PREMSTEM

Brain injury in the **prem**ature born infant: **stem** cell regeneration research network

H2020-SC1-2019-Single-Stage-RTD
SC1-BHC-07-2019 Regenerative medicine: from new insights to new applications

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Contents

Executive summary

This report provides an overview of the open innovation activities which took place in the PREMSTEM project as part of the work package aimed at increasing the visibility and impact of the project on health and society. These activities touched upon various aspects of this work package, including *Task 6.4: Involvement of patient/consumer representatives* and *Task 6.5: Exploitation and sustainability strategy*. Insights and outcomes arising from the innovation activities are important for shaping the project's communication and exploitation strategies.

Between June 2022 and February 2024, RMIT Europe organised ten online co-creation workshops and 16 one-on-one interviews via video call with representatives of different stakeholder groups. In total, 42 individuals participated in a workshop and/or interview. They represented a range of profiles of relevance to the project including patient associations, parents of children born preterm, adults who were born preterm, medical professionals, researchers and other stakeholder groups in the neonatal ecosystem. The participants came from many different countries and brought to the table a wealth of personal and professional perspectives and experiences.

Thanks to the co-creation activities, we have expanded our insights about the needs of patients who might one day receive a stem cell therapy to treat preterm brain injury. We have also uncovered obstacles and concerns from different stakeholders who would be involved in this treatment, including families and medical professionals. We have brought together different participants for deep discussions and to co-design solutions that could help us to achieve professional and societal acceptance of a future stem cell therapy for use in a medically vulnerable population.

Besides co-creation workshops and interviews, six student teams from the Industrial Design course at RMIT University were also involved in innovation activities. Submitted as part of a design studio, their projects aimed to find solutions for providing an optimal environment for service delivery of care to preterm-born babies in relation to PREMSTEM's expected research outputs.

Acknowledgements

The PREMSTEM team is grateful to have had the opportunity to work alongside a diverse group of people through innovation activities, not least the 42 participants of the co-creation workshops and interviews who voluntarily contributed to the process. We thank all our co-creation participants for their willingness to be involved, cooperation and openness to sharing their opinions and unique experiences.

The following participants have agreed to be acknowledged by name in this report:

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As the PREMSTEM partner coordinating the project's innovation activities, RMIT Europe thanks all members of the consortium for their support with recruitment, particularly our colleagues at the Cerebral Palsy Alliance, European Foundation for the Care of Newborn Infants and Chiesi.

We also thank the Industry Design students from RMIT University for their willingness to learn about a new topic and their creativity during the PREMSTEM design studio, as well as Susan Feitoza for connecting PREMSTEM to the Industrial Design team, the academic leadership provided by Judith Glover and Emma Luke, and the experts who provided the context for the students to gain an understanding of the topics: Bobbi Fleiss, Atul Malhotra and Amber Bates.

1. Introduction

1.1 What is co-creation?

The co-creation methodology invites the involvement of different stakeholders to work alongside an organisation (or project team) to diversify perspectives, for example in the design of a new service or a product. Co-creation allows two-way discussion between the organisation and external stakeholders, as well as discussion between interconnected parties who may not usually interact but have in common a particular product or service.

Co-creation gives stakeholders an opportunity to work alongside an organisation to provide feedback, describe experiences, offer suggestions and inputs on a particular idea, product or concept. Their involvement can help an organisation to see beyond its usual perspectives and preconceptions of what their end users need, want or expect. Co-creation has the potential to reveal insights that haven't previously been considered by the organisation thereby creating an opportunity to implement changes, improve and innovate their products or services based on real consumer feedback. This consultation and collaboration between an organisation and the consumer (and potential end users) may also lead to new ideas and is a way to create engagement between these groups.

The benefits of co-creation are two-fold. For the organisation, it means working directly with people who represent the end user of their services or products and gaining an improved understanding of their target markets. For external stakeholders, the co-creation process allows the chance to influence the ideation and design of services or products which they may use or benefit from in the future, thereby giving them the opportunity to shape the options available in the market and improve the user experience. They also get to exchange experiences and knowledge with other typical end users about the same service or product whose perspectives may differ to their own.

1.2 Why did we do co-creation?

Where possible, PREMSTEM is committed to involving stakeholders from the neonatal healthcare ecosystem in the project and allowing them an opportunity to voice their distinctive perspectives and concerns, as shaped by personal and professional experiences, in relation to a future stem cell therapy. Ultimately, this therapy will impact upon patients, caregivers and healthcare teams and their involvement in the project is important given the complexities and sensitivities generated by the topics of preterm birth, stem cells and brain injury.

We began to involve stakeholders early in the project by establishing a Patient/Consumer Advisory Board (PCAB) comprising six individuals located in different geographies, all with lived experience of preterm birth. We keep our PCAB members informed about the

scientific progress of the project and regularly consult them and invite their feedback on our communications activities and outputs.

Another way that we have engaged stakeholders is through open innovation and co-creation activities, which is the focus of this report. Co-creation methodologies allow a bottom-up approach, a circular, two-way communication with potential end users and an insight-driven process to complement our research efforts.

Through co-creation activities, we hoped to learn about potential challenges and obstacles to developing and bringing to clinical trial a stem cell therapy to treat perinatal brain injury. We wanted to hear about the ultimate outcomes of importance to stakeholders such as parents, patient representatives and healthcare professionals; we also hoped to include the voice of industry in these discussions. The overall aim was to broaden the vision of the project beyond the scientific investigations and uncover insights from key stakeholders. We hoped to co-design potential solutions to tackle concerns and challenges that could be incorporated into our communication and exploitation strategies to set ourselves up for future success, confident in the knowledge that representatives of end users and beneficiaries were consulted.

Over the course of around 18 months, our co-creation activities tackled the following challenge: *How might we lay the groundwork for societal and professional acceptance to perform clinical trials with stem cells in medically fragile preterm infants?* To address this challenge, we invited representatives from various stakeholder groups to participate in interactive, online workshops and a small number of one-on-one interviews to have a say about the research we're doing and our long-term goal of taking a stem cell therapy for the treatment of encephalopathy of prematurity to clinical trial.

