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Healthcare professionals', students', patients' and donors' perceptions of stem cell research and therapy: a systematic review protocol

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ABSTRACT

Introduction Stem cell research (SCR) and the biomedical potential of developing therapies are crucial topics in biomedicine. Like other biotechnologies, stem cells are context specific entities understood through local conceptualisations of culture, politics, nationhood, as well as their perceived therapeutic efficacy. There is a need to recognise how these developments are understood within the healthcare community and by those who may use them. This protocol describes a systematic literature review that aims to explore healthcare professionals', healthcare students', patients', and donors' perceptions of SCR and therapy (SCR/T) and the factors that influence their perceptions.

Methods and analysis Following Preferred Reporting Items for Systematic Reviews and Meta Analyses guidelines a systematic review will be undertaken. Web of Science, Scopus, Medline+Journals @Ovid and Ariti Library will be systematically searched for studies on healthcare professionals', healthcare students', patients' and donors' perceptions of SCR and developing therapies. All articles will be screened by a researcher for inclusion and evaluation based on 12 criteria for evaluating qualitative research. At least 20% of articles will also be reviewed by a second researcher and any disagreement will be solved via consensus. Data extracted from the articles will be analysed using thematic synthesis enabling the identification of concepts across studies and the development of new theory.

Ethics and dissemination As part of a larger research project, ethical approval has been provided by the Institutional Research Board (IRB) at Chang Gung Memorial Hospital. This review will be able to determine the impact that certain perceptions of SCR/T will have on the development of future medical knowledge and practice. The results of the study will be published in a peer-reviewed journal and disseminated at relevant conferences.

PROSPERO registration number CRD42018103627.

Strengths and limitations of this study

- The study is strengthened through its use of a search strategy that has been comprehensively informed by published recommendations for conducting studies on individuals' 'views' on a particular subject.
- Study screening, quality assessment of studies, data extraction and thematic synthesis will be conducted collaboratively, with a second researcher verifying at least 20% of the review process, which will increase the reliability of the study.
- Unique from other reviews, our team will be able to review literature published in four languages.
- By removing data from the context of the original study it will no longer be connected to the context of the original research questions or setting, presenting an analytical limitation; however, in the final stage of the analysis the study context will be considered during cross study comparison.
- The second limitation includes the synthesis relying on the data presented in each article, which may not be sufficient for our analysis or correspond with the original data set.

INTRODUCTION

Research into stem cells (SCs) and the biomedical potential of developing therapies are currently crucial topics in the biomedical community. Stem cell research (SCR) is an umbrella term that includes studies into the therapeutic potential of human embryonic stem cells (hESCs) and a range of developments in diverse medical fields including: oncology, haematology, plastic surgery, motor neuron diseases like amyotrophic lateral sclerosis, as well as the commercial production of synthetic red blood cells, the use of SCs in pharmaceutical discovery and predictive toxicology. SCR no long relies solely on hESCs but also adult, pluripotent, cord blood and amniotic fluid SCs, increasing the availability and applicability of SCs for research and therapeutic purposes.

As the breadth of perceived therapeutic potential of SCR becomes recognised, the diversity of people's perceptions of SCR and therapy (SCR/T) also broadens. The meanings, values and ethical implications around SCR/T vary based on sociocultural, political, economic, and organisational dynamics.[1] In

other words the significance of SCR/T is context specific. Factors as diverse as moral beliefs, notions of relatedness, bioethical and scientific standards and perceptions of the efficacy of new biotechnological developments may impact one's perspective of SCR/T. Such variation in SC meanings, practices, approaches and policies, are evident on an international scale. This is demonstrated by Thompson's comparative study of two famous stem cell laboratories one in South Korea and the other in Singapore.[2] However, these differences are not just across countries, they also develop between institutions or across professionals within singular cultures or even institutions.[3 4]

Perceptions of SCR/T are further complicated due to the limited scientific evidence to support the potential of the clinical application of these developments. The lack of a standardised reporting system between facilities conducting trials or initiating treatments prevents other researchers in the field, medical professionals, as well as potential users of such therapies from being informed.[5] Variation in research standards and policies governing research and translation into practice across countries may also raise scepticism about the efficacy of therapies developed in certain regions. Despite this uncertainty, these advancements and the recognised potential (even if overestimated) of developing SC therapies raise hope among those searching for a cure for currently untreatable conditions. Stem cell tourism has emerged out of this context of hope, lack of reporting, and over- and under-regulation, thus raising concerns about regulating such tourism, the responsibility of healthcare professionals in this, and the need to promote education and raise awareness.[5–8]

Within this complex context of the uncertainties of SCR and therapeutic advancements, limited regulation and standardisation across institutions/countries, a demand for (experimental) treatments by potential patients, and the cultural specificity of SCR/T, there is a need to better understand how healthcare professionals perceive SCR/T. Further, given their role in the training of tomorrow's doctors, understanding the implications their perceptions might have on future medical knowledge and practice is also of utmost importance.

