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THE DIGITALIZATION OF MEDICINE SUPPLY CHAIN

How to re-aim the shots in the dark?

Teijo Peltoniemi

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ABSTRACT

Healthcare expenses have been on the rise for decades. One of the key areas contributing to this ever-expanding growth is medicine expenses. Medicines are required to maintain a sustainable health system in a world of aging populations and pandemics. Novel medicines combat diseases previously considered incurable, and medicines help people with chronic conditions to live normal lives. Furthermore, in emerging economies, pharmacies are often the first and only interface to healthcare services, whereby other medical services are scarce or expensive. However, medicines are associated with costs. To maintain a sustainable health system, the growing expenses have to be managed.

There are different ways of controlling medicine expenses. In this age of digitalization, when multiple sectors have been disrupted by digital technologies, it can be argued that digital technologies have a role to play in the medicine supply field. This intersection of medicine supply and information systems has been, however, sparsely studied. This thesis seeks to fill this research gap by exploring the medicine supply chain and discovering obstacles and bottlenecks across the chain. The study also intends to identify how information systems and digital technologies can be utilized to remediate the problems and facilitate an efficient medicine supply chain.

The research approaches the medicine supply chain arena through the medicine supply chain concept. The supply chain is a highly complex world involving the pharmaceutical industry and the distribution, prescription and dispensing of medicines. This research examines this arena through cases from across the supply chain covered in four separate studies and related articles. The supply chain concept and the scene are set in one of the studies, followed by studies on the digitalization of pharmacies, medicine waste management in hospitals and the digitalization of the plasma derivatives supply chain.

The results of this research illustrate that the main role of digital technology in the management of the medicine supply chain relates to managing several information asymmetries across the chain. The key is to increase transparency between various stakeholders in the chain through novel digital solutions. Currently, the supply chain processes are largely based on rules of thumb rather than facts and evidence, and this should be addressed to maintain a sustainable chain and, subsequently, a sustainable health system.

KEYWORDS: Medicine supply chain, Digitalization, Medicine waste management, Blockchain, ePrescription, Information asymmetry

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TIIVISTELMÄ

Terveydenhuollon kulut ovat nousseet vuosikymmenien ajan. Lääkekulut muodostavat merkittävän osan terveysmenoista. Lääkkeitä tarvitaan kestävän terveydenhuoltojärjestelmän ylläpitämiseksi: lääkkeillä voidaan hoitaa aiemmin parantumattomia sairauksia sekä tukea ikääntyvää väestöä. Kehittyvissä talouksissa apteekit ovat usein myös ensimmäinen ja ainoa yhteys terveyspalveluihin. Lääkkeillä ja niiden kehittämisellä on kuitenkin kulunsa ja kestävän terveydenhuollon järjestelmän ylläpitämiseksi onkin kyettävä ymmärtämään ja hallitsemaan lääkekuluja.

Lääkekuluja voidaan hallita eri tavoin. Digitalisaatiolla voidaan ajatella olevan tässä myös roolinsa – useat toimialathan ovat muuttuneet merkittävästi digitaalisten ratkaisujen myötä. Digitalisaation ja tietojärjestelmien merkitystä lääkejakelussa ei olla kuitenkaan tutkittu laajasti. Tämän väitöskirjan tarkoituksena on täyttää tätä tutkimusaukkoa perehtyen lääkejakelun prosesseihin, niihin liittyviin esteisiin ja pullonkauloihin sekä digitaalisiin ratkaisuihin, joilla lääkejakelua voidaan tukea ja tehostaa.

Tutkimus lähestyy aluetta mallintaen lääkejakeluketjua. Lääkejakeluketju on monimutkainen globaali systeemi, joka kattaa toimijoita mm. lääketeollisuudesta, jakelusta ja logistiikasta, terveydenhuollosta ja vähittäismyynnistä. Tässä tutkimuksessa jakeluketjua tarkastellaan neljän tutkimuksen kautta, jotka liittyvät lääkejakeluketjun eri osiin. Aluksi esitellään lääkejakeluketjukonsepti, jota seuraavat tutkimukset apteekkien digitalisoinnista, sairaalan lääkehuollosta ja veriplasmatuotteiden toimitusketjun digitalisoinnista.

Tämän tutkimuksen tulokset havainnollistavat, että digitaalisten ratkaisujen päärooli lääkejakeluketjun hallinnassa liittyy varsinkin informaatiosymmetrioiden hallintaan sekä tiedon avoimuuden ja läpinäkyvyyden lisäämiseen ketjun eri sidosryhmien välillä. Nykyisin lääkejakeluketjun prosesseja leimaa epävarmuus ja faktoihin perustuva päätöksenteko on vaikeaa, mikä heikentää tehokkaan lääkejakelun ylläpitämistä.

