Research Article

Regenerative Medicine

Roles and responsibilities in stem cell research: a focus group study with stem cell researchers and patients

Lars S Assen*,[1], Karin R Jongsma[1], Rosario Isasi[2], Marianna A Tryfonidou[3] & Annelien L Bredenoord[4]

[1]Department of Medical Humanities, Julius Center for Health Sciences & Primary Care, University Medical Center Utrecht, Utrecht, 3508, GA, The Netherlands

[2]Department of Human Genetics & Interdisciplinary Stem Cell Institute, Dr. John T. Macdonald Foundation, University of Miami Miller School of Medicine, Miami, FL 3310, USA

[3]Department of Clinical Sciences, Faculty of Veterinary Medicine, Utrecht University, Utrecht, 3584, CM, The Netherlands

[4]Erasmus School of Philosophy, Erasmus University Rotterdam, Rotterdam, 3000, DR, The Netherlands

*Author for correspondence: l.s.assen@umcutrecht.nl

Background: The perspectives of researchers and patients regarding roles and responsibilities in stem cell research are rarely studied, but these could offer insights about responsible research conduct. **Method:** We have conducted a qualitative study consisting of focus groups with both early- (n = 7) and late-career stem cell researchers (n = 11) that are primarily based in Europe, and with Dutch patients with chronic lower back pain (n = 9). These focus groups have been analyzed thematically. **Results:** Four themes were identified: 1) roles and responsibilities in the laboratory, 2) responsibilities of and toward patients and the public, 3) the role of regulation and 4) structural hurdles for responsibility. **Discussion:** The results suggest that responsible research conduct could be improved by addressing grant application procedures, publication pressure and by providing support of dissemination activities for researchers. **Conclusion:** Responsibility in stem cell research could be enhanced by embracing open science initiatives and targeted training.

Plain language summary: What researchers and patients think about roles and responsibilities in stem cell research is not well known, but this information could help to deal with the ethical aspects of stem cell research. We have conducted focus groups with early and late career stem cell researchers based in Europe and with Dutch patients. Four overarching themes were identified: 1) roles and responsibilities in the laboratory, 2) responsibilities of and toward patients and the public, 3) the role of regulation and 4) structural hurdles for responsibility. The results suggest that responsible research conduct could be improved by addressing grant application procedures, publication pressure and by providing support for communicating the progress and results of research. More generally, open science initiatives and targeted training could help to improve dealing with the ethical aspects of stem cell research.

First draft submitted: 27 January 2022; Accepted for publication: 12 April 2022; Published online: 18 May 2022

Keywords: bioethics • open science • perspectives • qualitative research • stem cells

There have been fruitful efforts in identifying the ethical and societal challenges of stem cell research, including induced pluripotent stem cell and adult stem cell research, in both the preclinical and the clinical translation phase. Stem cell research raises several ethical challenges among others regarding donor material, storage of material and questions about ownership [1,2]. More translational questions include ethical challenges concerning the use of animals, safety, efficacy, side effects, stem cell tourism, and therapy costs [1,3,4]. Those discussions are closely tied to questions about responsibility. These include questions regarding who should be answerable to undesired actions and consequences, and who is responsible for dealing with, mitigating, or preventing the ethical and policy challenges of stem cell research. The importance of responsibility in stem cell research is stressed in overviews of the ethical landscape in academic literature as well as guidelines and regulations [1,5,6].

Future Medicine

However, little is known about stakeholders' perspectives on the ethical challenges of stem cell research, particularly regarding roles and responsibilities. These stakeholders including stem cell researchers and patients could offer a helpful insiders' perspective on the distribution of responsibilities in practice, perceptions of own roles and those of others, and possible obstacles for taking responsibility for or dealing with the ethical aspects of stem cell research. These perceptions are helpful for formulating more practice-based solutions and possibilities to enhance responsibility in stem cell research.

To better understand the types of roles and responsibilities of stakeholders in and around stem cell research, we have conducted focus groups with stem cell researchers and patients. Focus groups are a suitable qualitative research instrument for gaining deeper insights in concepts, perspectives, and experiences [7]. The goal of our research was to identify what stem cell researchers in the field of intervertebral disc regeneration, where cell-based therapies are in development [8], and patients with chronic lower back pain consider to be the roles and responsibilities in the field of regenerative medicine. The iPSpine consortium (www.ipspine.eu), a European collaboration of researchers who primarily work with iPS-based technologies for developing an advanced stem cell therapy for intervertebral disc degeneration from bench to bedside, served as a showcase. By providing insight into the perspectives of stakeholders on the roles and responsibilities in stem cell research and linking our results to the previously published literature, this analysis intends to contribute to the responsible development and translation of stem cell research.

Methods

We conducted a focus group study to identify the perspectives of relevant stakeholders on the roles and responsibilities in conducting stem cell research and its clinical translation. The study is reported in accordance with the consolidated criteria for reporting qualitative studies (COREQ) [9].

Participants, selection & recruitment

Three focus groups have been conducted for our study (Table 1). We conducted one focus group with late career stem cell researchers (n = 11). They were primarily full professors and associate professors. The researchers worked in France, Hong Kong, Ireland, Switzerland, The Netherlands and the United Kingdom. We conducted a second focus group with early till mid-career stem cell researchers (n = 7, henceforth early career researchers). They were PhD candidates, postdocs, one associate professor and one engineer. The researchers worked in France, Italy, Ireland, Switzerland and The Netherlands. The reason to make a distinction between these two groups is that early and late career researchers may experience their possible responsibilities and the role of legislation differently. In general, stem cell researchers were included based on being part of the iPSpine consortium, attendance to the iPSpine consortium meeting in January 2020, proficiency in the English language and work or have worked with stem cells. to get a broad perspective on the perceived ethical challenges, roles and responsibilities, efforts were made to include researchers who conducted fundamental or applied stem cell research. Potential participants were approached via the consortium-network by email and informed about the set-up and goals of the study by researcher LSA.

A third focus group was conducted with patients with chronic lower back pain (n = 9). Patients were included based on whether they were adults, were proficient in the Dutch language and had chronic lower back pain. The patients were recruited via a Dutch patient group, namely 'de Wervelkolom', who advertised our study via social media and their own website. Furthermore, the Dutch Arthritis Society shared our call within their network of lower back pain patients by e-mail. Using purposeful sampling, the groups were selected to balance disease history and gender [10].

People who refused participation in our study named a variety of reasons: six persons did not respond to our invitation, one person did not feel free to talk when recorded and one participant of the patient group dropped out due to technical issues.

Data collection

The focus groups were semi-structured and guided by a predefined topic list with open-ended questions that were based on relevant literature and discussed in our research team. The focus group covered the following topics: ethical challenges; the current role of legislation, researchers and patients in dealing with these challenges; the possible role of legislation, researchers and patients in dealing with the ethical challenges and what the different stakeholders would need or expect from each other to enhance responsible research in stem cell research.

