The information sheet described the effects of injury to the spinal cord, why stem cells are being considered as a treatment for SCI, the current state of the art, and the scientific and medical promises and risks of stem cell transplantation for SCI. Individuals who participated in the chronic arm of the study received the consent form in the mail and returned it either by mail or brought it to the focus group in which they participated. The consent form was hand-delivered to those who participated in

the sub-acute arm of the study and was returned at the time of the interview. All work was conducted under the approval of our institution's Behavioral Research Ethics Board.

Data Collection

Focus Groups—Chronic Injury Cohort We held five focus groups (FG) with two to five SCI participants each. The Project Leader (JR) led the groups, assisted by a professional facilitator. Groups were 60 to 90 min long and audio-recorded for later transcription.

Individual Interviews—Chronic Injury Cohort and Sub-Acute Cohort We conducted four one-on-one interviews (INT) with chronic post-injury participants who were unable to attend the focus groups, and 14 interviews with individuals in the sub-acute cohort. Interviews were approximately 30 min long and, like the focus groups, audio recorded and transcribed for analysis.

The groups and interviews focused on the following topics: sources of information about stem cells, perceptions of the benefits and risks of stem cells, factors that balance the possible risks against the benefits, receptivity to participating in clinical trials, decision-makers about clinical trials, perceptions about alternative therapies for stem cell treatment, and evolution of preferences about experimental treatments since time post injury.

Analysis

The output from each focus group and interview formed the basis for the rigorous and iterative process of qualitative analysis. We treated the data from the groups and interviews similarly, using a method of constant comparison. This involved segmenting the raw data (phrases, sentences, paragraphs), labeling and synthesizing the data, identifying categories and dimensions, and searching for patterns that could be associated and compared [23]. Our goal was to identify a broad range of perspectives, not necessarily a consensus among participants, and to deliver a coherent conceptual description of the data that captures thematic patterns and characterizes phenomena of interest while accounting for the individual variations within them. As with all interpretive research processes, data collection and analysis inform one another iteratively, shape the direction of inquiry, permit consideration of new emerging themes, and allow for the flexibility to accommodate views that evolve over the course of data acquisition. This methodology enables us to examine individual factors contextualized within the large picture of the narrative data collected [24].

In keeping with this approach, two researchers on our team identified themes from the data deductively, guided by the discussion questions, and inductively through intense coding of the transcripts for themes emerging in vivo. We used a rich coding strategy that allows for the attribution of multiple codes to segments of data. When there was a discrepancy between coding choices, the text in question was discussed and a code was chosen by consensus. We then grouped themes into conceptual categories to identify the relationships that meaningfully describe the data.

Results

Profiles of the Participant Cohorts

Participants Table 1 shows the demographics of the participants. Overall, there were 24 participants in the chronic cohort (CHR) and 14 in the sub-acute cohort (SA): 11 (79%) were men; there were 7 women in the chronic group (29%) and 1 (7%) in the sub-acute group. Fifty-five percent of participants were between the age of 30 and 45, however participants in the sub-acute group were generally younger (19–29 years of age; 11 were under the age of 40) than those in the chronic group, an unsurprising demographic given that participants in the chronic group were at least 1 year and up to 10 years post-injury. At the time of the study, 9 participants (38%) in the chronic group were employed or held some part-time employment; 15 were unemployed. Eleven (79%) of the recently injured participants held employment prior to their accident.

Knowledge Base Table 2 summarizes the sub-acute and chronic SCI participants' knowledge about living with their injury and their understanding of the risks and benefits of stem cells. These data must be considered in the light of the distinctly different contexts of the two cohorts: participants from the sub-acute cohort were in a rehabilitation facility; those in the chronic cohort were living in the community.

