Exploring Factors That Influence Trust in Non-standard Stem Cell Therapies Among Patients with Musculoskeletal Conditions.

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Abstract

Although stem cell interventions (SCIs) may offer some therapeutic potential, the development of regulatory frameworks for their safe clinical application remains a significant challenge. As the regulation of these innovative therapies is still being developed, it is crucial to examine the factors that shape patients' trust in these interventions that lack clear oversight. The purpose of this study is to explore the factors that influence the trust in non-standard SCIs among patients with musculoskeletal disorders as well as their understanding of the role regulatory bodies play in ensuring safe and effective treatments. This understanding will be relevant to policy development and regulatory reform for innovative regenerative medicine therapies, potentially addressing the role that professional regulation plays in providing oversight of this developing field.

This study employed a qualitative approach, using constructivist grounded theory. The data were obtained through in-depth, semi-structured one-on-one interviews with eight participants lasting from 45 to 75 minutes. The interview transcripts were analyzed initially with line-by-line coding, then focused coding. The codes were later collapsed and organized into categories, which guided theory construction.

The findings unveiled a range of factors involving the patients, their knowledge of the intervention, and their practitioners that influence their trust in non-standard SCIs. The results also suggest that health practitioners play a central role in guiding participants' consideration of non-standard SCIs. This role also extends beyond medical doctors and includes allied healthcare professionals, as patients with musculoskeletal conditions often seek their services to manage their symptoms. Lastly, the results indicate a strong and implicit trust that patients place in regulatory bodies; suggesting that patients hold expectations of these bodies without a full understanding of how they meet them.

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Dedication

To my parents, Hannan and Emad

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List of Abbreviations

CAM: Complementary and alternative medicine
MSD: Musculoskeletal disorders
OA: Osteoarthritis
PRP: Platelet-rich plasma
RM: Regenerative medicine
SCIs: Stem cell interventions

Transparency Statement

I used AI technology to assess the clarity of some sentences in the initial draft of this thesis only. While some sentences required no further editing, suggestions were applied to others, and some suggestions were disregarded. All of the original text was written by me, with revisions following editorial suggestions by my supervisor, my committee members and a student writing advisor. I acknowledge that I am solely responsible for maintaining the accuracy and academic integrity of this thesis. I confirm that no AI-technologies other than those listed above have been used to prepare this thesis.

Chapter 1: Introduction

1.1 Overview of Stem Cell Interventions & their Regulation

1.1.1 Stem Cell Interventions

Regenerative medicine (RM) is an emerging field focused on developing innovative therapies to repair or replace damaged body tissues and cells. It involves various approaches such as tissue engineering, gene therapy, and stem cell interventions, all aimed at promoting tissue repair, regeneration, or functional recovery (Mao & Mooney, 2015). Stem cells are types of cells with a unique ability to self-renew and differentiate into multiple cell types (Poliwoda et al., 2022). There are various sources of stem cells, including (though not limited to) bone marrow, adipose tissue, umbilical cord, and placental tissue, all characterized by their ability for self-renewal and proliferation, thereby providing a source of new cells to replace aging or damaged ones (Poliwoda et al., 2022).

Applications of stem cell interventions (SCIs) are currently part of standard care practice for some diseases. For example, stem cells are a standard of care treatment for leukemia patients who may benefit from receiving a stem cell transplant, often known as a bone marrow transplant (Pang et al., 2021). Additionally, SCIs have been scientifically investigated as a possible way to treat other chronic illnesses that current treatments may not be able to fully address. Previous studies have demonstrated promising outcomes for some conditions including diabetes mellitus, Parkinson's disease, and multiple sclerosis (Yazhen et al., 2020) (Jafarzadeh Bejargafshe et al., 2019). SCIs comprise various strategies, including the utilization of autologous cells (derived from the patient) or allogeneic cells (obtained from a donor) that retain their proliferative capacity, to directly aid in the formation and function of new tissues (Mao & Mooney, 2015). Due to the complexity and diversity of stem cell-based products and therapies, a significant number of regulatory challenges exist when it comes to their development and clinical use (Mao & Mooney, 2015).

1.1.2 Regulation of SCIs in Canada

In Canada, the regulation of health care is shared between the federal and provincial governments. Currently, drugs and medical devices are regulated by the federal government under the *Food and Drugs Act*, RSC 1985, c F-27. This legislation plays a crucial role in ensuring that pharmaceuticals and medical devices throughout the country are supported by evidence of safety and effectiveness. As already noted, there remains a significant number of regulatory challenges when it comes to the development of SCIs due to the complexity and diversity of stem cell-based products and therapies. For example, cell therapies derived from a patient's own cells (autologous), with identical function for both donor and recipient (homologous) are classified as minimally manipulated fall under Part C Division 5 (Drugs for Clinical Trials in Humans) and Division 8 (New Drugs) of the *Food and Drug Regulation*. However, the precise criteria for defining "minimally manipulated" therapies are still uncertain, as Health Canada has not outlined specific processing activities that constitute minimal manipulation or provided examples (Chisholm et al., 2019). In 2020, Health Canada did clarify its position that autologous cell therapy products meet the definition of drug under Canada's *Food and Drug Act* (Health Canada, 2020). However, it has yet to give clear guidelines about how autologous stem cell treatments, which are prepared and given using equipment approved under a medical device license, should be regulated. In its position paper, Health Canada warns that doctors might think that if the equipment used to make the stem cells is approved by Health Canada, then the stem cell products themselves are also approved. The document emphasizes that unless a device has been specifically approved for its cell therapy product, the *Food and Drugs Act* and its *Regulations* will apply to the product (Health Canada, 2020).

Although this position paper provided helpful guidance, it does not capture all forms of SCIs and Health Canada is engaged in regulatory reforms that are relevant to this field. In

June 2019, the federal government amended Canada's *Food and Drug Ac*t to create a distinct category of regulated products called "advanced therapeutic products" (ATPs) with the goal of establishing a legal framework for regulating innovative, personalized interventions (Government of Canada, 2022). It currently remains unclear whether and how new SCIs being developed will be incorporated into this new regulatory pathway. At present, Health Canada has not approved the use of stem cells to treat any conditions other than acute lymphoblastic leukemia (ALL), Adult B-cell Lymphoma, and Graft V Host disease (Government of Canada, 2019).

While drugs and medical devices fall under federal jurisdiction in Canada, the practice of medicine is regulated by provinces, with oversight typically delegated to professional regulatory bodies. For example, physicians are governed by their respective College of Physicians and Surgeons in whichever provinces and territories they are licensed in. Similarly, nurses and pharmacists, along with other healthcare professionals, are regulated by their respective regulatory bodies, such as the College of Nurses and the provincial Colleges of Pharmacists. These regulatory bodies are responsible for setting and upholding professional standards and ensuring the ethical conduct of their members. These colleges, mandated by provincial legislation (see e.g., *Medical Profession Act*, 1981, c M-10.1), oversee licensing standards and codes of conduct. Additionally, they evaluate the qualifications of new professionals, monitor their ongoing competence through continuing education, and handle complaints or disciplinary actions when necessary (Adams, 2020). Thereby, the development of clear regulations and robust oversight governing both the treatment products and their providers is essential for stem cell therapies to be safely translated into clinical practice.

1.2 Overview of SCIs in Musculoskeletal Conditions

Musculoskeletal disorders (MSDs) are conditions that affect the muscles, bones, tendons, ligaments, and other soft tissues in the body, causing pain, stiffness, swelling, numbness, and decreased range of motion in affected areas (Freemont & Hoyland, 2007). Musculoskeletal system conditions are common in Canada and are a leading cause of disability and morbidity (Gheno et al., 2012; Kopec et al., 2019). Treatment options for conditions that affect the articular cartilage are mostly focused on providing symptomatic relief through the use of pain relievers and anti-inflammatory medication (Anandacoomarasamy & March, 2010). These treatments are often geared towards alleviating symptoms and do not provide a cure; therefore, stem cell therapies present a promising avenue to explore. Previous research has shown some benefits of autologous cell therapy in reducing joint pain in some patients suffering from knee osteoarthritis (Zhu et al., 2021), but many questions remain about the potential risks and limitations of these interventions.

Osteoarthritis (OA) is a degenerative disease of cartilage and is one of the leading causes of disability, especially among the older adults (Birtwhistle et al., 2015). Patients with advanced-stage OA suffer chronic pain and functional impairments of their limbs, resulting in a reduced quality of life. The current treatments focus mainly on managing symptoms, rather than treating the disease itself (Chahal et al., 2019). The first Canadian trial of stem cell therapy applied to advanced knee osteoarthritis in 2019 showed that it could reduce joint pain and improve function by reducing inflammation (Chahal et al., 2019). The study showed a promising potential for stem cell injections to alleviate pain, however, it had a small sample size (n=12). Additionally, the heterogeneity of a condition such as OA demands multiple variations of treatment protocols to encompass the different manifestations of the condition.

Early successes in translational research studies have spurred interest in SCIs among the scientific community, as well as hope among patients to receive advanced medical care.

Nonetheless, the 2018 American Academy of Orthopaedic Surgeons and National Institutes of Health U-13 Conference consensus recommendations highlighted the inconsistencies found in research on stem cell therapies (Chu et al., 2019). This is due to many variables that affect the efficacy of each treatment that each needs to be examined thoroughly, such as tissue source, processing technique, culture conditions, and route of administration. The available data, therefore, cannot be generalized to make broad claims regarding the efficacy of SCIs in general or specific claims of achieving pain relief within a certain timeline.

1.3 Direct-to-Consumer Market for SCIs

Despite the need for significant advancements in scientific and regulatory domains, private market options are accessible to patients seeking SCIs for a wide range of conditions, including musculoskeletal conditions. This industry holds a significant presence both nationally and internationally across numerous jurisdictions (Connolly et al., 2014). The international market for unproven stem cell intervention has been studied for well over a decade and appears to be continually growing and developing into new arenas (Master et al., 2021; Turner, 2020). Although Health Canada has only approved the use of stem cell therapies for a limited number of medical conditions (Government of Canada, 2019), there is a private market in Canada for SCIs that fall outside the standard of care, and which have not been approved by Health Canada (Ogbogu et al., 2018; Turner, 2018). As reported by Turner (2018), a growing number of clinics have been offering a wide variety of unproven SCIs. As of 2018, 30 Canadian businesses were promoting these interventions through 43 Canadian clinics (Turner, 2018). Notably, physicians are the primary providers of these treatments (Ogbogu et al., 2018). Although, as noted above, Health Canada has clarified that at least some of these interventions likely fall under the authority of the *Food and Drugs Act*, there are challenges with enforcement, and some debate regarding whether some of these interventions should be governed as part of the practice of medicine (Mulligan, 2019).

Accordingly, where these interventions are provided by regulated healthcare professionals such as physicians, professional regulatory bodies play a critical role in providing oversight alongside the efforts of Health Canada. Since Turner's report in 2018, there has been no further assessment of the effectiveness of efforts by Health Canada in regulating these interventions, suggesting a need for further research. It is reported that the majority of these businesses focus on making claims about specific conditions, with nearly 50% advertising stem cells to treat orthopedic conditions (Knoepfler & Turner, 2018; Turner, 2021).

Previous research suggests that direct-to-consumer marketing of regenerative interventions tends to overemphasize benefits, understate risks, and promote regenerative options over the standard of care for musculoskeletal disorders (Kingery et al., 2019). Additionally, despite ongoing regulatory reforms aimed at enhancing regulatory compliance, there are still some gaps in clinical settings. For instance, some regulators have mandated treatment providers to conduct clinical trials to gather evidence supporting the clinical applications of various SCIs, which pose a risk of blurring the line between research and treatment (King, 2021). This requirement has resulted in a proliferation of "pay-to-participate" clinical trials (Turner & Snyder, 2021). These trials raise serious ethical concerns as well as new challenges for clinicians in ensuring patients understand whether they are undergoing a medical procedure or participating in a clinical trial (Ogbogu & Case, 2023).

The presence of this market gives rise to a number of policy issues concerning the lack of clear scientific consensus and a regulatory framework for these interventions and the potential risks they pose to the public (Zarzeczny et al., 2018). Although there is little evidence that many of these SCIs could be beneficial, there is evidence that they subject patients to a wide range of potential harms including loss of vision, stroke, and cardiac arrest (Bauer et al., 2018), raising concerns about health risks and impact on public trust in the field. Thus, the advancement of regulatory oversight in clinical practice is necessary for the

translation of safe and effective SCIs. It has been suggested that professional regulation may be an effective tool in responding to the risks posed by this private market for SCIs as it leverages the authority of regulatory bodies to guide physicians' involvement in recommending and providing these services, by providing clarification on their scope of practice and clinical standards (Zarzeczny et al., 2014).

This complex scenario also raises questions about patients' decision-making processes in face of these novel scientific and informational challenges and their understanding of the role regulatory bodies play in providing oversight. Consequently, there is a need for research to better understand the factors influencing trust in non-standard stem cell therapies among patients with musculoskeletal disorders. For the purposes of this research, the term non-standard is used to describe therapies that do not have a well-established treatment efficacy (College of Physicians and Surgeons of Saskatchewan, 2016) or treatments that are not specified by clinical guidelines (i.e., those which fall outside the standard of care). The findings from this research will contribute to the evolving evidence base available to inform ongoing regulatory reforms in this promising but complex field.

1.4 Statement of the Problem Area

This project is timely given the evolving oversight landscape for this burgeoning field of bioscience. As the regulatory landscape for these innovative therapies is still being developed, it is crucial to examine factors that shape patients' trust in these under investigated interventions that lack clear mapping of oversight. Many factors have been documented that motivate patients to pursue regenerative therapies as an option including reducing pain, delaying surgery, referrals by friends/family, and lack of options to cure their condition (Arthurs et al., 2022). However, there is a need for more in-depth insight into what factors are important for patients in their decision-making process about these treatment options and the practitioners who offer them. It is also unclear how patients perceive the

importance of regulation in ensuring safe and effective treatments, and in providing oversight of non-standard medical interventions.

