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SOCIAL PHARMACEUTICAL INNOVATION

Master's Thesis – Master Innovation Sciences

The Knowledge Capacity and Epistemic Contribution of Social Pharmaceutical Innovation Actors

by

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Abstract

Introduction | Unmet medical needs are still a problem for patients that suffer from severe diseases. Social Pharmaceutical Innovations are multi-actor collaborations that attempt to address these unmet medical needs. However, it is unknown how Social Pharmaceutical Innovation actors achieve this and what their individual contribution is to the knowledge of finding alternative medical approaches. Therefore, this thesis examines the process of knowledge creation, exchange, and application, or knowledge capacity, of Social Pharmaceutical Innovation actors and their epistemic contribution to this process. The aim of this thesis is to gain more insight into the management and execution of knowledge processes in Social Pharmaceutical Innovations. The case study of the off-label use of lidocaine on pain management for pancreatic cancer patients was used to represent this research.

Methods | Ten semi-structured interviews were conducted with key actors of Social Pharmaceutical Innovations and hospitals. In addition, document analysis was performed on the case study of off-label use of medication and lidocaine.

Results | The findings showed that knowledge is created through the sharing and assessment of knowledge. Knowledge is shared internally through meetings, discussion, and dialogue, and externally through written publications and congresses. Newly created knowledge is applied in new or changed projects, protocols, or techniques. Furthermore, Social Pharmaceutical Innovations involve and include various actors with different perspectives, expertise, and experiences. They collaborate toward a shared goal of identifying and addressing unmet medical needs.

Discussion/Conclusion | The analysis of the results showed that the exchange of knowledge is a continuous process that goes back and forth and is interconnected with the creation of knowledge. This knowledge is eventually applied to new projects or techniques. This process is performed by multiple actors that work toward a shared goal and plan to identify and address unmet medical needs. Further research is necessary for an in-depth examination of this process in Social Pharmaceutical Innovations.

Preface

Herewith, I present you my master's thesis: “The Knowledge Capacity and Epistemic Contribution of Social Pharmaceutical Innovation Actors.” This thesis is written to fulfill graduation requirements for the master’s program Innovation Sciences at Utrecht University. I was engaged in writing my research proposal and this thesis from November 2022 to June 2023.

During my master’s, I was mainly interested in digital innovations in the healthcare industry because of my biomedical background. However, I always have been interested in the social aspect of innovation and how this contributes to social problems. Therefore, I chose to finish my last project as a student with research focused on social innovation in the pharmaceutical and healthcare industry, particularly Social Pharmaceutical Innovation. I have learned a lot of new theories from the literature review I conducted. In addition, I also gained more experience with conducting interviews and executing qualitative research. This was professionally as well as personally very valuable for me.

I would like to thank my supervisor dr. Tineke Kleinhout-Vliek, for the guidance and support during the process. I appreciated the critical feedback, discussion moments, collaboration, and nice conversations. Thanks to my supervisor, I was able to challenge myself and write this thesis as the final product of my master’s.

And of course, I would like to thank you, my reader. I hope you enjoy your reading.

Samantha van Brakel

Houten, June 19th, 2023

List of Abbreviations

Dutch Pancreatic Cancer Group	DPCG
Ministry of Public Health and Environment	RIVM
Social Innovation	SI
Social Pharmaceutical Innovation	SPIN

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1. Introduction

Pancreatic cancer is the fourth leading cause of cancer-related death worldwide (Zhao & Liu, 2020). This type of cancer is an aggressive malignancy with a short life expectancy and suffering disease course due to the lack of effective treatment (Oberstein & Olive, 2013). It is predicted that moving towards 2030, pancreatic cancer will be the second leading cancer-related death worldwide (Andersson et al., 2022). Pancreatic cancer greatly impacts patients' quality of life (Andersson et al., 2022; Mackay et al., 2022). The most common impact of pancreatic cancer on a patient's quality of life is severe pain that becomes worse as the disease progresses (Coveler et al., 2021).

Pancreatic cancer-related pain is treated by opioids, such as morphine (Oberstein & Olive, 2013). This medication is not effective in the advanced stages of pancreatic cancer which leads to extra pain control, for instance, a surgery that anesthetizes nerves near the pancreas (Coveler et al., 2021). The side effects of these methods greatly impact the quality of life that results in mental and physical decline (Hameed et al., 2010; Zhao & Liu, 2020). Several studies have examined alternative treatments to address this pain and improve the quality of life. These alternative treatments include the off-label use of medication. Off-label use means that medication is used for an unapproved indication, age group, dosage, or route of administration (European Medicines Agency, 2022).

Strict standards and requirements need to be considered for the prescription of off-label used medication (Caminada et al., 2021). In the Netherlands, the off-label use of medication can only be prescribed by a CCPS-registered doctor if general guidelines or standards for the treatment have been developed (RIVM, 2017). However, if these standards are still in development, the prescriber must perform thorough research into the off-label treatment and is required to consult and discuss this with another doctor and pharmacist (Inspectie Gezondheidszorg en Jeugd, 2018; Rusz et al., 2021). After this consultation and discussion, the three professionals must agree on the prescription of the off-label medication prior to proposing it to the patient. This proposal includes all risks and side effects and must be signed by the patient for mutual agreement (Zorginstituut Nederland, 2021).

Off-label prescription is only proposed if it is mentioned for discussion by the doctor or patient. This means it is not a standard procedure that is considered during the treatment process and thus not offered to every patient. This can lead to an unfair treatment process as some patients are excluded from the knowledge that can possibly be effective solutions for their medical needs. This is known as epistemic injustice, which means unfair treatment in the sense of knowledge, participation, and understanding of an individual (Carel & Kidd, 2014; Fricker, 2007). Due to this, the medical needs of these individuals remain unaddressed. These needs are characterized as unmet medical needs, which are individual or

group medical-related needs that are not addressed by the current treatment or diagnosis (Zhang et al., 2021).

Currently, there are various healthcare-related socially driven organizations that attempt to address unmet medical needs. These social organizations are known as *Social Pharmaceutical Innovations* (SPINs). SPINs consist of a diverse set of actors that collaborate to address the problems and injustices concerning the accessibility, affordability, and availability of medication (Douglas et al., 2022). In the Netherlands, there are SPINs that collaborate on the study of LIDOPAN. LIDOPAN is a clinical study that examines the effect of intravenous infusion of lidocaine on pain in pancreatic cancer patients. Lidocaine is a local anesthetic with a narcotic effect and recent studies have discovered it also has an anti-inflammatory effect. (Berger et al., 2014; Cruz et al., 2017; Golzari et al., 2014; Karnina et al., 2021). Inflammation is recognized as a key factor in cancer-related pain and thus it is crucial to gain more insight into its potential role in cancer-related pain management (Ji et al., 2018; Laird et al., 2013; Omoigui, 2007).

The patient advocacy group *Inspire 2 Live* has taken the initiative to conduct the LIDOPAN study. Since 2020, this organization works globally with the mission to represent the patient by being *'the patient's voice in cancer'* (Inspire 2 Live, 2020). *Inspire 2 Live* strives for more patient involvement in their treatment process and encourages other health professionals to adopt and implement this. Furthermore, the *Dutch Pancreatic Cancer Group (DPCG)* is also engaged in the LIDOPAN study. This organization consists of various medical experts and researchers that aim to improve the diagnostics and treatment of pancreatic cancer patients that enhance their quality of life (Dutch Pancreatic Cancer Group, 2022).