2. Co-creation techniques and tools

2.1 Design thinking

Design thinking is a technique aimed at solving actual problems and real-world challenges based upon prioritising the needs of the end user, customer or beneficiary of a product or service. By interacting with stakeholders, this technique can help companies (or project teams) to identify pain points which they may not have known to exist. Design thinking lends itself to collaborative and innovative problem-solving and can be applied to many different challenges.

2.2 Human-centred design

Human-centred design is a mindset focussing on the end users or beneficiaries of the service, product, idea or concept at the heart of the co-creation challenge. Human-centred design demonstrates an openness to consult with external stakeholders – it shows that their views and needs matter and promotes a two-way conversation between the organisation (or project team) and the end user. The discussions and insights which arise from discussions using this methodology can be analysed and used to create solutions to their problems or concerns. The following mindsets are important when using human-centred design in the co-creation context:

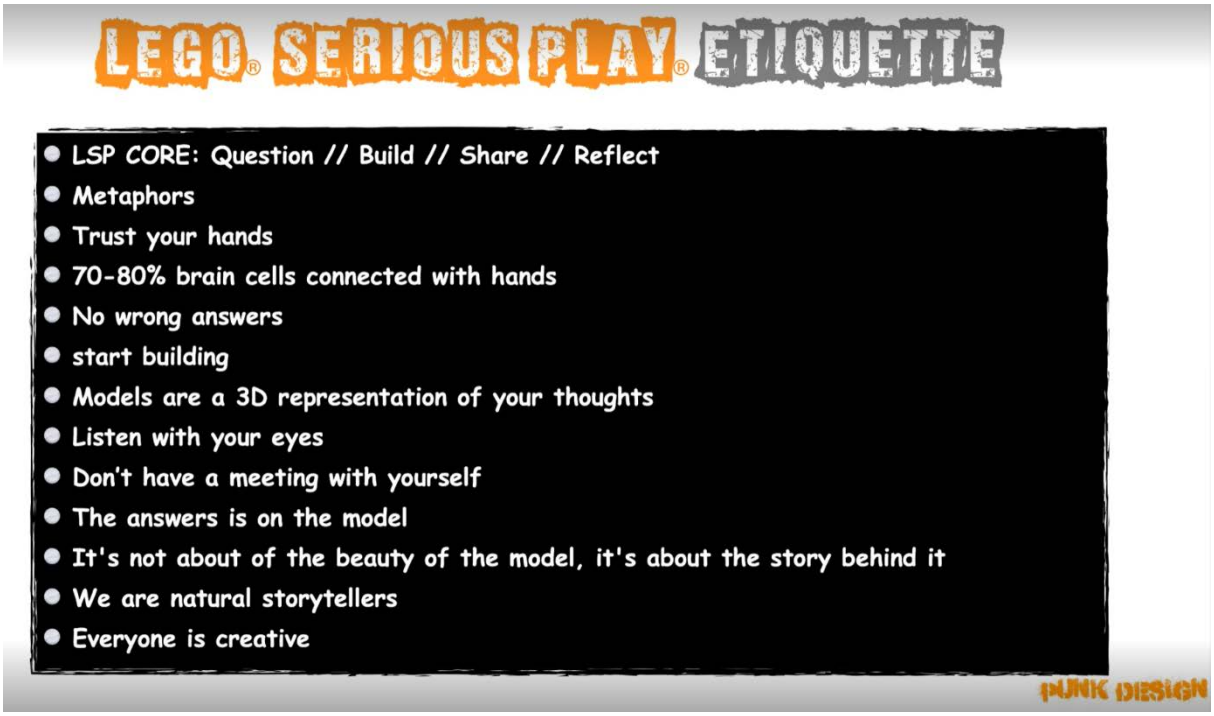
- **Empathy:** Understanding and respecting other peoples' feelings or emotions and imagining yourself in their position.
- **Learning by doing:** Being willing to create or build together.
- **Not being afraid to fail**: Testing ideas and potential solutions with end users or beneficiaries to see if they fit their needs.
- **Curiosity:** Keeping an open mind; being willing to find out why and how things are happening and what the problem, situation or context is like from the end user's point of view.
- **Iteration:** Coming back to the proposed solution or idea and modifying it based upon knowledge, perspectives and experiences revealed by the end user. Asking if it addresses the users' needs, if it's possible from a technical perspective and if it covers the requirements of the business.
- **Creative confidence:** Not being afraid to be creative.

2.3 LEGO® SERIOUS PLAY®

LEGO® SERIOUS PLAY® is a problem-solving methodology created by Lego in the 1990s. It is the result of over ten years of research in which the company looked at business psychology and the role of play, discovering that 70-80% of the cells in our brain are connected with our hands. The methodology taps into this finding and the notion that our hands are the 'search engine of our mind'. In sessions involving LEGO® SERIOUS PLAY®,

participants are assured that there are no wrong answers, that everyone is a natural storyteller and that everyone is creative.

During LEGO® SERIOUS PLAY®, participants are tasked with using everyday objects to build a model to tell a story or answer a question. The models they create become a 3D representation of their thoughts. The methodology is designed to tap into and draw out both conscious and unconscious knowledge. The goal is not about creating a work of art; it's about explaining ideas, solutions or a point of view using visual metaphors inspired by their model.



Credit: Punk Design

2.4 Online tools

With all PREMSTEM's co-creation workshops taking place in a virtual environment, the facilitator used uncomplicated online tools that allowed participants to focus on the activities without the need for training on the technology. These included Google Sheets, Google Slides, Google Docs and Padlet for collaborative brainstorming and individual exercises.

3. Preparation for co-creation activities

3.1 Human ethics approval

Prior to commencing co-creation activities with members of the public, RMIT Europe sought human ethics approval from the RMIT University STEM College Human Ethics Advisory Network to ensure that the activities met the requirements of the *National Statement on Ethical Conduct in Human Research* (NHMRC, 2007). Formal human ethics approval was recommended due to the link between the co-creation activities and a future clinical trial. This advice was consistent with the *National Statement on Ethical Conduct of Human Research*, RMIT University Research Policy and the Human Research Ethics Procedure. The low-risk application was reviewed and approved by the STEM College Human Ethics Advisory Network (CHEAN). It was submitted via RMIT's Research Ethics Platform (https://researchethics.rmit.edu.au/).