The focus groups with stem cell researchers were conducted in English and took place in person in January 2020 in Nantes, France. They lasted for approximately 70 min. The focus group with the patients lasted for 64 min,

Table 1. Respondent groups.

Respondents	Early career stem cell researchers (n = 7)	Late career stem cell researchers (n = 11)	Lower back pain patients (n = 9)
Sex			
– Male	3	5	3
– Female	4	6	6
Age (years)	26–42	41–59	46–76†
Years of research experience			
– 0–2	1	-	n/a
– 3–5	1	-	n/a
– 6–10	2	-	n/a
– 11–15	2	-	n/a
– >15	1	11	n/a
Academic position			
– PhD candidate	2	-	n/a
– Post-doc	3	-	n/a
– Associate professor	1	3	n/a
– Full professor	-	6	n/a
– Other	1	2	n/a
Phase of stem cell research			
– Fundamental	3	5	n/a
– Development/applied	5	7	n/a
– Implementation	-	1	n/a
– Differentiation	1	-	n/a
– Translational	-	2	n/a
Ethical training during education			
– Did follow	4	7	n/a
– Did not follow	3	4	n/a

†One respondent did not disclose their age.

was conducted in Dutch and took place online in October 2020, using the web application for videoconferencing Webex. By conducting the focus group with the patients in Dutch, it was inclusive to people with different educational backgrounds. This focus group with patients took place online for two reasons: first, due to Covid restrictions in The Netherlands it was impossible to meet in person. Second, for patients with chronic lower back pain traveling is often difficult to plan and could aggravate pain.

All focus group participants filled in a short demographic questionnaire and all participants had the opportunity to ask questions before providing their informed consent in writing. The focus group with the early career researchers and patients was moderated by KRJ (trained qualitative researcher, female, assistant professor) and LSA (trained qualitative researcher, PhD-candidate, male) took notes and provided administrative support. The focus group with the late career researchers was moderated by ALB (trained qualitative researcher, female, professor) and RI (trained qualitative researcher, associate professor, female) took notes and provided administrative support. After informing the participants about the research and the signing of the informed consent forms, the actual focus group took place. The focus groups were audiotaped, transcribed verbatim, and pseudonymized.

Data analysis

The pseudonymized transcripts were analyzed thematically – an approach to qualitative analysis aimed at identifying themes and patterns that extend across all data [11]. Transcripts were coded using the academic software *NVivo*. The analysis process was structured according to the constant comparative method [12]: data were systematically reviewed for supportive and conflicting evidence for emergent themes. The coding process was used as a first step to categorize the data, after which these were further analyzed and abstracted from, to develop overarching themes and sub-themes. LSA conducted the initial coding. to achieve inter-reliability of results, the research team (LSA, KRJ and ALB) frequently compared and discussed codes in light of text fragments. This was done by discussing

the analysis process, going back and forth between the data and the results to develop and revise themes and sub-themes, while also ensuring agreement about the results. In our study we reached saturation in terms that subsequent conversations no longer brought up new issues ('coding saturation') and the formulated themes were sufficiently understood ('meaning saturation') [13]. Representative quotations were chosen to illustrate themes and were translated into English where necessary by the research team. Due to the passing of time between the focus groups and the analysis of the data, we did not conduct a member check with the participants.

Results

The analysis of the results of the focus groups has led us identify four themes namely 1) roles and responsibilities in the laboratory, 2) responsibilities of and toward patients and the public, 3) the role of regulation and 4) structural hurdles for responsibility. Below we will elaborate on respondent's accounts of these challenges and their suggested solutions.

Theme 1. Roles & responsibilities in the laboratory

Early and late career researchers identified various roles for themselves within the field of stem cell research. These included: researcher, trainer, manager and supervisor. Early career researchers considered their role primarily as a researcher. The corresponding responsibilities to this role, were to ensure that experiments are properly designed and conducted. Late career researchers identified their role primarily as a managerial and supervisory one, in which they lead by example (Table 2, Quote 1). They felt a strong responsibility for making sure that their PhD students are trained well, thereby promoting research integrity. In light of that, late career researchers found it important that their PhD students receive the correct information about research and the laboratory and do not copy bad habits, such as deviating from research protocols. Therefore, many late career researchers considered it to be important that when their PhD students have questions, they would go to those persons that the late career researchers trust, such as members of the technical staff (Table 2, Quote 2). This trust is based on technical staff members' experience in the laboratory and their knowledge of research processes. Patients mentioned different responsibilities surrounding the clinical translation of stem cell research. In that respect, several respondents found it important that the therapy is safe, has no or minor side-effects and that it is clear what effect the therapy has on the patients' body (Table 2, Quote 3). Moreover, one respondent remarked that in the translation of research there should be attention for what the therapy might mean for a patient's psychological wellbeing when a chronically ill person becomes (completely) healthy (Table 2, Quote 4).

Several late career researchers expected of their PhD students to have some knowledge of the ethical guidelines and one researcher mentioned the importance of learning to write an internal ethics application themselves (Table 2, Quote 5–6). Many late career researchers regarded it important that their PhD students are familiarized with the ethical aspects, such as guidelines and applications, of their job. However, some early career researchers did not consider the ethical aspects to be part of their job, nor considered it to be a feasible part of their job (Table 2, Quote 7–8). Moreover, late career researchers generally had a broader conception of ethics than early career researchers. Early career researchers perceived the ethical implications to be limited to ethics approval and did, for example, not consider their work with human tissue to have any further socio-ethical implications. Specifically, they did not perceive problems with the use of cells of adult patients in comparison to embryonic stem cells (Table 2, Quote 9). However, late career researchers identified several ethical challenges in conducting research with patient-derived stem cells, such as making sure that they have an ethical authorization and whether patients, from which the cells were derived from, should share in the potential financial profit of the research. To enhance the feasibility of dealing with the ethical aspects, all early career researchers preferred to have guidance in writing ethics applications and other documentation or to have a database with relevant regulatory information (Table 2, Quote 10). Another option that was considered is to delegate the administrative responsibilities to a dedicated body that is specialized in regulatory affairs.

Late career researchers stated that they have a lack of oversight of the activities of early career researchers. More specifically, they argued that they cannot oversee everything early career researchers do, such as whether the early career researchers are following the instructions they were given (Table 2, Quote 11). In addition, late career researchers argued that they are unable to go through all the raw data that early career researchers produce. This is due to the time constraints, but as well due to the practical reason that the early career researchers work with new technologies, of which late career researchers may lack sufficient knowledge (Table 2, Quote 12). Despite these challenges, many late career researchers considered themselves to be accountable for the research results of their

Table 2. Roles and responsibilities in the laboratory.