SPINs collaborate to create new possible medical solutions that are of importance for addressing unmet medical needs. However, SPIN is a relatively new concept since 2022, and the understanding of its nature of processes still has some limitations (Douglas et al., 2022). It is still unknown how the process of knowledge creation, exchange, and application is managed and executed in SPINs, and what the contribution of the various actors is to this process (Douglas et al., 2022). In addition, it is not clear how actors' knowledge is valued and included in this process (Douglas et al., 2022), thus raising questions about epistemic injustice. Therefore, the goal of this research is to gain more insight into how knowledge is created, exchanged, and applied by SPIN actors and what their epistemic contribution is to this process. This will be performed by addressing the following research question:

"*How do Social Pharmaceutical Innovation actors create, exchange, and apply knowledge, and what is their epistemic contribution to this process*?"

This thesis will give more insight into pharmaceutical and healthcare-related social innovation. Since the pharmaceutical and healthcare industry is highly regulated and institutionalized, it is essential to re-think innovation in these sectors to create more space for alternative innovation pathways (Douglas et al., 2022). SPINs have the potential to address this and thus it is crucial to gain more insight into their processes. This thesis contributes to the existing literature on the nature of SPIN processes concerning their capacity to create, exchange, and apply knowledge, and how the various actors in this collaboration contribute to this process. These factors are key to understanding how SPINs collaborate, involve and include different actors' knowledge, and generate new innovative and alternative solutions to address unmet medical needs (Douglas et al., 2022).

Furthermore, the obtained knowledge of these processes in SPINs is valuable for the contribution to a better socio-technical analytical framework for understanding and helping to improve the implications and impacts of pharmaceutical R&D practices (Douglas et al., 2022). In addition, this thesis can be valuable for other healthcare, research, and governmental institutes to gain more insight into the importance of finding alternative approaches to address unmet medical needs.

The outline of this thesis will start with a literature review that addresses the concepts of social innovation, knowledge creation, exchange, and application, SPINs, and epistemic injustice. This is followed by the methodology that elaborates on the research design and data collection, and the explanation of the results. Furthermore, a comprehensive discussion will be given resulting in a conclusion concerning the research question.

2. Literature Review

The Role of SPINs in Healthcare-Related Social Innovation

The literature review will shed light on the concepts of social innovation, knowledge creation, exchange, and application, SPINs, and epistemic injustice. First, a definition of social innovation will be given followed by an explanation of its relationship to knowledge creation, exchange, and application. After this, the concept of SPINs will be elaborated upon, and the definition and link with epistemic injustice will be explained.

2.1 Social Innovation and Its Transformation Towards Empowerment

Social innovation (SI) has various definitions. Moulaert et al., (2005) define it as a phenomenon that leads to a better inclusion of excluded groups and individuals and thus increased social justice. On the other hand, Avelino et al., (2019) define SI as changing social relations involving new ways of knowing, organizing, framing, and doing. In addition, Avelino et al., (2019) highlighted the intricated issues of (dis)empowerment because SI frequently involves numerous groups of people and there is no evident group of actors that should or should not be empowered. Other scholars define SI as collaborations to address unmet social needs and improve the welfare or well-being of individuals, groups, or an entire society (Grimm et al., 2013; Osburg & Schmidpeter, 2013). Others again define it as a process of empowering and promoting collective action through transforming power relations in multi-actor collaborations where end-users are involved (Medina-García et al., 2022). Important commonalities between these definitions include the transformation of social relations, collective action, and inclusion of individuals or groups. These definitions differ most importantly in aspects of their goals, for example, Moulaert et al., (2005) emphasize increasing social justice as Grimm et al., (2013) and Osburg & Schmidpeter, (2013) highlight the fulfillment of unmet social needs. I conclude that social innovation is a process that includes and empowers neglected individuals or groups by changing their social relation dynamics and creating new relationships. Thus, for SI, different collaborations are needed between groups or actors (Pache et al., 2022).

Social innovation typically comprises multi-actor collaborations, or active collaboration between various actors, including academia, civil society, politics, and the private sector, as well as end users (Avelino et al., 2019; Medina-García et al., 2022). Involving end-users and/or neglected individuals and groups can be difficult. An important reason is that these individuals or groups often do not have the required knowledge and expertise to understand the concepts that are discussed (Callens, 2023). Because of this, an important role of these collaborations is to identify a common language to communicate and develop a better understanding of existing problems (Brix, 2017). The knowledge capacity, or the ability

to generate, distribute, and apply new knowledge (Fong, 2003), is a crucial part of such a common language and understanding of multi-actor collaborations (Castaneda & Cuellar, 2020).

2.3 Knowledge Capacity in Multi-Actor Collaborations

The process of knowledge capacity is rather complex in multi-actor collaborations. To better understand the creation, exchange, and application of knowledge, or 'knowledge practices', I will delve deeper into each individual knowledge practice, starting with the creation of knowledge.

2.3.1 Knowledge Creation

Knowledge creation, or the generation of new knowledge, is a social and cognitive process that can be performed individually or socially (Mulyaningsih et al., 2016). In multi-actor collaborations, this is executed on a social level because multiple actors contribute to this process (Medina-García et al., 2022). The actors in these collaborations have different backgrounds, perspectives, experiences, and expertise which varies their knowledge base (Medina-García et al., 2022). These different knowledge bases can be bundled together in multi-actor collaborations to identify knowledge gaps and generate new ideas (Fong, 2003). This is performed by discussing complementary themes, listening to arguments, and developing a joint solution (Fong, 2003).

Effective knowledge creation is dependent on the ability to learn, or absorptive capacity (Cohen & Levinthal, 1990). Cohen & Levinthal, (1990) define absorptive capacity as the ability to acknowledge, combine, and apply new knowledge. This ability is necessary to understand, interpret, and absorb knowledge that is shared (Cohen & Levinthal, 1990; Yildiz et al., 2019). Therefore, the exchange of knowledge is interconnected with effective knowledge creation (Yildiz et al., 2019).

2.3.2 Knowledge Exchange

Knowledge exchange involves the distribution of knowledge between individuals or groups (Pérez-Luño et al., 2019). This process can occur in different ways, such as publications, reports, workshops, and dialogue (Castaneda & Cuellar, 2020). Nevertheless, not all knowledge can be easily shared and understood. Knowledge can be divided into tacit and explicit knowledge. Tacit knowledge refers to an individual's experience, thinking, and feeling, while explicit knowledge refers to knowledge that can be communicated, for instance, verbally or in written documents (Kothari et al., 2012). Tacit knowledge is hard to communicate in a logical form because it is something an individual possesses subconsciously (Kothari et al., 2012; Venkitachalam & Busch, 2012; Zheyu et al., 2021). To better understand the process of sharing tacit and explicit knowledge, Nonaka developed a dynamic model that explains this process in different stages. Nonaka, (1995) describes the stages of socialization, externalization, internalization, and combination (Figure 1).