1.5 Purpose of the Study:

This project aims to explore the factors that motivate patients with musculoskeletal conditions to place their trust in non-standard therapies and the practitioners providing them. This understanding will be relevant to policy development and regulatory reform for innovative regenerative medicine therapies.

Primary research question:

What factors motivate trust in non-standard stem cell therapies among patients with musculoskeletal disorders?

> *As noted above, for the purposes of this question, the term non-standard is used to describe therapies that do not have a well-established treatment efficacy (College of Physicians and Surgeons of Saskatchewan, 2016) or treatments that are not specified by clinical guidelines (i.e., those which fall outside the standard of care).*

Secondary research question:

How do patients with musculoskeletal disorders understand the role of professional regulation in providing oversight and how does that impact their trust in healthcare providers?

1.6 Overview of Thesis Structure

The current study is presented in five chapters. Chapter 1 provides an overview of key concepts and maps out the problem area. It also presents the study's purpose and research questions. Chapter 2 reviews existing literature on factors that influence patients to consider non-standard treatments, including complementary and alternative medicine and stem cell interventions. Chapter 2 also reviews unique challenges faced by patients exploring stem cell

interventions such as misinformation and the association of these novel therapies to public trust. Chapter 3 presents the methodology that has guided this study, detailing the selection process of the qualitative design, introducing the role of grounded theory in the study, and delving into the different stages of research procedures. In Chapter 4, the research findings are presented. This section covers the main categories and subcategories that were generated, offering detailed descriptions of their properties. Chapter 5 presents and discusses the emerging theory from the data. Chapter 5 also highlights the main findings in relation to the existing literature. The chapter concludes with a discussion on the implications of the study for policy and practice, as well as limitations of the study.

Chapter 2: Literature Review

The literature review played a vital role in establishing the groundwork for this study, contextualizing my research within existing scholarship on patient interest in non-standard treatment options. Additionally, it helped me identify gaps in research, pinpointing areas where further investigation is needed to enhance our understanding of this topic, as outlined in the study purpose. I began this process by exploring factors driving patients towards non-standard treatments, including complementary and alternative medicine (CAM), then focused on literature related to patient experiences and perspectives on SCIs. It is important to note that this literature review is not intended to be exhaustive. Given the vast and constantly evolving body of research on these topics, I have selected and highlighted studies that are most relevant to my research objectives and questions.

2.1 Why Do Patients Use Non-Standard Treatments?

Patients' interest in pursuing non-standard treatments, such as CAM, has been the focus of previous studies examining factors relevant to their decision-making process. According to the National Institutes of Health, the term complementary and alternative medicine refers to medical products and practices that are not part of standard medical care (National Cancer Institute, 2023). Examples of CAM include reiki, herbal medicine, and homeopathy. During 2015-2016, approximately 56% of Canadians utilized at least one CAM therapy (Esmail, 2017).

A systematic review revealed that the primary drivers behind CAM utilization included positive attitudes toward CAM such as expected benefits and perceived safety of CAM, dissatisfaction with conventional medicine, and various influences such as social networks, recommendations from healthcare providers, having an internal health locus of control, defined as preferring to decide choices of health treatments for oneself, and cultural tradition (Phutrakool & Pongpirul, 2022). In a recent qualitative study exploring the

perceptions of Hawaiian adults who use CAM to treat their symptoms, researchers categorized their findings into two main groups: "push" factors, which signify reasons for dissatisfaction with conventional medicine, and "pull" factors, which indicate a desire for a more holistic or proactive approach to health (Odegard et al., 2022). Participants in the study expressed a range of perspectives on CAM. Some held positive "push" views, believing CAM to be effective and superior to conventional medicine, while others had positive "pull" perceptions, viewing it as supportive of overall well-being. Conversely, negative perceptions included doubts about CAM's effectiveness and concerns about its lack of scientific backing and regulatory oversight. Additionally, some participants maintained neutral attitudes, considering CAM to be safe on occasion and viewing it as a natural alternative. It is important to note that this study, along with the other studies referenced throughout this thesis, were conducted across diverse jurisdictions with varying regulatory landscapes, which warrants a consideration of potential hidden influences resulting from geographical contexts.

Similarly, previous studies have looked into the reasons why patients pursue SCIs and others investigated the public opinion on using stem cells as a potential treatment option (Puzzitiello et al., 2021; Rachul, 2011). Rachul's (2011) study, which analyzed personal blogs, highlighted characteristics of stem cell therapy patients, including their motivation to actively engage in their recovery and their desire to understand available options for various diseases and conditions.

In another study that focused on orthopedic applications, Arthurs et al., (2022) reported the main reason patients with musculoskeletal conditions express interest in SCIs was to avoid or postpone joint replacement or tendon repair, closely followed by the desire to treat or alleviate pain. Additionally, some patients cited SCIs as a preferable alternative to surgery because of its less invasive nature or perceived superiority compared to standard treatments such as steroid injections, medications, or physical therapy.

Previous research indicates that patients consider a variety of factors when expressing interest in non-standard SCIs. These include their personal experiences with the disease, perceptions of treatment risks, benefits, and effectiveness, as well as their understanding of stem cell science and its clinical applications (Kawam et al., 2023). Other factors that contribute to this interest include trust in medical and scientific authorities, confidence in one's social support network, and the availability of resources, such as adequate funds for treatment (Kawam et al., 2023). In another study of orthopedic patients considering SCIs, some viewed improvement as a hopeful prospect rather than an expected outcome of treatment. Nevertheless, they still expressed some expectations for symptom alleviation, enhanced mobility, pain management, or cartilage regeneration (Kenihan et al., 2020).

Another survey examining public opinions on the utilization of SCIs in orthopedics revealed that reports of their safety and effectiveness in research, alongside endorsements from medical professionals, hold the greatest influence in decisions to pursue such therapies (Puzzitiello et al., 2021). Additionally, the respondents of this survey indicated that they would consider stem cells if their doctor recommended it, regardless of evidence supporting their effectiveness.

These findings are consistent with another study involving patients who received or were in the process of receiving SCIs, the findings of which suggested that the primary source through which patients acquired knowledge about treatment was healthcare providers, while sources like clinic ads, websites, and social media had less influence (Ogbogu & Case, 2023). This survey also indicates the majority of participants received information about these side effects from their treatment providers, yet it remains unclear which specificity or the accuracy of the side effects participants were briefed on.

These previous studies on patients considering SCIs have mainly taken a quantitative approach or relied on surveys. Although their findings are valuable, there is a need for more

in-depth qualitative exploration into the factors motivating patients with musculoskeletal conditions to consider these options, along with their understanding of the role of professional regulation. The qualitative design of this study provides an opportunity for participants to explain their rationale, expand on their reasoning, and contribute their unique perspectives. Thus, this approach facilitates a nuanced exploration of participants' decision-making processes and attitudes towards professional regulation. The interviews used in this qualitative study allow for a detailed investigation of patient concerns, priorities, and the information they seek to receive during their treatment journeys. This study will also shed light on how patients assess risk of non-standard SCIs when safety and effectiveness are yet to be proven.

Additionally, many previous studies have primarily focused on including patients who have already received or are in the process of receiving SCIs, thus limiting our understanding of attitudes and intentions towards SCIs among the broader patient population. This study did not establish inclusion/exclusion criteria based on patients' history of pursuing or receiving any regenerative medicine treatments, including SCIs. The study's focus is on understanding how patients with musculoskeletal conditions make treatment decisions, and what factors they consider important when weighing non-standard stem cell-based treatment options, rather than exploring the reasons behind their previous treatments. Thus, this study helps build on previous work and will help fill a current gap by including the perspectives of individuals who have not undergone non-standard stem cell interventions, thus exploring the diversity in attitudes towards SCIs.

2.2 Non-standard SCIs: A Complicated Science and Misinformation

While the exploration of non-standard treatments by patients is not a new phenomenon, the emergence of SCIs introduced unique challenges, due to complexity of the topic on a scientific level, compounded by the prevalence of pervasive misinformation online.

It has been reported that when patients with chronic conditions exhaust standard treatment options, they may start looking for other non-standard options (Bunnik & Aarts, 2019). Patients exploring non-standard SCI options may encounter marketing from providers who emphasize health benefits, downplay risks, and portray their practice as scientifically supported (Smith et al., 2020). This is significant as patients increasingly rely on the internet for health information, leading them to becoming more knowledgeable about treatments developing around the world (Bunnik & Aarts, 2019). The rise in popularity of direct-to-consumer SCIs for a range of medical conditions likely stems from both unmet medical needs and the perceived promise of SCIs to address those needs (Arthurs et al., 2022).

Patients may come in contact with endorsements of these interventions through many sources online such as blogs and social media, or in person through patient education seminars arranged by clinics (Hawke et al., 2019; Knoepfler, 2016). Marketing tactics involve using endorsements from patients and celebrities, registering for clinical trials, using complex language, getting accreditation, partnering with scientific institutions, misrepresenting scientific information, and falsely claiming support from published studies to appear scientifically credible (Kawam et al., 2023; Sipp et al., 2017).

The novelty and complexity of these interventions make it all the more challenging to discern quality when patients are faced with mixed messages from the scientific and medical community. For example, some scientific organizations, including research societies and regulators (i.e., the United States Food and Drug Administration), caution patients about unproven SCIs, while others, mostly providers, do not echo this sentiment (Center for Biologics Evaluation and Research, 2021; MacGregor et al., 2019).

It remains unclear how patients with musculoskeletal conditions navigate this complex information environment when deciding whether to pursue non-standard treatments. Specifically, there is uncertainty regarding how they assess the risks of treatments lacking

proven efficacy and safety, as well as the factors that shape their trust in such interventions and in the healthcare professionals who provide them. Furthermore, little is known about their understanding of the role regulatory bodies play in ensuring the safety and effectiveness of treatments. The study aims to address this gap, and hopefully the results from this project may uncover valuable targets for patient education to address misinformation.

2.3 Trust in Regenerative Medicine

Trust in healthcare professionals and the health institutions is vital to building provider-patient relationships as well as to the functioning of our healthcare system as a whole. Trust is theorized to operate on an interpersonal level between specific patients and providers as well as on an institutional level, also known as public trust, directed toward societal institutions, systems, or collective entities (Hall et al., 2001). Four broad categories were proposed to influence public trust in the healthcare system (Van der Schee et al., 2007). These are: institutional guarantees (i.e., regulation of health providers), media exposure (i.e hype, media scares and scandal), network knowledge (i.e., family, friends and support groups), and lastly personal experiences with the health care system (i.e., interactions with providers). Other studies suggest a bidirectional relationship between institutional trust and interpersonal trust (Krot & Rudawska, 2021) whereby public trust can influence how patients engage with healthcare providers, and conversely, the experiences patients have with healthcare institutions and their professionals can also affect their trust in the system (Krot & Rudawska, 2021). Thus, public trust serves as an indicator of how patients and the general public perceive the healthcare system's ability to deliver services and achieve its goals, while also providing a crucial measure of the level of support for the healthcare system as a whole (Peters & Youssef, 2014).

This trust can be influenced not only by the past experiences of a particular patient or their generalized social confidence in public institutions but also by the experiences of others

and by the mass media (Gille et al., 2016). Van der Schee et al., (2007) argued that public trust encompasses broad perceptions of professional institutions, which are shaped by personal experiences, and social cues such as protective legal or regulatory measures. This project aims to broadly investigate how patients come to trust non-standard treatments by delving into their experience navigating their musculoskeletal conditions within the system as well as their understanding of the role regulatory bodies play in ensuring safe and effective treatments. This understanding will be helpful in informing regulatory reforms that are consistent with patient expectations and maintain their trust. Although this research engaged with elements of interpersonal trust between participants and their healthcare providers, the study findings will be more pertinent to public or institutional trust.

Trust in a field, such as regenerative medicine, is also connected to public acceptance of the field and the related concept of social license. The term social license refers to stakeholders' support of a field and its ability to operate, including its practice standards (Dixon-Woods & Ashcroft, 2008). This concept extends beyond formal regulatory requirements and expects institutions engaged in potentially controversial initiatives, such as novel stem-cell based interventions to adhere to voluntary codes promoting trustworthy behavior and transparency (Dixon-Woods & Ashcroft, 2008).

According to Boutilier and Thomson (2020), social license is defined as the ongoing approval of a local community and other stakeholders to a project. The social license stems from the beliefs, perceptions, and opinions carried by the local community and other stakeholders about the project and thus the social license is granted by the community. It is dynamic and ever-changing due to beliefs, opinions, and perceptions changing when new information comes into play. Therefore, the social license must be earned and continuously maintained.

As many SCIs remain in early stages of development, with uncertainties about clinical application and regulatory oversight, the future success of this field requires that it maintain public confidence, and that it develops in line with public concerns and interests. The current gap between public expectations and actual progress of stem cell-based therapies in the clinics threatens regenerative medicine's social license to operate (Cossu et al., 2018). In an effort to outline how social license can be pursued, Cossue et al. (2018) suggest increasing trust in the field through competence, openness and accountability. This requires professionals involved with SCIs to conduct rigorous science, address the public's concerns, increase accessibility to scientific findings, and accept responsibility. This current study aims to understand patient expectations of non-standard stem cell therapies for musculoskeletal conditions, and the factors that shape their trust or mistrust in these interventions. This knowledge will be useful in addressing the gap between the public expectations of regenerative medicine as a field and the reality of non-standard stem cell therapies, ultimately supporting efforts to enhance trust and confidence in these novel interventions through transparent communication and accountable practices.

Chapter 3: Methods

3.1 Research Study Design

A qualitative research approach was chosen for this study to gain a rich, in-depth understanding from individuals with lived experience of musculoskeletal conditions. More specifically, the study utilized constructivist grounded theory methodology (Charmaz, 2006), chosen for its emphasis on inductive inquiry, which aligns with the study's aim. This project aims to explore the perspective of patients with musculoskeletal disorders and, more specifically, to explore what factors are relevant to them when they consider non-standard SCIs. Thus, I utilized principles of emergent design during the process of data collection and analysis. The process of grounded theory involves three key elements: (a) systematically gathering data, (b) employing the constant comparative method for qualitative analysis, and (c) generating theory (Charmaz, 2006). The purpose of this approach is to foster the generation of ideas throughout the research process, ultimately leading to the emergence of a unified theory deeply rooted in the data itself. Unlike quantitative research, the focus is not on verifying pre-existing ideas, but rather on deriving theory directly from the data (Richards et al., 2007).