1	LCR1: So lead by example? ALL: Yes. LCR11: This is a question the students ask me when I go through the ethics courses with them is that we're the supervisors. I think a lot of them when we've finished training them, the rules and regulations they kind of enjoyed it, but yet they say: Well, when I go back into the lab nothing changes. I think at the end of the day, the future is really making sure every researcher keeps talking and practicing in the lab so generate that culture within the lab for compliance.
2	LCR8: I guess it's the same. I don't know. It's not only about research, it's the same in a factory; the CEO of a factory is not checking every item going out of the factory so you have to, in a way, delegate and trust people that they do the thing they're supposed to do. So, you can implement some measures to make sure that everything goes along in the right way but you have to delegate.
3	PT4: What are the long-term effects? Or what the short-term effects could be, but as well what on the long run this could do to your body.
4	PT4: Imagine that you have a lot of physical complaints and instantly you will get rid of them, then your life will change a lot. Imagine that… and this might be a bit utopian, but a lot of people hope for it, that it will help a lot of people, and that your life could change fundamentally. And it could be the case that you will need psychological guidance because you will be a different person, though the people around you treat you in the same fashion as they did before. We hope to get rid of our pains, but considering that we, often for years, have learned to live with pain and adapted to it. When life is turned around instantly, it could be difficult to enter this new life. So, I think it is not only medical aspects, but that you could be affected psychologically – And as well from your environment.
5	LCR11: We trained students so they get a basic understanding what the necessary procedure is and what necessary guidelines they need to know.
6	LCR5: Every research student has to put in their own internal ethics approval. It's a long line system. They have to go through that for their own project even if we've got overarching ethics to collect human samples from (Organisation), students have to read and understand the ethical permissions that you got and then portray that in terms what exactly they're doing. I think that's really good.
7	ECR5: Not really. I take the cell and make differentiations so we don't care about ethical, not really. ECR1: You don't deal with it in your everyday? ECR5: Nothing. Every day, for me, it's really new and I really don't care about that in my job. Maybe it's more common because I take from the human. For me, it's really not a problem in my job.
8	ECR2: For me, not entirely. The senior researchers still have the lab work but not all the iPSpine project being done by the student researcher because they have a post doc PhD doing the research and so they can focus as well on the ethics. ECR1: So you see the ethical aspects really are separate from your lab work? ECR6: I don't think it's separate it should be part of it but for a literal sense it's too much to deal with. ECR2: Yes, it's too much
9	ECR8: Yes, I actually don't think about it a lot when you work in the lab. I'm quite happy that we work with IPS cells and not embryonic stem cells because it would be more difficult, I think. But still, yes, they're from a patient and, yeah, it's good to think about it a little bit more so I think this is nice to do. ECR1: Do you mean 'difficult', more ethically difficult like in ethical terms or is it also more difficult to work within the lab like more ethically? ECR6: More ethical because iPS cells are just from a patient, somebody's somatic cells.
10	ECR8: Yes, it's nice if someone could teach you how to do it and not just say you have to do it: Look how you do it yourself. ECR1: So some more guidance in that part? ALL: Yes, that would be nice, yes.
11	LCR5: But it's the only way you can do things as well when you've got a bigger group, you can't possibly supervise everyone all the time so you have to trust.
12	LCR11: These days, what students do you can't do. You don't know what they've done. […] This is a challenge most of us face because our training is so different. I trained decades ago so some of these new technology I really don't have a good sense.
13	LCR13: With me the same. I am prepared to retract data if it's wrong, and I will be the first one to say that not all data I know exactly but I'm prepared if somebody says it's wrong I will retract it.
14	LCR13: But in a bigger group, I have a big group so post docs, PhD's I completely delegate, I don't necessarily have them engaged, but you can have technical staff which are consistent and can manage; they have basic principles, they can record the data and they can sign off every week so you can implement systems in the big lab. When my lab was small then I would do it myself.

early career researchers, some arguing that that they would for example retract the data if necessary (Table 2, Quote 13). The late career researchers argued that a solution for the lack of supervisional oversight is suggested to be found in intervening in the structure of institutes. Since late career researchers cannot be on top of all the research activities, they need to trust their early career researchers and delegate tasks to other researchers or the technical staff (Table 2, Quote 14). Some late career researchers had good experiences with the technical staff assessing research data and giving approval.

Theme 2. Responsibilities of & toward patients & the public

Dissemination of research findings and the progress of research to the public was considered important by all groups. Patients considered it the researchers' responsibility to disseminate research findings. Patients saw a role for themselves to be part of dissemination activities as a bridge toward other patients by talking about what the research project involves (Table 3, Quote 1). Furthermore, patients and late career researchers both argued that dissemination should be directed at creating transparency, managing expectations and hype (Table 3, Quote 2–3). Therefore, late career researchers considered it important to communicate about the importance of animal research. One researcher mentioned the importance of clarifying why it is necessary to use stem cells for research purposes. Moreover, the respondent found it important to state that they do not (primarily) work with human embryonic stem cells (hESCs), since the public often equates stem cells with hESCs and has bad associations with hESCs (Table 3, Quote 4). Furthermore, late career researchers considered dissemination as a possibility to create transparency about their research, such as why they use certain (human) stem cells and what the source of those cells is (Table 3, Quote 4). Patients stressed that the information should not be too technical, be communicated in an understandable form, give insights in the risks and long-term effects of a new intervention and that the information should be easily findable through websites and social media (Table 3, Quote 5–6).

Informing the public and patients about research could have benefits in terms of transparency and expectation management, it was also stressed that the interaction between the public and patients and researchers could similarly have benefits for stem cell research itself. Late career researchers experienced that disseminating to and interacting with patients is motivating. It helps them to understand the perspective of patients and to get clearer why their research matters (Table 3, Quote 7–8). Similarly, patients stated that they themselves could convey why a new treatment is necessary and what the potential benefit of the new treatment is. In addition, some patients liked to be involved in early stages of the research, instead of merely the later stages in which they as a research participant might undergo experimental treatment (Table 3, Quote 9). In light of dissemination, patients identified a role for themselves to help disseminating and generating information: they could function as a bridge to other patient groups (Table 3, Quote 1). This could foster understanding and support for stem cell research. Likewise, patients see a role for patient associations in the dissemination of information (Table 3, Quote 10).

Some early career researchers seemed to have prejudices about the difficulties with communicating to the public, where many early career researchers had bad experiences with public dissemination. These early career researchers mentioned that the general public often does not understand their research, specifically the use of animal models (Table 3, Quote 11). One factor that affected whether the experience was positive, or negative, is the assumed level of education of the public. The higher the assumed level of education, the more positive the experience of the early career researchers was (Table 3, Quote 12). However, one early career researcher had positive experiences with disseminating to the public. What was considered helpful was the support of a science communication department of the university (Table 3, Quote 13). The early career researchers stated to have had additional positive experiences with dissemination activities with patients, because patients were perceived as being more understanding than members of the public for the type of research that is needed, such as animal models (Table 3, Quote 14).