First, socialization is the transfer of tacit knowledge from one individual to another (Nonaka, 1995). This phase requires prior knowledge and shared experiences to learn by direct action (Pérez-Luño et al., 2019; Sarayreh et al., 2012). An example of this is observing another individual's behavior in the same environment (Zheyu et al., 2021). Second, tacit knowledge is transformed into an understandable form of explicit knowledge through externalization (Nonaka, 1995). Nonaka, (1995) describes this as the articulation of one's own tacit knowledge which are images, ideas, words, or metaphors. Thus, externalization can be performed by, for instance, expressing ideas in words or metaphors face-to-face among individuals or groups (Sarayreh et al., 2012). Following this, explicit knowledge is shared among groups in the combination phase. In this phase, explicit knowledge is shared, for instance, through documents, briefings, e-mails, and databases (Brix, 2017). Lastly, internalization takes place when explicit knowledge in individuals is absorbed and understood into tacit knowledge (Kothari et al., 2012; Nonaka, 1995). The new tacit knowledge is 'actionable' through learning, experimenting, and performing actions, such as the actual doing or through simulations (Sarayreh et al., 2012; Venkitachalam & Busch, 2012).

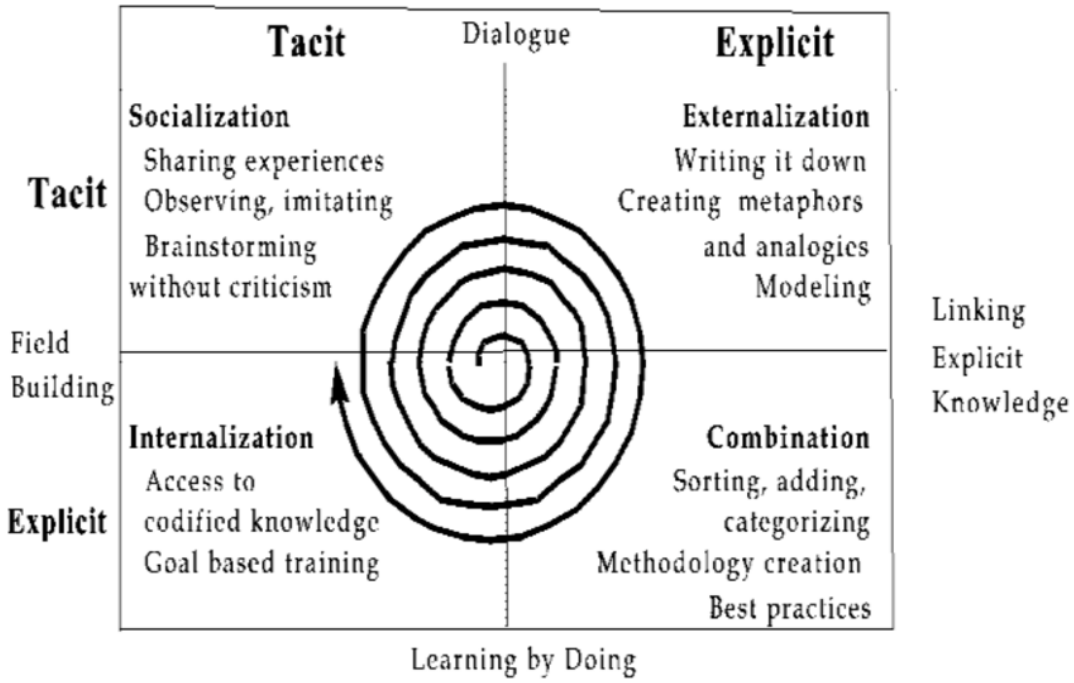

Figure 1: Overview of the knowledge exchange process of Nonaka. First, socialization occurs through dialogue that transmits tacit knowledge from individual to another individual. Second, externalization transforms this tacit into explicit knowledge. Then, this explicit knowledge is transferred among group, which is called combination. Lastly, the explicit knowledge is transformed to tacit knowledge within the group. This process is known as internalization (Markopoulos & Kornilakis, 2016; Nonaka, 1995)

After the process of knowledge exchange, new knowledge can be created. This newly created knowledge can be applied to existing solutions or real-world problems and is a key facilitator for innovation and performance (Ode & Ayavoo, 2020).

2.3.3 Knowledge Application

Knowledge can be applied, for instance, to new or changed policies, programs, products, and case studies (Pérez-Luño et al., 2019; Sarayreh et al., 2012). Effective knowledge application depends on clear communication, capabilities, and resources (Ode & Ayavoo, 2020). Gold et al., (2001) highlighted that the process of knowledge application is not well examined and documented because it is often taken for granted. In addition, Song et al., (2005) mentioned that knowing when to apply knowledge is a talent and therefore this process is hard to analyze.

The process of knowledge capacity can be valuable for multi-actor collaborations to enhance innovation (Brix, 2017; Fong, 2003). Particularly in highly regulated and institutionalized industries, such as the pharmaceutical and healthcare industry, innovation is essential to find alternative approaches that address existing problems, for instance, unmet medical needs (Douglas et al., 2022). Therefore, they developed the concept of SPIN which are novel forms of multi-actor collaborations that break with standard pharmaceutical innovation practices to produce accessible, effective, and safe alternative approaches (Douglas et al., 2022).

2.4 Knowledge Capacity in Social Pharmaceutical Innovations

Douglas et al., (2022) identify three types of SPINs. The first type engages in the development of other forms of licensing and provision, for instance, public sector manufacturing, magisterial preparations, usage, and early access schemes (Douglas et al., 2022). The second type focuses on alternative regulatory frameworks for coverage, including pricing and reimbursement schemes (Douglas et al., 2022). Lastly, the third type is novel R&D partnerships across public, not-for-profit, and private sectors. These collaborations can contribute to novel technological platforms, systems, and the development of new medication (Douglas et al., 2022).

It is known this type of SPIN works on diagnostics, development of new medication, repurposing existing drugs, and incentive clinical research (Douglas et al., 2022). However, in-depth knowledge about how they work on these solutions is lacking (Douglas et al., 2022). It is not clear how they use and manage their knowledge capacity to develop innovative medical solutions (Douglas et al., 2022). This information is needed to understand the internal processes of this type of SPIN (Douglas et al., 2022).

In addition, studying knowledge capacity in SPINs is particularly relevant to examine the individual contribution of different actors to this process. Douglas et al., (2022) highlighted that this type of SPIN emphasizes the crucial role of collaboration between various actors which includes the significance of patient empowerment that guides research based on their needs (Douglas et al., 2022). Nevertheless, how these actors contribute to the process of knowledge capacity is still unknown. There is a possibility that the voices, experiences, and knowledge of actors are not valued and are considered irrelevant (Byskov, 2021). This phenomenon is described as epistemic injustice (Fricker, 2007).

2.5 Epistemic Injustice and Social Pharmaceutical Innovations

Fricker, (2007) defines epistemic injustice as the neglect of an individual's knowledge to be not relevant enough and thus undervalued. This can be experienced by individuals who are unfairly discriminated against their knowledge, including silencing and exclusion (Byskov, 2021).