ASIASANAT: Lääkejakelutketju, digitalisointi, lääkejätehuolto, lohkoketju, e-resepti, informaatioepäsymmetria

Acknowledgments

My dissertation work and post graduate studies have been a lengthy journey and they have been both immensely productive and rewarding. They have afforded me a chance to immerse myself in an interesting topic on a long-term basis, something I have truly enjoyed. As I near the completion of my dissertation work, I am very much looking forward to contributing in this field in the future. As always, the end of one journey is a beginning of the next.

The age of global pandemics emphasizes the significance of this research area. As I am writing this, the COVID-19 pandemic continues to adversely affect communities globally. There is, however, light in the end of the tunnel and without question an efficient medicine supply chain, supported by efficient information systems, will play an important role in mitigating this and future pandemics.

It is now time to express my gratitude to those who have supported me over the course of this journey. I cannot thank my supervisor in this work, Reima Suomi, enough for all the support and encouragement he has provided to me during various ups and downs. I have truly enjoyed the discussions and debates. I also wish to thank my reviewers, professors Mirella Cacace and Pirkko Nykänen, whose comments and advice have been highly appreciated, and Matti Mäntymäki for evaluating the work and for his advice at the beginning of the project. I am also honored to have Mirella Cacace as my dissertation opponent. I also wish to thank Liikesivistysrahasto for their funding support. Furthermore, I would like to express my sincere gratitude to all those who have collaborated with me on my research, namely Jarkko Ihalainen, Sirpa Peura, Markus Lähteenoja, Hanna Kivikoski, Kirsti Torniainen and all the staff at Turku University Hospital pharmacy.

Many thanks also to all my friends, relatives and colleagues, who have had the patience and interest to discuss and spar with me on this topic – I can guarantee that each discussion has helped me to further improve my analysis and develop my understanding. Finally, I wish to thank my parents, siblings and, last but not least, my wife and children.

18.6.2021
Teijo Peltoniemi

Table of Contents

Tables

Figures

List of Original Publications

This dissertation is based on the following original publications, which are referred to in the text by their Roman numerals:

I Peltoniemi, T. The digitalisation of the medical value network - how information asymmetries can be managed with digital innovations. *International Journal of Telemedicine and Clinical Practices*, 2017; Vol. 2, No. 4: 298-317. https://doi.org/10.1504/IJTMCP.2017.091939.

II Peltoniemi, T., Suomi, R., Lähteenoja, M. & Peura, S. The electronic prescription as a driver for digitalization in Finnish Pharmacies. Submitted to *BMC Health Services Research.*

III Peltoniemi, T. & Suomi, R. Eliminating medicine waste in a Finnish university hospital — a qualitative study. *Journal of Pharmaceutical Policy and Practice*, 2019; Vol. 12, No. 27: 1-7. https://doi.org/10.1186/s40545-019-0188-8.

IV Peltoniemi, T. & Ihalainen, J. Evaluating blockchain for the governance of the plasma derivatives supply chain: how distributed ledger technology can mitigate plasma supply chain risks. *Blockchain in Healthcare Today*, 2019; Vol. 2: 1-13. https://doi.org/10.30953/bhty.v2.107.

1 Introduction

1.1 Background

Healthcare expenses have continued to increase significantly over the past decades. Annual per capita expenditure almost doubled from 1970 to 2016 (OECD, 2019b). There is no indication this trend will change, and it is, undoubtedly, a societal issue that needs to be solved. The question is how to maintain a sustainable health system.

There are several factors contributing to this trend. One of them is the aging population in the developed world. People live longer, and when they become old, they require more health services. Countries such as Finland try to solve the issue, whereby there is an aging demography and increasingly fewer taxpayers, while the requirement is still to run a quality healthcare system. This turns the issue of rising health expenses into a question of productivity.

Health systems vary depending on the country. The highest spending country has traditionally been the United States, which spends twice as much as other high-income countries (Papanicolas, et al., 2018). The suggested reasons for this include population growth and aging, chronic disease prevalence (Dieleman, et al., 2016) and increasing prices in the healthcare and pharmaceutical market (Papanicolas, et al., 2018).

The topic is complex, and there are varying and often conflicting explanations for the ever-increasing expenditure. For example, the economic growth in the developing world typically leads to increased pollution and, therefore, may degrade health and increase healthcare expenses (Wang, et al., 2015).