As part of the ethics process, we produced a participant information sheet, consent form and data release form. These documents were provided to participants interested in taking part in co-creation workshops and/or interviews. Human ethics approval for co-creation activities not only provided the framework to protect participants and their personal data but allows for quantitative research outcomes to be published and/or disseminated, if desired.

The following is a summary of the main commitments of the human ethics application related to data management:

- All documents and files related to co-creation, including workshop recordings, to be stored and managed by RMIT Europe in dedicated RMIT University SharePoint folders and shared with Punk Design (the facilitator) and PREMSTEM partners only as required.
- Participants to use a self-assigned alias (first name and last name) in all workshops and one-on-one interviews to protect identities.
- Documents containing participants' actual names and email addresses to be accessible only by RMIT Europe.
- RMIT Europe to liaise directly with participants.
- RMIT Europe to manage the signing of participant consent forms and store them on the RMIT University SharePoint.
- Neither Punk Design nor PREMSTEM to intentionally collect sensitive personal data such as medical history data from co-creation participants.
- Participants to have the right to have any unprocessed data withdrawn and destroyed, providing it can be reliably identified and not necessitate the destruction of group session data.

- In reporting, any reference to insights and inputs revealed in co-creation activities to be attached to the broad stakeholder groups rather to an individual participant to protect participant anonymity.
- Any identifying information to be removed or changed in interview transcriptions to protect participant anonymity.

The human ethics application set out the following main commitments for participants taking part in the co-creation workshops and interviews:

- Participation to be voluntary.
- Participants to be free to withdraw from the activities at any stage.
- No costs to be associated with participating, nor would participants be paid.
- Participants to self-identify as a representative of one of the stakeholder groups defined by PREMSTEM.

3.2 Facilitator recruitment

RMIT Europe managed the PREMSTEM co-creation activities, working alongside an external facilitator experienced in co-creation methodologies, design thinking techniques and human-centred design. The external facilitator was required to:

- Propose a plan of co-creation activities with clear timelines.
- Facilitate online co-creation workshops and provide a report of outcomes and implementable recommendations.
- Conduct in-depth one-on-one interviews with key stakeholders, analyse the outcomes and provide implementable recommendations.
- Produce a final report on co-creation insights and outcomes with implementable recommendations to inform the PREMSTEM exploitation plan and communication strategy.

RMIT Europe ran two calls for a co-creation facilitator – in September 2020 and May 2021 – as a change in employment would have caused a conflict of interest for the original facilitator. In the second call, the refined co-creation brief invited proposals to include RMIT University students in the activities. The following tactics were employed by RMIT Europe to attract proposals from suitable facilitators:

- We invited five external service providers with expertise in design thinking and creative methodologies to quote, according to recommendations from other Horizon 2020 projects and the original facilitator.
- We asked experts working in co-creation and design thinking to share the brief with their networks, e.g., the REACH network and the Health Cascade Horizon 2020 project partners and network.

- We ran an open call for proposals on PREMSTEM social media channels for two weeks and encouraged the consortium to share the details within their networks.

As a result of these efforts, two organisations submitted strong proposals. Of the three other recommended organisations, one was unable to quote due to a lack of resourcing and the other two did not respond. To assess the submissions, colleagues from RMIT Europe and RMIT University carried out individual analyses and a scoring based upon the two proposals and video calls with a company representative who was asked about:

- Their background in facilitating co-creation activities; what they most enjoy about the work that they do.
- The proposal submitted for PREMSTEM, highlighting any standout elements.
- Past work to support why they would succeed in the PREMSTEM co-creation tasks.
- Their approach to situations where the audience is unfamiliar with co-creation or there is resistance to taking part.

The assessors from RMIT Europe and RMIT University recommended engaging Punk Design (https://www.punkdesign.barcelona/) to facilitate the co-creation workshops and interviews, highlighting the following strengths:

- A nuanced level of understanding of co-creation, design thinking and science.
- The IDEO experience, tools mentioned, approach and methodology.
- Goal orientated but with flexible methodologies.
- A comprehensive and well-structured roadmap of activities and an intention to focus deeply on a small number of audience profiles to get more useful insights.

Punk Design uses human-centred design, design thinking, play and creativity 'to galvanise, guide and inspire businesses to engrave their spirit within differentiating strategies through play and creativity'. Enrique Conches facilitated all of PREMSTEM's co-creation workshops and interviews. He is a specialist in design thinking and LEGO® SERIOUS PLAY® trained at IDEO online university – a leader in creativity, innovation and design thinking. Nohemy Veiga, a design thinking specialist with a focus on health and science, supported the facilitation of the first four workshops. Other members of Punk Design worked behind the scenes on tasks such as analysis of data and reporting.

The Punk Design proposal included ten workshops and 18 one-on-one interviews whose profiles would be defined by co-creation workshop participants. Partly a result of the COVID-19 pandemic, all activities were held online. Workshops were scheduled at 8am CET (Central European Time) to allow Australian participants to take part. This made sense given that one of the consortium partners responsible for co-creation recruitment was the Cerebral Palsy Alliance based in Sydney. This start time meant we didn't have participants from the Americas in the workshops, although there was flexibility for them to take part in one-on-one interviews.

Punk Design envisaged that workshop discussions would build on each other without disadvantaging participants who hadn't attended before. Nonetheless, it was recommended that participants try to attend multiple workshops for the purpose of consistency. The plan was to tackle the co-creation challenge progressively, using different techniques to uncover different knowledge and insights, give participants the freedom and empowerment to delve deep into the topic and co-create solutions and outcomes that can contribute to PREMSTEM's communication and exploitation strategies.