Participants in the sub-acute cohort described their initial rehabilitation and preparation for discharge to the community. They were early in the process of adjusting to their injury and redefining their life situation, as exemplified by: "I'm still here… in a rehab facility. I go home on weekends. I don't have to work at the moment; I don't have to commute to work. I don't have to do a lot of things that life involves so… It's a huge change from here to the outside world." (SA Int 24 Thoracic). Participants in the chronic cohort described their efforts to maintain or enhance their quality of life, and described how their life situation has been redefined as they adjust to change and re-establish their life within their families and communities: "…Ten years later now I'm okay where I am…I'm halfway there…we've got a house, everything is fine, but it's still a loss…" (CHR FG 04 Thoracic).

Table 1 Participant demographics

	Chronic		Sub Acute	
	Neurological Level		Neurological Level	
	Cervical	Thoracic	Cervical	Thoracic
Number of Patients	12	12	6	8
	Asia Grade Scale		Asia Grade Scale	
	A	B	A	B
Number	19	5	6	8
Years Injured	4 - 11	4 - 11	Interviewed within 7 months of injury	
	Gender		Gender	
Male	17		13	
Female	7		1	
	Age Range		Age Range	
19 – 29	2		8	
30 – 45	17		4	
46 to 60	5		2	
	Employed		Employed	
Yes	9		11	
No	15		3	
	Education Level		Education Level	
Some High School	5		1	
High School Graduate	7		6	
College/Technical	8		3	
Under Graduate Degree	4		4	

Emerging Themes

Four major themes emerged from the analysis of 21 h of audio recordings from the chronic and sub-acute participants and resulting 1,032 segments of coded data:

- *Readiness for clinical trials*: Receptivity to clinical trials in consideration of risks, benefits, and the context of a person's life situation.
- *The here and now*: Current needs related to quality of life, autonomy, and level of functioning.
- *Wait and see*: Views about participating in stem cell trials given the state of the art in research and translation.
- *Informed hope*: Evidence and information that is scientifically grounded, balanced, and curated by experts, enabling informed decisions and promoting realistic expectations about clinical trials with stem cells.

Readiness for clinical trials:

Chronic Cohort Participants suggested that enrollment in a stem cell trial would constitute a major life change to an already vast array of changes imposed by their SCI. They further reported that even a beneficial physiologic change from an intervention would be accompanied by enormous adjustments in their daily life, their sense of identity and thus require additional redefinition of their life situation. "The transition was hard enough the first time; I don't want to go through it again." (CHR FG 07 Cervical). For some participants, another round of rehabilitation and adjustment seemed too overwhelming to contemplate: "As a cervical patient, I have less functionality and thus, more to lose than other people". (CHR FG 09 Cervical).

Participants with thoracic injuries indicated a greater readiness to participate in clinical trials than those with cervical injuries; they tended to be less accepting of the *status quo*, anticipated opportunities for change positively,

Table 2 Participant knowledge of spinal cord injury and stem cells

	Sub-acute Cohort	Chronic Cohort
Knowledge of SCI	Minimal references to quality of life issues.	Identify quality of life issues such as independence, engagement with others, recreation, relationships.
	Naïve about services/costs to sustain self in the community.	High degree of awareness of costs associated with equipment, supplies, ongoing therapy, and vocational opportunities to maintain selves in the community.
	Minimal exposure to alternative therapies.	More aware of and use alternative therapies—acupuncture, massage.
Knowledge of stem cells; risks and benefits	Exposure to the media and Internet minimal and over a short duration.	Have accumulated knowledge over time from the Internet and media.
	Naïve about risks and benefits.	Persons with cervical injuries prioritize hand function over walking. Other physical functions indentified were the primacy of bladder/bowel; motor and sensory functions that enable them to stand, transfer, experience sensation; improved circulation; sexual function; reduced fatigue, spasm, pain.
	Knowledge primarily gained from information sheet provided by project.	Able to identify risks/benefits in general and in particular, i.e., how benefits are relevant to their personal situation.
	"Don't know what they don't know".	Identify the "ripple" effect of risks/benefits, for example, how managing toileting contributes to more social interaction, more spontaneity, and improved morale.
		More skeptical of risks/adverse events related to previous personal experience of invasive surgeries and concerns about loss of existing function, pain and spasm.

