Decision-making in stem cell trials for spinal cord injury: the role of networks and peers
Marleen Eijkholt, Brian K Kwon, Ania Mizgalewicz and Judy Illes

DOI: [http://dx.doi.org/10.2217/rme.12.32](http://dx.doi.org/10.2217/rme.12.32)
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Full Text:

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**KEYWORDS**

decision-making; ethics; informed consent; peer support; spinal cord injury; stem cell

Much excitement and trepidation surrounded the launch of the first clinical trial to test the safety of embryonic stem cells for subacute spinal cord injury (SCI). This first translational attempt with an embryonic stem cell product by Geron Corp. came with high hopes for progress, but also raised controversy about the question of who to recruit in these trials, and the role of patient networks in the decision-making process [1-8]. The controversy related to the unprecedented use of embryonic stem cells in humans, the risks and uncertainties of participation in the trial, and also the selection of the trial population itself. The recent suspension of the trial provides an opportunity to take a step back and reflect on how to best develop and implement future research and clinical testing.

Whether or not the Geron trial will be taken over by another company, other trials will be initiated, or existing trials will be opened to new populations [101], the question of how to ensure informed decisions about participation in stem cell trials remains a source of ethical inquiry and debate. In the stem cell trials undertaken to date, different challenges have arisen. For example, the Geron trial, which was based in the USA and ran from October 2010 to November 2011, targeted subacute SCI patients [102]. Over the course of the trial, Geron implanted four patients with oligodendrocyte progenitor cells derived from human embryonic stem cells 7-14 days after their spinal cord injury [103]. Eventually, Geron even injected a fifth person who had been consented just prior to trial termination [104]. Individuals meeting eligibility criteria in this trial had to make a decision about participation almost immediately after their injury occurred, without having had much time to adapt to the life-changing circumstances. Furthermore, in an ongoing European trial, Stem Cells Inc. is implanting neural stem cells into the spinal cord of patients 3-12 months post-injury [105]. Although these participants have more time for decision-making, they still face uncertainty about the novel technology.
In the past, commentators have explored empirical, theoretical and scientific arguments about the suitability of recruiting individuals in the subacute phase of SCI for research trials \([4,5,7,8]\). Discussions have focused on the putative vulnerability of these individuals and the lack of information people possess shortly after injury. In particular, questions have been raised about the decision-making capacity of injured individuals during in the subacute phase of SCI and their ability to provide informed consent to participate in a clinical trial \([4,5,8]\). The studies have largely focused on the perspectives of the injured person, but have disregarded the position of networks that surround the injured person and the important role they play in the decision-making process \([1-4,9]\).

Here, we advance the discussions by exploring if, and how, the network of healthcare professionals on the one hand, and the network of family and friends on the other, can offer decision support. Desire for such decision support is illustrated by previous work with individuals with SCI \([4]\), and is highlighted by vulnerable trial populations themselves in other contexts, such as the cancer trial setting \([3,4,9,10]\). We examine the challenges of informed decision-making from the perspectives of these networks, and analyze which consent models would best address ensuing ethical issues. Our findings are situated in the context of stem cell interventions for SCI, but extend to other trial situations where vulnerable participants face high risks and uncertainty. In light of the rapid pace of translational efforts and the promises of stem cell science, the need to address these issues is urgent.

**Materials & methods**

We acquired focus group and interview data from individuals in two networks surrounding people with SCI: the network of healthcare professionals (i.e., physicians and allied healthcare workers), and the personal network of family and friends. Both networks take part in the decision-making process and can serve as stakeholders in decisions about clinical care and participation in research.

Network participants were recruited through a provincial Canadian database housed at the sole SCI referral center for a population of approximately 4 million people. The study was approved by the Behavioral Research Ethics Board of the authors' institution. Data collection ran between June 2009 and February 2010. Participants received a consent form and an information sheet about spinal cord injury and stem cells, not further specified for type of stem cell, in the mail prior to participation. All participants provided informed consent.