Theme 3. The role of regulation

During the focus groups, rules and regulations have been considered as a broad set of prescriptions for researchers to adhere to, for example following rules and filling in applications and forms. Patients argued that they find it important that researchers are aware of the rules and regulation surrounding research (Table 4, Quote 1). While most early career researchers agreed that rules and regulation are important, not everyone was aware of them or did encounter them; for example, when someone else takes care of the administration (Table 4, Quote 2–3). It was observed that researchers often considered the regulation of stem cell research to be the same as the ethical aspects of stem cell research. In light of this, most early career researchers mentioned that they (would like to) share the responsibility for, among others, receiving ethical approval and documentation of forms by having administrative

Table 3. Responsibilities of and toward patients and the public.

1	PT3: Us being a patient, or as a participating patient, you can create a bridge to larger patient groups. By showing what is happening and talking about the content of the research and what the research will be in the following years.
2	PT4: I think that it is important that the information is translated as much as possible in such a way that you as a layperson could understand it. Besides, I think that it is important that people do not have too high expectations and think that it is the solution to their problems. So, I think that it is important that you share honest information.
3	LCR13: It's managing expectations and hype. We, as a community, not us around the table, but we as a community have done a complete disservice to the public in creating hype of a technology and have not delivered on it.
4	LCR5: I also do sessions on ethics on stem cells as well with public, doing multiple different sessions with public or have debates with them. It's really important to get them to understand the actual true science behind why you would need to use these cells and what the cells are as well. Often, the perception of the public when you say 'stem cells' is they always assume it's an embryonic stem cell, and even with embryonic stem cell they assume what you're doing is you're killing a baby to get there which, of course, that's not where these kinds of things come from.
5	PT3: I was thinking about your question "what type of information we would like to see". I realize that when things are getting technical, about which material is being used and so on, I lose interest.
6	PT4: I think that it is important that people… because nowadays everybody uses google for finding information, that a website would come in handy. And in that case it is important that the information would be communicated in such a fashion that every patient would be able to understand it.
7	LCR4: It helps you to realize the type of burden people who have the disease you're working on have. That motivates you.
8	LCR1: But is it that research is explaining to patients what they're doing or is it patients giving input for what kind of research that needs to be done, so what direction it is? ALL: Both ways. LCR8: So we could get feedback.
9	PT3: Yes, and I think that patients should be included in the pre-phase. To show in the preliminary stage: okay, the impact is huge, just look at this and that person. If we could realize something with this research that could lead to results, yes, what kind of financial and societal impact that is going to produce. I think that you should include that already.
10	PT6: So, de "Wervelwind", the magazine of the association for patients with back pain, contains so much information. When you could provide feedback to them, then we will be automatically informed.
11	ECR 3: Sometimes the public doesn't really understand the importance of the in vivo models in medical technologies that they themselves benefit from, and for that reason I don't really talk about it to other people about the animal work I do because I feel like they won't understand because I'll just get judgement, you know, sometimes get frustrated.
12	ECR6: I think if you try to talk with someone who has a lower educational level I find it then more difficult.
13	ECR2: Basically, it's how we can engage with the community and tell them in layman terms. Also, we have, for example, involving various talks. You just went through the streets and then just talk about your research so people will understand. People will ask you about what you're doing and then why you're doing this research and so on.
14	ECR6: if you talk to a patient group the response you're going to have is different from the general public. I think the patient group would be a bit more emotional and connected to the topic.

support (Table 4, Quote 4). Some early career researchers mentioned that their supervisor should or could take responsibility for it. Late career researchers had much experience with regulation and referred to how the number of rules and regulation change over time. A few respondents recognized that often more rules come into place after an incident showcased possible risk (Table 4, Quote 5).

All researchers thought that regulation could be useful for promoting responsible research. A late career researcher argued that regulation and filling in forms, could have an instrumental value. Where in light of getting samples, it helps to reflect upon the research aim and which questions one wants to ask (Table 4, Quote 6). One early career researcher mentioned that following the rules helped to protect themselves. A different early career researcher stated to trust the rules enough that following it will lead to ethically sound research (Table 4, Quote 7). Conversely, researchers mentioned that regulation can hamper research progress. All researchers have experienced that regulation is not always in congruence with the practice and that it leads to bureaucracy and accompanying paperwork (Table 4,

Table 4. The role of regulation.

1	PT1: A first question that I would like to ask is whether you – as a patient – find it important that researchers are up to date about the rules and regulations of stem cell research. PT6: I would think that to be very necessary.
2	ECR1: But with regulations and the rules, is it something you encounter or not so much? ECR5: Not so much. ECR1: Is there someone else in your lab that is doing that? ECR5: No, my chief takes care of that, not me. It's not my job really.
3	ECR8: Honestly, I don't really know about the regulations. The cells are just there. So, yes, that's it.
4	ECR3: Just because it's kind of new and there is a lot of regulations and a lot of extra work involved with all this, it would be nice if institutions have a dedicated body to help the researchers follow the rules and do all the paperwork so I'm not expending all my energy trying to figure it out and do it. If I have somebody to help then I can focus on doing science and making discoveries. I think if they're going to have the rules in place, facilitate it and not put all the responsibility on me to figure it out.
5	LCR5: Partially, because often if an event has happened, which obviously highlights there's a risk somewhere, then sometimes the answer is to have more rules to ensure everyone can't do that again.
6	LCR5: It makes you think about the questions you're trying to do with your samples. If you have to fill in that bit of paperwork, you have to think: What is it I'm actually doing? What are the questions I want to ask? Whereas if it was a lot easier and you could just get the sample, you might not think through those processes as well. I think it is important.
7	ECR8: I don't know exactly what the rules are but I trust them enough that what I do is ethically okay. So yes, I get there are rules that you cannot do anything you want.
8	LCR5: That was fine in those days and it has improved for the better but it's getting a balance between making sure there is support and paperwork there at the right level without making it too cumbersome with paperwork you can't get research as well.
9	ECR2: Sometimes you just put a rule just based on the paper but not practical.
10	ECR3: I realize it's necessary. I understand it's important but on my level when I'm just completely overwhelmed with planning experiments and labwork and data analysis and so one more thing, then it's a little bit overwhelming because there are so many rules and regulations in doing the work. I have to learn all of it, and I just need somebody to tell me: Here, just do this. Theoretically, yes, it could hamper my work but I understand that it also needs to be made a priority.
11	ECR5: if you really want to make a discovery, do you need to follow the same rules as everybody? Because it's a fundamental question that we need to make discoveries, we need to do science; then it's kind of contradictory past and respect ethics and to do discovery by doing the same as other people.
12	LCR2: Do you think in that way you run a risk of people losing a sense of ethics and just thinking: As long as I tick all the boxes I don't have to think what I do is right? I have a feeling that's happening at the moment. So, in a way, you lose your sense of ethics just because you can put it back to the rules: I did everything I needed to do.
13	PT4: I think that there are rules and regulations for protection, but they can as well hinder developments that potentially could help a lot of people. If that is the case, it might be helpful to involve politicians to make legislation less strict.
14	ECR8: I don't know. I don't have enough knowledge. I don't know enough about the rules but it's nice if they involve researchers setting up these rules and regulations so we can have influence from it.
15	PT3: It would be nice if you [a researcher] could spend time together with a regulator. That you could create a relationship between the two and they could work together toward something, instead of merely: well, show us what you got, and this is what we think of it.
16	LCR11: This is a question the students ask me when I go through the ethics courses with them is that we're the supervisors. I think a lot of them when we've finished training them, the rules and regulations they kind of enjoyed it, but yet they say: Well, when I go back into the lab nothing changes. I think at the end of the day, the future is really making sure every researcher keeps talking and practicing in the lab so generate that culture within the lab for compliance.