3.1.1 Grounded theory: an overview

Grounded theory, introduced by sociologists Barney Glaser and Anselm Strauss in the 1960s, is a qualitative research methodology aimed at developing theories that are "grounded" in empirical data. According to Glaser and Strauss (1999), grounded theory is an inductive methodology that allows researchers to generate a theory from the perspective of participants by listening closely to the ideas of those participants. Unlike traditional deductive approaches, where researchers start with preconceived theories or hypotheses, grounded theory begins with observations and data collection, allowing theories to emerge from the data itself (Charmaz, 2006). Over the years, grounded theory has evolved through various

traditions, with the most recent being constructivist grounded theory proposed by Kathy Charmaz, which I adopted for this study.

As Charmaz (2006) elucidates, the central tenet of grounded theory is to understand social phenomena through a process of systematically gathering data, coding, and constant comparison, leading to the generation of concepts and theories that are deeply rooted in empirical evidence. Constructivist grounded theory acknowledges the interpretive nature of qualitative research, emphasizing the role of the researcher in actively constructing knowledge through engagement with the data (Charmaz, 2006).

3.1.2 Grounded Theory: Rationale

After exploring different qualitative methods, I decided that a constructivist grounded theory methodology was the most suitable for my research goals, based on the following reasons.

Firstly, the theory-generating aspect of grounded theory methodology aligns with this research's aims to provide a thorough exploration of the factors patients consider when they evaluate non-standard SCI treatment options. This project aims to explore the perspective of patients with musculoskeletal disorders and, more specifically, to explore their reasoning if they were to consider non-standard SCI treatment options. The grounded theory methodology involves developing inductive theories that are rooted in systematically collected and analyzed data. Grounded theory is especially valuable in exploring topics with limited prior research. As mentioned in Chapter 2, there is uncertainty about the process by which patients assess the risks of treatments lacking proven efficacy and safety, as well as the factors that shape their trust in such interventions and in the healthcare professionals who provide them. Furthermore, little is known about their understanding of the role regulatory bodies play in ensuring the safety and effectiveness of treatments.

Secondly, constructivist grounded theory acknowledges multiple realities. It suggests that creating knowledge involves collaboration between the researcher and participants, in a specific context, embracing an interpretive understanding of the data (Charmaz, 2006). This aspect of grounded theory was appealing for me as a researcher as it provided space for me to acknowledge my prior experiences and how they shape my role in the research, as discussed in Section 3.1.3. This study aims to explore the subjective experiences of considering non-standard SCIs as a treatment option as well as patients' understanding of professional regulation. Thus, it aligns with the constructivist approach that recognizes understanding is gained through the interpretation of subjective perceptions rather than assuming the collection of facts. Grounded theory methodology provides a nuanced and insightful approach, for the purposes of this project.

Additionally, it was crucial to incorporate interviewing to understand patients' experiences exploring treatment options and how they respond to different factors in their decision-making journey, and interviews work well as a data collection strategy in constructivist grounded theory methodology. It was important to use this data collection approach as the majority of the studies previously conducted on patients considering SCIs were of a quantitative nature, and/or have relied on surveys, and have not explored the patients' understanding of the role regulatory bodies play to ensure safe and effective treatments. To gain a deeper understanding of their process, I utilized intensive interviewing as the primary method for collecting data. Interviewees were asked questions to explore how different factors affect their trust in a non-standard treatment and expressed their understanding of the role regulatory bodies play in approving new treatments. They were also asked to elaborate or clarify some parts of their answers. This approach is consistent with Charmaz (2006) as it aims to draw out each participant's personal interpretation of their experience.

Before starting the interviews, my plan was to complete both data collection and analysis simultaneously. However, due to unexpected factors like participant availability, I often ended up scheduling interviews back-to-back or even fitting in two interviews in a single day. As a result, I lacked sufficient time for editing the auto-generated transcript and conducting the necessary line-by-line coding but I had the opportunity to listen to the audio and review the unedited transcripts. This constant comparison method helped identify gaps or areas I wished to learn more about and seek this data on my next interview.

3.1.3 Situating Myself as a Researcher

As a researcher, I did not enter into this research project without my personal opinions, perspectives and preconceptions of the subject. Charmaz (2006) indicates that "we construct our grounded theories through our past and present involvements and interactions with people, perspectives, and research practices" (p. 10). Thus, a researcher must explicitly state their position. Charmaz refers to this concept as reflexivity, in which the researcher scrutinizes his or her research experience, assumptions, biases, and positionality, and how these may influence the research inquiry (2006). Charmaz explained "Without engaging in reflexivity, researchers may elevate their own tacit assumptions and interpretations to 'objective' status" As a researcher I understand the importance of revealing my motives in conducting this study.

My interest in learning about the human body began at a young age. Around the age of eight, I picked up reading as a hobby and I spent hours every day reading about health, physical activity, nutrition, and all things related to wellness. I would cut up interesting articles out of the newspaper and make a scrapbook. I later flew some of these books with me to Canada from Egypt. I believe this experience piqued my interest in the holistic nature of health and instilled in me the idea that health impacts all aspects of our being and is also impacted by more than I think. As I reached the time to select my undergraduate degree, I

chose to pursue a degree in kinesiology where I spent four years learning about human anatomy, physiology, biomechanics, pathophysiology and learned about exercise as medicine. Thus, I believe all these experiences shaped what I know about musculoskeletal diseases and my perceptions of how it impacts people's lives.

My journey through undergraduate studies in kinesiology was not just about learning scientific content, it gave me the opportunities to work with patients with musculoskeletal diseases in both volunteer and professional roles. I have always been interested in helping this population to navigate the disease and achieve the highest possible quality of life through exercise. I worked as a physiotherapist assistant for over a year where I applied for a variety of treatments such as (i.e., ultrasound massage, interferential current) and helped patients perform specific exercises as part of the plan of care. I have also had the opportunity to talk to patients on a daily basis and learn about their lives and see first-hand the limitations it poses on their lives. Nonetheless, my perspectives may have been influenced by past encounters and the insights into the disease, patients' preferences and decision-making acquired through my education and professional experience.

The outcome of constructivist grounded theory does not present a single objective and universally applicable account of the patient's experience. Rather, it presents a subjective interpretation rooted in the temporal and context-specific interactions between the researcher and the participants (Charmaz, 2006). This interpretation reflects the researcher's own construction or understanding of these interactions and represents merely one of several possible interpretations (Charmaz, 2006). As a result, as a researcher, I must cultivate self-awareness to acknowledge the influences of my experiences, assumptions, interpretations, and decisions on this inquiry (Charmaz, 2006).

3.2 Data Collection

Data were gathered using in-depth semi-structured interviews suitable for exploring individuals' experiences. One-on-one interviews allow for free exploration of participants' feelings, thoughts, and past experiences (Josselson, 2013). In semi-structured interviews, an outline of questions with no rigid script is prepared by the researcher. Thus, when the questions are asked, the participants have the opportunity to reflect and speak on their past experiences without restriction. In my research, participants often told stories of themselves or family members who were faced with a choice of a non-standard treatment option. By being allowed to answer questions freely, they were able to provide refined reflections and build rapport with me. The interviews also created an opportunity for me to actively observe the participants' verbal and non-verbal cues (i.e., pauses and silence), which cued me to further explore some answers. After the first exploratory interview, the initial interview guide (Appendix A) was edited to make the terminology more accessible, and an amendment was submitted to and approved by the Research Ethics Board (Appendix C). The interviews were conducted via Zoom and were audio recorded. Using Zoom features, an electronically generated transcript was produced at the end of each session and then edited with the help of the audio recording.

The interviews were conducted online between January 2024 and March 2024 and lasted from 45 to 75 minutes. I asked for consent to continue at the one-hour mark; all participants were eager to continue. The identities of participants were kept anonymous throughout all data processing. The interview started with an overview of the consent form, then covered the following areas: general knowledge, non-standard SCIs related questions, and ending questions. Please refer to Appendix A for the interview guide.

3.3 Participants

The study participants were recruited using a purposive sampling strategy that targeted various groups within the University of Regina (i.e., the Centre on Aging and Health, Seniors' University Group, and Faculty of Kinesiology and Health Studies). The recruitment material was disseminated using physical posters placed in Seniors' University Group Lounge as well as online advertisements distributed via social media and the University of Regina listserv. The inclusion criteria for the study required participants to be adults 18 years old or older, proficient in English, residing within Canada and diagnosed with a chronic musculoskeletal condition.

The study specifically focused on patients with diagnosed diseases rather than individuals with knowledge through loved ones. Patients with diagnosed diseases have direct experiences and interactions with healthcare practitioners, providing unique insights into their personal experiences, hopes, fears, and concerns regarding new interventions. By including the patients themselves, the study gains authenticity, credibility, and relevance to the patient population, enhancing the applicability of the research findings. Being knowledgeable or experienced in regenerative medicine was not a criteria for participation since participants were provided with prompts as needed during the interview process to explain key concepts they were not familiar with such as relevant background on regenerative medicine. These prompts are included in the interview guide attached as Appendix A. As will be discussed in the limitations section, this participant recruitment process had inherent limitations due to avenues by which the project information was shared as well as the requirement for computer access, email, and Zoom. These requirements may have influenced the types of participants willing to volunteer for the study, potentially introducing selection bias. As a compensation for their participation, all eligible participants are to be entered into a draw to win one of three Amazon gift cards valued at 50 dollars.

In this study, there were eight enrolled participants, aged between 30 and 77 years old, the majority of whom resided in Regina, Saskatchewan. One participant was located outside the province in British Columbia. In the beginning of the interview, each participant was asked to rate the severity of the impact caused by their musculoskeletal condition on a scale from one to ten, with one indicating minimal impact and ten signifying significant impact on their daily activities. All participants rated their condition's impact within the range of five to nine. Reported conditions among participants included osteoarthritis, dystonia, chronic back pain, and rheumatoid arthritis. Notably, some participants reported experiencing a combination of these conditions or the same condition affecting different parts of their bodies. Of the eight participants, seven have attained some level of university education. The recruitment strategies used in this study may have introduced selection bias, impacting the characteristics of the participants. This aspect is further discussed in the limitations section, highlighting the potential implications for the study's findings and conclusions. Table 1 provides a summary of the participants' characteristics in this study.

Participant #	**Location**	**Age**	**Self-reported Condition**	**Self - reported Impact**	**Post-secondary education attained**
P1	Regina, SK	77	OA	Provided a description not an exact number	Yes
P2	Moose Jaw, SK	49	OA	1 to 9	Yes
P3	Regina, SK	30	Chronic back pain + Schmorl's node	8	Yes
P4	Victoria, BC	54	OA	7	Yes
P5	Regina, SK	65+	OA	6 to 9	Yes
P6	Regina, SK	73	OA + Degenerative	5	Yes

			disk disease + Rheumatoid arthritis		
P7	Regina, SK	70	Dystonia	6	No
P8	Regina, SK	60	OA	7	Yes

Table 1. Summary of Participants' Characteristics

In grounded theory, it is suggested that data collection should be terminated when theoretical saturation is reached. Theoretical saturation is defined as "when gathering fresh data no longer sparks new theoretical insights nor reveals new properties of [the] core theoretical categories" (Charmaz, 2006, p. 113). Although eight participants is not a large number, the point of theoretical saturation was reached after conducting six interviews. Subsequent interviews in the research process yielded minimal or no new categories, and redundancies began to surface. Nonetheless, the last interviews were conducted with the purpose of confirming or testing the emerging theories. Although eight participants may not be a large sample, I am confident that the data from these rich, in-depth interviews were sufficient to support the development of a preliminary theory, which I present below in Section 5.1. As will be discussed further in Chapter 5, future research with a larger number of participants located in different provinces and territories, and recruited via non-University based avenues, may help further refine and enrich this theory.

3.4 Data Analysis

The interviews were electronically recorded, and an automatically generated transcript was produced, which I then edited using the recordings. While reading and editing the automatically generated interview transcripts, I had the opportunity to conduct an initial overview of the presented information. The initial stage of the research journey consisted of self-observation and self-reflection while reviewing the data, which created the opportunity to understand what the data revealed about the experiences of participants seeking treatment for

their chronic musculoskeletal condition. Constructivist grounded theory emphasizes the importance of theoretical sampling and constant comparison, which are crucial for producing a rich and elaborate theory; allowing me to refine my understanding and generate new theoretical insights as I progress. In the early stages of comparing data and after recognizing tentative categories, Charmaz (2006) recommends employing a theoretical sampling approach by “seeking pertinent data to develop your emerging theory” (p. 96). Therefore, through continuous comparison and analysis of data while simultaneously collecting it, the researcher is able to identify areas requiring additional data collection, leading to the development of a more refined theory. This process is also essential for the generation of valuable connections and critical ideas from the data. Charmaz (2006) characterizes this phase as one where the researcher is actively engaged in gathering data rather than adopting a stance of passive observation in pursuit of scientific objectivity. The data analysis included three elements: initial coding, focused coding, and memo writing.

3.4.1 Initial Coding

Using NVivo 14, the transcripts were uploaded for analysis and coded line by line. Each line was meticulously examined and assigned a code reflecting the action or event described within it (Charmaz, 2006). This approach not only helps researchers to approach the data from fresh angles but also ensures they stay closely connected to the dataset, enabling the construction of analysis "from the ground up" (Charmaz, 2006). Whenever possible, the codes were crafted using the language of the participants themselves, a technique known as "in-vivo coding". Table 2 provides an example illustrating how a response was coded line by line.