The aim of this systematic review is to explore healthcare professionals' and healthcare students' perceptions of SCR/T, as well as the perceptions of others in the medical realm (ie, recipients of SCs or their care-decision-makers and donors) that may impact the perceptions of healthcare professionals and students. The specific research questions may develop as the systematic review progresses.

Research question

What perceptions do healthcare professionals, healthcare students, prospective stem cell patients (or their care-decision-makers) and donors have about SCR and developing therapies? And what factors influence their perceptions?

Sub questions:

a. What factors (demographic, cultural, education, sources of knowledge and so on) appear to influence these stakeholders' perceptions of SCR and SCT?
b. What are the differences in the perceptions that exist between and within these stakeholder groups, and in which ways do their varying perceptions influence the perceptions of those in other stakeholder groups?
c. How do perceptions around SCR and developing therapies influence the information that particular stakeholders relay to others?

METHODS AND ANALYSIS

Protocol and registration

This systematic review protocol was developed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) Protocols guidelines, which intend to assist researchers in developing the rationale for their review or meta-analysis, and preplan the methodological and analytical approaches they will use.[9] This protocol has been registered with PROSPERO International Prospective Register of Systematic Reviews.

Literature search

We will search the following English databases: Web of Science, Scopus, Medline+Journals @Ovid. We will also search one Chinese database: Ariti Library. Search terms have been developed across three themes using terms that are associated with stem cell related research and therapy, the target population and their perceptions and attitudes. The search strategy has been prepared with the assistance of a research librarian. (See online supplementary appendix 1 for the search strategy for the Medline Journals@Ovid database.)

To ensure all literature has been covered, we will review the reference lists of included studies or relevant reviews identified by the search. Additionally, we will look for studies in relevant journals on medical and health education as well as specific social science journals we have identified by reviewing the reference list of a review article on stem cell related research published in the Annual Review of Anthropology.[10] The selected journals will be searched using the key term 'stem cells'. Key articles already identified by the research team will also be included.

Defining the eligibility criteria

This review focuses on particular individuals' perceptions of SCR/T. By perceptions we broadly mean individuals' opinions and views in terms of what they think about SCR/T and what they understand SCR/T to be, individuals' attitudes and values towards SCR/T (eg, their moral considerations and understandings of ethical dilemmas concerning SCR/T), and individuals' personal experiences with and interpretations of SCR/T. Given this, both qualitative and quantitative studies that explicitly explore the views of the target population will be included. As noted by Harden *et al*,[11] however, some quantitative studies that examine views may be unsuitable for our analysis and therefore will be excluded.

This review will consider SCR and therapies that use various cell types (embryonic, adult, mesenchymal and induced pluripotent cells), alongside well established, government regulated SCT and experimental therapies. The review will explore perceptions on topics from the use of embryos in SCR to patients' use of experimental therapies. It will also include the issue of establishing 'legitimate' research centres and competition between researchers. In other words, we do not intent to limit the topics related to perceptions on SCR/T that are covered in this review. Our aim is to gain a broad understanding of the topics with which the target population is concerned and their views on these specific topics.

The target population comprises individuals interacting in the healthcare setting. This includes a broad range of healthcare professionals, healthcare students, patients or those who make healthcare decisions on patients' behalf (ie, parents) and donors. Donors will include individuals who donate ovas or embryos specifically for SCR (with this clearly stated in the studies being reviewed) and those who donate blood cells, bone marrow or other tissue for SCR/T. We have chosen to include patients, their parents and donors because these individuals may interact with healthcare professionals and students and impact their perceptions. Ethicists, scientists and researchers have been included as their opinions may also influence those of healthcare professionals and students, as well as the fact that they may also be practising medical personnel.