4. Recruitment of participants

4.1 Workshop recruitment

4.1.1 Target stakeholder groups

Prior to recruitment, PREMSTEM partners identified the below target stakeholders to involve in co-creation workshops:

Stakeholder group	**Why it is important for this stakeholder to participate in co-creation**
PREMSTEM Patient/Consumer Advisory Board or patient/consumer organisation/advocacy groups	These stakeholders represent the voices of the end users of the research, i.e., those born preterm, parents and carers.
PREMSTEM Ethics/Institutional Review Board committee	These stakeholders are knowledgeable on ethical issues related to the science.
Parents/carers of a preterm baby or young child who might be eligible for a future stem cell treatment and/or adults who were born preterm	These stakeholders represent people who will make the decision as to whether their baby or child receives the stem cell treatment in the context of clinical trials. People born preterm represent the eventual end users of the stem cell therapy. The people in this group have first-hand insights, perspectives and experiences related to preterm birth.
Parents/carers of a child with no known health issues	These stakeholders could have a distinct perspective on testing experimental therapies on babies or young children in clinical trials compared to parents who

	have had the experience of having a sick child.
Clinicians or other health professionals	These stakeholders represent those who will be directly involved in clinical trials, discussions with families and potentially the recruitment of participants.
Researchers (preferably in the health sciences)	These stakeholders are those with the most scientific understanding of the research taking place and the barriers which may be faced in bringing the therapy to clinical trial.
Policy makers	These stakeholders can provide insights to help shape the PREMSTEM exploitation strategy and increase the impact of the research.
Governance/regulatory bodies	These stakeholders can provide insights into what will be required to apply for regulatory approval to conduct clinical trials. First-hand knowledge in this area would help to shape PREMSTEM's exploitation strategy.
Other interested parties	These stakeholders represent the wider audience we inform about the project through accessible communications.

4.1.2 Recruitment strategy

The initial call for submissions of expression of interest to take part in the co-creation workshops was promoted through personalised emails, social media (including X, LinkedIn and Facebook), EDM (Electronic Direct Mail) and newsletters (Cerebral Palsy Alliance, European Foundation for the Care of Newborn Infants, RMIT Europe), webpages (PREMSTEM, Cerebral Palsy Alliance) and word of mouth. Subsequent calls for new participants and the promotion of upcoming workshops were circulated on PREMSTEM's social media channels. Individuals signed up via Eventbrite or expressed their interest directly to the RMIT Europe team via the PREMSTEM website contact form or email account.

Recruitment among certain stakeholder groups was more difficult than envisaged. The initial call for expressions of interest attracted 37 potential participants but not all responded to email or returned their consent forms. We initially aimed to have around 20-25 participants in each workshop, with representatives from each stakeholder group. In the end we advised individuals who had expressed an interest in participating in co-creation workshops of upcoming sessions by email and accepted all those who RSVP'd to attend. For every workshop, more people registered than attended – there were always last-minute dropouts due to other commitments – and the average number of attendees was around seven. Nonetheless we realised early on that the workshops ran well with a small group. In fact, participant feedback indicated that this was a positive point. In terms of workshop attendance, most sessions included at least one representative from the following groups:

- PREMSTEM Patient/Consumer Advisory Board or patient/consumer organisation/advocacy groups.
- Parents/carers of a preterm baby or young child who might be eligible for a future stem cell treatment and/or adults who were born preterm.
- Clinicians or other health professionals.
- Researchers.

4.2 Interview recruitment

4.2.1 Target stakeholder groups

We aimed to recruit representatives of the profiles detailed in the below table for one-on-one interviews with Punk Design. The interview profiles were a result of the co-creation process – brainstormed, defined and refined by participants in workshop five. The participants in this session agreed that these profiles represented the people with whom the PREMSTEM team should communicate about a future clinical trial.

Stakeholder group	Interviewee profile	Target number to interview	Actual number interviewed
Parents, families and patients	Parent of a preterm child with experience of having their child participate in a clinical trial	3	5
	Parent of a preterm child who didn't accept an offer of their child being part of a clinical trial	2	0

Stakeholder group	Interviewee profile	Target number to interview	Actual number interviewed
Research teams, researchers and physicians	Neonatologists who have worked on a clinical trial involving preterm-born babies or children	3	3
	Nurses who have worked on a clinical trial involving preterm-born babies or children	2	2
Adults who may have been eligible for a clinical trial*	Adults with an existing neurological injury who may have been eligible for treatment when they were a child	5	5
Media experts	Journalists, TV producers, podcasters etc.	3	1

* The *Adults who may have been eligible for a clinical trial* group replaced the regulatory body profile proposed by workshop five participants. Although it was agreed that this group would be important to communicate with, various PREMSTEM partners indicated concerns about being able to recruit regulatory professionals for an interview and even if we did, it would be unlikely that they would be able to reveal particularly deep insights. Given the nature of their sector, regulatory professionals are unable to readily comment or provide guidance on therapies in development such as PREMSTEM's. To acquire specific advice from this type of profile usually requires paying a consultancy fee not budgeted for as part of PREMSTEM's co-creation activities. We therefore opted to seek insights from the patient perspective instead and were fortunate to be able to talk to five *Adults who could have been eligible for a trial as an infant*, all of whom were born preterm and three of the five living with cerebral palsy.

4.2.2 Recruitment strategy

The recruitment strategy for interviewees was more targeted as we planned to speak to a small number of people with specific profiles. The strategy leveraged off the PREMSTEM network, with two of the three neonatologist interviewees recommended by consortium members. The European Foundation for the Care of Newborn Infants and Cerebral Palsy Alliance circulated the opportunity through their networks which attracted interest from parents and adults who may have been eligible for a trial. The main communications methods used to recruit interviewees were personalised emails and word of mouth. RMIT

Europe also did online searches to reach out to potential participants for the nurse and media professional profiles.

4.2.3 Selection of participants

Participants in the interviews had to match the profiles listed in the table above. We made an exception for a participant in the parent group whose child was not born preterm but who otherwise fit the criteria. We received interest from many parents of preterm-born children about taking part in an interview but who did not have the experience of either accepting or declining a clinical trial for their child. These parents were not called to an interview but were invited to attend future co-creation workshops (time zone permitting).