Transcript	Initial codes	Focused code
"It would be trying to figure out whether there were people whose conditions were made worse as a result of having the intervention. And I know it wouldn't always be possible to show a direct cause and effect relationship. But if it seemed that people who had treatment did not get better, then I would say, that's a risk."	Learning about other patients experiences with intervention Understands not always black and white Treatment outcome risk perception	Concerns about safety of intervention

Table 2. Example of transcript analysis through initial coding and focused coding

3.4.2 Focused Coding

The next coding phase was focused coding. Building upon the initial coding, this stage entails identifying the most significant codes that encapsulate key themes and patterns within the dataset. This was also a crucial part of the data analysis process as I carefully examined the initial codes and decided which initial codes made the most analytical sense and could be used as a lens to categorize the rest of the data. This process was informed by my understanding of the literature and previous related research. During analysis, initial codes were combined and simplified into focused codes based on what made the most sense from an analytical standpoint, as shown in Table 2, This meant bringing together codes that shared similar ideas and condensing those that were repetitive or overlapped, making sure the analysis stayed clear and focused. This process consisted of constant movement between different parts of the data, enabling the synthesis of new ideas and connections. It was during this flexible process that I was able to critically think about earlier data in new ways. This allowed for significant realizations to occur, contributing to a richer understanding of each participant's perspectives.

Charmaz (2006) emphasizes that "the strength of grounded theory coding derives from this concentrated, active involvement in the process" and that "focused coding checks your preconceptions about the topic" (p. 59). I believe my experience with coding resonates strongly with these assertions. My previous experiences interacting with patients with musculoskeletal conditions may have influenced my beliefs on how they process their illness and their expectations of a treatment plan. However, although I entered the study with my own preconceptions, opinions, and beliefs, the rigorous grounded theory coding process ensured that the categories generated through this process were based on repeated patterns in the data. This method helped ensure that the results reflected the participants' experiences rather than being overly influenced by my own interpretations.

3.4.3 Memo Writing

The third part of the data analysis process which enriched the current study is memo writing. According to Charmaz (2006), “memos catch your thoughts, capture the comparisons and connections you make, and crystallize questions and directions for you to pursue” (p. 72). Thus, memos were an instrumental part of my data analysis as they facilitated reflexivity by allowing me to critically examine my assumptions, biases, and perspectives. This process also helped me to explore the richness of interview data and make connections and organize the emerging categories. By using Charmaz’s flexible guide to constructivist grounded theory, I was encouraged to carry an interpretive lens throughout data analysis and explore the factors that shape patients' trust in non-standard stem cell interventions.

3.4.4 Quality Considerations

Reflecting on the study and assessing the quality and trustworthiness of the data and findings is essential. The most widely recognized criteria for evaluating a qualitative research study are credibility, transferability, dependability, and confirmability, as proposed by Lincoln and Guba (1985). The terms of this criteria were discussed by Korstjens and Moser

(2017), where they provide practical guidance to support qualitative researchers. The first criteria is credibility, which is the confidence that the research findings are valid; transferability addresses the applicability of findings to other contexts; dependability focuses on the consistency of findings over time; and confirmability ensures that the findings reflect the respondents' situations rather than the researcher's subjective views (Korstjens & Moser, 2017). The authors provide strategies used to ensure credibility such as prolonged engagement and persistent observation (Korstjens & Moser, 2017). During this project, I adopted practices aligned with these strategies. Prolonged engagement involved maintaining a significant presence during the research and data analysis phases. During interviews, I asked probing questions to gain a deep understanding of the participants' contexts and experiences. Additionally, my data analysis was comprehensive and involved revisiting the data multiple times, to generate initial codes through line-by-line coding and a second review to develop focused codes. This thorough approach ensured a full review of the data, minimizing the risk of missing anything.

Korstjens and Moser (2017) also emphasize that a study's quality relies on the dependability and confirmability of its findings. Transparency in research steps, explicit process descriptions, and detailed reporting create an audit trail for the study. I built confidence in the study's dependability and confirmability through a grounded-theory approach. Although I faced uncertainties during coding and analysis, I frequently revisited the methodology to ensure proper understanding and application, as described by Charmaz (2006). To mitigate personal bias, I employed several strategies throughout the study. During interviews, I avoided guiding or leading questions, opting for broad, open-ended questions to let participants direct the conversation. In data analysis, the grounded theory methodology allowed me to develop line-by-line codes using participants' words, reducing the influence of personal bias. Lastly, in the discussion of the study findings, I included direct quotations from

participants to provide an accurate and transparent representation of their experiences. By meticulously following the processes described by Charmaz and thoroughly reviewing the data, I ensured that the study achieved dependability and confirmability.

Chapter 4: Findings

4.1 Introduction to Categories and Subcategories

In this section, I present the categories and subcategories that were generated through my analysis of the data. I then introduce and explain the factors that this research suggests shape trust in non-standard SCIs for the participants, each of whom identified as someone with a chronic musculoskeletal condition. These factors include: Patient Factors, Information about the Intervention, Healthcare Provider Characteristics, and Perspectives on Professional Regulation. In the final section of this chapter (4.6), I will discuss the relationship between these categories and present an accompanying theory of how they serve to influence trust in non-standard SCIs.

4.2 Patient Factors

Participants shared their experiences with their condition(s), discussing how it affected different aspects of their lives. Each participant was impacted differently and had their own ways of managing the disease. In the first segment of the interview, participants shared their current symptoms, pain levels, and how they cope with their conditions on a day-to-day basis. Participants exhibited different levels of interest in non-standard interventions based on how they perceive their illness, their current circumstances, and attitudes towards SCIs. Three key factors stood out as being particularly prominent in motivating why these participants would consider non-standard stem cell treatments.

Desperation

Participants shared their experiences managing their condition and how it had impacted their daily activities in different ways. Developing a chronic musculoskeletal condition posed new challenges as some participants had difficulties enjoying their hobbies, maintaining productivity at work and some suffered extreme pain due to having multiple comorbidities. When participants were asked which aspect they would like to learn about

before receiving a non-standard treatment, some participants alluded to the fact that their choice may be driven by desperation.

Participants reflected on their current condition and shared that pain may be a motivation for them to consider non-standard SCIs. **P3** related how her severe chronic back pain prevents her from doing the thing she enjoys:

"I probably would definitely go for it because of the fact that living with this pain that I live with, it's some days it's unbearable, and it just it. It really sucks because I have, you know, I do have a son, and he's very athletic and likes being active, and I enjoy being active like prior to this, my back, getting messed up, and everything and the way that, like my pain is, I was very active. I was out, you know, bike riding, and, you know, running around with my son. Now I can barely go to the grocery store and walk".

This participant recognized that her condition severely limits her, indicating that desperation to alleviate her pain could be a significant driving factor. Another participant, **P1**, who also suffers from OA, carefully examined factors that she would consider regarding a non-standard SCI and toward the end of the interview, she concluded:

> *"I think it would be my desperation level. You know I would try everything I could within the health system and if that wasn't helping, and it was limiting my quality of life. I would probably listen to the professional within the health system and try it".*

Similarly, **P8** linked her consideration of this treatment to the severity of her pain. She shared:

> *"I think it might also depend on how bad what's your what's my quality of life like and how bad it has the pain gotten"*

Dissatisfaction with Current Treatments

Participants shared accounts of how their musculoskeletal condition(s) impacts their daily activities and rated the severity of this impact on a scale from one to ten, with one signifying low impact and ten high impact. The participants gave varying answers but fell on the five to nine range. They also shared what they do to cope with the associated challenges. Their strategies ranged from adjusting their environment and adopting exercise regimens to taking medications and other treatments provided by healthcare providers. Nonetheless, some participants expressed dissatisfaction with the current options available to them, leading them to consider non-standard interventions. Multiple participants expressed their worries about the limits of current treatment options.

P1 who leads a very active lifestyle shared her worries:

> *" [the doctor] he said that I would lose my range of motion if I had surgery, so he didn't refer me".*

This same worry was revealed by **P6,** who viewed non-standard SCIs as less invasive than traditional joint replacement surgery:

> *" I think they are less invasive than traditional joint replacement. And I would prefer to try the stem cell route".*

Participants, such as **P4** in this extract, also say they have considered the chronic nature of musculoskeletal conditions and the potential side effects of long-term management:

> *"I really try to minimize taking any medications just because of the impact on my liver."*

P2 echoed this sentiment:

> *"Yes, and because it is something new. It doesn't involve drugs for me, that even being on painkillers, I have worried because my family has a whole history of alcoholics. I'm always terrified. I'm going to be addicted to pain medication"*

Participants demonstrated that dissatisfaction with current treatment options and concerns about invasiveness and potential side effects may drive their interest in non-standard interventions. It is also important to note that this dissatisfaction with traditional treatments, such as medication, may persist or increase if they are considered for long-term management.

Curiosity

Participants also expressed some acknowledgment of personal attitudes that influence their decisions when it came to considering non-standard treatments. Some participants expressed curiosity towards non-standard treatments including SCIs while other participants demonstrated a more reserved attitude. Participants reflected on how their approach to evaluating risk could be a contributing factor to their trust in non-standard SCIs.

For example, when **P5** was asked if they would consider a non-standard treatment that is still being investigated, she responded:

> *"I don't like taking risks… I'm not sure that I really would trust their advice when it comes to non-standard treatment. And yeah, I'm a little more skeptical".*

P1 made similar comments:

> *"You know again, if it helps some people, but not a lot of people, you know, then you would question it as well. So I yeah, I would ask a lot of questions……. I would hesitate a great deal. I probably wouldn't go forth with it."*

These participants were curious to learn about SCIs and shared the kind of information they would want to acquire before deciding on a non-standard treatment. However, they were not comfortable with a level of risk where certain information is unavailable or unknown.

Additionally, other participants acknowledged that they process risk differently and demonstrated an overall more optimistic attitude about non-standard interventions. In the face of knowing that some information could be still unknown about the treatment, **P2** acknowledged her comfort with risk:

"And so for risk, I tend to take more risks than a normal person, just because of my background in agriculture. you know, risk, there's there's always more of a risk, no matter what you do" .

The journey towards considering non-standard treatments begins with the patient. Musculoskeletal conditions vary widely in their impact, with each patient experiencing them uniquely. The severity of the condition and its effects differ greatly from person to person. For some patients, the pain they endure drives them to seek new and unconventional interventions such as SCIs, especially if they feel dissatisfied with current treatment protocols. Additionally, patients recognize that they assess risks and uncertainties differently, which influences their level of trust in new non-standard treatments. It is important to acknowledge a level of interconnectedness between these factors as it is possible that a patients' prolonged dissatisfaction with current treatment could lead them to feel more desperate to treat their condition using a non-standard treatment.

4.3 Knowledge about the Non-Standard Intervention

Participants were asked about the information they would want to have before deciding to pursue non-standard SCIs. They were asked to elaborate on each factor. Participants showed interest in learning about several key aspects, including; safety, effectiveness, success rates, costs involved, degree of invasiveness or discomfort associated with the procedure, recovery period following the intervention, and regulatory status of the treatment.

Concerns About Safety

Participants identified safety as one of the aspects they would like to receive information on before deciding to pursue a non-standard treatment. Most participants expressed that the safety of the intervention is very important to them and wanted to know

about potential side effects to the intervention, how invasive or painful it is likely to be, and the anticipated recovery time as well as future follow-ups, if any after the procedure.

When asked about which factors would contribute to their decisions about whether to pursue a given treatment, several participants emphasized their concerns about safety.

P7 responded:

> *"I guess I would like to know how invasive the process was. I would like to know potential side effects from it."*

P4 said:

> *"[safety]That's important. Yeah. I would say a on a scale of 1 to 10. That would probably be an 8 out of 10, or maybe even a 9 out of 10."*

P6 echoed this sentiment as well:

> *"it's important to know what the risks are… I would want to know both sides of the story so risks and what's the percentage or likelihood of success."*

Although all participants mentioned safety as one of the aspects they would like to be informed about, participants had different approaches to assessing safety including consulting health providers, reading online resources, and learning about other patient experiences. Participants were also asked about their approach to evaluating risk when considering a non-standard intervention still under investigation, for which there remain scientific uncertainties. They unanimously expressed reliance on their medical team for risk assessment, involving both medical doctors and allied health professionals.

For example, **P2** shared:

> *"I'd like to talk to my medical practitioner, our general practitioner, because he is a very smart young man, and I would like him to get his okay on it. But I think just basically, him would be the main scientific support."*

P4 also expressed a similar approach to assessing treatment safety, stating:

"Oh, having a conversation with the medical practitioner just based on their experience. talking about what the side effects they've seen may be and also what those risks might entail."

Additionally, most participants mentioned their use of online resources to supplement their knowledge about potential treatments. Furthermore, all participants demonstrated an understanding of the importance of accessing reliable information sources. As a result, they emphasized consulting with their healthcare team and seeking information from reputable sources such as government websites, renowned research institutes like Mayo Clinic, and medical associations such as Arthritis Society Canada. They also highlighted the need to avoid relying on social media, blogs, and advertisements for information.

P5, who is an experienced adult educator and helps older adults navigate health information online, commented:

"a lot of things to take into consideration with one of the primary ones being the source of that information. So is it a research institution that has reliable, credible information?"

She also believes there could be some bias when seeking information from providers who advertise their services. She explains:

"And I don't think that's necessarily the most reliable information. So it would be places where there's not a specific connection with a business orientation"

It is also worth noting that some participants discussed the difficulty they face with navigating health information online due to the large amount of information and the inaccessibility of the content for experts. For example, **P6** emphasized the importance of consulting with her medical team while learning about a non-standard intervention due to the complexity of content available online; adding:

"well, trying to read research papers. Of Course I wouldn't. The language will be medical language will be required to follow."

Concerns About Effectiveness

Most participants expressed a desire to learn about the effectiveness of a non-standard SCI and its potential outcomes for their condition before deciding whether to pursue it as a treatment. However, there was variation in their attitudes towards the importance of treatment effectiveness. While some prioritized a high success rate, others expressed interest in receiving a non-standard treatment even if this treatment had not yet proved to be effective. Factors such as the level of desperation, the pain associated with the procedure, and treatment costs seemed to have a more notable influence on how much emphasis participants placed on effectiveness as a factor in their decision-making process.