Carel & Kidd, (2014) highlighted that patients are particularly vulnerable to epistemic injustice due to a lack of attention to individual needs. Patient testimonials are often considered irrelevant, too emotional, time-consuming, and confusing (Grimm et al., 2013). Other scholars mentioned that patients cannot contribute relevant knowledge because they do not have medical expertise (Kidd & Carel, 2017; Pot, 2022). The involvement of the knowledge of this group is important to understanding and improving current problems in this industry (Grim et al., 2019; Kidd & Carel, 2017). SPINs attempt to involve this group of actors in their collaboration (Douglas et al., 2022). However, Kok et al., (2022) highlighted that involvement does not guarantee understanding and valuation of knowledge of these actors. Kok et al., (2022) also point out that institutionalized structures can promote or hinder the epistemic contribution of an actor (Kok et al., 2022). Epistemic contribution is the ability to express the epistemic subjectivity of an individual by sharing their beliefs and interpretations (Fricker, 2015). Since this is an important feature to consider in the knowledge capacity to empower this group (Fricker, 2015), I will investigate the epistemic contribution of SPIN actors to this process.

In conclusion, SPINs are multi-actor collaborations that aim to find alternative medical approaches to address unmet medical needs. However, the process of knowledge capacity in SPINs on how they develop these solutions remains unknown. In addition, the actor's contribution, or epistemic contribution, to this process is not clear. Therefore, I aim to address these questions in this thesis.

3. Methods

3.1 Research Design and Methods

This thesis aims to examine the knowledge capacity of SPIN actors and their epistemic contribution to this process. SPINs consist of actors with various backgrounds and expertise, for instance, doctors, surgeons, researchers, lawyers, nurses, and patients. Therefore, a qualitative research design was chosen to better understand the concepts, opinions, and experiences of these diverse actors (Hashmi et al., 2017). Data were collected through document analysis and interviews.

3.1.2 Document Analysis

Document analysis is a method to interpret, review, and evaluate written documents, such as newspapers, webpages, memoranda (written diplomacy messages), and books. The researcher interprets these written data to give voice and meaning related to the research question (Bowen, 2009).

3.1.3 Semi-Structured Interviews

Semi-structured interviews were conducted based on the combination of predetermined and spontaneous open questions. These interviews allow the interviewer and interviewee for open-ended responses, follow-up questions, and free-flowing thoughts and opinions to perform an in-depth examination of particular responses (Adams, 2015; McIntosh & Morse, 2015).

3.1.4 Triangulation

The combination of document analysis and semi-structured interviews leads to triangulation. Triangulation is a research technique using multiple data collection methods, data sources, or theories (Nightingale, 2020). This technique can help improve credibility, identify biases, and increase the ability to interpret the findings (Carter et al., 2014; Thurmond, 2001).

3.1 Data Collection

3.1 Document Analysis

Data was collected for document analysis on memoranda (n = 2) and public reports (n = 2) of the Ministry of Public Health and Environment of the Netherlands (RIVM), and webpages (n = 2) of DPCG and Inspire 2 Live concerning the use of off-label medication and lidocaine. The memoranda were written by two independent law firms and obtained from a respondent active in the patient advocacy group Inspire 2 Live.

3.2 Semi-structured Interviews

The interviews consisted of two parts. The first part considered the thoughts, beliefs, and experiences on the off-label use of medication, in specific lidocaine. This part was asked in detail to participants that had a function familiar with this topic, such as doctors and researchers. Participants that were not familiar with off-label use were given a short elaboration on the topic and asked about their opinion on this. This gave insight into ideas and opinions on the off-label use of medication and lidocaine by different actors. Other questions in this part addressed the collaboration between patients and doctors, the valuation and assessment of opinions and knowledge of patients, and the quality of life of pancreatic cancer patients. The second part focused on questions about the organization and its knowledge capacity. The questions in this part addressed the in- and external collaborations, the generation, distribution, assessment, and application of knowledge, and the type of actors active in the organization. The interview guide for these predetermined questions is available in *Appendix I.*

A total of 10 participants were interviewed in the Netherlands. The interviews were conducted with representatives from patient participation and client board groups from academic hospitals (n = 2), nurses (n = 2), patient advocacy groups (n = 2), and research institutes and universities (n = 4). These participants were selected based on their function in relevant organizations. The interviews were performed and recorded between 2021 and 2023 in person or in Microsoft Teams. The duration of the interviews was approximately between 30 and 60 minutes long.

3.2 Data Analysis

The interviews were transcribed in the program Microsoft Word. This was done by performing non-verbatim transcription which does not describe every sound made during the interview. All transcriptions were checked for prevention of misunderstanding of quotes and statements by reading and simultaneously listening to the recording.

Data from document analysis and semi-structured interviews were analyzed through inductive coding. Inductive coding is a process that consists of open, axial, and selective coding, whereby written data is read and interpreted to develop concepts or themes (Chandra & Shang, 2019). First, open coding was conducted to structure the data into meaningful expressions by labeling concepts through single-word codes. Second, axial coding was performed to break down the research core topic by relating and creating linkages between data and order codes into categories. Lastly, selective coding was used to find relationships between categories and define them into one core category (Campbell et al., 2013). The coding process was performed in the program NVIVO 14. The coding schedule is presented in *Appendix II*.

3.3 Reliability and Validity

Several factors were considered to minimize threats to reliability and validity. Reliability and validity refer to the replicability and trustworthiness of the research (Leung, 2015). These concepts can be divided into credibility, dependability, confirmability, and transferability.

Credibility refers to the believability of the research findings by giving an accurate representation of the included participants (Shenton, 2004). Data triangulation was used to achieve credibility. The combination of multiple data collection methods helps to examine the consistency of the findings (Carter et al., 2014). In addition, credibility was addressed by the representativeness of the sample interviewees. This consisted of various actors that were affiliated with the research topic.

Dependability is the possibility to replicate the research and obtain similar findings (Shenton, 2004). This is achieved by making the interview guide and coding schedule available for other researchers. Similar findings should be obtained if similar participants are interviewed.

Confirmability is the degree to which the findings can be confirmed by others (Shenton, 2004). This was addressed by contacting participants to corroborate the results. This was done if there were any doubts considering the interpretation of quotes or statements. Participants were contacted by e-mail and asked for extra elaboration on particular quotes or statements.

Transferability refers to the generalizability of the research into other contexts (Shenton, 2004). The findings and conclusions can be used by other researchers to put it in a different perspective. For instance, this can be done by examining the processes of knowledge capacity and epistemic contribution in other or similar (social) organizations.

3.4 Ethical Issues

This thesis aimed to avoid ethical issues by allowing voluntary participation in the interviews. Participants are free to opt in or out of the research at any point in the process. This was done by asking participants to sign an informed consent. An informed consent (see *Appendix 1*) is a document that states the purpose of the research and the expectations from the participants. In addition, the identity of participants was made anonymous. No personally identifiable data was collected and published in this thesis. After completing the research, the thesis was shared with the participants.

4. Results

This chapter is divided into two sections. The first section will address the results of the knowledge capacity of SPIN actors. The second section will be focused on the epistemic contribution of these actors to this process. I will start with the findings of the knowledge practices exchange and creation.