Some authors have also questioned the importance of the aging population and suggest that reasons such as quality of healthcare, lifestyle and social protection are key factors contributing to growing expenditure (van den Heuvel & Olaroiu, 2017). Some other authors have highlighted the importance of social spending (Papanicolas, et al., 2018). For example, these authors suggest that the main drivers for expenditure growth in the United States include higher price levels of goods and labor than in other high-income countries (Papanicolas, et al., 2018). Nevertheless, this discussion underlines the uncertain and complex nature of the domain – whereby information is seldom available in an open and unambiguous manner, often due to strict regulations for health-related data.

Pharmaceutical breakthroughs have also had a role to play. The invention of antibiotics led to preventing deaths from infections, which subsequently enabled people living longer and rather suffering from heart diseases and cancers due to longer life (Weisbrod & LaMay, 1999). These are costly conditions, given they are long-term and chronic and may require intensive treatment.

This illustrates the difficult nature of healthcare services: putting a price tag on health leads to difficult discussions on who should pay for what and who should be treated. To illustrate the paradoxical nature, consider smokers – a smoker may generate more healthcare costs during a short period, whereas a nonsmoker will accumulate more costs during the 10–15 years he is outliving the smoker (Kleinke, 2001). Health expenditure is also a complex issue for politicians, and governments may fail when trying to solve it (Milne, 2019).

Various solutions have been suggested. One of the key elements in managing the increasing healthcare spending is, however, the medication. Broadly speaking, it is often argued that having people consume medicines at home and reducing the amount of hospital stays is cost-effective (Kleinke, 2001). Putting it bluntly, the aim is to maintain elderly people and those with chronic conditions at home for as long as possible. However, it should be noted that the actual impact, if any, of the medication to healthcare expenses and decreasing hospital stays is challenging to isolate or prove.

From the OECD (2020) health expenditure data, as illustrated in Figure 1, it can be noted that pharmaceutical expenditure has increased moderately compared to overall health expenses. The chart depicts the development of pharmaceutical and healthcare expenses as percentages of gross domestic product and the development of hospital stays in days. It should be noted that the figures are incomplete, as they do not include pharmaceuticals consumed in hospitals and for day-care treatment (OECD, 2019a). It can be observed that hospital stays have decreased over the past decades. However, medication is only one potential influencing factor, and its impact is difficult, if not impossible, to single out.

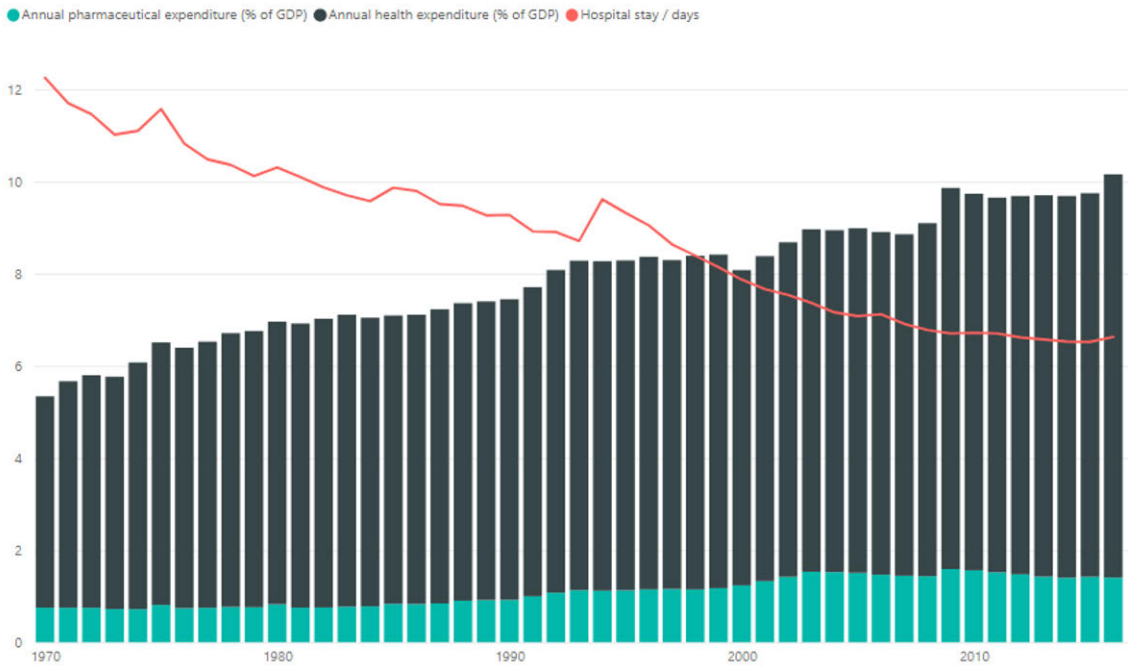

Figure 1. OECD health expenditure (OECD, 2020).