5. Overview of co-creation activities

5.1 Workshops

In total we ran ten online workshops of three hours each. Hannah Tribe from RMIT Europe joined all workshops as the PREMSTEM representative and assisted the facilitators from Punk Design with queries about the project or aims of the co-creation process. The structure of each session was similar, beginning with a warm-up activity or game to encourage the use of skills that would help participants to get into the co-creation mindset. In all but the very last workshops, one participant then recounted a story to the rest of the group during what was known as the *empathy moment*. The purpose of the empathy moment was to share with the other attendees a situation or story related to preterm birth that they had experienced and remembered for a particular reason, feeling or learning. The goal was to create understanding and empathy among the group and to discuss how the story was perceived by different stakeholder representatives. The remainder of each workshop involved individual and/or group activities focussed on specific tasks related to the co-creation challenge. At the end of each session the participants reflected on the discussions and on what had been achieved as a group. After each workshop the participants were invited to take a short survey to provide feedback to shape or improve future sessions.

5.2 Interviews

As part of PREMSTEM's co-creation activities, we conducted 15 interviews between March and June 2023 with the following stakeholder groups:

- Parents who have a preterm-born child that participated in a clinical trial.
- Neonatologists and nurses who have worked on a clinical trial involving preterm-born babies or children.

- Adults who may have been eligible for a clinical trial when they were a child, for example because they were born preterm.

We also interviewed one media professional in September 2023. The aim of this qualitative research was to learn about real-life experiences of clinical trials and what could have been done differently to improve the process, and to understand current knowledge and acceptance of stem cells as a treatment in the preterm population. All interviews were conducted by Enrique Conches via video call and in English.

The interview scripts were based upon the activities which took place in workshop five in which participants brainstormed what they would like to learn from each stakeholder group. Feedback from the PREMSTEM consortium and PCAB members was incorporated to finalise the scripts, all of which included questions to gather demographic and biographic information about the interviewee to create personas in the analysis stage. There were also questions about the types of information or knowledge that would be useful for a parent or medical professional taking part in a future clinical trial with a stem cell therapy. The remaining questions differed according to the interview profile. The interview goals for each profile were as follows:

- Parents: To learn about the clinical trial they enrolled their child in; the type of information they looked for or needed; the steps that were followed in the clinical trial process; their main concerns; the roles they interacted with; their emotions; their knowledge or opinion about stem cells.
- Neonatologist and nurses: To learn about the clinical trial they participated in; the type of information they looked for or needed; the steps that were followed in the clinical trial process; their main concerns; their opinion about PREMSTEM's research into a future stem cell therapy.
- Adults eligible for a clinical trial: To learn about their pre-existing knowledge and feelings about clinical trials; their knowledge or opinions about stem cells; the information they would need before taking part in a clinical trial with a stem cell therapy; the roles they would expect to interact with; the types of situation that should be avoided; the emotions they would expect to feel if taking part in a trial.

RMIT Europe arranged all interviews and as per the human ethics approval for co-creation activities, all correspondence went through this partner. To protect anonymity, there was no direct correspondence between Punk Design and the participants. Participants used an alias in the online interviews and were referred to by this alias in the interview transcripts. All interview transcripts were automatically generated in Microsoft Teams, reviewed by RMIT Europe and then shared with the participants to allow the opportunity for them to remove or edit any of the content.

Key achievement: Qualitative research about real-life experience of clinical trials, current knowledge and acceptance of stem cells as a treatment in the preterm population

The one-on-one interviews generated many insights from key stakeholders in the neonatal ecosystem which can be reviewed and taken into consideration in the design of a future clinical trial. We talked to two stakeholder groups with first-hand knowledge of taking part in a clinical trial: parents who had enrolled their child, and medical professionals who have worked on trials. From these conversations, it is clear to see that their perspectives and priorities are not necessarily aligned. The interviews are useful for knowing what is of importance to each stakeholder profile, hearing insights into real-life experiences and the emotions that they generated, and revealing potential areas of tension between the two stakeholder groups and feedback on what could be improved. The interviews showed differences in the experience of trials according to factors such as geography and the concept of follow up reporting, The conversation with the media professional was useful for the project's communication strategy as it revealed insights that can help with pitching news about the project's future results (and possible clinical trial) to the media and achieve traction.

6. Summary of co-creation activities

PREMSTEM's co-creation challenge was: *How might we lay the groundwork for societal and professional acceptance to perform clinical trials with stem cells in medically fragile preterm infants?* We tackled this challenge by:

- **Inviting representatives of defined stakeholder groups to engage in conversations about these key themes through workshops.** Creating this space for different stakeholders brought about a diversity in the discussions that wouldn't have occurred in a workshop with representatives of just one group.
- **Delving into deeper discussions with specific stakeholder profiles through one-on-one interviews.** The interview questions explicitly addressed the topics of stem cell research and clinical trials in preterm populations and aimed to uncover preconceptions, concerns and experiences that can be taken into consideration in the design of a future clinical trial. We can learn from negative experiences to make a future clinical trial as stress-free for parents as possible, also ensuring they receive the updates and reporting they need.
- **Addressing how communication can be pivotal for achieving acceptance for a future stem cell therapy to treat preterm brain injury.** We had many in-depth discussions, brainstorming sessions and activities related to the communication of scientific results and a future clinical trial, including the types of audiences that are

important for PREMSTEM to communicate with, how to communicate with these audiences (especially parents) and when.

- **Considering how a clinical trial should be designed, bearing in mind the needs of different stakeholders, and coming up with ideas for how to maximise the experience, especially for parents.** Workshop participants co-designed a roadmap to help parents to understand the full process of a clinical trial which includes reminders to the trial team about checking on the parents' mental health and different communications needs. In the final workshops, the participants generated ideas for an app that could support the parent and patient experience during a future clinical trial. In the workshops, we also talked about the idea of a 'bridge' role to facilitate interactions between clinical trials teams and parents.