4.1 Knowledge Creation, Exchange, and Application of SPIN Actors

4.1.1 Knowledge Exchange and Creation

Knowledge is shared internally and externally in different forms. The most common manner of knowledge sharing internally is through meetings and dialogue onsite or online. These meetings and conversations take place daily, monthly, or a couple of times a year.

> *"(...) in the end, there were six people who consulted daily from 9.30 to 10.30 A.M. for at least two and a half months about how we take this further, how do we get this out on the table, et cetera." (Participant 10, Patient, July 5, 2021)*

> *"We have a meeting every month to discuss things usually about AMC-related issues." (Participant 4, Hospital Client Board Member, March 14, 2023)*

> *"(...) and then we meet 4 times a year and on the same evening we have a workgroup meeting afterward." (Participant 7, Surgeon, February 27, 2023)*

According to Participant 8, (Patient Advocate, March 2, 2023), they had a virtual meeting every month on Wednesday from 3 P.M. until 5 P.M. These meetings focused on different themes concerning patient priorities, such as registries, pain management, personalized medicine, and tobacco control. It was highlighted that the topics are always related to the interests of cancer patients. The meetings are accessible before 3 P.M. to first have an informal chat. At 3 A.M. a presentation is given based on the content that will be discussed in the meeting. After the presentation, the others can ask questions, and bring up discussion points or input.

Participant 7 (Surgeon, February 27, 2023) mentioned that they have workgroup meetings 4 times a year. These meetings discuss a selection of new or the progress of existing research projects and allow others to ask questions, file for discussion, and give input. The results of the meetings will be discussed, and together new or adjusted research protocols will be developed step-by-step (Participant 7, Surgeon, February 27, 2023).

Both participants agreed that these meetings are valuable for effective collaboration. In addition, Participant 4, (Hospital Client Board Member, March 14, 2023) mentioned that through discussion and dialogue that consists of different opinions from a variety of actors with diverse backgrounds, one coherent opinion is eventually created. This indicates that knowledge is created through knowledge sharing and assessing it on opinions, expertise, experiences, perspectives, but also peer review. Peer review occurs throughout the process of the creation of new knowledge and before the application to, for instance, projects or publications. These organizations are also asked to peer review knowledge, such as project applications or publications, from other organizations.

> *"This is done through the classic scientific way, peer review. And so, peer review, but also discussion, is there a better method, but also the consideration of what is ethically correct." (Participant 8, Patient Advocate, March 2, 2023)*

> *"We are also asked as a scientific committee. Coincidentally, this week I wrote a letter about this, if someone submits a grant application, they ask us to send that protocol to the scientific committee, which will be assessed by us when we have a meeting." (Participant 7, Surgeon, February 27, 2023)*

The assessment of knowledge requires input from different perspectives and therefore patients are also involved in this process. According to Participant 5, (Researcher, March 24, 2023) it is mandatory to have a client board or patient participation group within the organizational structure of hospitals. Research institutes are also obligated to involve the opinion of patients (Participant 8, Patient Advocate, March 2, 2023). However, Participant 7, (Surgeon, February 27, 2023) mentioned that this group of actors often does not have in-depth medical expertise and finds it hard to understand the concepts that are discussed. Patients must have a certain knowledge base to fully understand and interpret these in-depth discussions. There are patients that are familiar with specific concepts because they do plenty of self-studies, for instance, by reading scientific articles (Participant 8, Patient Advocate, March 2, 2023). Patient Participation Organizations of hospitals offer courses to patients that are actively involved to help them to better understand medical concepts and extend their knowledge (Participant 6, Hospital Coordinator Patient Participation, March 13, 2023).

4.1.2 Knowledge Application

After the process of knowledge sharing and creation, these collaborations aim to apply the newly created knowledge. This is done by applying this knowledge in written publications, discussing the results at (inter)national congresses, and implementing new knowledge into new techniques and protocols. The application of knowledge is executed after all actors agree upon a shared vision that is valuable to apply (Participant 8, Patient Advocate, March 2, 2023; Participant 4, Hospital Client Board Member, March 14, 2023)

4.2 Epistemic Contribution of SPIN Actors

According to Participant 8, (Patient Advocate, March 2, 2023) the prescription of off-label treatment is a thorough process. Doctors must perform extensive individual research on the off-label treatment that is thereafter discussed with other health colleagues. Detailed information is given to the patient about all the benefits and risks if all parties agree on responsible treatment. The patient must always sign a document that states they agreed upon the prescriptive off-label treatment. In some cases, it is mandatory to deviate from standard protocols.

> *"(...) and the patient must always give consent and agree to the treatment by signing a document. So, the doctor must inform well, but the patient makes the final decision." (Participant 8, Patient Advocate, March 2, 2023)*

> *"As a rule, a doctor should be aware of treatment protocols and adhere to them. The doctor can, or in some cases even must, deviate from the treatment protocol, if the standard protocol for treatment of the patient's disease does not offer a solution and will not be a successful treatment." (Mischie, 2022)*

The process of the prescription of off-label used medication is similar to the participation in clinical trials. Participants can voluntarily apply, for instance, for the LIDOPAN study. This is done by discussing with their doctor whether they are eligible for this trial. The doctor gives detailed information on the advantages and disadvantages, such as risks and side effects. The participant is required to sign a consent form and is allowed to withdraw their consent at any time (Weda & Hegger, 2006).

The LIDOPAN study was set up to gain more insight into the efficacy of lidocaine on pain management for pancreatic cancer patients, and if this is valid for this indication.

> *"(…). So, that is a medicine that is registered for a technique that is already used. It is just not used specifically for this group. Only that is the difficult thing about off-label. This is a registered medicine and therefore not experimental, just not registered for this indication. It is now examined in this study whether it is also valid for this indication." (Participant 7, Surgeon, February 27, 2023)*

It was initiated in Rotterdam by anesthetists that contacted one of the co-founders of Inspire 2 Live and an advisor. In some hospitals, this is used as a standard pain treatment, and the literature shows that it is effective, however, for this indication it is believers and non-believers (Participant 11, Researcher, June 29, 2023). There is limited information on the effects, complications, and duration of intravenous lidocaine on pain. Pancreatic cancer patients are currently treated with morphine, but this still does not control their pain. It is mentioned that lidocaine is less intensive than morphine. Morphine is an effective type of pain management but decreases the quality of life which makes patients tired, sick, and inactive. Another option is surgery whereby doctors sedate nerves in the pancreatic ducts with endoscopy but that is an invasive intervention (Participant 8, Patient Advocate, March 2, 2023). According to Participants 8 and 11, (Patient Advocate, March 2, 2023; Researcher, June 29, 2023), lidocaine can function as an intermediate step prior to using morphine or surgeries.