and weighed benefits over risks. Those with cervical injuries were more pragmatic about their life situation, had more experience with invasive procedures, were skeptical of medicine, and tended to weigh risks over benefits. They also introduced the caveat that they did not want to lose any current function—no net loss. In particular, those with cervical injuries identified that a net loss of function could have a major impact on them: "If I lost my arms, I would be suicidal". (CHR INT 01 Cervical). This represents an awareness of the impact that the level of neurologic injury has on functioning. For example, for a C7 quadriplegic with triceps function and the ability to transfer independently, the deterioration of a neurologic level to become a C6 quadriplegic would have considerable functional implications. By contrast, a T7 paraplegic with the loss of a neurologic level to become a T6 paraplegic would likely have little functional effect. Together, the responses from the thoracic and cervical SCI individuals suggest a spectrum of receptiveness to stem cell transplantation therapies that is more weighted towards a risk tolerant perspective for the thoracic group and a risk-averse perspective for the cervical group, but with considerable overlap in a middle ground of mitigated risk. This is depicted in Fig. 1.

Sub-acute Cohort When participants in the sub-acute cohort were asked to reflect on whether they would have considered a clinical trial with stem cells at the time of acute injury, many indicated a readiness to proceed. "If I was lying on the emergency table, yes, I would have said yes."(SA INT 22 Cervical). "I probably felt like I had nothing to lose at that point." (SA INT 26 Thoracic). They described the interplay of factors that influence their perspectives in the acute period: fear; the influence of pain and medication; lack of knowledge about the benefits and risks of different intervention options; the range, severity, and permanence of the sequelae of spinal cord injury; the effect of rehabilitation on their ultimate level of progress; and, their adjustment to life as a spinal cord injured person. Improvement in functional abilities over time is associated with greater aversion to risk. Concerns over loss of rehabilitative function cause participants to give increased weight to evidence of clinical effectiveness. "If there would be a loss of function that could be quite devastating particularly for quads, every level means so much…every level is a muscle group that helps." (SA INT 21 Cervical).

While both sub-acute and chronic groups of participants suggested that those who are newly injured would likely be the greatest beneficiaries of stem cell treatment, they qualified this view with concerns about the ability to make informed decisions at this early stage: "I do worry about the newer injuries being first on the list because I know how that feels… all you want to do is walk again, whatever it takes, it doesn't matter. So that scares me a little bit." (CHR INT 03 Cervical).

The here and now:

Chronic Cohort The need to focus on quality of life issues in the here and now emerged as a major theme for the participants in the chronic cohort. They stressed the importance of maintaining functioning and participating