Quote 8–9). Late career researchers noticed that regulation could hamper research when regulation is not feasible in an actual research setting. Some early career researchers considered the regulatory bureaucracy to be overwhelming (Table 4, Quote 10). Moreover, one respondent was worried that the translation of ethics into rules and regulation is hampering the pursuit of science so much that it prevents extraordinary science (Table 4, Quote 11).

Late career researchers questioned whether all ethical challenges could be accommodated by regulation. Some of them expressed the fear that regulation could reduce ethics into a 'tick-the-box exercise'. By merely following the 'legal requirements', researchers are not stimulated to reflect upon ethical aspects of their work and that researchers might lose a sense of ethics (Table 4, Quote 12). Some patients worried that ethical aspects may (unnecessarily) hinder the development of new therapies. Yet, some of the patients argued that discussions about protection and hindrance should rather be done on a political level (Table 4, Quote 13).

All groups mentioned several improvements for regulation that would lead to responsible research. The early career researchers acknowledge that when formulating and enforcing rules and regulation, it would be helpful to involve researchers so they can have (some) influence on it (Table 4, Quote 14). Similarly, patients stated that regulation is ideally an actual collaboration between scientists and regulators that is directed at making it in congruence with the actual research practice. This should involve that regulators act parallel to researchers and that regulators advice researchers as well (Table 4, Quote 15).

Moreover, all stem cell researchers mentioned the value of training. In the group of late career researchers, some noticed difficulties when their early career researchers were trained in rules and regulation. While new researchers developed knowledge about the rules and regulation, this did not automatically lead to changes in the laboratory. More specifically, the training could provide all kinds of relevant information to teach research integrity, it does not mean that this information is automatically integrated in the working environment. to stimulate research integrity, the respondent argued that researchers should continue the conversation about compliancy to the rules and continue practicing to generate a culture for compliance (Table 4, Quote 16).

Theme 4. Structural hurdles for responsibility

Responsible conduct was considered important by all groups. All researchers mentioned several issues that hamper stem cell researchers to take more responsibility for the direction and execution of research, which are closely related to scientific culture. All researchers acknowledged that there are different kinds of pressure in the scientific community. Publication pressure was experienced by early career researchers to 'grow' in the field of science. More specifically a pressure of publishing positive results and as a consequence the pressure to produce positive results, since publishing negative results is not rewarded (Table 5, Quote 1). Both early and late career researchers remarked that this type of pressure could result in unethical or morally grey behavior (Table 5, Quote 1–2).

Late career researchers stated that the direction in which science progresses is dependent on funding possibilities. They mentioned that the way that stem cell research is funded, negatively affects the potential of research ideas and possibilities for societal impact (Table 5, Quote 3–4). Late career researchers stated that funding goes primarily to research that is appealing, without risks and is applied or translational (Table 5, Quote 5). Moreover, early career researchers mentioned that researchers and their grant applications are judged based on whether they have published in journals with a high impact factor.

As a result of how funding agencies divide their financial means and evaluation how grant proposals are evaluated, late career researchers identified several barriers to take responsibility for supervising and creating consistency between fundamental and translational research. First, since funding dictates the direction and possibility of research, late career researchers need to spend a lot of their time into writing grants, which is an uncertain process and prevents researchers to work on the research that already got funded (Table 5, Quote 6). Second, funding is often allocated to either fundamental or translation research. This isolates fundamental and translational researchers, which complicates whether and how applied and fundamental researchers could communicate with each other. Consequentially, this affects the (internal) responsibility of researchers to ensure whether certain translational research is viable (Table 5, Quote 7). Third, when fundamental research is not funded, necessary scientific insights for conceptualizing and conducting translational or applied research cannot be studied, which could backfire scientific progress (Table 5, Quote 8).

Late career researchers considered themselves to be responsible for changing the way how funding agencies work and how it directs research (Table 5, Quote 9). Some late career researchers opted the importance of fundamental research could be stressed by communicating why fundamental research is important for translational research. In addition, they stated the importance of communicating what kind of impact their research could have on society

Table 5. Structural hurdles for responsibility.

1	ECR4: You have the right to make a mistake. Research doesn't allow that. I mean, look at publications; publications are based on positive results. They tried in the past to make some publication about negative. It didn't work at all. Because we have this inability to fail it's pushing people to do unethical things; and it's only about that because if you don't have possible results, if you don't fulfill the requirement.
2	LCR8: Like you said, sometimes students could be under pressure and do things that are not totally right.
3	LCR5: One of the things that can probably be improved is researchers knowing when to change direction, but the trouble is the directions that research goes in is not often driven by what we want to do or what we think the results are; it's actually on which grants we get funded for. You have put in so many for grants and whichever grants you get, well, that's the work you do. That's how it works. Really, that's wrong because we know that one will probably have much more chance getting there but it's not as sexy.
4	LCR1: If I hear you correctly, you say our research would be better and more successful and then have a more societal impact if we would have more freedom in the study ourselves what direction we should go to? ALL: Yes.
5	LCR4: In a way, if you leave the total responsibility up to reviewers you're leaving the responsibility up to a committee. We all understand that when you make decisions by committee you don't make the bravest decisions; you usually end up making the safest decisions which usually meet the lowest denominator. Which begs the question: Is that really the way you want drive science?
6	LCR5: And we wouldn't have to spend a lot of time writing the next grant rather than actually concentrate on the grant we've got, and getting on with what we should be doing rather than just write and write grants which keep getting rejected.
7	ECR8: I think it's also, our responsibility, internal responsibility communicating between fundamental and people that are more doing translational because translational is just before the clinical trial. So we're giving the signal: Oh we're ready, when we're not always ready. I think it's a good combination. We're struggling because sometimes we disagree; sometimes the fundamentalist: No, we're not ready and sometimes the translational are: Yeah, we're going. I think we should keep talking. We should keep having this mixed community and sometimes we're separated because of the funding. You know, sometimes we say: Well, you should do translation, and I say no. It's true because of the funding. There is a separation of the committee because of the funding.
8	LCR4: Because if the (Place) national agency had decided to give money to translational research this is probably because the people who are making these really bullshit decisions is because they don't discuss with the fundamental researcher and they don't understand what will be researched in (Place) in 30 years. If we stop giving money to fundamental research, in 30 years what are we going to do? We are going to make a hole in the bone of a rabbit and inject biomaterials?
9	LCR1: Whose responsibility is it to change this? LCR13: Ours, we're the grants.
10	LCR7: I just want to say so maybe we so far failed in explaining correctly to society how important also fundamental research is, that maybe in a hundred years from now this can be used for very, very promising treatment or application
11	LCR4: If we agree that the research we're conducting now could have a huge societal impact in terms of improving quality of life and patients and so on, I think we should have very early in the project discussions with patients and with society, and patients the PAB we have in this project.
12	LCR1: If I hear you correctly, you say our research would be better and more successful and then have a more societal impact if we would have more freedom in the study ourselves what direction we should go to? ALL: Yes.