We assembled spinal cord injury professionals in seven focus groups. They comprised physicians (three groups) and allied health professionals (four groups) involved in acute care, rehabilitation and inpatient and outpatient care. In addition, we invited the network of family members and friends to share their experiences and views. These persons were associated with individuals with thoracic or cervical injuries. We based the final
number of participants on data saturation when no new themes emerged during data analysis and data collection, two processes that we conducted concurrently.\cite{11}

We gathered the perspectives of members of both networks with guiding questions about receptivity and readiness for stem cell trials. We recruited over a wide age range, experiences and relationships. Each participant in the personal network group was independent, and had no prior relationships to the others.

A project investigator and facilitator led the groups and interviews, which were 60-90 min long and audio-recorded for later transcription. Interviews were set up similarly to the focus groups in terms of recruitment, consent, recording and transcription. We used a grounded-theory approach and constant comparative analysis to identify salient themes. Two researchers independently coded the focus group and interview data qualitatively. This involved segmenting raw data (phrases, sentences and paragraphs), labeling and synthesizing the data, identifying categories and dimensions, and searching for patterns of intersection to finally structure the data into a coding scheme.\cite{12} This process shaped the direction of inquiry, permitted consideration of new emerging themes, and allowed flexibility in integrating the views and themes that evolved over the course of data collection. Together, the methodological and analytic process led to a contextualized descriptive account of the narrative data.\cite{13}

Discrepancies in coding were settled by discussion and return to the text. The researchers conducted a final critical inquiry of the themes in order to identify overarching conceptualizations of ideas and relationships that could meaningfully describe the data. Finally, we adopted a normative lens to interrogate the findings and highlight conclusions. Quotations provided here are representative of major themes.

**Results**

The study generated over 60 h of discourse from 50 members of the two networks. Tables 1 & 2 show the demographics of the participant cohort.

Results illuminated a complex picture of each network's ability to support injured individuals in decisions regarding stem cell trial participation. Both networks spoke to the desirability of decision support for the injured individual:

"I think mostly the patient, the surgeon and their family-" (Professional)

"Yes, he should definitely get educated about the whole process, probably by the physician or the researcher." (Personal)

However, the data also suggested that networks are not currently equipped to offer
stable decision support. We identified three obstacles to this goal: personal dimensions of risk; limited insights for decision support; and deference. The novelty of stem cell research enlarges these obstacles, as professionals pointed out:

"-some things we know we don't know and some things we don't know we don't know."
(Professional)

"We don't yet know the impact of injecting something into the spinal cord."
(Professional)

* Personal dimensions of risk

Many study participants contended that risk is not an objective concept with well-defined precedent, but rather is entangled with the individual perspectives of the injured person. Concepts of risk are deeply intertwined with variables such as expectations, experiences, and the injured person's perceptions of quality of life. Our data indicated that these variables influence risk perceptions and risk assessments, and leave the network to deal with factors that they do not always comprehend.

In relation to risk perceptions, for example, participants from both network cohorts referred to the quality of life and the personal dimensions of decisions:

"the quality of their life, at any given time, in combination with in their mind and the reasons they have to live, will probably affect how risk-adverse they would be."
(Professional)

"[In] spinal cord research - there's this trend to saying, well, patients want it, let's do it. But that makes me nervous. Just because they want it, you know, they've really got to understand the risks and they really have to understand it in a consensual way."
(Professional)

"And I know in talking with [son] because we talked a little bit he said it didn't matter what surgery he had, he wouldn't want to jeopardize the quality of life that he has now at the cost of having less than what he has already now. Like he thought if he lost any more function, he wouldn't go down that path." (Personal)

Different variables affecting expectations and experiences between the injured person and the network appeared equally in the distinctive layers of the risk assessment they could adopt. For example:

"The layers of risk are different for clinicians than they are for patients." (Professional)
"And once, as we hear on this floor, every injury is very unique and even though they can have the injury at the same level it affects them in different ways." (Personal)

Participants suggested that it would be possible to distinguish between risks that affect quality of life and those that do not have such effect. Some risks are purely physiological or without clinical effect and do not necessarily affect quality of life, and vice versa. In turn, injured individuals and their networks may appreciate these differently.