6.1 Recurring themes

Through stakeholder engagement we uncovered several themes which regularly came up in discussions, both during the workshops and interviews. They can be summarised as follows:

- Communication: Ensuring clear communication between medical professionals (including clinical trials teams) and parents; using plain language in clinical trial documents and conversations; being inclusive; breaking scientific language down into accessible terms; engaging the media at key moments of the project; creating a 'bridge' role between medical team and parents to aid understanding of information and provide support; sharing stories of people involved in the preterm journey (parents, families, clinicians, researchers); generating engagement with a future clinical trial through storytelling and explaining milestones; creating a safe environment for discussion; translating and disseminating scientific findings in lay language; keeping parents informed about trial results through reporting.
- Involvement of parents and patient representatives: Using a human-centred design approach in the planning of a future clinical trial by involving key stakeholder groups; seeking parent experts to review and provide input into communication and information materials; allowing the opportunity for peer-to-peer support; creating empathy and understanding between parents and clinicians.
- Engagement with decision-making stakeholders: Devising a strategic plan to engage with policy makers regarding the exploitation of scientific results.
- Mental health: Ensuring that the clinical trials team realises the emotional impact and distress that parents experience when their child faces an unexpected medical condition; encouraging empathy with the parents will help clinicians and nurses to

understand how and when to approach them about clinical trials; considering how to support the mental health of parents and medical staff in a clinical trial.

- Shared goals: Understanding that clinicians, researchers and parents have the same objective – to do what's best for the child; communicating shared goals can help to break down perceived barriers between different stakeholder groups, despite differences in background or perspectives.

6.2 Insights from interviews

An analysis of the interviews revealed various themes and insights for each interview profile.

Parents:

1. The difficult nature of the (medical) situation and concerns about the baby's health can lead parents to be more willing to accept a clinical trial for their child. Parents of babies with more severe medical conditions are more open to participating in clinical trials.
2. Parents must have an active voice in the healthcare system. Parents feel that a patient-centred mindset and co-creation is missing in the current approach to planning clinical trials.
3. In a clinical trial, there should be a 'bridge' role between the medical team and the parents. This is seen as an independent role that can communicate effectively with clinicians, researchers and parents. The idea of this dedicated role is to fill a gap when the medical staff cannot dedicate an adequate amount of time to the parents. The role is important for ensuring parent understanding. This role can take care of the parents, provide them with companionship in a stressful environment, help them to understand technical information they're given by medical team and play a role in protecting parents' rights. The person in this role should have a sufficient understanding of the medical side of the trial to explain to parents what the treatment is about and how the trial works.

Additional findings from the interviews with parents include:

- Parents with a scientific background* find it easier to make a decision about enrolling their child in a clinical trial.
- Enrolling a child in a trial can be emotionally traumatic for parents, making it difficult for them to understand or absorb the information provided to them about the clinical trial.
- Parents often participate in trials because they want answers about their child's medical condition.
- Addressing parents' mental health is crucial during the trial process.
- Timing is critical when approaching parents about enrolling their child in a trial.

- Parents often do not understand how a trial works or what lies ahead.
- There is a lack of knowledge and awareness about the consequences of participating in a trial which can lead to misconceptions.

* Workshop participants noted the limitations of the insights uncovered in PREMSTEM's interviews as all five parents had some scientific knowledge or a scientific background.

Neonatologists and nurses:

1. Recruitment is the most difficult part of a clinical trial and can be stressful and complex. It can be difficult to meet recruitment targets and to not overlook eligible patients. The way that the research team and medical professionals approach parents about enrolling their child in a trial is important.
2. The data management aspect of a clinical trial is hugely time consuming.
3. Neonatologists believed that parents need to make an extra effort to understand all the information related to a clinical trial.

Additional findings from the interviews with neonatologists and nurses include:

- Missing data is a big issue. Managing and ensuring the quality of collected data is time-consuming.
- Scientific evidence and addressing an important clinical question are crucial for medical professionals to engage in a trial.
- Informing parents about the trial's goals and the importance of their participation is vital.
- Information should be presented in plain language and multiple languages.
- Trust is crucial in clinical trials.
- Informed consent is crucial; parents need to fully understand what they are signing up for.
- The concept of the 'doctor's ego' – some doctors may not invest enough time with parents or underestimate the parents' ability to understand information.
- There is an absence of a patient-centred mindset and a need for a 'bridge' role to impartially take care of parents.
- Concerns about safety and side effects of the treatment.
- Research nurses play a vital role in trials.
- Professional reward and creating a real impact are important triggers for participating in a trial.

Adults eligible for a trial:

1. Information related to a clinical trial must be in plain language to ensure that parents feel comfortable with what is expected and can then make an informed decision about whether their child is enrolled.

2. Parents should be put first – the clinical trials team should spend time with them, not rush their decision to enrol their child, and take care of them.
3. The clinical trial design should be co-created with parents to create alignment in the trial goals.

Following these 15 interviews we aimed to speak to three media professionals. This was a difficult profile to recruit but we were able to speak to a journalist. Some observations which came from this conversation:

- There is a lack of information about stem cells available for parents.
- There are many unknowns among the general population about what preterm babies need.
- There is a lack of unified information about preterm babies available – parents need to search for it.
- Journalists are seeking exclusive news, e.g., about innovative technologies.
- People need to feel that the news (e.g., about the trial, the therapy) is available (i.e., a possibility) to them and not only to an exclusive section of society.
- News should be crafted for the target audience; medical professionals are not interested in emotive scientific news – this is more appropriate for the general population.

6.3 Achievements

PREMSTEM's co-creation activities were more extensive than originally envisaged by the consortium members, with workshops and interviews taking place over an 18-month period. Using co-creation methodologies has added an additional component to the project that complements the work taking place in our labs, going beyond what research projects traditionally do. Through co-creation activities, we have reached out to external stakeholders in the neonatal ecosystem and invited them to contribute to a project whose outcomes could one day affect someone like them. We hope that the insights uncovered in this research can be used to improve a future clinical trial experience for different stakeholders, including parents of preterm-born children and clinicians. Some of the key achievements of the co-creation activities are:

- Through interactive, online workshops and a small number of one-on-one interviews we have given stakeholders a voice. They have had their say about the research we are doing and long-term goal to take a stem cell therapy to treat preterm brain injury to clinical trial.
- We have uncovered a vast quantity of insights, feedback and concerns from different stakeholder groups that can help to shape PREMSTEM's communication and exploitation plans as well as a future clinical trial design. We have gathered lots of views, real life experiences and perspectives by talking to real people. This

can help the PREMSTEM team to make future decisions not just based on gut feelings or presumptions about the needs of the end user. These insights can help to create outcomes that consider what is of importance for stakeholders in the neonatal ecosystem.