and on the quality of life of patients (Table 5, Quote 10). It was mentioned that when the potential societal impact of fundamental research is acknowledged, that patients could be included much earlier in the process of research. All late career researchers agreed that this would help to explain the necessary methods of their research and to receive input from patients to understand what kind of research is needed (Table 5, Quote 11). This is in line with what patients have expressed. Patients perceived a specific role for themselves in being involved early on in the research progress, because they could clarify why certain research is of importance by explaining which practical effects the research outcomes could have on their lives (Table 3, Quote 9). Another solution that is considered by late career researchers is to have more leeway over the direction of their research, claiming that it could lead to more societal impact (Table 5, Quote 12).

Discussion

The goal of our research was to get insights in what stem cell researchers and patients with chronic lower back pain consider to be the roles and responsibilities in the field of stem cell research. The iPSpine consortium, working primarily with iPS-based technologies, served as a showcase. Below we will reflect on the implications and relevance of our empirical study for responsible research and translation of stem cell therapies in regenerative medicine. Furthermore, we will relate its findings to the broader literature, and identify areas for further research. The findings of the focus groups show a close resemblance with open science initiatives or problems that those initiatives try to overcome. These involve accessibility of science – such as transparency and dissemination – alternative metrics for rewarding scientific impact and collaboration between scientists.

Our study shows that stem cell researchers did primarily discuss the ethical dimension of their work in terms of research integrity and ethical permits and to a lesser extent the quality of life of patients, the social value and use of financial societal means. Our findings are in line with the conclusions of a 2015 study, where healthcare professionals and researchers in the field of regenerative medicine consider certain societal impacts to be important but focus primarily on costs and risks [14]. Such risks are often conceptualized in ethical permits and application forms. Similarly, stem cell researchers from Saudi Arabia consider informed consent and following the right research methods to be the important ethical aspects of stem cell research [15]. Notably, ethical challenges related to the field of stem cell research, such as cell tourism, increase in healthcare costs, social justice (e.g., promoting inclusion in research and preventing discriminatory practices [5]) and other societal impacts have not been mentioned, while these are considered to be of importance [2,16]. It should be noted that some late career researchers hinted at the need of ethical action besides merely following guidelines, by claiming that a sense of ethics should not get lost. If this sense of ethics is important for conducting responsible stem cell research, it should be cultivated and/or trained. This could for instance done by education, workshops and interventions [2]. As such, research integrity could, for instance, be promoted through a virtue-based approach [17,18]. The rationale of this approach is that by internalizing ethical values, such as honesty and accuracy, researchers will behave in accordance with such values.

Regarding accessibility of science, both the late career researchers in our study as researchers of an interview study [19] consider it the responsibility of researchers to communicate their research to the public, more specifically, the innovative and problematic aspects of research. In our focus group, early career researchers faced difficulties in disseminating problematic aspects of their research, such as the use of embryonic stem cells and animal studies. A possible explanation for why some of the early career researchers experience these challenges is that they have specific ideas of the goal of dissemination. The findings show that many early career researchers consider dissemination to be explaining their research to the public. This idea of dissemination is related to an educational activity [20] or the 'deficit-model' of science communication, where the underlying belief is that the public does not have knowledge about the research itself and it is the task of the researcher to present this knowledge [21]. The downside of such a model is that it does not include different types of expertise and worldviews, outside the ones that is advocated by the researchers. Researchers could broaden their view by taking ideas, desires and wishes of society into consideration. As such, researchers could consider how society could be benefitted by their research. Therefore, it is helpful to think differently about dissemination, and to consider forms that opt more for dialogue. A dialogue leads to that both researchers and the public could learn from one another without necessarily reaching consensus [21]. To accommodate more fruitful and positive interactions with the public, researchers can embrace different dissemination goals, other than educating the public. In addition, they could get training on strategies for disseminating morally sensitive aspects of research. This could be pursued by using the different dimensions of Responsible Research and Innovation (RRI), such as anticipation, reflexivity, inclusivity and responsiveness as a source of inspiration for the creation of learning goals for curricula of biomedical students [22]. Moreover, accessibility of science could as well be improved by including patients in dissemination activities. The focus group with patients saw a role for patients themselves to help communicating about research to other patients. Literature suggests as well that letting patients being involved in early stages of the research project and be part of dissemination activities, where they help to explain the research, are inherent to meaningful patient engagement [23].

In respect to maintaining and improving research integrity, our findings and existing literature [24,25] show that academic pressure needs to be alleviated. Open science initiatives [26,27] could contribute to reducing academic pressure and finding different incentives for conducting research. This initiative focuses, among others, on open access publishing, public engagement, and new ways to recognize and reward researchers. Specifically, the aim to judge researchers no longer (exclusively) on journal impact factors and h-indices, but rather by the societal impact

of their research and their educational and professional performances, may mitigate publication pressure. This is in line with finding alternative metrics for understanding scientific impacts. Results of the early career researchers group suggest that academic pressure could as well be alleviated indirectly by having administrative support, which has as well been reported by, among others, biomedical researcher [28]. Having administrative support enables researchers to spend time on other aspects of their work.

There is a gap in responsibility of the ethical conduct of stem cell research that concerns collaboration between scientists, which can be explained by a gap in knowledge and lack of time. First, late career researchers do not always have the insights to supervise early career researchers about the specifics of new research technologies, making it difficult for late career researchers to control – without any assistance of others – whether early career researchers have used the technology properly (in compliance with research integrity). Second, early career researchers often do not have experience with the oversight of the research project for the ethical rules and regulations concerning it. Late care researchers do have this oversight but often lack time. As a result, early career researchers could potentially make unintended mistakes. For the responsible conduct of stem cell research, these gaps should be overcome. A possible solution for this gap can be found in the hierarchical structures of research institutions. Here, late career researchers could delegate certain supervision to people whom they trust, based on their knowledge and experience in the laboratory.