> *"What we do with the lidocaine, well, you have paracetamol and ibuprofen that is all still fine. Then morphine is, a lot of patients have morphine but that is you get a lot of patients who are addicted, and you have people with side effects. And in many patients, it does not work or is not good enough. And we want as a step between the morphine and the invasive operations, so lidocaine is a good step to hope that patients need to use less morphine on the one hand." (Participant 11, Researcher, June 29, 2023)*

Now, LIDOPAN included 15 pancreatic cancer patients. These patients are given intravenous administration of lidocaine for 2 hours. They receive questionnaires about the effect of lidocaine on their pain after the treatment. Participant 11, (Researcher, June 29, 2021), mentioned that they measured this parameter through SF12, EQ5D, BPI questionnaires, and NRS scores to observe the level of pain and the effect of the treatment. This study is intended to improve the quality of life of pancreatic cancer patients, and it is mentioned that such studies are important to involve patients, listen to their needs, and co-create a plan to address these needs.

"I think with pancreatic cancer it is important to look at the involvement of patients because you see that sometimes doctors prefer other things, so it is good that more attention is paid to that. I think this will improve in the future; however, I am not sure that the use of lidocaine for pain management will become a 100% treatment, but I think that there will be more attention and that is helpful. So, I think the fact that there is more attention to this is most important." (Participant 11, Researcher, June 29, 2021)

The involvement of patients is often difficult because patients do not know that these trials or alternatives exist. This is because doctors do not always feel responsible to communicate these options with their patients (Participants 1 and 2, Researchers, March 30, 2023).

"I think many patients felt heard, but it is not I think that is the most important thing encountered, the doctor does not necessarily come up with things like that [alternative treatment options]. It is the patient who came up with that in many cases and some doctors were very aware that they also gave other options, for example from clinical studies to off-label use. But yes, there were fewer I think indeed especially patients themselves who also had to proactively ask for it, look for it, and then you get a very clear difference in which patient could eventually receive an off-label treatment and which one could not." (Participants 1 and 2, Researchers, March 30, 2023)

Doctors suffer from high responsibility when they prescribe an alternative treatment. Due to possible risks, doctors often discard the option to propose such options.

"Doctors have become somewhat hesitant over the last 10 or 20 years. Wrong developments also in the U.S., where doctors are quite often taken to court, but a little bit is starting to blow over to Europe." (Participant 8, Patient Advocate, March 2, 2023)

Another point made about involvement is that this does not automatically means that their input, opinions, experiences, and knowledge are heard and considered important.

"What is striking is that there is a lot of shouting that patients should be involved, but somehow that is very complicated. Or that does not work well, or patient organizations feel they are not heard or seen." (Participant 5, Researcher, March 24, 2023)

Participant 9, (Hospital Nurse, April 27, 2023) mentions that in some cases patients do not wish for further treatment but doctors insist and convince them to continue. In addition, Participants 9 and 3 (Hospital Nurse, April 27, 2023; Hospital Nurse, March 20, 2023), mentioned that patients also experience that they are not taken seriously due to the high workload in hospitals.

> *"Yes, and we wanted to have time for that, but that was a shortage of staff and there was simply too much pressure in the department. So yes, you had very little time really for that personal bit of attention to the patients. (...) yes, it is just factory work, I think. You are basically just a number there." (Participant 3, Hospital Nurse, March 20, 2023)*

This is not always the case for patients. Participant 8 (Patient Advocate, March 2, 2023) mentioned, as a personal statement, that they had good experiences with their doctor and mutual communication.

> *"I have very good experiences with doctors. (...) and that three-quarters of the time the doctor is looking at the screen and that the patient occasionally makes some noise, but that the doctor still adapts to what he or she has in mind. And what do you think about that yes that is of course just wrong." (Participant 8, Personal Communication, March 2, 2023)*

Participants 9 and 3, (Hospital Nurse, April 27, 2023; Hospital Nurse, March 20, 2023), also mentioned that doctors and other health professionals must perform under high workload conditions that can cause misunderstanding of effort towards patients. This means that patients feel they are taken seriously and that their doctor does not care about their feelings.

> *"(...) that were also surgeons that did these conversations at the outpatient clinic, say they did a combination, and I also spent a day there and they have only 10 minutes for patients and that was it. And then you must go to the next one, so there really is not a good conversation and attention, because it is just discussing results and continuing." (Participant 3, Hospital Nurse, March 20, 2023)*

> *"I think that a patient's opinion will be heard by a doctor, provided that the doctor takes enough time to address the needs of patients. Now, that seems impossible, since they often have many patients, and a day has too few hours for this." (Participant 9, Hospital Nurse, April 27, 2023)*

5. Discussion

In this thesis, I have examined the process of knowledge capacity of SPIN actors, and their epistemic contribution to this process. In this chapter, notable observations from the results will be discussed as well as the limitations of the research.

5.1 Knowledge Capacity in SPINs

First, SPINs commonly share knowledge through discussion and dialogue within groups. SPINs execute this internally through meetings and discussions, and externally through publications and congresses. Compared to the knowledge-sharing model of Nonaka, this correspondent with the combination phase. The combination phase is described as the exchange of explicit knowledge in groups (Nonaka, 1995). I can confirm that SPINs share knowledge in an understandable form in their meetings because multiple actors can interpret and intervene in this. In addition, this knowledge can be described as explicit knowledge because it is shared in an understandable form. This is also aligned with the literature that states that explicit knowledge refers to knowledge that can be communicated verbally or written (Brix, 2017; Kothari et al., 2012). However, the findings do not in-depth indicate how SPINs are performing in the phases of socialization, externalization, and internalization.

The socialization phase is described as the transfer of tacit knowledge between individuals (Nonaka, 1995). SPINs share experiences but often in an understandable manner. Tacit knowledge in SPINs is not precisely identified in this research. Therefore, it is not clear how SPINs perform in this phase and how they interpret and learn from the shared tacit knowledge. The literature stated that this phase requires prior knowledge and shared experiences to learn from this (Pérez-Luño et al., 2019; Sarayreh et al., 2012). This in turn is addressed by the findings because it is found that SPINs do need a certain level of prior knowledge to correctly understand and interpret the shared knowledge.

Furthermore, the externalization phase of the Nonaka model describes the transfer from tacit to explicit knowledge that can be communicated in an understandable form, for instance, by using words or metaphors (Nonaka, 1995). As mentioned earlier, I examined that SPINs do share knowledge in an understandable way, however, in this phase, it is not clear how they transfer tacit to explicit knowledge.

The internalization phase is the absorption of explicit to tacit knowledge in individuals meaning that the knowledge is ‘owned’ by the individual (Nonaka, 1995). The results indicate that SPIN actors understand and absorb the knowledge that is shared because all actors can actively participate in meetings and discussions. Nevertheless, the findings lack in-depth information about the ‘actionability’

of the knowledge and how actors learn from this to make it their 'own' unconscious knowledge. This is a characteristic of the internalization phase (Sarayreh et al., 2012; Venkitachalam & Busch, 2012).

I think it is crucial to get more insight into the socialization, externalization, and internalization phases of knowledge sharing to have an in-depth understanding of how SPINs perform in these processes. In addition, it is thus essential that there is a clear identification of tacit and explicit knowledge in SPINs to examine this. However, I think the internalization phase of SPINs can be hard to examine because it is rather a complex process. There is a possibility some actors have more difficulties with understanding and absorbing knowledge than others. For instance, it is possible that doctors do understand medical concepts better than patients. This refers to the absorptive capacity of individuals (Cohen & Levinthal, 1990). These concepts are not particularly addressed in this research. However, they are important concepts to understand the knowledge-sharing process. For further research it would be interesting to gain more insight into the identification of tacit and explicit knowledge, how these types of knowledge transfer and are transformed through the socialization, externalization, and combination phase, and what effect the actors' individual absorptive capacity has on this.