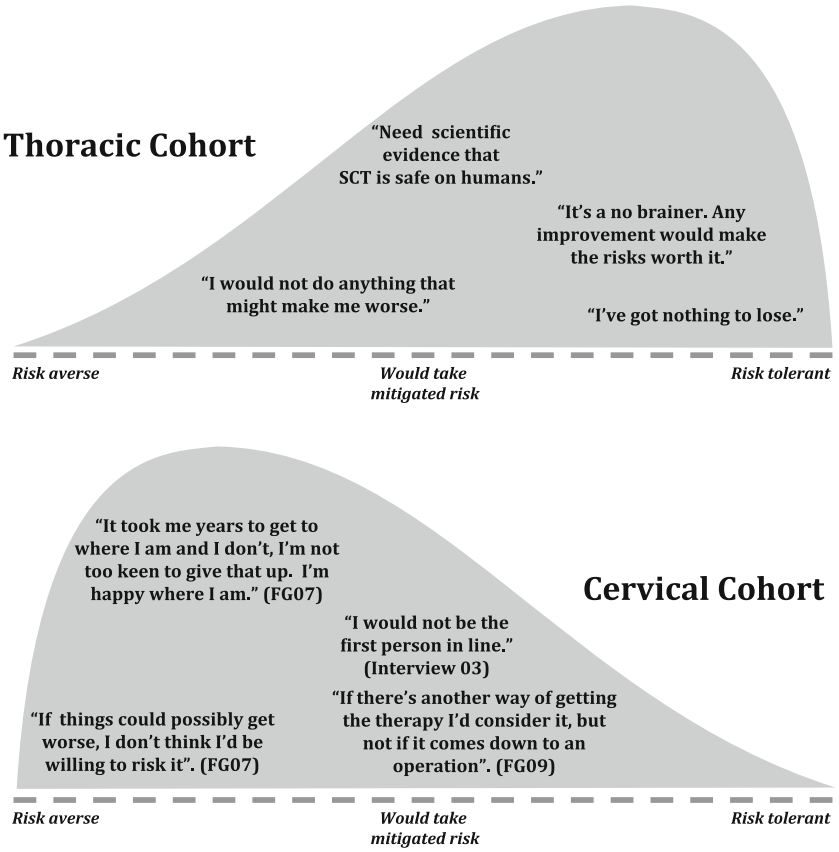

Fig. 1 Schematic representing attitudes of the chronic participant group towards risk. The responses of the individuals with thoracic and cervical SCI suggest that those with cervical injuries tend to be more risk averse. This may arise from the recognition that localized damage from a stem cell transplantation to the spared regions around the injury site can have significant functional consequences. The figure, however, illustrates the range of perspectives on the issue of risk and the considerable overlap between the groups

fully socially and recreationally. They expressed frustration about the lack of facilities once discharged from rehabilitation and identified a need for greater support in community-based facilities, particularly in relation to ongoing therapy to maintain function. They expressed that the funding for stem cell research, which may not benefit them in their lifetime, may be taking away from resources that could otherwise be allocated to more immediate and proven benefits. Stem cell treatment is not necessarily visible or real for participants in this cohort overall: "I also realize that this [stem cells] could be not in my lifetime so my focus is on today." (CHR INT 03 Cervical). Frustration exists about navigating health care once outside rehabilitation, such as completing forms to access services, obtaining modern equipment, using community-based exercise facilities, and accessing and paying for complementary therapies.

Sub-acute Cohort The here and now did not emerge as a significant theme for participants in the sub-acute group. They were still in rehabilitation and not yet integrated into their community.

Wait and See:

Chronic Cohort The wait and see theme emerged for the chronic cohort consistently in the context of scientific progress related to stem cell trials for SCI: "The science has to be there first of all." (CHR FG 03 Thoracic). In fact, some participants compared themselves to experimental models: "I don't want to be a guinea pig. I would wait until many trials have been completed before I would try". (CHR FG 07 Cervical).

Sub-acute Cohort The wait and see perspectives of the participants in the sub-acute cohort is consistent with their day-to-day post-injury reality that is still evolving: "So a lot can happen in the course of my therapy here …I'm getting improvements. I don't know how far I'm going to progress with the injury… if at some point down the line I didn't improve, I would be looking at stem cells." (SA INT 32 Cervical). Unlike the chronic group, the wait and see for this group focused on the internal evaluation of functional progress rather than on external developments in stem cell research.

Informed hope:

Participants in both chronic and sub-acute groups reported that they would like their physicians to be a key source of information about stem cell research and trials: "Doctors don't provide much information relevant to stem cells… There's a real fear of healthcare practitioners to give any

information to people with SCI that they think might lead them into some sort of false sense of hope."(CHR FG 09 Cervical). Overall, however, they indicated that they rely primarily on television, the Internet, and other persons with SCI for information. A few reported accessing medical journals as secondary source; some noted the technical language used in professional reports and difficulties in interpreting it.