"So I think one of the risks is that you could have - improvement in an academic way in either more sensation or more movement or something, but you could at the same time have deterioration because of increased spasticity or increased pain." (Professional)

"It's important to evaluate 'the capacity of resilience' in this patient." (Professional)

"-back it up with the information, the research, you know, that would lead him down that road, but ultimately it would be his decision." (Personal)

Further complicating risk assessment, the networks observed that neither risks, nor benefits, can be expressed in a purely medical framework:

"-the top 10-15 post-injury complications and.. you lay on top of that, the individual perspective, then you get the specific things that people ask for." (Professional)

The perception of what constitutes risk depends on the specific injured individual:

"And, you know what, you might find that you might have to tweak it for each individual patient; it may not be just for the population or for people with the same injury." (Professional)

"But, you know, and you find with every, well [son] is a risk taker. That's partly why he's here. So but I think there is a bottom line to that risk and I guess he's the only one that'll know what that is." (Personal)

An adequate assessment of risk, accordingly, requires knowledge about the whole identity of the injured person. Statements from both networks illustrate how risks connect to expectations:

"I think it most depends on the expectation the client has - that even if he understands
the risks he always will have expectations." (Professional)

"And I can actually understand that, it's a risk and I'm not the one walking it out, he's the one walking it out-" (Personal)

Furthermore, personal experiences surrounding the injury played a significant role in the perspectives around potential therapeutic benefit:

"I think the benefits should be how the patients perceive their needs." (Professional)

"Of those key functions, I mean those are key social functions, that limit us from participating so, you know." (Personal)

Risk and benefits, accordingly, have different features and relate to personal experiences. Connections between subjective quality-of-life experiences and the risk-benefit picture - that is, the personal dimensions of risk - prevented networks from offering objective information and contributing confidently to the decision-making equation:

"One of my thoughts regarding the ethics of patient stem cell research is that I worry that with all the risks that we do know a client could even make a fully informed decision without having found out how good life can be even with a spinal cord injury. So in an acute stage, they might feel like their life is over as they knew it and I don't care if I get infections, rejection of cells or tumors because right now I'm in my worst hell ever. Whereas if they had gone through their process of rehab and acceptance - the odds might be totally different. So I wonder if someone can actually give fully informed consent - in their early stages post-injury - I think would have to be considered by an ethics committee." (Professional)

* Limited insight

Both networks expressed insufficient familiarity with the priorities and quality-of-life perspectives of the injured person to be able to inform or support decision-making, at least at early time points post-injury. Healthcare professionals reported limited knowledge regarding the context, experiences and expectations of injured individuals:

"-nor do we really that well understand what the patient's expectations are like. They may be sitting there in their chair thinking they're going to be walking and be back to normal - so unless the expectations and the understanding of the risks match, you cannot really allow the patient to make an informed decision. All of our interventions are based on informed consent on the part of the patient and you can't get that in the current environment." (Professional)
"I think the correlation between the two [risks and quality-of-life perceptions] is extremely tenuous, extremely tenuous [sic] if you have people with tremendous physical disabilities who self-report a very high quality of life. Then you have people with almost no perceptible impairment from a neurological point of view that self-report a horrific quality of life, worse than any sort of high lesion quadriplegic, and the link between the two is not linear and is in many cases tenuous." (Professional)

The personal network described a similar point of view:

"-it's your decision, it's your legs, it's your life, I couldn't do that." (Personal)