Furthermore, the results showed that the process of knowledge creation in SPINs is dependent on knowledge sharing. SPINs share knowledge through discussion and dialogue that consist of different opinions from various actors. From this, they create one coherent opinion of multiple opinions, expertise, experiences, and perspectives. This process is continuous that goes back and forth to create and assess new knowledge. This aligns with the literature that highlighted the importance of knowledge sharing in the creation of knowledge (Medina-García et al., 2022), and that these processes are interconnected (Yildiz et al., 2019). The assessment of knowledge of SPINs in this process is commonly performed by peer review and discussion. This research does not address the assessment of knowledge in detail, but it is an important factor of knowledge capacity. Peer review is the most common method to critically assess the quality of (written) work by colleagues or other specialists in a particular field (Rowland, 2002). It would be interesting for further research to gain more insight into other assessment methods SPINs use in this process.

The application of knowledge of SPINs does not differ from the classical knowledge capacity process. SPINs apply knowledge in written publications, discuss results at congresses, and implement knowledge into new projects. This aligns with the literature that states knowledge can be applied to changed programs, case studies et cetera (Pérez-Luño et al., 2019; Sarayreh et al., 2012). In addition, the literature stated that effective knowledge depends on clear communication, capabilities, and resources (Ode & Ayavoo, 2020). Following the results, SPINs apply knowledge after all actors agree upon the decision that is made and is valuable to apply which makes clear communication a crucial variable in this process.

However, it is not clear what capabilities and resources are essential for SPINs to apply knowledge. These perhaps can be networks, funds, or other financial resources. For instance, funds are required to set up and execute a new project. The literature stated that talent is needed to estimate when to apply knowledge (Song et al., 2005), thus this could also be a capability for knowledge application. This would be interesting to address in further research to gain more in-depth information on the capabilities and resources needed for the application of knowledge in SPINs.

5.2 Epistemic Contribution of SPINs

Second, the results showed that patients in general often feel neglected and not understood. This aligns with the literature that highlighted patients are particularly vulnerable to epistemic injustice (Carel & Kidd, 2014). This is a common problem in hospitals where the knowledge, opinions, experiences, and input of patients are neglected which results in unmet medical needs. The findings showed an important reason for this is the lack of in-depth medical knowledge. In addition, doctors do not always feel responsible or are afraid to share information on off-label or alternative treatment options due to possible risks. This indicates that patients are not involved in discussions concerning their medical treatment process. SPINs attempt to involve these neglected actors in their collaboration. However, the results mentioned that the involvement of neglected actors does not automatically guarantee they are taken seriously and understood. This also corresponds with the literature that highlighted the involvement of individuals does not mean the knowledge of these actors is valued and understood (Kok et al., 2022). In addition, the neglect of these individuals could have an influence on medical needs and thus can impact their epistemic contribution, or the ability to express the epistemic subjectivity of an individual by sharing their beliefs and interpretations (Fricker, 2015; Kok et al., 2022).

In multi-actor collaborations, such as SPINs, this is a complicated problem because it is impossible to address all actors' wants and needs. SPINs endeavor this by developing a shared goal. A shared goal is a proper way to include knowledge of various multiple actors and create space for their wants and needs but still follow a certain vision (Schöttle & Tillmann, 2018). The shared goal of SPINs is to identify unmet medical needs and to include various actors with different perspectives to effectively achieve this. They co-create a plan together to address these unmet medical needs. The identification and action plan to address these problems increase the epistemic contribution of neglected actors. Herewith, SPINs attempt to address the problem of epistemic injustice.

5.3 Limitations

Furthermore, this thesis has some limitations. Due to time constraints, 10 interviews were conducted. The perspective on SPINs from a governmental perspective, such as RIVM, would be interesting to add to further research. This gives insight into their opinion about SPINs and if and how they interpret the future perspective of these organizations. In addition, this might trigger governmental institutes to be aware of the importance of the identification and addressing of unmet medical needs and what role SPINs can have in this. In addition, a larger number of interviews and documents will strengthen the reliability and validity of the research.

Another limitation is that this thesis is focused on one case study, which is the off-label use of lidocaine in pancreatic cancer patients. Including multiple case studies of alternative treatments in different countries would be interesting to examine if these SPINs have similar knowledge capacity and if they are attempting to address epistemic injustice. Interesting platforms to consider are, for instance, MyTomorrows. MyTomorrows is an international platform that helps patients discover and access (alternative) treatments (MyTomorrows, n.d.).

6. Conclusion

SPINs are multi-actor collaborations that create, exchange, and apply knowledge to produce accessible, effective, and safe interventions that attempt to address unmet medical needs. In this thesis, the following research question is addressed "*How do Social Pharmaceutical Innovation actors create, exchange, and apply knowledge, and what is their epistemic contribution to this process*?".

I conclude that the exchange of knowledge in SPINs is a continuous process that goes back and forth and is the fundamental building block for knowledge creation. From discussions and dialogue in knowledge sharing, one coherent opinion is created. Knowledge creation in SPINs is thus a process dependent on knowledge sharing. This new knowledge is applied in different forms, such as written publications, congresses, or new protocols and projects through clear communication.

Furthermore, SPINs put emphasis on the involvement of various actors, particularly patients. Besides involving these actors, SPINs value and include their knowledge to identify unmet medical needs and collaborate towards a shared goal to address these problems. Considering the case study, the LIDOPAN study was set up to gain more insight into the efficacy of lidocaine in pain management for pancreatic cancer patients, and if this is valid for this indication. I conclude that the identification and the shared goal of addressing unmet medical needs is the epistemic contribution of SPIN actors to the knowledge capacity process.

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9. Appendices

9.1 Appendix I: Informed Consent and Interview Guide

Research topic — **The Power of Knowledge:** Knowledge Creation, Exchange, and Application of Social Pharmaceutical Innovations on the Off-Label Use of Lidocaine Concerning the Quality of Life of Pancreatic Cancer Patients in the Netherlands.

Goal: — This research aims to gain more insight into the process of knowledge production, valuation, and application in healthcare solutions within SPINs.

Why — This research is performed for my master's thesis at Utrecht University.

Your role — Contribute to knowledge and insights on how knowledge is created, exchanged, applied, and assessed within SPINs. In addition, what the role of SPINs is concerning epistemic injustice within healthcare?

Informed consent

1. Participation is only needed for this interview today.
2. I would like to record this interview.
3. Information provided by you during this interview will be used for academic purposes only. It is about your personal thoughts and experiences, thus there are no right and wrong answers. You can decline to answer the question and end this interview at any time. Please take as much time as you need to answer the question.
4. Your responses will be anonymized in reporting the results, but I will mention the initiative itself.
5. Do you have any questions at this point?
6. Do you confirm that:
    a. You are satisfied with the information you received concerning the research.
    b. You have been allowed to ask questions and these questions are answered to your satisfaction.
    c. You have been allowed to carefully consider your participation in this research.
7. Do you agree that:
    a. The interview will be recorded, and the collected data are being stored for scientific purposes.

b. The collected and anonymized data can be shared and reused by scientists and researchers to address other research questions.