When asked about how important it is that the treatment is likely to work, some participants were not open to consider a non-standard treatment option without some sort of a guarantee. When **P5** was asked to elaborate on how important the effectiveness of a non-standard treatment is to her, **P5** answered:

"On a scale of 1 to 10? 10…..if it's not going to improve my condition, then I don't think it's a wise thing to do"

Similarly **P1** answered**:**

"I'd have to be assured that it would be worth the effort, you know. do they really know? And how, you know, what. If it's passed the clinical tests? And it's already into the process of assisting people with medicine or with illnesses then I would have to trust it….. And so, if I could feel some confidence that this could give me kind of my life back in this direction, too, that I could have a positive outcome. I'd probably go for it. But when it's really iffy, I don't know and I don't think I would know until the option was presented to me"

However, some participants regarded effectiveness as a secondary concern to safety. They expressed willingness to consider this treatment option even if it is not proven to work, as long as there are no identified safety concerns. This finding could stem from patients' desperation to treat their condition despite the uncertain efficacy and potential costs associated with non-standard treatments. When asked to elaborate on how important effectiveness is to her, **P4** responded:

> *"I think that that [effectiveness] would. It would be minimal for me, because I'm I'm sort of desperate to get it to get it treated, and so I think if I were to get the procedure I would. I would look to get the procedure done in hopes that it would improve my function"*

Similarly, **P3** acknowledged her hopes for improvement but also expressed comfort in exploring alternative therapies, regardless of their potential effectiveness. She reflected on past disappointments with other treatments and responded:

> *"If it weren't to work. it's really not. I don't think it would be a huge deal. I really hope that this works and it's effective, and it helps with my pain and everything, but also because of the fact that I've dealt with disappointments, with treatments, not working and everything like that. I've kind of just been like, okay, well, what's the next thing that I can do?"*

Interestingly, during discussions about effectiveness, participants were able to recall past personal experiences with treatments that lacked proven efficacy, prompting further exploration of their willingness to consider additional non-standard treatments. The majority of participants had previously sought out alternative treatment options which could be considered non-standard, such as healing touch. Additionally, three out of eight participants have undergone platelet-rich plasma (PRP) therapy injections. Platelet-Rich Plasma (PRP) therapy involves using a patient's own blood to extract platelets and plasma, which are then

injected into the affected area to promote healing (Han et al., 2019). The unclear number, frequency, and preparation of PRP injections necessitate further research to establish efficacy and resolve these uncertainties (Han et al., 2019). Consequently, PRP is not currently recommended in Osteoarthritis Research Society International (OARSI) treatment guidelines (Bannuru et al., 2019). Nonetheless, **P6** wanted to explore this option explaining:

"I just thought if there's been any positive result, I had to try it"

When asked about how important the effectiveness of a non-standard SCI was to her, **P6** shared her disappointment with a previous PRP injection. Despite this previous disappointing experience, she expressed willingness to consider other non-standard treatments that might not guarantee effectiveness, provided they are affordable. **P6** responded:

"Working is one thing. Whether it's safe is a different matter. I would want to know that it is safe. I've already taken a chance on a stem cell treatment that did not work and cost me money. I guess it would depend on the costs."

Although participants hope for some symptom relief after treatments, those who express dissatisfaction with their current treatment options and feel desperate to alleviate their condition may place less significance on treatment effectiveness.

Regulation Status of the Treatment

Most participants demonstrated keen interest in learning about the safety and efficacy of treatments through diverse sources such as practitioners, reputable journals, and patient experiences. However, when discussing the information required to consider a non-standard SCI, some participants also expressed curiosity about its regulatory status. **P1**, who has a family member involved in drug development research, shared insights, stating:

"And so I understand a lot of the processes that have to go through before it even, you know, gets Federal approval to be used. And so. you know there would be that level of trust."

Similarly, **P6**, who knew individuals who received a stem cell intervention in Canada for a musculoskeletal condition before its suspension, expressed a desire to know if Health Canada approves the treatment, saying:

> *"I would want to know if Health Canada approves it. I guess it's not going to happen otherwise."*

However, most participants showed more interest in exploring different aspects such as safety and effectiveness. To better understand the participants' comprehension of the current treatment approval process in Canada, they were all asked to explain what they knew about it. Most participants had limited and vague knowledge, with some admitting that they do not know much about it. It is possible that some participants did not make any mention of the regulatory status of a treatment because they did not fully grasp the drug approval process. Without full awareness or comprehension of regulatory procedures, they may not have viewed it as a pivotal factor in their decision-making process regarding treatment options. It is also possible that participants assumed that if they were able to access a treatment option, it would be Health Canada approved. **P1** explained:

> *"It's to me it sounds like common knowledge that everybody knows that before a drug appears on the shelf, that it has been tested thoroughly"*

Nevertheless, when provided with a prompt regarding Health Canada's role in ensuring the safety and effectiveness of new treatments, most participants agreed on its importance. Many participants shared the view that the drug approval process in Canada is lengthy, potentially lagging behind other countries. However, there was a divergence of opinions on whether this perceived delay is beneficial or detrimental.

Some participants perceived the lengthy process as necessary to protect the public from potential side effects. For example, **P1** expressed the belief that Health Canada plays an important role:

"I think they do, absolutely. And and you know the more stops along the way that you know something has to be of a certain standard the better for everybody".

Making comparisons between healthcare systems, another participant expressed preference for the lengthy Canadian process over others. **P7** said:

"I say that based on what I see go on in the US. And how they pop drugs out into the public without maybe a lot of care. I always have thought that Health Canada does their due diligence in studying at before they approve drugs for use in the public."

However, other participants perceive this lengthy process as disadvantageous to some patients in Canada. **P2** explains:

"The lack of speed getting things done on their end seems to hold back our forward motion. That's why we're behind. If that makes sense".

Similarly, **P3** was conflicted in her response in that she believes Health Canada plays an important role in ensuring proper approvals of treatments but also perceives some drawbacks. **P3** explained:

"I want to say yes and no. I want to say yes, because they're there to make sure that stuff is done, you know, properly, policy wise. There's no infliction on human rights…. but also no……ff the Health Board decides no, this isn't something that we should put into general circulation, medication wise, operation wise.. they could actually be hindering somebody's ability to live their life with, you know, a better quality of life."

In this study, participants seemed to have a limited understanding of Canada's treatment approval process. While most participants acknowledged the importance of Health Canada's role, they differed on the benefits of the lengthy approval process. Some saw it as protective, preferring it over other systems, while others viewed it as hindering progress, potentially limiting access to treatments.

4.4 Healthcare Provider Characteristics

In this section of the results, I will be exploring factors related to healthcare providers that these participants indicated would be important considerations for them if offered a non-standard SCIs. Participants emphasized three key provider characteristics in discussing what might incline them to accept such an intervention. These characteristics included: medical expertise, patient centeredness, and professional standing.

Medical Expertise

Participants were asked about the aspects of a provider that would be significant to them if they were recommended a non-standard treatment. The majority of participants highlighted the importance of the provider's qualifications as well as their level of experience before considering such intervention. More specifically, nearly all participants highlighted the importance of the provider's experience in administering the non-standard treatment. This sentiment is echoed in the following responses.

> **P1:** *"If they've had a lot of positive experience then that would help towards that decision."*
>
> **P4:** *"somebody who has been involved in the research, who has actually done, provided the treatment in others, and can articulate what the outcomes…I would say somebody that has experience, their own experience."*
>
> **P5:** *"It would be a provider that I know has had experience with that particular condition with other patients…. if they know they've recommended it to other patients. and it's worked well and improved their condition."*

P8 reflected on her experience with a knee injection (specifics unknown) and highlighted the significant role of perceived expertise and effective communication in shaping her trust in a non-standard treatment. **P8** shared:

"I guess I think about when I got the shot. whatever I got in my knee that didn't work and it was non-standard and the I because the person was a sports, a doctor with specialization of sports medication. And they talked about. They they gave me lots of information about it. Then I went back, and I and I had another conversation with them. And they were very upfront about whether it would work or not, which it actually didn't but because of the training, I guess, because of what I saw as their expertise, their certification, and their way they communicated about the treatment. I went ahead with it."

Participants also emphasized the importance of treatment providers' medical expertise, mentioning their credentials including educational background and experience in the field as indicators of competence. Additionally, they considered the practitioner's level of specialization. Given the diverse and complex nature of musculoskeletal conditions, these participants discussed having often sought specialized advice, leading them to consult with a diverse healthcare team. As a group, they were eager to receive guidance from a variety of practitioners including doctors, physiotherapists, massage therapists, chiropractors, and naturopaths. For example, **P1** shared her journey of consulting with multiple healthcare providers after receiving a diagnosis of severe osteoarthritis. She emphasized the importance of specialized advice when deciding between different treatment options, noting discrepancies in opinions among her family doctor, chiropractor, and massage therapist. **P1** shared:

"First of all, my family doctor told me I had severe osteoarthritis and just simply said. You know, because you're active, you'll lose your range of motion. So I'm totally aware that family doctors have to have a very broad knowledge, but it's shallow. They can't have the depth of a specialist in every topic. It's impossible. So I talked to my chiropractor about that, and the chiropractor tended to disagree and suggested the

sports doctor. My massage therapist again, was very concerned. He was the one that actually made me take action because he was afraid I would end up needing knee replacement as well from the strain of my body being out of alignment".

P1's comments highlight patients' recognition of the importance of consulting multiple healthcare providers to obtain diverse perspectives. Additionally, they reflect the appreciation that many of these participants have for the critical role that allied healthcare professionals, such as chiropractors and massage therapists, play in supporting proactive steps towards managing their health.

Some participants discussed having previously sought information from multiple practitioners when considering non-standard treatments. For example, **P4** described consulting with a doctor and a naturopath before receiving a PRP injection, noting her trust in her naturopath's thorough research:

"[my naturopath]. I trust her. She has a very solid . She does a lot of research, and the research that she has done aligns with what my physician has said… I will go to see her as my primary care provider over my family physician" and later she says "my naturopath had suggested PRP, and then my family physician suggested PRP".

P6 also weighed the expertise of different practitioners, stating:

"I think the expected answer is the physician. but I have been to a physiotherapist, too, who is...certainly very knowledgeable. I have to weigh things. I don't know that I can come straight out and say one over the other."

Participants in the study emphasized that they need to perceive medical expertise and specialization when selecting healthcare providers, particularly in the context of navigating treatment options for musculoskeletal conditions, but it is notable that they did not necessarily prioritize the medical expertise of physicians over other types of healthcare professionals. Further, participants also actively seek expert advice by consulting with

different practitioners, valuing credentials such as educational background and experience in the field. This holistic approach to seeking healthcare reflects the complexity of managing musculoskeletal conditions and the participants' desire for comprehensive care.

Patient Centeredness

When considering what would be important to them before they would pursue a non-standard treatment, participants in the study prioritized an aspect of healthcare providers known as patient-centeredness. This concept refers to an approach of care that respects and responds to individual patient preferences, needs, and values, ensuring that these values guide clinical decisions (Edgman-Levitan & Schoenbaum, 2021). During the interviews, participants emphasized the importance of perceiving a high level of patient-centeredness in practitioners who recommend new treatments. For example, **P2** articulated her appreciation for a healthcare provider who is responsive to her medical condition while also considering her values. **P2** expressed:

> *"They're always thinking of what? What can be done on a different aspect. What's new? What's something that will help eliminate the drug dependency. He's just very proactive, willing to try new techniques to help eliminate pain, and I feel that aligns with my thoughts and processes in my head."*

Similarly, **P8** reflected on her experiences with different doctors in managing her condition. She contrasted a practitioner in Saskatoon who solely focused on injections without considering her response to previous treatments with a physiatrist who takes a collaborative approach. **P8** remarked:

> *"The physiatrist that I see always wants to know exactly how did I react to the last round? What did I think I needed?... So she takes more of a team approach as opposed to: I'm the doctor, this is what we're doing, end of discussion. It's a 45-minute*

appointment of her listening to me and what I have to say and then adjusting accordingly."

Similarly, when **P5** was asked which factors are important to her in deciding to follow a practitioner's advice, **P5** stated:

"Someone that I know that I've seen before that takes time to ask questions and not just immediately say, you need to do X without understanding the complete situation... Someone who is good at asking questions and good at listening to responses, and then makes practical suggestions that are things that I think I can easily do."

The participants in the study highlighted the importance of patient-centeredness when evaluating different treatments. They emphasized the need for healthcare providers to consider individual patient preferences, needs, and values in recommending such treatments. More broadly, effective communication and collaboration emerged as key factors in ensuring that patients feel heard and involved in their treatment choices.

Professional Standing

In addition to sharing their thoughts on the regulatory status of the treatment, participants reflected on the regulated status of healthcare professionals more broadly. This aspect was similar to, yet distinct from, the regulatory status of the treatment itself. The participants in the study also emphasized the significance of a provider's professional standing when considering non-standard treatment options. They touched on various aspects such as affiliation with public research teams, respect within the medical community, and the reputation of their practice. Only one participant explicitly mentioned professional regulation when asked which aspects of the healthcare provider would contribute to her trust if she were to receive a non-standard treatment. However, when probed, all participants agreed that belonging to a regulatory body would influence their receptivity to non-standard interventions offered by a healthcare provider. It is noteworthy that the importance of

professional regulation to participants' decision-making did not emerge unprompted, and yet when raised, participants unanimously agreed it is relevant. The fact that it was not brought up unprompted may be because the notion of regulation is so ingrained that its absence is not considered. One participant, **P8**, elucidated this by stating:

> *"I make an assumption that if you have a medical degree from the University of Saskatchewan, and you are a member of the Saskatchewan Medical Association, you're a member in good standing. You've met all of the standards, and that's because I'm not a doctor, and I don't know what all of those things are."*

This response appears to underscore the implicit trust placed in regulated professionals, including physicians. Similarly, **P1** highlighted the importance of knowing a practitioner's professional requirements and qualifications:

> *"Yes, I hadn't thought of that to say it, but absolutely that would be important…. because there are plaques out there, and you do need to know their professional requirements….. If they have their qualifications, their, you know, their truly been trained in a respected school. and they've had a lot of positive experience then that would help towards that decision. Absolutely".*

P6 echoed this sentiment, stressing the need for regulation to ensure adherence to established rules and standards. **P7** emphasized the accountability instilled by professional regulation, acknowledging its imperfections but valuing the existence of guidelines and entrance exams as safeguards within the profession. **P7** responded:

> *"I guess to me, when they're regulated. There's a body that they have to answer to. There should be guidelines that they need to follow. I know that doesn't guarantee that they all do. but at least they've proven cause they have to pass whatever entrance exams whatever to practice in Saskatchewan."*

The study participants highlighted the importance of professional regulation in healthcare, revealing their implicit trust in regulated professionals. This demonstrates the essential role that regulation plays in fostering trust and ensuring standards of competency and accountability. Participants articulated the significance of knowing a practitioner's qualifications and adherence to established rules, reflecting a broader understanding of the importance of transparency and credibility in healthcare delivery. Their unanimous support for regulation as a safeguard for patients and a marker of professional competence highlights its critical role in shaping perceptions and practices within healthcare. These findings carry significant policy implications, suggesting the need for continued emphasis on robust regulatory frameworks to uphold standards of care and protect patient interests when it comes to non-standard treatment delivery.