"I would be much more conservative because I wouldn't, I'm speaking for someone else's body and future and possible side effects or risks involved and that's more difficult than if I'm making it for myself personally." (Personal)

Furthermore, the personal network described uncertainty due to changing perspectives and insights that run parallel to the dynamic experiences of the injured person. In other research with networks of chronically injured individuals [Eikjhol M et al., Unpublished Data], they described how their reactions to injury evolved over months. The network only came to understand the injury and the perspectives of the injured person several months after the injury, as time allowed for maturing of ideas and more reflection. Networks of subacutely injured individuals hinted to such nascent perspectives as well, although, in the present study, they were not yet able to articulate it as clearly as individuals in the chronic network.

"We can't predict how it's going to affect them. It's not standardized or and I don't see that it would ever really be standardized." (Personal)

* Deference

Both networks emphasized that decision-making should not be the sole enterprise of the injured person. As we mentioned above, at early time points post-injury, individuals are unlikely to have adjusted to their new life situation and the process of recovery to make a fully informed decision:

"When you think about ethics and research, for me the only big difference between, you know, using spinal cord injured patients versus any other patient out there that we do research on is the big, the big issue of someone doesn't know what their life can be like when they haven't been given that opportunity to live it, to experience it." (Professional)

"It's a balancing act at first when they're in acute care. They need you as their advocate
because they're so vulnerable. They're just trying to survive. And then there comes a point when they're trying to find their voice for their advocacy and also they still need some assistance at times because sometimes the drugs they've been on too, have, they haven't been able to take in some of the information that's been given along the way and they have not retained it." (Personal)

Where both networks alluded to a desire for decision support, they disagreed about where decision support should come from. Professional networks suggested that decisions about participating in stem cell research should derive from a deliberative process that includes multiple players, and that considers not only immediate outcomes, but also perspectives of those involved in ongoing care and management of complications:

"There are different perspectives for the acute care providers and for the rehab providers. And the outcomes that are sometimes selected by the acute care providers aren't necessarily what we would select." (Professional)

"We hold the bag for the rest of the time (-) and we will face problems and we will deal with these patients for the rest of their lives." (Professional)

"I think you should involve whoever is going to manage the complication of the intervention - I don't think people should be doing this if they can't manage the complication of it." (Professional)

Professionals reasoned along the lines of medical responsibility and, furthermore, were adamant that the personal support system should be a factor in decision-making. They perceived a connection between personal support structures, stability and the context in which the injured individual will later function:

"They had that support structure before the injury they've had and that may or may not have changed in its dynamic or its components with the injury. And those people should be involved." (Professional)

By contrast, members of the personal support system did not necessarily picture themselves as being an integral part of the decision-making process. They maintained a distance from the decision-making process and described their role more as that of a sounding board than as one that is instrumental to decisions:

"And like if he would look into it then he could bounce off, ideas off of me but I would not try to make up his mind for him that would be definitely his doing. I could just give him ideas - a sounding board, yeah." (Personal)
It has to be their [injured person’s] decision and we will support them if this is what they want." (Personal)

This idea persisted even after consideration of how the injury would affect them by extension:

"ultimately it would be his decision because it's his life. I mean, it's interesting because I mean one thing you learn here, yes, they had the accident, but it was an accident that affected all of you. It changed your whole lives." (Personal)

A perceived lack of expertise about science and medicine also factored into the sense of limited insight of the personal network:

"I'd probably get a lot more involved with understanding. And for me, you know, it's going to be his life, so he'd have to make that decision and I would totally leave it with him. I wouldn't influence him one way or the other, other than, you know, I would like to see him walk again and I don't think that's possible at this point, so-" (Personal)

The personal network referred to and deferred to the professional network for decision-making support. Professionals were perceived as trustworthy authorities in decision-making and as gatekeepers to successful trial participation:

"If he asked me, I would be very hard-pressed to say what I was thinking. I would say 'ask the doctors,' I would say 'please ask the doctor'-" (Personal)