Most participants commented that information on the Internet needs to be filtered: "There's obviously a pile of things on the Internet, some of which is true, some of it isn't true. I guess I'm not a hundred percent confident in just going straight to the Internet and reading all about stem cells because there's probably some very good news and some very bad news and the actual news is probably somewhere in-between hopefully." (SA INT 24 Thoracic). They were clear in expressing that education about SCI in general is lacking. Overall, they urged the creation of a centralized, credible resource for information that is scientifically based and curated by experts. This would serve to meaningfully translate advances in research to the interested public and support their decision-making in this context. "I like to get the information from the guys that are the scientists—the people that are doing it right now that have had success with it." (CHR FG 04 Thoracic). They also highlighted: "… a need for researchers to be better connected." (CHR FG 03 Thoracic).

Conclusion

In this qualitative study of the perspectives of individuals with thoracic and cervical SCI in chronic and sub-acute post-injury stages, we discovered a complex and multidimensional set of perspectives about participation in stem cell trials. Across the four groups—chronic and sub-acute, thoracic and cervical—four major themes emerged: *readiness* (no net loss), *informed hope*, *the here and now*, and *wait and see*. *Readiness* and *informed hope* were shared themes. *The here and now*, a priority for the participants in the chronic group, and *wait and see*, the orientation of the participants in the sub-acute group, were distinguishing themes between the groups.

Although biomedical science is targeting fairly acute time points for stem cell clinical trials for SCI [2, 11], our findings suggest that this is the time when a person with SCI is most vulnerable, poorly informed about the evolution of the condition and options for intervention and is unlikely, therefore, to be able to make an informed decision about participation. Thus, we have discovered a disparity between the practical necessities of the science of stem cell therapy and perspectives about when it would be ethically optimal to perform these trials from the viewpoint of those who are the ultimate beneficiaries. A number of salient solutions are available to bridge this gap.

First, the timing of stem cell trials should consider the evolving readiness of patients and their understanding of risks and benefits. On the one hand, while participants in this study felt they were least equipped to make a decision about invasive therapy early post-injury, the bulk of preclinical science justifies intervening earlier than later. An overwhelming majority of studies—as many as 95%—report on transplantation time windows of 7 to 14 days post-injury, and only a handful of preclinical studies, representing an extremely small proportion of cell transplantation studies, have reported some benefits in the chronic context [1]. One simple explanation is that it is considerably easier to demonstrate a beneficial effect in a sub-acute cell transplantation paradigm than in chronic animal experiments, and much less expensive to do so. Moreover, at the early time point, cellular therapies offer the potential to provide some degree of neuroprotection to the cord, enhance the spontaneous local axonal sprouting and plasticity, and then replace cells that are lost. At a later time point when the injury has become chronic, the cell therapy can replace lost cells and provide trophic support with hopes of stimulating further axonal regeneration and sprouting, but at a time point when spontaneous plasticity has already largely subsided. The fact that the latter is a much more challenging environment was demonstrated by the transplantation of human embryonic stem cell-derived oligodendrocyte progenitors—a technology that Geron Corporation has now brought to clinical trials [11]. When these cells were transplanted one week post-injury in an animal model, they remyelinated axons and promoted functional recovery of the animals. In the same report, the transplantation of cells in animals eight months post-injury did not result in functional recovery. Consistent with the efficacy data demonstrated preclinically, the Geron clinical trial is recruiting SCI patients at an early time point post-injury (1–2 weeks).

More preclinical success with stem cell transplantation in chronic models of SCI is clearly needed to support the interests of individuals with chronic SCI, and to address the complex question of preparedness for clinical trials. Ironically, despite the paucity of scientific evidence supporting the efficacy of cell transplantation treatments in models of chronic SCI, the majority of clinical trials that are ongoing around the world have involved individuals with chronic SCI [13, 15–20]. Nevertheless, given the state of the science, we expect that in coming years there will be a growing number of trials initiated with a similar sub-acute time window of enrollment that is being used in the Geron trial.