- We have identified target audiences for project communications based on the views of our stakeholders.
- We have heard first-hand experiences of clinical trials and generated ideas to enhance the experience for different stakeholders.
- We have learnt about barriers in communication between clinicians and parents and that there is some disconnect between what parents (or patient representatives) want and what clinicians are providing. Clinician insights such as "It's very difficult to give all the basic information in a very complicated environment" can help us to tackle such findings and come up with solutions.
- Clinician interviews revealed the pressures that they're under which can help to explain some of the disconnect with parents. These insights are useful for us to find solutions in a future clinical trial design.
- The roadmap for parents – co-designed by parents, parent association representatives, researchers and health professionals – can be refined and incorporated into the project's exploitation plan as a tool to enhance the clinical trial experience.
- The brainstorming about an app that could be offered to participants in a future clinical trial takes into account parent and scientist viewpoints and can be considered as a communication channel in a future trial.
- The co-creation process has been a positive and collaborative experience for workshop participants – an opportunity for different stakeholder groups to interact, collaborate and learn from each other and inspire innovative ideas. We provided an inclusive, safe environment for participants to speak freely and share experiences. The length of the co-creation process meant that topics could be discussed at a deeper level.
- The empathy moments in the first workshops were important for building compassion among the participants and opening their eyes to experiences of other stakeholders in the neonatal healthcare system. These moments may positively influence their future interactions with similar stakeholders.
- Participants showed a high level of commitment and involvement in all workshops and conversations were always respectful, genuine and insightful.
- We used a human-centric mindset to uncover the needs and feelings of different stakeholders involved in clinical trials.

6.4 Participant feedback

42 people took part in PREMSTEM's co-creation activities by participating in a workshop and/or interview. Their comments in workshops and post-workshop surveys indicated that their experience was overall a positive one.

- Participants often found it humbling to hear the personal stories of parents of preterm-born children during the co-creation workshops. One clinician said he found it 'powerful' to put a face to the parent stakeholder group.
- Participants indicated that by learning about different stakeholder experiences, PREMSTEM would be able to build something better for the patient.
- Although it is not easy to do and is time consuming, participants found co-creation to be a positive approach. One participant remarked "I observed things in a completely different way". Another said "It's quite unique to speak to many people that have different perspectives".
- One participant commented that the LEGO® SERIOUS PLAY® exercise had opened her mind to different perspectives and made her think bigger and wider about the topic. Another participant said she loved the model building and found it fun.
- Participants agreed that an exciting part of the workshops was the dialogue and being able to work together. One participant said "I have the impression that through these co-creation sessions and interviews we'll be able to uncover unknown concerns and barriers and map them out before they become problems". A parent said "I really like that we can exchange different perspectives, different experiences, and as I always say, this is a safe place".
- One clinician said that it had been a great experience having direct conversations with parents and that she felt inspired to implement some of the ideas discussed during the workshop in her own work. Another clinician said "It's been a very positive experience for me. I expected to contribute more than receiving and I received a lot".
- In the final workshop, the participants celebrated the completion of the roadmap for parents and discussed the potential benefits it could bring. They expressed hope that the roadmap will provide clarity for parents and improve the clinical trial experience. They hoped that the roadmap could be used as a model for other areas of research, not just neonatology.
- About the roadmap, a parent remarked that "Now we have an outcome based on interview outcomes, not only based on feelings. When we started two years ago, it was a blank page". This comment indicates that participants feel that progress has been made through co-creation.

6.5 Lessons learned and recommendations

To help other research groups who are interested in incorporating co-creation methodologies into their projects, we have reflected on lessons learned over the 18-month process and provided some recommendations based on our experience.

Recruitment and ongoing participation:

The initial Expression of Interest (EOI) process through Eventbrite was moderately successful. We received 36 EOIs representing different stakeholder groups and in different countries. Of the target stakeholder groups, we were unable to attract EOIs from the following: 1) Policy makers and 2) Governance/regulatory bodies. Indeed, throughout the activities these were the most difficult groups to reach.

Additional Eventbrite events were created throughout the co-creation process to promote individual workshops which allowed us to attract new participants beyond the original pool of EOIs. New workshop participants were also recruited through word of mouth and promotion through partner networks. We used these same methods to recruit for the one-on-one interviews, in which the European Foundation for the Care of Newborn Infants and Cerebral Palsy Alliance played key roles. RMIT Europe's interview recruitment strategy involved online research and individual emails. RMIT Europe also promoted the interview opportunity in the NHS nursing network.

Although the initial aim was for the same people to attend all workshops, this turned out to be impractical for various reasons, such as availability of participants. It was particularly difficult for *Clinicians or other health professionals* to commit to multiple three-hour workshops given the nature of their profession (long hours, shiftwork and being on call). There was a lot of enthusiasm from this stakeholder group to take part but given the nature of their work, they often could not.

We found it difficult to engage some of the target stakeholder groups, for example *Governance/regulatory bodies*. These types of professionals receive a high number of requests to take part in external initiatives and are unable to participate in them all. It is also commonplace to engage regulatory professionals through paid consultancy services rather than voluntary activities such as ours.

Overall, it should be noted that recruitment for co-creation activities is a time-consuming process and requires extensive liaison between the co-creation project manager and potential participants. There is also a lot of information to be provided in relation to the co-creation activities and to conform to ethics requirements. This can be overwhelming and off-putting for potential participants.

Recommendation: Aim to have a core group of participants throughout the whole co-creation process. The consistency provided by a small number of participants will help to

incorporate new or less frequent attendees into sessions as they have the ongoing knowledge of the process, previous discussions and tasks. They can also become advocates of the co-creation process and drive enthusiasm among the wider group.