"I guess if at this point Dr. [name] recommended or felt that there was a very strong chance that [son] might have some great success and provided us with the information that we could deliberate over it. " (Personal)

"He would listen if it was information that was dispensed to him from somebody specialized in the field, you know, had knowledge and said, you know, you might want to consider this." (Personal)

"Yeah, I guess I would start with the medical profession. And probably the current doctors that are, are around [husband], yeah." (Personal)

Discussion

Our results highlight a significant and multilayered problem in decision-making for stem cell clinical trials for networks of individuals who are in the subacute phase post-SCI.
The data illustrate that networks of professional and personal networks, which fulfill an important role in decision support for vulnerable populations\[^{3,4,9}\] have an unclear understanding of the decision-making framework. The highly personal dimensions of risk assessment and the perceived quality of life of the person with SCI complicate the perceived ability of the network to offer decision support. This opacity fundamentally characterizes the problem: both professional and personal networks express limited insight into these personal dimensions. One network defers decision support to the other, even in the face of agreement that decision-making about trial participation should not be left to the injured person alone. The dynamic state of embryonic stem cell science adds to this complexity and further impedes meaningfully informed decisions.

Questions of whether informed decisions can be achieved in trials involving individuals in the subacute phases of SCI have been previously discussed in theoretical discourse,\[^{5-8}\] as well as in empirical studies that focused on the perspectives of injured individuals\[^{4}\]. Both discussions highlight uncertainties around the ability of the injured individual in early post-injury stages to make an independent, free, and voluntary decision based on the understanding of risks and benefits\[^{4,6,8,14}\]. The studies elaborate, for example, on the physical and psychological risks for a subacutely injured individual and the risk of therapeutic misconception\[^{5-8}\]. However, these discussions do not assess the position of the networks surrounding the SCI patient, which have an important supporting role to play in decision-making processes\[^{2-4,9}\]. This study fills the gap.

Our results support the natural intuition that personal experiences of individuals are essential to risk-benefit analyses\[^{15}\], as both networks emphasize the interconnection between personal experience and risk. Our data illustrate that, where the goals and experiences of an injured individual are multifaceted, and risk is defined as a potential harm for the objectives of a person or group, risk and personal experience are inherently connected. Furthermore, our results indicate that despite the subjective nature of risk, decision-making about stem cell-based interventions should be a partnered effort. According to the networks, a framework of support for assisting in decision-making would be helpful. This corresponds with views of injured individuals and patients, who reveal a desire for decision support\[^{3,4,9}\]. A traditional model for consent and decision-making, in which individuals are perceived sole decision-makers is, therefore, suboptimal for decisions about trial participation.

Moving from a traditional consent model to a supported decision model is not inherently problematic. Such a model could fit, for example, with the approach of relational autonomy or shared decision-making\[^{10}\], where a wide context of individuals contribute to and influence the process of decision-making\[^{12,16,17}\]. Relational autonomy promulgates the idea that persons interconnect and do not exist as isolated thinkers\[^{18}\]. It holds that surrounding networks can provide expertise and support for an individual to maintain a sense of self and goals\[^{12}\], and the approach balances responsibility for decision-making with care relations\[^{19}\].
The deference of each support network to their counterparts, however, challenges the feasibility of relational autonomy for the SCI stem cell context. The personal networks refer to professionals as the supporting authority while the professionals, paradoxically, defer to the personal network. Both networks acknowledge that familiarity with the individual's experiences, preferences and values is essential for providing decision support, but both perceive limited insights into these issues. The finding that each network shifts decision-supporting tasks to the other network, accordingly, does not only contrast with the role patients desire for networks,\textsuperscript{[3,4,9]} but also impedes relational autonomy.