4.5 Perspectives on Professional Regulation

The second purpose of this study was to explore how patients with musculoskeletal disorders understand the role of professional regulation and how that impacts their trust in healthcare providers. In the last section of the interview, participants were prompted to share their perspectives on the role of professional regulation in ensuring treatment safety and effectiveness in the context of considering what is important to them when making decisions about specific treatments offered by a particular provider. The results presented in this current section discuss patients' perspectives on the importance of professional regulation in general in terms of ensuring treatment safety and effectiveness, and how they integrate this consideration into their decision-making process, without singling out a specific treatment or a specific provider. These findings are related to, but distinct from, those presented above. During the discussion, participants not only shared their understanding of regulatory bodies but also articulated their expectations and the factors influencing their trust. Through this

dialogue, two key categories were generated, emphasizing their expectations of accountability and a hopeful attitude.

Expectation of Accountability

During discussions regarding the role of regulatory bodies, participants emphasized their important function in holding practitioners accountable to protect the public. Recognizing the inherent power imbalances in healthcare settings, participants underscored the necessity of these bodies in protecting patients. For instance, when asked about the importance of regulatory bodies in ensuring safe treatment, **P3** noted:

> *"I've seen that there's some doctors who like have abused their power and everything like that as a medical professional, and everything like that. And it's I feel like it's important that there are like, there's a way to hold those people accountable… I think it's important to be able to have somebody that you can hold that person accountable to, so that they don't abuse their their power or their knowledge".*

Another participant shared a personal experience, recalling a time when a family member was dissatisfied with certain procedures and the treatment received from the healthcare system. Despite her limited knowledge about professional bodies, she took the initiative to reach out to Saskatchewan Health Authority and the Ministry of Health. Reflecting on this experience, **P1** concluded:

> *"What I trust is that if I find a deficit in a doctor or in any medical aspect, I can report it because nothing can be changed if nobody knows about it".*

Furthermore, participants echoed the importance of these bodies in ensuring accountability. When discussing their role in guaranteeing safe and effective treatments, **P7** highlighted the necessity of regulatory guidelines, stating:

"I know there's certain standards they had to meet to become part of that body... Without guidelines, you've just got a bunch of cowboys running around doing what they want. So you gotta have rules and regulations."

Through their discussions, participants emphasized the critical role of regulatory bodies in ensuring accountability and addressing power imbalances within healthcare. Their narratives underscore the critical function of such bodies in safeguarding patient well-being and maintaining trust in medical practices. These insights highlight the imperative for robust regulatory frameworks to uphold standards and promote transparency when delivering non-standard treatment options.

A Hopeful Attitude

After participants discussed their expectations regarding the role of regulatory bodies, they went on to elaborate on the factors that motivate their trust in these regulatory entities. Participants acknowledged their limited understanding of these processes, yet they demonstrated optimism regarding the efficacy of existing regulatory bodies. For example, when asked why she has confidence in our current regulatory bodies in ensuring safe and effective treatments, despite the lack of clarity on the specific processes, **P8** responded:

"I would hope that they would, because they're clinicians, and they would have expertise in dealing with actual patients. But I don't know how their, how, their, how their processes work within those organizations to ensure that".

Some participants showed a strong sense of trust, underpinned by their identity as Canadian taxpayers and a hope that these institutions prioritize their well-being, **P2** stated**:**

"We are just supposed to trust them like non blinding trust because we're Canadian Taxpayers, we're hoping that they have our best interests at heart".

Some participants were able to more clearly articulate their understanding of professional regulation, and why they trust these processes. **P4**, a regulated health practitioner herself,

provided insights into the role of professional regulatory bodies, emphasizing their adherence to specific standards aimed at preventing negative outcomes and addressing some ambiguities in practice. **P4** stated:

> *"So they're making sure that the physicians or healthcare practitioners are using, you know, scientific evidence to ensure the pub. Their role is to ensure the safety of the public.….The college isn't there to say you can use this or that treatment or just making they just want to make sure that the person is practicing safely and using evidence-based practice."*

When prompted to delve deeper into her confidence in regulatory bodies, **P7** offered a perspective based on her extensive career within the ministry of health. Highlighting the inherent challenges faced by regulatory bodies, **P7** concludes:

> *"in any profession you're going to get those that think they know better than the guys writing the policies…. I've always just believed they've done the regulatory bodies in Saskatchewan do the best they can".*

Chapter 5: Discussion & Conclusion

5.1 Constructing the Theory

In this chapter I will be explaining how the findings from this study relate to and build upon the existing literature. As mentioned above, the aim of this research was to explore the factors that motivate trust in non-standard stem cell therapies among patients with musculoskeletal diseases, along with their comprehension of professional regulation's role. In this section, I will present a theory of how participants consider different factors and trust non-standard SCIs and I will highlight the most prominent findings of this study and contextualize them in existing literature. A visual representation of the theory is presented in **Figure 1**. This flowchart was developed through the observation of emerging connections in the data during analysis. The shapes were assigned according to international guidelines (Wilkins, 2020): ovals for start and end points, parallelograms for inputs (as shown in Figure 1), rectangles for processes, and a diamond to signify decision point.

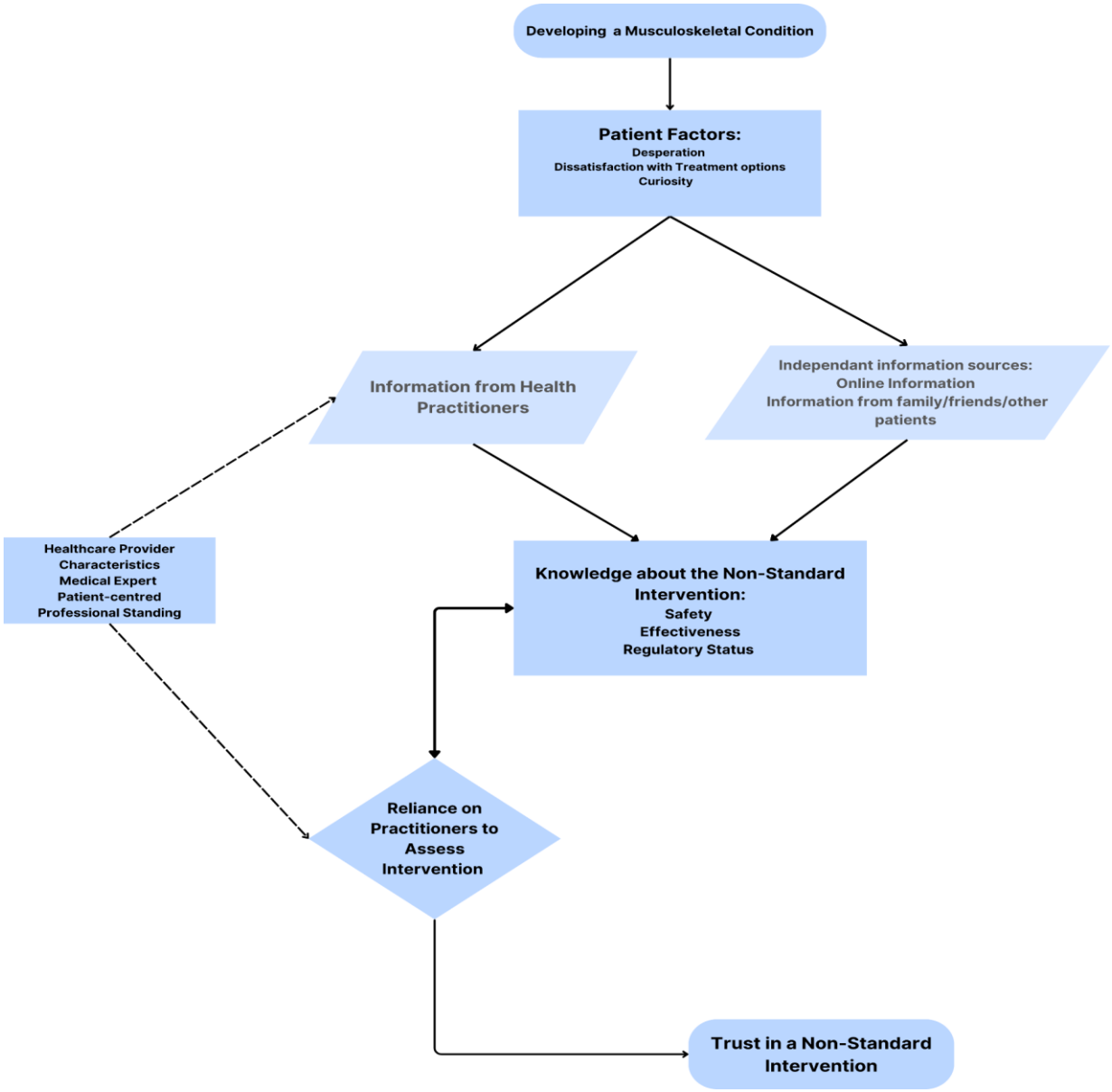

Figure 1: The process of developing trust in non-standard SCIs.

The patients' exploration begins with an internal evaluation process wherein patients assess their situation from diagnosis impact on their lives to available treatment options, driven by discomfort and dissatisfaction with current treatments, which sparks interest about potential alternatives. As shown in Figure 1, patients begin their journey upon developing a condition, navigating through various aspects outlined in the *"Patient Factors"* node. These factors describe how patients process their condition over time which includes dissatisfaction

with available treatments, a sense of desperation to treat their condition, and curiosity about non-standard treatments. Participants of this study often described the pain they experience and how it limits their ability to carry on some daily activities and discussed other non-standard treatments they have tried.

As their journey continues, they begin learning about different treatment options from various sources. This includes information they independently gather through online searches and discussions with family, friends or other patients, as well as insights obtained from conversations with different healthcare practitioners, as shown in Figure 1. The node *"knowledge about the non-standard intervention"* demonstrates this process where patients synthesize detailed information about non-standard interventions, including safety, efficacy, procedural steps, recovery time, cost, side effects, and documented patient cases. Although participants demonstrated interest in learning about different aspects about non-standard SCIs, they considered safety to be the most important aspect to learn about, with some expressing priorities related to potential side effects, both short and long-term, recovery time, and any associated risks. Three aspects about the intervention were particularly relevant for participants; these included are safety, effectiveness, and regulatory status.

The interplay between patients' understanding of their medical needs and the nuances of non-standard treatments is largely mediated by the practitioners they encounter. Most study participants explicitly expressed their reliance on practitioners to evaluate risks and highlight qualities that foster trust in non-standard interventions. As shown by the double-headed arrow in Figure 1, participants rely on practitioners to assess the suitability of a non-standard intervention, integrating providers' opinions into their knowledge base. This reliance on practitioners forms a crucial part of participants' understanding. They seek opinions from practitioners, integrate this knowledge, and then often seek additional opinions to refine their

knowledge and evaluate the intervention further. This cycle of seeking and integrating opinions contributes significantly to participants' trust in non-standard treatments.

The findings from this study also suggest that certain practitioner attributes are critical in processing the suitability of suggested non-standard treatments from the patient perspective, as shown in the node *"Healthcare Provider Characteristics".* Participants identified particular practitioner characteristics as valuable, which are suggested to influence patients' perceptions of the provider's opinion at various stages, as highlighted by the dashed arrows. These characteristics encompass two dimensions. The first related to perceived clinician qualities observed during patient interactions, including medical proficiency (e.g., years of experience and specialized knowledge) and patient-centeredness. The second dimension relates to professional standing, which is less emphasized and signifies the alignment of healthcare providers with regulatory standards.

In this study, participants evaluated the credibility of advice based on their perception of the practitioners' expertise. Factors contributing to this perceived expertise include the practitioner's level of experience, positive experiences, research about the subject, and overall familiarity with the treatment. Participants expressed a preference for practitioners who can articulate information fluidly when they seek clarification about a non-standard treatment. Additionally, they preferred practitioners who demonstrate a high level of patient-centeredness, being inquisitive about their medical needs and addressing concerns about their current treatment protocol and potential future treatments. Lastly, the study revealed that the participants strongly preferred healthcare professionals associated with a regulatory body, despite their limited understanding of professional regulation or the standards it entails for registrants. Nonetheless, participants believed that professional regulation plays an important role in ensuring the safety of healthcare practices. This implicit yet strong trust in professional regulatory bodies is a crucial factor to consider as regulatory reforms for SCIs

progress. It is imperative to monitor how these reforms may impact patient perceptions and to take into account patients' expectations of regulatory oversight to prevent undermining patient trust.

This current study utilized grounded theory methodology, emphasizing subjective interpretation grounded in temporal and context-specific interactions between the researcher and the participants. Thus, the resulting theory is tailored to the participants included in this study, with no claims regarding its transferability to other contexts. To further enhance understanding of patient perspectives, it would be valuable to explore its applicability in different settings, such as with diverse patient groups or in various jurisdictions.