There will be no limitations on the type of study design, however, only primary research studies published in peer-reviewed journals will be included, in addition to conference abstracts if sufficient information can be extracted from the abstract. Commentaries, letters, editorials, short communications and unpublished data will be excluded. The publication year of the included studies will be limited to 2000–2017. In order to gain a global understanding of perceptions of SCR/T, the setting in which studies took place will not be limited by region or country. However, studies will be limited by publication language given the language skills of the research team. Thus, studies published in Chinese, English, Slovenian and Spanish will be included.

Study selection and quality assessment

All studies identified by the database and specific journal searches will be imported into EndNoteX7. Duplicates will first be removed by using the automatic function, and second by hand. A researcher will screen the titles and abstracts of the remaining articles, and at least 20% of the articles will be subject to cross checking by the lead researcher to ensure a cohesive assessment. The research team will discuss any discrepancies.

The full texts of the selected articles will be obtained and uploaded into ATLAS.ti8. First, the quality of qualitative studies will be assessed using 12 criteria identified by Thomas and Harden.[12] The criteria covers three core quality issues: the quality of the reporting of study aims, context, rationale, methods and findings; the sufficiency of the approaches taken to establish the reliability and validity of research methods, analytical approach, and research findings; and the evaluation of the appropriateness of the methods to ensure that findings were based on the perceptions of the individuals' studied. The research team will discuss any studies that are found to be methodologically questionable, and those deemed as poorly designed or reported on will be excluded. If necessary, a fluent speaker will cross check the Chinese, Slovenian and Spanish publications. We will present the study selection process in accordance with the PRISMA Flow Diagram.[13]

Data extraction and analysis

Harden and colleagues emphasise that studies on people's 'views' or 'perceptions' may use various methods, which may be difficult to categorise as qualitative or quantitative.[11] As our intention is to extract data that voices the perceptions of the individuals' studied, while identifying key concepts that stretch across various studies, we will consider findings from both qualitative and quantitative studies as appropriate using thematic synthesis.

First, the general characteristics of the included studies will be extracted (eg, year of publication, study aim and questions, population, country, number of participants, methodology, analysis: see online supplementary appendix 2 for data extraction table). The findings and results sections of the articles will be the focus of the thematic analysis. Thematic synthesis involves three overlapping stages: the coding of text line-by-line of each study, the organisation of the codes into 'descriptive themes' and, last, the formation of broader 'analytical themes' that group various 'descriptive themes' together.[12]

To conduct the line-by-line coding, two researchers will read a subset of the studies, inductively creating the codes so they reflect the meaning and context of the original data. The researchers will then discuss the developed codes, agree on the codes and create a shared terminology for each. One researcher will then continue coding the remaining articles, adding to the coding list as the process progresses and modifying established codes if necessary. Regular team meetings will review these developments. Once all studies have been coded, codes will be grouped into themes looking at the similarities and differences between them to create descriptive themes.

The final analysis stage will involve using the descriptive themes identified during the initial analysis stage to address the systematic review questions. This will be done through a collaborative discussion process. At that time we will also consider similarities and differences across studies, as we look at the descriptive themes in relation to other characteristics of the studies (eg, study population and context). This may allow us to explain differences in the perceptions expressed across the studies.[14]

The findings from any quantitative studies that are included in the review will be analysed descriptively in accordance with the thematic coding framework that is developed.

Patient and public involvement

No patients or the public were involved in the development of this systematic review protocol, nor will they be involved in the actualization of the review.

DISCUSSION

Insights from the proposed review will allow us to better understand the various perceptions that healthcare professionals, students and others involved have of SCR and developing therapies. It will shed light on the diverse factors that influence these populations' perceptions and any differences in perceptions across cultures and regions or those between stakeholder groups.

Building on the conceptual translations identified by this thematic synthesis we will be able to determine what implications these perceptions might have on the development of future medical knowledge and practice in specific contexts, and the impact that certain perceptions have on the learning of future healthcare professionals. It will inform the development of necessary educational programmes for healthcare professionals and the creation of recommendations to guide healthcare professionals in determining their responsibility in raising awareness among potential patient groups.

The key findings from this synthesis will be used to inform a qualitative study on the impact that healthcare professionals' perceptions of SCR/T has on the learning of healthcare students and trainees in Taiwan. The review will be published in a peer-reviewed journal and presented at relevant conferences.

Contributors MKS conceived the idea for the study. MKS and MB, in discussion with LVM, designed the study and developed the protocol. MKS drafted the protocol manuscript with input from MB and LVM. MB prepared the search strategy for Medline Journals@Ovid and data extraction table. All authors have read and approved the final manuscript.

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