Thus, while a decision support model seems straightforward, its implementation may not be: members of both networks lack confidence to support the decisions at hand, and perceive that their counterparts in the complementary network are better situated for the purpose. Combined with suggestions that a shared-decision making model may lead to abdication of responsibilities on the part of the physician or the family\textsuperscript{[20,21]}, the model alone is unhelpful for effective decision support. Adopting the approach of relational autonomy alone is insufficient to resolve the problem of informed consent in the trial setting.

Staged consent has been proposed as another alternative to the traditional consent model\textsuperscript{[4,22,23]}. Staging - alone or in combination with another model of consent - anticipates extended contact between the physician and the injured person, and more communication, insights into expectations, risks and benefits and deliberation about individual priorities\textsuperscript{[23]}. Extended contact between the physician and the injured person allows for more communication, insights into expectations, risks and benefits, and deliberation about the individual's priorities. Can staging, however, practically result in free and informed consent? What staging structure would enable understanding of the risks and benefits, specifically in the SCI context? How would participants who are initially consented under such a model feel about withdrawing at later time points? At present, these remain unanswered questions.

Consideration of a third model of consent - one of peer support - is justified given the limitations of the other two decision models (Figure 1). Peer support is defined as:

"The provision of emotional, appraisal, and informational assistance by a created social network member who possesses experiential knowledge of a specific behavior or stressor and similar characteristics as the target population, to address a health-related issue of a potentially or actually stressed focal person" \textsuperscript{[22]}.

This model pairs a recently injured person with an injured individual who is further along in recovery. For example, a subacutely injured individual may be coupled with a person in the chronic phase post-injury, who has had more time to reflect on post-injury quality of life and other factors, and who is open to sharing insights\textsuperscript{[4]}. Peers in this model, accordingly, are not patient advocates who have different goals and play an important
but different role. Peers are discussion partners matched, for example, for age, education level and marital and employment status. They take a newly injured individual through relevant experiences and deliberations with the primary goal of enabling the newly injured person to mature and personalize a framework for reasoning. This model offers secondary benefit by bringing more insight to the existing support networks [24]. Past research, in contexts such as cancer and diabetes, show that peer support is inexpensive, easy to establish and effective [16,17], as it places the experiences of an injured individual at center-stage [25]. Although the present context is different than these other settings, since persons with SCI suffer an impact injury with instantaneous life-changing implications and have had little time to reflect on these circumstances, it is still reasonable to expect success of the peer support model in this setting. Factors such as stress, anxiety and potential depression are common in both contexts and can be addressed similarly and proactively under this model. Furthermore, an issue such as the therapeutic misconception [5,26,27] may arise in both settings and could be anticipated and managed under this model. There is already backing for such a model in the system evidenced in our data:

"Or even peers in clinical trials. Like I know in cancer treatment people - often talk to people who have been through clinical trials and what, why they did that? Was it a risk, was it a benefit, why didn't they go with more traditional treatment and hearing about other people's choices and their experiences" (Professional)

Inherent differences between focus group and interview data, differences in numbers of professionals and personal participants, relatively small and geographically bound participant cohorts, and subjective lenses of multiple coders are limitations of this study. Yet the voice of both stakeholders is a vital force in ensuring ethically guided stem cell research and translation. Data saturation and the discursive nature of the analytic process are key controls to these limitations and permit the data to contribute to the development of ethical and pragmatic guidance for this field.

We conclude that introducing a peer support system for decision-making is a solution worth considering for the complex problem of enrolling participants in trials at early post-injury time points. The combination of vulnerable individuals, deferring networks and the particular risks and uncertainties of stem cell trials warrant optimized informed consent procedures. Peer support brings the personal experience of the individual to center-stage and focuses on the subjective dimensions of risk in the decision-making procedure. Whether a staged consent process should complement the proposed peer support [4] remains an open question for further empirical inquiry and deserves further investigation, as do questions about the specific design features of the peer support model. Developments in stem cell research are advancing rapidly, with constant pressure for translation from bench to bedside. Critical engagement and guidance both protect prospective human research subjects and safeguard public trust in science.