Recommendation: Ask project partners to identify people in their own networks who represent one of the stakeholder groups then send personalised emails inviting suitable connections to take part.

Workshop length:

All workshops lasted three hours and the tasks were well planned to fit within this time. Although there were few criticisms from participants who attended a three-hour workshop, the reality is that it is difficult for participants to consistently dedicate this amount of time on these kinds of activities given other life commitments (employment, family etc.). It is especially difficult for medical professionals who are often on call or working shifts. We also must bear in mind that these activities were voluntary and that participants received no monetary compensation for their time.

Recommendation: If possible, include a budget to reward or compensate participation, especially in a lengthy co-creation process such as PREMSTEM's.

Engagement levels:

Throughout the co-creation process, we were able to count on a small number of highly engaged workshop participants. We realised early on that smaller sessions facilitated the establishment of a safe space and allowed for productive discussions. According to feedback, participants felt more comfortable to openly share their thoughts and personal experiences in a smaller group.

Recommendation: Avoid setting a preferred group size beforehand. Instead, consider what type of environment will be appropriate for the type of topics that might be discussed to ensure the most comfortable setting for the participants to engage freely in dialogue.

Use of alias:

The PREMSTEM grant agreement required EOIs for co-creation activities to be anonymous, identifying participants with an ID number rather than their names, and for participants to self-identify as belonging to one of the 'pre-defined and broad stakeholder groups'. We asked co-creation participants to assign themselves an alias (alternative first and last name) rather than an ID number when signing up to a workshop or interview. They were asked to go by this alternative name in all sessions.

The request to create an alias was sometimes misinterpreted or not followed and, in these cases, needed follow up by RMIT Europe. The main stakeholder group to query the use of aliases was the *Clinicians or other health professionals*. For some individuals, the use of an alias was unnecessary as they believed it would be relatively easy to identify their real name based on the insights and experiences they discussed. One person from this group suggested that using an alias might devalue his professional achievements. On the other hand, a parent in the co-creation workshops thought that, in some way, anonymity had helped participants to feel that they were on an equal playing field with other stakeholders during the discussions.

Recommendation: The use of an alias could be at the discretion of the participant – a possibility but not obligatory – unless there is a need for them to be protected by anonymity, for example for legal reasons.

6.6 Next steps for PREMSTEM

For the communications plan:

- Review the *Shared model of the three stakeholders to influence through communication* (workshops one, two, three) and *Affinity diagrams of each key stakeholder group* (workshop three) to refine target audiences for scientific results and future clinical trial and think about how to engage with the media for the promotion of scientific results.
- Review the *Affinity diagram showing the different concerns and obstacles to gaining societal and professional acceptance of a future therapy* (workshop four) to consider whether the points can be addressed in project communications.
- Review the *Clinical trials roadmap for parents* (workshops seven, eight, nine) co-designed by parents, clinicians and researchers to find opportunities to enhance the communication approach and messaging before, during and after a future clinical trial.
- Review the *Co-design of an app that parents can use during a future PREMSTEM clinical trial* (workshop ten) as a communications tool that can be built in a future clinical trial.
- Review the *Qualitative research about real-life experience of clinical trials, current knowledge and acceptance of stem cells as a treatment in the preterm population* from the one-on-one interviews and the messages that arose. Look for negative experiences and insights that can be addressed through project communications. Look for opportunities to raise awareness on topics discussed or to create new resources for the project.

For the exploitation plan:

- Review the *Affinity diagram showing the different concerns and obstacles to gaining societal and professional acceptance of a future therapy* (workshop four) to learn about barriers and concerns according to PREMSTEM's key stakeholder groups and consider how they can be addressed in the design of a future clinical trial.
- Review the *Clinical trials roadmap for parents* (workshops seven, eight, nine) co-designed by parents, clinicians and researchers and see how it can be incorporated into the exploitation plan to enhance the experience of a future clinical trial for different stakeholders.
- Review the *Co-design of an app that parents can use during a future PREMSTEM clinical trial* (workshop ten) to see if it can be incorporated into the design of a future clinical trial.
- Review the *Qualitative research about real-life experience of clinical trials, current knowledge and acceptance of stem cells as a treatment in the preterm population* and look for opportunities to avoid making similar mistakes in the planning of a future clinical trial and therefore optimise the experience for all key stakeholders.

7. Conclusion

Innovation activities have given PREMSTEM an opportunity to go beyond what is traditionally expected of a research endeavour by reaching out to external stakeholders and inviting them to contribute their voice to the project. What we have learned through these activities will help us to make future plans that consider the perspectives of potential end users and benefit them.

Through co-creation workshops and interviews, the PREMSTEM team has heard diverse perspectives from outside of the consortium, including from parents of children who were born preterm, patient representatives, researchers and medical professionals. We have been able to get a glimpse into real-world situations of preterm birth and clinical trials, as well as insights into how stem cell research is perceived.

Hearing personal stories and experiences in the co-creation workshops not only helped to foster empathy among the participants but brought about a deeper understanding of the challenges and realities faced by different stakeholders. Through these findings we hope to apply a more compassionate and human-centred approach to future strategies that impact our different stakeholders.

For participants, co-creation has provided an unusual but welcome opportunity to converse and collaborate with stakeholders who experience preterm birth in a different way to them. They often expressed their thanks to PREMSTEM for bringing them together and allowing the chance for these conversations and interactions to come about through co-creation workshops.

Co-creation has allowed an opportunity for participants to work towards shared goals and on specific tasks, often building on previous work as part of a step-by-step process. This collaboration has led to many ideas co-designed by participants that can be considered and refined in PREMSTEM's communication and exploitation strategies. By bringing together diverse perspectives and encouraging open dialogue, co-creation has fostered innovation and the development of new ideas and solutions.

Finally, we should mention one further innovation activity not related to the co-creation workshops and interviews that took place at PREMSTEM consortium member, RMIT University. Through a design studio, undergraduate Industrial Design students were given the chance to work with PREMSTEM to gain experience in working on a real-life challenge with a real-life industry partner.