Second, our findings support the need for a shift in content emphasis in informed consent, from a general

consideration of the risks and benefits of a trial to the specific risks and benefits as they intersect within the context of an SCI person's life situation. This is consistent with Feudtner's (2008) critique of the complexity of clinical decisions [25]. In this commentary, he highlights the need to clarify the values of people and their families and to explore often inevitable trade-offs, particularly when new therapeutic interventions push the boundaries of what is possible and desirable. It also goes hand in hand with the work of Robertson (2010) who commented, "*the science* [of stem cells] *is complex, the risk of therapeutic misconception is high, and the patient's condition, especially in neurological research may be grave*." [26]. Sahni and Kessler (2010) similarly advocated that the translation of stem cell science to clinical trials must take into account severity and level of injury, type of cell, and therapeutic goal [3]. Adding to these insights, Taylor (2010) has recommended a new model for oversight of innovative therapy [27]. He urges close attention to vulnerability: *"…the physician proposing innovative therapy looks at this patient, not participants as a class as an IRB would do. Specifically, there must be a way to understand how the patient weighs the alternative outcomes, so that with their probabilities, even given the unknowns, the choice is both ethical for the clinician to offer and not clearly inappropriate for a given patient who decided to receive innovation therapy."*

Third, we propose the introduction of a staged consent process that would provide SCI candidates eligible for stem cell trials sufficient time to rationally consider information available to them. Without affecting the fundamental right to withdraw, staged consent would offer structure and the opportunity to exchange information and could positively reinforce the choice to participate in a clinical trial. Systematic staging, albeit a slower process than single-stage consent, has been shown to contribute to a more informed decision-making in other populations [28–30]. In one study, not signing the consent at the initial discussion was found to be an independent factor for improved knowledge scores [31] and, in another, delay led to more questions and active participant involvement in the consent process [32]. As staged consent may also lead to more prolonged contact [33] between a prospective participant and the researcher or physician, it can serve to build trust [28]. As Sugarman (2005) suggests, clinical trials with stem cells should follow ethical principles that guide all clinical research. This includes efforts to assure that participants with high hopes and no alternative effective treatments understand key features of the trial. No doubt, modifying and measuring informed consent can be difficult, but ways to enhance a process that Wade et al. (2009) called a black box [34], by allowing more time for deliberation, by explicitly eliciting and addressing participants' concerns, and by integrating individual patient-based or networks of support, need to be explored. The introduction of interactive computer media to convey complex details between face-to-face contact points [35] may a viable and modern strategy to further support such efforts.

We appreciate our findings and recommendations in the context of the limitations of the study. For example, participants were recruited from one location in Western Canada and in the data were taken in a snapshot of time. SCIs are not uniform and the perspectives and priorities of people may vary over time. Focus group data do not allow us to derive findings or interpretations in relation to age or gender since individuals are not identified in analysis. Many of the participants in the sub-acute group knew little about stem cells beyond the information sheet provided by the project. Finally, although we specifically probed about stem cells, we cannot know to what extent our findings, particularly those that relate to communication, are unique to stem cells and SCI, or are generalizable from any novel therapy for SCI, other disorders of the CNS, or indeed other diseases overall.

The mandate of this study was to bring the voices of individuals with SCI to stem cell translational research, and the results of this effort can inform both the biomedical-science of trial timing and the social-science of consent. Participants identified many opportunities to create a culture of collaboration and knowledge exchange across all stem cell stakeholder groups: researchers, health care professionals, and persons with SCI and their network of family and friends. While researchers produce results, and physicians and health care professionals create the bridges between the science and practice, people with SCI must not only seek the fruits of those gains, they must have the opportunity to contribute their experiential, contextualized knowledge to the unfolding story: "*Put my voice in there, so it's actually not just the doctors and physiotherapists doing all the research stuff without having input from the people with the actual spinal cord injuries*." (CHR FG 07 Cervical).

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