This is in line with the open science initiative stressing that scientific efforts and achievements are nowadays more considered as a team effort. Science should not be considered as an individual practice or the outcome of individual researchers; a complementary team of researchers address scientific challenges, which include also challenges regarding responsibility and ethics. For example, a team including the technical staff, assistant professors and post-docs could have the role to ensure whether researchers adhere to the research protocols of the laboratory and ethical demands concerning the use of tissues or experimental animals. This could help to hold researchers accountable for their actions and create a culture of compliance and improve research integrity. Although, it should be noted that responsible research and innovation demands more than merely compliance to rules and regulation.

Moreover, the role of regulation in stem cell research has been heavily discussed in our focus group by researchers and patients. It was observed that rules and regulation was used interchangeably in our focus group studies. A possible explanation for this is that in practice researchers adhere to research protocols, which could be based on both rules and regulation.

Limitations of our study & recommendations for future research

Our results should be considered considering the following limitations. The sizes of the conducted focus groups (n = 7–11) is within a normal range for focus group studies [7], as is the total sample size (n = 29). Qualitative studies, such as our study, aim for analytic rather than statistical generalizability. The analysis revealed abstractions with regard to ethical conditions for responsible research conduct that could be transferable to other situations [29]. As such, the larger theoretical concepts are transferable to other situations when scrutinizing the procedure, methods and analysis strategies [7]. Furthermore, the analytic generalizability has been increased by analyzing the interviews with multiple members of our team and by triangulation with existing literature [29].

Another point of interest is that the focus group with the patients was conducted online. While all focus groups shared the same topic lists, the online setting could have affected the dynamics of the focus group with the patients. For example, eye contact is difficult in online sessions, as well as picking up on body language, which could result in that people feel inhibited to speak up. However, the data of the online focus group are most likely of similar quality as focus groups that are conducted in person. Research suggest that online focus groups lead to shorter answers, but that the actual content and quality of the data do not differ from focus groups that have been conducted in person [30]. Furthermore, the focus group with the patients might have had a cultural bias, as all patients were Dutch. Their experience is primarily based on living in The Netherlands, being part of the Dutch health care system and being a patient with chronic lower back pain.

The focus groups with the researchers were conducted by two different couples of researchers, while using the same topic list. The consequence is that there could be differences in how questions were asked and how the discussion was moderated. Moreover, the focus group was conducted with primarily European-based stem cell researchers. Apart from one researcher who worked at a university based in Hong Kong, all stem cell researchers worked at European research institutes. It is possible that the ethical challenges of stem cell research and accompanying roles and responsibilities are perceived differently in other countries and cultures, which would be worthwhile to explore in future research.

Future research could continue to explore the perspectives of other stakeholders, such as the technical staff and legislators, to improve responsible research conduct. As the late career researchers stated that the technical staff do and could play an important role in enforcing research integrity, the perspective of technical staff members on their role and responsibilities could generate input for improving ethical behavior in the field of stem cell research. Staff members could offer insights on, among others, their experiences with training new researchers, and in their role or possible role for establishing a culture for compliance and research integrity. These insights could be gained through a focus group or interview study. The perspective of legislators is potentially helpful for a more complete understanding of the role of regulation. Exploring this perspective could provide insights in which motivations and intentions play a role in (the creation of) regulation in the stem cell research field. In turn, these insights could help to consider how responsibility in stem cell research could be enhanced. In addition, our findings and existing literature [15] suggest that many stem cell researchers do not consider the broad range of ethical challenges of stem cell research, for example, indirect consequences and societal impacts, or consider them to be the most important ethical challenges of stem cell research. To raise awareness and possibilities to take responsibility for the broad range of ethical challenges, it would be helpful to understand which methods could be helpful to educate researchers about the broad range of ethical challenges. Literature on transformative learning and ethics education could offer insights about which methods could be helpful in an educational setting.

Conclusion

The results of the focus groups bring several insights that could contribute to enhancing responsible stem cell research. While our study focused on research around stem cell-driven intervertebral disc regeneration, our insights could help to improve the responsible conduct of stem cell research and biomedical research in general, because most challenges, roles and responsibilities are not limited to the case study.

Researchers stated different hurdles for taking responsibility for the ethical aspects of their work due to lack of time, knowledge of regulation and new technological advancements and not recognizing/acknowledging that those ethical aspects might be part of their work. Moreover, structural hurdles could be found among late career researchers who have responsibility for the research in their laboratory, lack of oversight of all the research activities in their lab and that early career researchers experience academic pressure. To eliminate these hurdles, the field of stem cell research could be improved by adopting open science initiatives, such as accessibility of science, alternative metrics for rewarding scientific impact and collaboration between scientists. These initiatives could improve research integrity and create possibilities and interactions to ensure that research includes the wishes and needs of society and patients. Open science in combination with practical solutions that reduce administrative overload could contribute to reducing academic pressure and promote research integrity as well.

Moreover, as many researchers considered the ethical challenges primarily in terms of research integrity and permits, expanding the awareness of a broader idea of the ethics of stem cell research could help to enhance responsible stem cell research through identification and possible actions. Within this context, follow up exploratory research with regulators and the technical research staff could contribute to more insights in the dynamics of regulation and the practicalities surrounding fostering moral behavior in the laboratory and thereby enhancing responsible research conduct.

Author contributions

LSA, KRJ & ALB prepared the focus groups. KRJ moderated the focus group with the early career researchers and patients, LSA took notes during these focus groups. ALB moderated the focus group with the late career researchers and RI made notes during this focus group. LSA conducted the initial coding and was checked during cross-coding sessions with KRJ & ALB. LSA, KRJ & ALB prepared the initial draft. RI and MAT made contributions to early versions of the manuscript. All authors read, contributed to, and approved the final version.

Acknowledgments

We thank all the participants of our focus group discussions. We also thank Frances Bach and Deepani Poramba Liyanage for helping us to practice a focus group with them.

Financial & competing interests disclosure

This project has received funding from the European Union's Horizon 2020 research and innovation program iPSpine under grant agreement no. 825925. MAT receives funding from the Dutch Arthritis Society (LLP22) and is a scientific advisor of SentryX. 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 all the participants involved.

Summary points

Background

- Little is known about stakeholders' perspectives on the ethical challenges of stem cell research, particularly regarding roles and responsibilities.
- Focus groups with stem cell researchers and patients could offer a helpful insiders' perspective to promote the responsible conduct of stem cell research.