5.2 Relationship to Existing Literature

5.2.1 Patients' Experience with Condition

The study findings align with existing literature regarding the motivations behind patients' consideration of non-standard stem cell interventions. In a qualitative study conducted by Waldby et al. (2020) involving Australian patients and carers, dissatisfaction with standard medical practice emerged as a theme. Patients expressed dissatisfaction with standard medical practices, which often drove them to seek alternative stem cell therapies. Particularly, patients suffering from pain highlighted feelings of desperation, viewing it not only as a symptom of their condition but also as a consequence of unsatisfactory standard medical treatment. In this study, participants demonstrated a similar pattern, with many expressing dissatisfactions with the current approaches to managing chronic musculoskeletal conditions and demonstrating more interest in non-standard treatment options as a result. Participants in this study exhibited a range of motivations for considering stem cell interventions as preferable to current options, including the potential to delay surgery, the perception of it being less invasive than surgery, and a preference for natural alternatives, consistent with findings from Arthurs et al. (2022).

5.2.2 Patients' Expectations of Treatment

The participants in this study also demonstrated a significant concern for safety, with the research delving into their inquiries regarding side effects, procedure invasiveness, and recovery time. Similarly, in a survey conducted by Ogbogu & Case (2023), safety emerged as a primary theme of concern among participants. Additionally, participants varied in their concerns regarding treatment effectiveness, with some expressing a desire for improvement but also a willingness to consider the treatment even if its efficacy is still under investigation. In another study involving orthopedic patients considering stem cell interventions, conducted by Kenihan et al. (2020), some viewed improvement as a hopeful outcome rather than an expected outcome of treatment. Nonetheless, they still expressed expectations for pain alleviation and enhanced mobility. Some participants in my study attribute their willingness to try stem cell interventions to their desperation to treat the condition. They express concern that their condition may worsen or have experienced previous disappointments with other treatments, leading them to feel more open to exploring alternative options.

5.2.3 Patients' Reliance on Health Practitioners

One of the most interesting and potentially important findings uncovered in this study is the participants' reliance on health practitioners to evaluate risk. All participants expressed their intention to consult with practitioners to assess the risk of the intervention, seeking to amalgamate information from various sources to determine its safety. Some participants in my study noted that they might not find online information as reliable or productive in this regard. This finding echoes the results of Puzzitiello et al.'s (2021) survey, which investigated public opinions on the use of stem cell interventions (SCIs) in orthopedics. The majority of respondents expressed willingness to consider stem cell therapies if recommended by their doctor, regardless of evidence supporting their effectiveness. Similarly, as per Ogbogu and Case (2023), healthcare providers were the primary source of information about the stem cell

interventions, with secondary sources like clinic advertisements, websites, and social media playing a smaller role.

Another finding from this study, particularly related to musculoskeletal patients, is that these participants relied to a large extent on allied health practitioners to access information. Musculoskeletal patients seek treatment frequently from various allied services such as physiotherapy or massage therapy. Thus, even though these practitioners may not be directly involved in administering SCIs, they play a role in sharing information and advice with patients, thereby offering opportunities to promote evidence-based practice through leveraging these relationships.

5.2.4 Patients' Understanding of Regulation

Lastly, this study highlights that some patients lack clarity regarding the regulatory frameworks for new treatments. Fortunately, Health Canada has taken steps to address this issue by releasing a position paper aimed at ending the administration of SCIs through clinics nationwide to protect the public. Nonetheless, studies conducted in various countries have shown confusion and misconceptions about the regulatory oversight of treatments that are still in the investigational stages (Waldby et. al, 2020). Thus, it becomes very important to prioritize raising awareness and promoting transparency about the approval process as components of effective patient education initiatives.

Various studies have gathered data from patients who have already undergone non-standard stem cell interventions, potentially contributing to the confirmation bias observed among participants who believe these treatments are beneficial. This study adds to this knowledge base by capturing the perspectives of patients who have not undergone non-standard SCIs. By including these individuals, this research aims to gain a deeper understanding of the factors influencing some patients' decisions regarding these interventions. Additionally, this is the first qualitative study, to my knowledge, contributing a

nuanced understanding derived from in-depth interviews with Canadian patients with musculoskeletal conditions regarding non-standard stem cell interventions. This study provides deep insights into what factors a small number of individuals with chronic musculoskeletal conditions consider when exploring non-standard SCIs. Although small in scope, these rich insights help advance the larger body of work relevant to these topics and, as discussed in greater detail below, will hopefully contribute to the ongoing discourse surrounding healthcare regulation and patient safety in Canada.

5.3 Policy and Practice Implications

This study suggests that healthcare providers play a critical role in assisting patients in evaluating the risks associated with non-standard stem cell interventions. Healthcare providers serve as crucial intermediaries, helping patients navigate and interpret the information they receive from various sources. The study findings emphasize the importance of professional regulation in providing oversight, given the central role providers play in patients' decision-making processes. The participants highlighted practitioners as trusted sources of information to guide their consideration of non-standard SCIs. Therefore, it becomes critical to consider the responsibility of regulatory bodies to oversee professionals and help ensure patient safety through ethical practices that adhere to the standard of care. Thus, these regulators should aim to be equipped to provide robust oversight. Moreover, considering limitations in resources and capacity within Health Canada, it becomes crucial for professional regulatory bodies to engage in robust oversight of their members' professional practices. Ensuring that professional regulatory bodies are equipped to provide meaningful oversight of providers who offer non-standard SCIs is likely particularly important in the context of the direct-to-consumer market in general, and especially for emerging interventions that may not have a clear regulatory pathway under the current *Food and Drugs Act*.

Additionally, these findings suggest there is a pressing need to prioritize professional development initiatives and continuing education programs tailored to healthcare providers, including allied healthcare providers, who work with musculoskeletal patients. These programs should aim to bolster their expertise in this rapidly evolving field and equip them with the necessary knowledge to effectively address patient concerns. It is imperative to extend these educational opportunities to allied health practitioners, as they frequently interact with musculoskeletal patients. Collaborating with allied health professionals can leverage their existing relationships with patients to combat misinformation and promote evidence-based practices. By incorporating these practitioners into training programs, healthcare providers can harness a multidisciplinary approach to patient care, ensuring a comprehensive and cohesive response to the challenges posed by non-standard interventions. Furthermore, addressing the educational needs of healthcare professionals should encompass understanding regulatory frameworks governing non-standard interventions. This includes familiarizing healthcare providers with the regulatory standards and guidelines applicable to these treatments. By enhancing their understanding of regulatory requirements, healthcare providers can navigate legal and ethical considerations with greater confidence, ultimately safeguarding patient welfare and upholding professional integrity.

Lastly, the study's findings contribute to the existing research on the factors that influence patient trust in SCIs. Kawan et al. (2023) emphasizes the need for further research into factors motivating patients' interest in SCIs to ensure that persuasive education strategies are firmly grounded in empirical evidence. They advocate for integrating persuasive education to combat and correct misinformation and mitigate the risks associated with non-standard stem cell interventions.

Kawan (2023) argues that persuasive education aims to address patient biases, thus enhancing patient autonomy in decision-making. Moreover, beyond fostering autonomy,

persuasive education can play a critical role in reducing social harm by improving public understanding of stem cell science and increasing confidence in institutions and actors responsible for safeguarding public health (Kawan et al. 2023). For example, persuasive education can be used to address some of the negative bias against the lengthy process to approve these treatments on the institutional level and shed light on the complexity of the challenges these interventions pose to the current regulatory framework. Therefore, it is crucial to thoroughly examine the study's findings and develop detailed educational strategies based on empirical evidence. Although providing recommendations regarding educational strategies is beyond the scope of this project, its findings may be useful to future work on that issue.

5.4 Limitations of the study

There are several important limitations of this study, with associated implications for further research on factors driving patients to explore non-standard SCIs. These limitations primarily center around three key aspects: research methodology, sample size, and participant recruitment. The present study employed a constructivist grounded theory methodology, which emphasizes a subjective interpretation grounded in temporal and context-specific interactions. Consequently, the theory derived from the data of this study is specific to the participants involved and may only be applicable to this particular point in time. Thus, as with all qualitative research, caution is advised when generalizing findings. It would be beneficial to investigate its applicability in diverse contexts, such as with different patient groups or in different jurisdictions.

Secondly, in this research study, only eight participants were enrolled to conduct the individual interviews. Despite the thorough analysis conducted on these interviews yielding sufficient theoretical depth, the limited number of participants raises an important consideration. It is essential to recognize that with such a small sample size, there is a

possibility that unforeseen insights or perspectives could have been introduced by additional participants. This aspect highlights a potential limitation of the study, suggesting that future research with a larger and more diverse participant pool might provide a broader understanding of the factors being examined.

Thirdly, another limitation of the study relates to the recruitment method since participants were mainly recruited through emails, virtual or physical posters they encountered through their association with the University of Regina in some capacity. This approach may have led to a bias in the data, as it likely attracted individuals who were either interested in the study or sought to voice their opinions. Additionally, the patients represented in the study may be more research-proactive or educated than individuals recruited through other avenues. For instance, seven out of the eight participants have completed some form of university education, while the eighth participant, who did not pursue higher education, had a lengthy career with the Ministry of Health. This is especially relevant to the study as this patient sample may have a stronger ability to critically evaluate research regarding treatment options online or be more aware of the importance of evidence-based practice. Additionally, it is important to note that most of the study participants possessed prior work experience in the healthcare or public sectors. Therefore, while the insights from the interviews are valuable, they can be refined further through investigations in broader contexts.

Lastly, another potential limitation is the use of Zoom in this study. While it enabled participation from individuals both within and outside the province, it may have excluded those without internet access. Additionally, the online format might have impacted participants' attention and engagement, as the absence of in-person, face-to-face interaction may affect the rapport between researcher and participants, potentially influencing the depth of the data collected. Furthermore, due to the resource limitations of this project, the data analysis was conducted by a single coder. The absence of an additional coder means the

analysis lacked the benefit of cross-verification, which could lead to potential biases or missed insights.

5.5 Conclusion

SCIs, marketed online and surrounded by complex science, create ample opportunity for misinformation for patients with unmet medical needs, including those managing musculoskeletal conditions. These emerging interventions introduce new challenges for patients, practitioners, and regulatory bodies alike. This study indicates that patients may consider non-standard SCIs interventions for various reasons, and health practitioners play a central role in their journey as they guide them through different treatment options and the information they come across online. The results of this research also emphasize that alongside physicians, allied healthcare professionals have an important place in this support system as patients with musculoskeletal conditions often seek their services to manage their symptoms. Thus, they also have a role in providing information. The institutional trust patients have in professional regulation is invaluable and points to important policy recommendations regarding future governance of non-standard SCIs. It is my hope that the theory generated from this project contributes to understanding that promotes consideration of patients' expectations of regulatory bodies when designing reforms to regulate regenerative medicine interventions.

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Appendix A: Interview Guide

Background Questions

Name:
City:
Age:

Which chronic musculoskeletal conditions do you suffer from? For how long have you had this condition/these conditions?

On a scale of 1 to 10, with 1 representing minimal impact and 10 meaning a significant impact, please assess how severely your condition impacts your daily activities (for example, work, housework, driving, childcare, social life, self-care)?

Knowledge Assessment Questions:

Question 1: How do you currently manage your musculoskeletal medical condition(s)?

Question 2: Had you ever heard about regenerative medicine before this interview? How about stem cell interventions?

2.a. If so, can you please tell me what you knew about regenerative medicine broadly and stem cell interventions specifically prior to this interview?

2.b. Have you ever heard about stem cell therapies for joint and tendon pain/disorders? What have you heard about them?

Prompt (if participant asks for more information): *Regenerative medicine is a relatively new field where scientists and clinicians are trying to develop new treatments to fix or replace damaged body tissues and cells. Regenerative medicine is a broad term and can describe areas such as tissue engineering (i.e., artificial cartilage), gene therapy, and stem cell-based therapies.*

Stem cells are special cells in the body that can renew themselves and turn into different types of body cells. There are different kinds of stem cells, like embryonic and adult stem cells, each with its own unique features and treatment potential.

Question 3: Can you please tell me about any experiences you've had gathering information about potential stem cell treatments?

Follow-up (if needed): For example, have you researched the topic online or discussed it with professionals or non-professionals, including perhaps friends, family, or people you interact with online? Have you heard about it in the news or other media?

Question 4: Are you aware of any ethical dilemmas that surround the use of stem-cells to treat diseases?

4.a. If so, what ethical dilemmas come to mind?

4.b. Do you think those kinds of ethical questions would influence whether you would want a stem cell treatment? If so, in what way?

Question 5: To your knowledge, have you ever received an intervention that would be classified as regenerative medicine (i.e., platelet-rich plasma therapy), including a stem cell treatment? If so, can you please tell me about your experience?

<u>Research questions (and follow-ups):</u>

Question 1: In addition to how you are currently managing your chronic musculoskeletal condition, do you anticipate wanting to explore stem-cell based interventions as a potential treatment? Why or why not?

Follow-up: What factors would you consider? What information would you want to have before deciding?

Question 2: Would you be interested in receiving a stem cell treatment-based treatment if you were told that it is not yet known whether the treatment is likely to work, or if it is safe? Why and why not?

Follow-up (if needed): How important is it to you that the treatment is likely to be effective? How important is it to you that research has shown that the treatment is safe? How do you assess risk when treatments are still being investigated and there are a lot of unknowns about them? What level of scientific support would you like to see?

Question 3: How do you go about seeking information on new potential treatments for your condition?

Follow-up (if needed): How do you evaluate different kinds of information (i.e., your doctor, information you find online from medical websites, information from providers advertising treatments, information from other patients) about treatment options?

If you find information from multiple sources, which one has the most weight, in your view?

Question 4: What kinds of healthcare providers have you seen for treatment for your conditions? (e.g., doctors, nurses, naturopaths, physios, etc.)? And how do you decide what provider(s) to see?

Follow-up (if needed): How do you decide whether or not to follow their advice? What factors are important to you?

Question 5: If one of your healthcare providers were to recommend a non-standard treatment option, such as a non-standard stem cell treatment, what aspects about the provider would matter to you in deciding whether to pursue it?