Future perspective
Over the next 5-10 years, new trials will likely be initiated to test the safety and efficacy, and may even seek to optimize stem cell products for SCI. They will further explore the nature and behavior of cells in relation to injury type. Developments in stem cell science will undoubtedly also intersect with the rapid movement in personalized medicine. Advances in the field will underscore the importance of ethically appropriate recruitment, enrollment and participation criteria in trials. Informed decision-making remains a cornerstone of ethically sound research participation and is a timeless concern. The burden to deliver adequate decision-making systems falls to the academic sector, but there will be increasing financial and ethical imperatives for the private biotechnology sector to collaborate with academia in translational efforts.

Table 1. Sample characteristics (personal).

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Table 2. Sample characteristics (professional).

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Executive summary

* The recent withdrawal by Geron Corp. of the first trial designed to test the safety of embryonic stem cells for acute spinal cord injury (SCI) provides an opportunity to reflect on the question of how best to organize trial participation.

* There is a need for decision support in stem cell trials involving individuals with SCI, especially in the subacute phases of injury.
Definitions of risk and benefits in stem cell trials are deeply interconnected with an injured person's perspectives on quality of life.

The complexity of the risk-benefit assessment limits the ability of personal and healthcare networks surrounding an injured person to offer decision support in stem cell trials for SCI.

Mitigated insights lead each network to defer the task of decision support to the other network.

A peer support model for informed consent that places the experiences and expectations of the injured person at center-stage could potentially enrich and complement the knowledge base and support decision-making of all stakeholders.

CAPTION(S):

Figure 1. Informed consent models in stem cell trials for spinal cord injury.

Illustration of different IC models in stem cell trials for spinal cord injury and various layers of patient support. The inner circle represents the core of the IC process. Intermediate fields represent additional support systems for consent, including those that might derive from a model of relational autonomy. The peer support model, represented in the outer circle, encompasses the full potential for IC by enriching and complementing the knowledge base and supporting decision-making of all stakeholders.

IC: Informed consent.

References

Papers of special note have been highlighted as: * of interest ** of considerable interest

1 Shannon-Dorcy K, Drevdahl DJ. "I had already made up my mind": patients and caregivers' perspectives on making the decision to participate in research at a US cancer referral center. Cancer Nurs. 34(6), 428-433 (2011).


3 Cox K, Avis M. Psychosocial aspects of participation in early anticancer drug trials.

* Examines patients' decision-making in clinical trials.


** Empirical analysis of the perceptions of individuals with a spinal cord injury (SCI) about their readiness and receptivity to stem cell clinical trials.


** Questions and comments about the design of the Geron Corp. trial, especially related to the inclusion of participants with SCI and the risk of therapeutic misconception, from a theoretical academic perspective.


** Comments on the rationale and design of the Geron trial, particularly in relation to the questions raised by Bretzner et al. from the perspective of Geron.


** Questions the meaning of vulnerability in clinical trials, and discusses potential pitfalls of first-in-human (stem cell) trials.


* Scrutinizes inclusion criteria, risks and the issue of therapeutic misconception after elaboration on the design of the Geron trial as set out by Wirth et al.

** Examines the role of informal caregivers as an unrecognized population for patient support.


** Discusses principles, strategies and features of the peer support system.


* Websites


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Acknowledgements

The authors gratefully acknowledge J Reimer and S Parke (National Core for Neuroethics at UBC) and M Sharp (Edge Consulting) for their contributions to data collection, coding and analysis, and E Borgelt (National Core for Neuroethics at UBC) for editorial assistance.

Financial & competing interests disclosure

Supported by NCE/Research 9/5251(CT8; F Miller). J Illes is the Canada Research Chair in Neuroethics. BK Kwon is a CIHR New Investigator and M Smith Foundation for Health Research Scholar. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.
No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

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