Results

- Patients like to be involved in early phases of the research process and in dissemination activities.
- Both early and late career researchers state that academic pressure, such as publication pressure, could lead to unethical or morally grey behavior.
- There is a gap in responsibility of the ethical conduct of stem cell research, due to a gap in knowledge and lack of time. This complicates supervision of PhD students.
- Early career researchers faced difficulties in disseminating problematic aspects of their research, such as the use of embryonic stem cells and animal studies.

Discussion

- Patients could contribute to making stem cell research more accessible by partaking in dissemination activities with other patients and the general public. Moreover, they can make meaningful contributions in early research phases.
- Academic pressure could be alleviated by adopting alternative metrics for rewarding scientific impacts and by offering administrative support for (early career) stem cell researchers.
- Late career researchers could delegate certain supervision to people they trust, based on their knowledge and experience in the laboratory.
- Training researchers about different dissemination goals and strategies for communicating morally sensitive aspects of research could help to accommodate more fruitful and positive interactions with the general public.

Concluding remarks

- Our insights could help to improve the responsible conduct of stem cell research and biomedical research in general, because most challenges, roles and responsibilities are not limited to our case study.
- The field of stem cell research could be improved by adopting open science initiatives. These initiatives could improve research integrity and create possibilities and interactions to ensure that research includes the wishes and needs of patients and society.
- More exploratory research with regulators and the technical staff in research laboratories could contribute to more insights in the dynamics of regulation and the practicalities surrounding fostering moral behavior in the laboratory.

References

Papers of special note have been highlighted as: • of interest; •• of considerable interest

1. MacPherson A, Kimmelman J. Ethical development of stem-cell-based interventions. *Nat. Med.* 25(7), 1037–1044 (2019).

•• **This article provides an overview of the ethical challenges related to translational stem cell research.**

2. Assen LS, Jongsma KR, Isasi R, Tryfonidou MA, Bredenoord AL. Recognizing the ethical implications of stem cell research: a call for broadening the scope. *Stem cell reports* 16(7), 1656–1661 (2021).
3. Sipp D, Caulfield T, Kaye J *et al.* Marketing of unproven stem cell–based interventions: a call to action. *Sci. Transl. Med.* 9(397), eaag0426 (2017).
4. King NM, Perrin J. Ethical issues in stem cell research and therapy. *Stem Cell Res. Ther.* 5(4), 1–6 (2014).

5. International Society for Stem Cell Research (ISSCR). Guidelines for stem cell research and clinical translation. (2021). www.isscr.org/policy/guidelines-for-stem-cell-research-and-clinical-translation
6. Lee TL, Lysaght T, Lipworth W *et al.* Regulating the stem cell industry: needs and responsibilities. *Bull. World Health Organ.* 95(9), 663–664 (2017).
7. Krueger RA, Casey MA. *Focus groups: a practical guide for applied research (3rd ed.)* Sage Publications, Inc., CA, USA (2000).
8. Williams RJ, Tryfonidou MA, Snuggs JW, Le Maitre CL. Cell sources proposed for nucleus pulposus regeneration. *JOR Spine* 4(4), e1175 (2021).
9. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *Int. J. Qual. Health Care* 19(6), 349–357 (2007).
10. Coyne IT. Sampling in qualitative research. Purposeful and theoretical sampling; merging or clear boundaries? *J. Adv. Nurs.* 26(3), 623–630 (1997).
11. Vaismoradi M, Turunen H, Bondas T. Content analysis and thematic analysis: Implications for conducting a qualitative descriptive study. *Nurs. Health Sci.* 15(3), 398–405 (2013).
12. Boeije H. A purposeful approach to the constant comparative method in the analysis of qualitative interviews. *Qual. Quant.* 36(4), 391–409 (2002).
13. Hennink MM, Kaiser BN, Marconi VC. Code saturation versus meaning saturation: how many interviews are enough? *Qual. Health Res.* 27(4), 591–608 (2017).
14. Niemansburg SL, Tempels TH, Dhert WJ, Van Delden JJ, Bredenoord AL. Societal impacts of regenerative medicine: reflections on the views of orthopedic professionals. *Regen. Med.* 10(1), 17–24 (2015).
15. Alahmad G, Aljohani S, Najjar MF. Ethical challenges regarding the use of stem cells: interviews with researchers from Saudi Arabia. *BMC Med. Ethics* 21(1), 1–7 (2020).
16. Chan S. Current and emerging global themes in the bioethics of regenerative medicine: the tangled web of stem cell translation. *Regen. Med.* 12(7), 839–851 (2017).
17. Pennock RT, O'Rourke M. Developing a scientific virtue-based approach to science ethics training. *Sci. Eng. Ethics* 23(1), 243–262 (2017).
18. Goddiksen MP, Gjerris M. Teaching phronesis in a research integrity course. *FACETS* 7(1), 139–152 (2022).
19. Wäscher S, Biller-Andorno N, Deplazes-Zemp A. "I don't want to do anything bad." Perspectives on scientific responsibility: results from a qualitative interview study with senior scientists. *NanoEthics* 14(2), 135–153 (2020).
20. Dudo A, Besley JC. Scientists' prioritization of communication objectives for public engagement. *PloS one* 11(2), e0148867 (2016).
21. Reincke CM, Bredenoord AL, van Mil MH. From deficit to dialogue in science communication: the dialogue communication model requires additional roles from scientists. *EMBO Rep.* 21(9), e51278 (2020).

•• **This article presents an overview of different types of science communication.**

22. Gerrits EM, Bredenoord AL, van Mil MH. Educating for responsible research practice in biomedical sciences. *Sci. Educ.* 1–20 (2021).
23. Supple D, Roberts A, Hudson V *et al.* From tokenism to meaningful engagement: best practices in patient involvement in an EU project. *Res. Involv. Engagem* 1(1), 1–9 (2015).
24. Tijdink JK, Verbeke R, Smulders YM. Publication pressure and scientific misconduct in medical scientists. *J. Empir. Res. Hum. Res. Ethics* 9(5), 64–71 (2014).
25. Mejlgaard N, Bouter LM, Gaskell G *et al.* "Research integrity: nine ways to move from talk to walk". *Nature* 586(7829), 358–361 (2020).

• **This article discusses several possibilities to improve research integrity.**

26. DORA. San Francisco declaration on research assessment. (2012). https://sfdora.org/read/
27. UNESCO. UNESCO recommendation on open science. (2021). https://unesdoc.unesco.org/ark:/48223/pf0000379949.locale=en
28. Haven T, Pasman HR, Widdershoven G, Bouter L, Tijdink J. Researchers' perceptions of a responsible research climate: a multi focus group study. *Sci. Eng. Ethics* 26(6), 3017–3036 (2020).
29. Yin RK. Validity and generalization in future case study evaluations. *Evaluation* 19(3), 321–332 (2013).
30. Woodyatt CR, Finneran CA, Stephenson R. In-person versus online focus group discussions: a comparative analysis of data quality. *Qual. Health Res.* 26(6), 741–749 (2016).