Prompt: A non-standard intervention *is one that is still being researched, and /or which hasn't been proven to be safe or effective through the regular process in Canada. In other words, non-standard interventions include treatments that are not part of the accepted standard of care for a specific condition.*

For example, stem cells are a standard of care treatment for leukaemia patients who may benefit from receiving a stem cell transplant, often known as a bone marrow transplant. However, there are other kinds of stem cell treatments advertised that fall in the non-standard category

Follow-up (if needed): What makes you trust (or not trust) a health care professional's advice? Does it matter to you whether or not they are regulated? Why or why not?

Prompt (if needed): *Healthcare professions typically have regulatory bodies, like medical boards or nursing associations. These organizations set rules, licensing standards, and codes of conduct for healthcare professionals. They evaluate the qualifications of new professionals, track their ongoing competence through continuing education, and handle complaints or disciplinary actions when needed.*

Question 6: What is your understanding of how new medical treatments are approved in Canada?

Prompt (if participant asks for more information): *Health Canada is the federal department responsible for overseeing various aspects of public health, including regulatory approvals for drugs and medical devices, food safety, health promotion, and disease prevention. On the other hand, policies for the practice of medicine are regulated by provinces, which assign this authority to the Colleges of Physicians and Surgeons.*

Follow-up: Do you think Health Canada plays an important role in making sure treatments offered to patients are safe and effective? Why or why not?
Do you think professional regulation (such as the colleges of physicians and surgeons) play important roles in making sure that treatments offered to patients are safe and effective? Why or why not?
What factors influence your level of trust in regulatory bodies when it comes to ensuring safety and effectiveness of new treatments?

Ending Questions:

Question 1: Can you please tell me about your previous education or professional background?

Question 2: How would you describe your support network as it relates to managing your condition? (Do you live with someone who provides support?)

Appendix B: Consent Form

Project Title:

Exploring Factors That Influence Trust in Non-Standard Stem Cell Therapies among Patients with Musculoskeletal Disorders

Researcher(s): Marina Shaker, Graduate Student, Johnson Shoyama Graduate School of Public Policy, University of Regina, 647-702-0180, MSP201@uregina.ca

Supervisor: Dr. Amy Zarzeczny, Associate Professor, Johnson Shoyama Graduate School of Public Policy, University of Regina, 306-337-3345, amy.zarzeczny@uregina.ca

Purpose(s) and Objective(s) of the Research:

- This research project aims to understand what factors influence patients' trust in non-standard stem cell interventions (SCIs) and how they perceive the role of regulatory bodies like Health Canada in evaluating and supervising these treatments. Stem cell interventions (SCIs) have been investigated as a possible way to treat chronic illnesses that current treatments may not be able to fully address. Previous studies have demonstrated promising outcomes for some interventions while others highlighted a diverse array of potential risks. This project aims to explore the factors that motivate the trust of patients with musculoskeletal conditions in non-standard therapies and the practitioners providing them, and to examine understanding of the role of professional regulation. This understanding will be relevant to policy development and regulatory reform for innovative regenerative medicine therapies.
- This research is an essential component of my master's degree requirements. The data collected from this study will be included in my master's thesis. The outcomes of this study may be disseminated through academic publications and presented at conferences to contribute valuable insights to the broader scientific community and policymakers.

Procedures:

- If you decide to participate in this research, you will be invited to a single interview that will take approximately 45 minutes to 1 hour. In the event the interview exceeds the allocated time of 1-hour, I will ask for your verbal consent five minutes before the end of booked interview time and will confirm with you if you would like to stop the interview (1), consent to continue until all the interview questions are discussed (2), or reschedule for another time (3). Please note that if you opt for option 3, we need to re-obtain your verbal consent at the beginning of

the rescheduled interview. After obtaining your consent, it will be logged, and a record of all consents will be securely stored in a password-protected file on FILR, the University's managed data storage system.

- The online interviews will be held via Zoom, an online video/audio meeting software service. You do not need a Zoom account to join meetings as a participant. Access to the meeting space is secured using a unique meeting ID number and passcode. A link, containing the meeting ID and passcode, will be provided to you by the host. Following the link will open your web browser, or an installed version of the Zoom desktop or mobile client (see https://zoom.us/download), and take you to the virtual meeting. The meeting ID and passcode will also be sent to you, and you can enter that information directly into the Zoom web interface (at https://zoom.us/join) or the installed program. Participants will enter a waiting room where the principal investigator will admit them to the meeting. The meeting will be subsequently locked to prevent anyone else from joining the meeting once the interview begins.
- With your permission, the interview will be recorded and then transcribed for analysis. All recordings will be stored on FILR, which is the University's managed data storage system and will be accessed through the primary researcher's computer –which is password protected (and not to a Zoom cloud server).
- During this session, you will be asked about your thoughts on stem-cell based therapies to manage your condition, and about different factors that contribute to your levels of trust in these interventions. At the start of the interview, you will be asked a few personal questions about your experience managing your condition. These will be followed by questions around different factors that shape your trust in stem cell-based therapies and how they are regulated. **Please note that you do not need to have any prior knowledge or experience using stem cell therapies** as you will be provided with sufficient background information during the interview. You also don't have to answer any questions that you don't feel comfortable with.
- Please feel free to ask any questions regarding the procedures and goals of the study or your role.

Funded by:

This research is related to a project funded by the Stem Cell Network, as part of the Translation & Society Team Award Program. The title of the related project is "Law, Public Policy and Social License for Next-Generation Regenerative Medicine". The results of the research could be shared with those who provided funding.

Potential Risks:

There are no known or anticipated risks to you by participating in this study interview. However, if you feel any discomfort during the interview, please inform the interviewer if you would like to reschedule or terminate your participation. We acknowledge that there are inherent security issues when using zoom and email as a communication tool. Zoom ensures the security of the communication amongst all participants through encryption of data in

transit and at rest, and meets industry and security organization standards (SOC 2; FedRAMP; GDPR,CCPA, COPPA, FERPA, and HIPAA; Privacy Shield Certified; and TrustArc Certified Privacy Practices and Statements). By default, emails are not encrypted and are vulnerable to interception by outside sources or someone may see that you are involved in this research if you leave your browser open. We will use the phrase "Regulation of Stem Cell Therapies" in the subject-line of all email correspondence. Thus, you will know the email is from us and recommend you submit any email queries using the same term.
It is possible that the topics of discussion may cause some participants emotional discomfort. The following resources are available for counselling and support:
https://sk.211.ca
HealthLine 811 - https://www.saskatchewan.ca/residents/health/accessing-health-care-services/healthline;
Canadian Mental Health Association - https://cmha.ca/find-help/find-cmha-in-your-area/
Crisis Services Canada - https://www.crisisservicescanada.ca/en/
Mobile Crisis Services (Saskatchewan) - https://mobilecrisis.ca

Potential Benefits:

There is no guarantee that you will benefit directly from participating in this study. However, the interviews will provide you with the opportunity to voice your opinion on innovative medical interventions and will hopefully be relevant to policy decisions regarding future governance of stem cell interventions.

Compensation:

- For participating in this research project, you will be entered in a draw to win one of three Amazon gift certificates valued at $50 each. The participants' pseudonyms will be entered into a computer-generated random selection website to choose the winners. The odds of winning this gift card will depend upon the number of participants who complete the interview, but will be less than 50%. In order to comply with University policy, recipients of cash or gift cards must sign a Participant Receipt of Compensation Form. Participant Receipt of Compensation Forms will be stored for 7 years in a sealed envelope within a secure file in Financial Services at the University of Regina. The envelope will only be opened in the event that the file is part of a financial audit. The only information in the file will be your name and the type and amount of compensation you received. All email communications will not contain any information about the study and will be deleted immediately upon receipt of the form.
- You will still be eligible to win even if you stop the interview or withdraw later from the research.

Confidentiality:

- You will be asked to join the interview from a private space where your responses cannot be overheard. You will be asked to turn off your camera to ensure the recording captures audio data only.

- All digital copies of documents and recordings will be identified only by a code number or pseudonyms and will be kept on FILR, which is the University's managed data storage system and will be accessed through the primary researcher's computer –which is password protected. No hard copies of transcripts will be made. You will not be identified by name in either the recording or the transcript. Participants will not be identified by name in any reports after the study is completed.

- The data from this research project will be published and presented at conferences; however, your identity will be kept confidential. Although we may report direct quotations from the interview, you will be given a pseudonym, and all identifying information (i.e location, etc) will be removed from our report. The use of a pseudonym will protect your privacy. If we decide to use a quotation from you in a report or publication that may identify you, we will check it with you first. To protect your confidentiality, you will receive the quotation and a Transcript Release Form as password protected files in two emails (one email will contain instructions to access the transcript and the other will contain the password to access the transcript). If you do not respond to this email or a subsequent reminder, we may include quotation but will keep any identifying information confidential.

- We will use email for communication. We acknowledge that there are inherent security issues when using email as a communication tool. Typically, emails lack encryption and can be susceptible to interception by external parties. There's also the possibility that your involvement in this research may be visible if you leave your browser open. To address these issues, we will consistently use the subject-line "Regulation of Stem Cell Based Therapies" in all email communications, allowing you to easily identify our messages. We recommend you submit any email queries using the same phrase. We also encourage you to refrain using or providing your work email and use your personal email account instead.

- All data will be collected by the principal investigator, Marina Shaker. The principal investigator will be responsible for data storage. Both the transcript and the recorded data from the interview on Zoom will be saved as a file on the principal investigator's password protected FILR account. The automatic transcript feature will be enabled during the Zoom session to generate live transcripts that will be extracted and saved on FILR as well. The automatic transcript will be used as the basis for preparing a corrected transcript with the aid of the recording. The final transcript will receive a code and will be saved in a file on the principal investigator's FILR account and will be accessed through password protected computer for analysis, and the audio recording will be deleted. Zoom cloud will be

disabled to ensure none of the study data will be saved on the cloud. The principal investigator will use Zoom and NVivo 12 (for data analysis) and has access to licensed accounts purchased by the University of Regina.

- The identifiable information collected such as full name and email will be stored on master list sheet kept on FILR, the University's managed data storage system, and will be accessed through the primary researcher's computer. Your contact information will be deleted after data collection is completed. After seven years, all of the digital data collected for this research, such as transcripts or any notes, will be deleted. Additionally, my thesis supervisor, Dr. Amy Zarzeczny, will maintain secure access to all the study files post study to assure that if there were participant concerns that information is accessible to my supervisor even after I graduate.

Right to Withdraw:

Participation in any phase of this study is completely voluntary. You are free to answer only those questions that you are comfortable with. Should you wish to withdraw, your decision to withdraw will not influence your relationship with the researcher in any way, and you will still be entered in the gift card draw. If you decide to participate in the interview now, you may withdraw in the future without any explanation/reason required, or any consequences.. **You will have 1 week after the interview to decide to withdraw your data**. After that time, your data cannot be withdrawn due to the nature of the data anlysis. At this stage, the research team will begin the process of constructing themes, concepts, and categories from de-identified data. If you decide to withdraw during that time, please contact the principal investigator

Follow up:

Once the interviews are completed and data are analyzed, we plan on disseminating the final findings through peer-reviewed journals. In the event that the dissemination of our research findings through peer-reviewed journals is expected to take some time, we want to assure you that we are committed to ensuring you have access to our results in a culturally appropriate and accessible manner. You will be able to view the study findings through the University of Regina library: https://ourspace.uregina.ca by searching up the primary researcher's name Marina Shaker to find the completed thesis, which is expected to be available sometime in 2024-2025. Your participation in this study is greatly appreciated, and we are dedicated to keeping you informed in an accessible way.

Questions or Concerns:

- If you have any further questions, concerns, or want clarification regarding this research and/or your participation, please contact the principal investigator using the contact information at the top of page 1.

- This project has been approved on ethical grounds by the University of Regina Research Ethics Board on (insert date). Any questions regarding your rights as a participant may be addressed to the committee at (306-585-4775 or research.ethics@uregina.ca). Out of town participants may call collect.

VERBAL CONSENT

You can provide your consent verbally at the beginning of the interview. I will read the key sections of the consent form and you need to indicate verbally that you understand the description provided. You are also given the opportunity to ask questions before providing your verbal consent.

I agree for my email address to be entered into Amazon.ca so I can obtain the gift card. Yes / No

_____	_____	_____
Name of Participant	*Researcher's Signature*	*Date*

Appendix C: Research Ethics Board Approval Certificate

[Converis] REB Application #411 Exploring Factors That Influence Trust in Non-Standard Stem Cell Therapies Among Patients with Musculoskeletal Disorders

R research.ethics@uregina.ca
To: msp201@uregina.ca

Reply Reply all Forward ...
Thu 12/21/2023 3:43 PM

Status change comment:
Happy holidays and good luck with your research. Kim

Research Ethics Board (REB): Application # 411
Title: Exploring Factors That Influence Trust in Non-Standard Stem Cell Therapies Among Patients with Musculoskeletal Disorders

Approval Date: 21-Dec-2023
Renewal Date: 21-Dec-2024

- PI: Marina Shaker
- Supervisor: Amy Zarzeczny

The University of Regina Research Ethics Board has reviewed the above-named research project. The proposal was found to be acceptable on ethical grounds. The principal investigator has the responsibility for any other administrative or regulatory approvals that may pertain to this research project, and for ensuring that the authorized research is carried out according to the conditions outlined in the original protocol submitted for ethics review. This Certificate of Approval is valid for the above time period provided there is no change in experimental protocol, or related documents.

Any significant changes to your proposed method, procedures or related documents should be submitted as an amendment for Research Ethics Board consideration in advance of implementation.

ONGOING REVIEW REQUIREMENTS
In order to receive annual renewal, a status report must be submitted to the Research Ethics Board for consideration one month in advance of the current expiry date each year the study remains open, and upon study completion. Please refer to the following website for the renewal and closure forms:
https://www.uregina.ca/research/for-faculty-staff/ethics-compliance/human/ethicsforms.html

- Kim Dorsch
  Research Ethics Board Chair
  University of Regina