8. Do you understand that:
    a. You have the right to withdraw your consent for the use of the data at any time in the research.
    b. You have the right to review the report afterward.

Interview Questions

General Questions

1. What is the organization you are active in?
2. What is your function within this organization?
3. What is the goal of your organization?

I – Off-label Use of Lidocaine and Justice

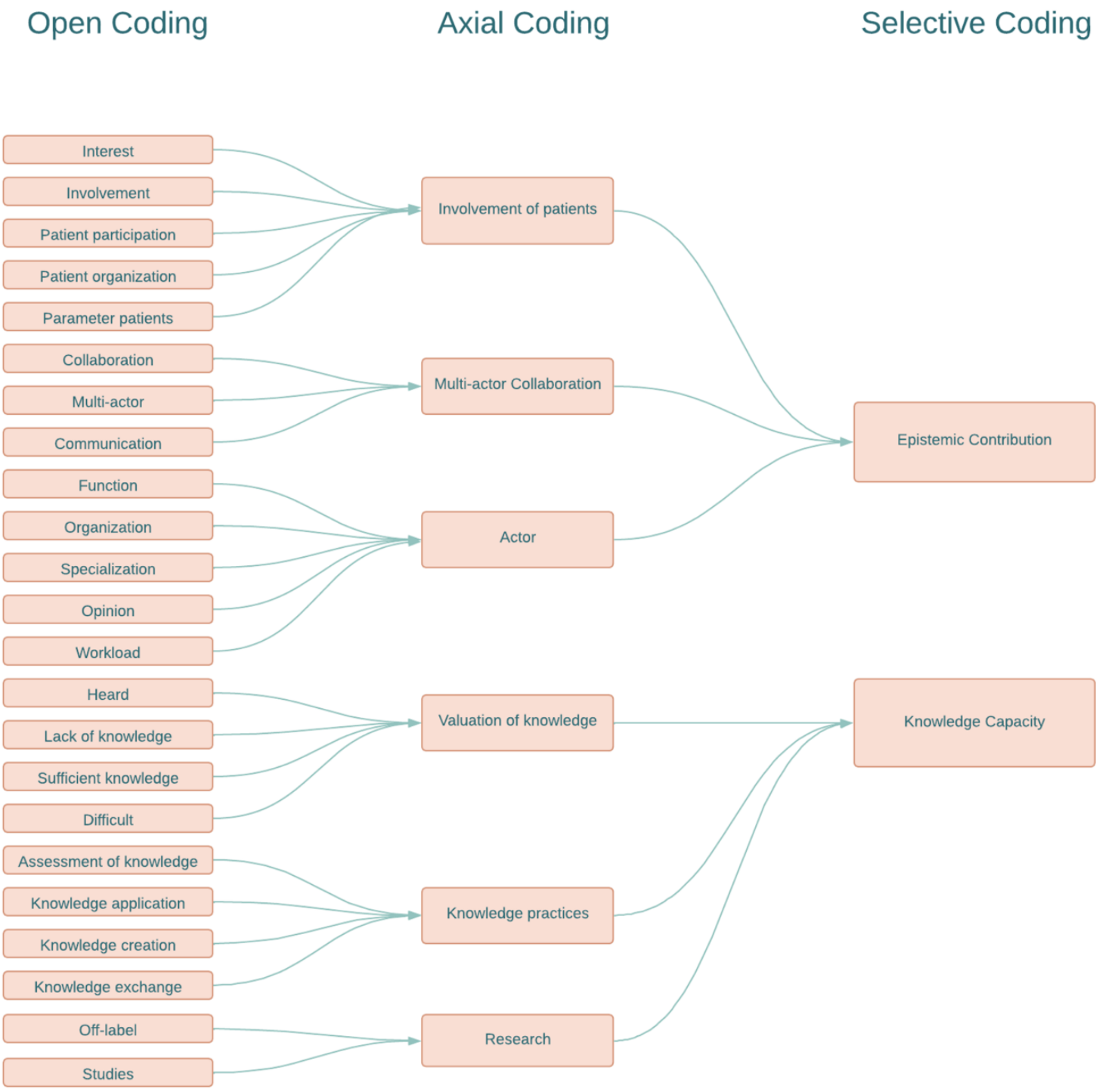
a. What is your opinion on the use of off-label medication?
b. Currently, the use of lidocaine is not a standard treatment for pain management for pancreatic cancer patients. What do you think about using off-label lidocaine for pain management?
c. Do you think the off-label use of lidocaine could influence the quality of life of pancreatic cancer patients? Please elaborate.
d. What is your opinion on the cooperation/relationship between health professionals and patients?
e. Do you think patients' voices are neglected in their treatment?
f. Do you think patients are taken seriously enough in their treatment?
g. Does the above answer have an influence on the quality of life of patients?
h. Are patients experiencing injustice regarding their opinions/knowledge of their medical treatment?
i. If yes, what should in your opinion be changed to address this problem?

II – Organization and Knowledge

a. How is the organization organized? What kind of people are active in the organization?
b. How does the organization work internally? By this it meant how various actors work together within the organization.
c. Considering the internal collaboration, how is knowledge generated? By this it meant how knowledge within the organization is created.
d. What type of knowledge is generated within the organization?
e. How is this knowledge exchanged within the organization?
f. How does the organization collaborate with (external) partners?

g. Concerning the collaboration with (external) partners, whom is the organization collaborating with? What kind of people/organizations/institutes are these?
h. How does the collaboration work? How is knowledge being exchanged within these partnerships?
i. How is knowledge considered sufficient or insufficient within these partnerships?
j. Do you think this is the right way to assess knowledge? Please elaborate.

9.2 Appendix II: Coding Schedule and Description



Open Codes	Axial Codes	Category	Description
Interest, involvement, patient participation, patient organization, parameter patients	Involvement of patients	Patient involvement	Describes why it is important to involve patients and what they desire concerning different processes and how this is managed and executed
Collaboration, multi-actor, communication	Multi-actor collaboration	Collaboration of different actors	Describes how collaborations are managed with different actors and how they communicate with each other
Function, organization, specialization, opinion, workload	Actor	Characteristics of different actors	Describes the characteristics of different actors: function, organization, specialization, opinions, and workload they experience
Heard, lack of knowledge, sufficient knowledge, difficult	Valuation of knowledge	The valuation and assessment of knowledge from different actors	Describes if actors are being heard or not and if they have a sufficient level of knowledge on the topic of interest and what the difficulties are of the involvement of these actors
Knowledge assessment, knowledge creation, knowledge application, knowledge exchange,	Knowledge practices	Process of knowledge capacity	Describes how and which types of knowledge is generated, shared, assessed, and applied
Off-label, studies	Research	Research concerning off-label use and epistemic injustice	Describes the studies and clinical trials to the off-label use of lidocaine. In addition, it describes the studies to epistemic injustice