It is suggested that low-cost essential medicines treating common health problems are key to maintaining a cost-effective health system (Management Sciences for Health, 2012). However, medicines do not come without costs.

The volume of medicines consumed today is staggering. There are more than 4,000 pharmaceuticals used in healthcare (Arnold, et al., 2014). The medicine expenses account for roughly 20% of overall health expenses in OECD countries (OECD, 2017). Considering the four largest EU markets – France, Germany, Italy, Spain – and the UK, the medicine expenses vary between 11% and 19% of the total healthcare expenditure (Espin, et al., 2018). According to Newhouse (1992), this is unlikely to decrease: he suggests that half of the healthcare expense increase is due to technological advances and innovation, including those relating to pharmaceuticals. This is not an unfounded position: it is suggested that new specialty drugs, such as oncological drugs, comprise one-third of total pharmaceutical spending (Belloni, et al., 2016). It is, however, estimated that new drugs have had an impact on the reduction of life years lost in a cost-efficient manner. For example, Lichtenberg (1998) suggested that an R&D investment of USD 15 billion in the pharmaceutical industry saves 1.6 million lives annually, which can be valued at USD 27 billion. However, the prices of new drugs tend to be high, and it is not always clear whether the benefit exceeds the costs (Belloni, et al., 2016).

Another aspect is adverse drug reactions (ADRs). For example, the U.S. Food and Drug Administration (FDA) reported a significant, almost threefold, increase in ADRs between 1998 and 2005 (Light & Lexchin, 2021). One factor is the aging population and the growth in terms of polymedicated patients. ADRs may be fatal, and the associated costs are scarcely included in medicine expense estimates (Light & Lexchin, 2021).

Nevertheless, global pharmaceutical spending is on the growth path, which does not seem to be slowing down. It is estimated that global spending will reach USD 1.5 trillion by 2021, which is USD 370 billion more than in 2016 and almost double the spending in 2007 (QuintilesIMS, 2016). Considering Europe, the publicly funded part of medication expenses varies from Finland's 50% to Germany's 70% (Aanestad, et al., 2017a).

Authorities ought to monitor the development of these costs meticulously to keep them under control. For example, in Finland, there were 30.8 million prescriptions processed in 1995, while in 2018, the amount had risen to 63.3 million, of which 43.43 million were publicly subsidized (Lääkealan turvallisuus- ja kehittämiskeskus Fimea ja Kansaneläkelaitos, 2019; Kansaneläkelaitos, 2020).

The factors affecting pharmaceutical spending typically includes, in addition to the launch of new drugs, changing prices and quantities (Mousnad, et al., 2014). Various policy interventions can be used to mitigate the spending, including those steering the pricing of medicines in different markets. However, this is not always straightforward, as the pharmaceutical industry must stay incentivized to maintain an adequate level of R&D investment.

The delivery channels for medicines include pharmacies and hospitals. This forms an alternative endpoint for evaluating expenditure: Can the efficiency of the supply and delivery of medicines be increased? Medicine waste is a relevant example here – for instance, the estimated loss caused by prescription medicine waste in Finland is between EUR 95 million and EUR 125 million (Apteekkariliitto, 2016). Waste is a symptom of an inefficient delivery system and an example of areas that, if remediated, would contribute to lowered pharmaceutical expenditure. However, how can these pain points be addressed? Are there tools that can be used to remediate these inefficiencies?

Digitalization has been one of the buzzwords through the 2000s. It denotes the sociotechnical, comprehensive transformation organizations undergo when deploying digital technologies and modifying processes and organizations around them (Tilson, et al., 2010). Digitalization has disrupted several sectors, including finance, hospitality and transportation. One of the key aspects digitalization is commonly understood to address is productivity, which is expected to increase in various sectors (Pohjola, 2014). Perhaps digitalization also has a role to play in the medicine supply chain.

1.2 The market profile and research gaps

The healthcare market has been widely researched. It is a peculiar market, as proven by Arrow (1963) in his seminal article. One of the key findings is that the market is heavily impacted by information asymmetries and policy interventions. Patients have significantly less information on treatments than physicians, physicians or insurers rarely know whether patients follow prescriptions and so forth. Therefore, it is typically understood that the market cannot be left to self-regulate. Instead, the information asymmetries must be reduced by tight regulations.

The pharmaceutical market can be considered a closely related entity, which has been widely researched as well. Newhouse (1992) suggested that several decades of continuing expansion of healthcare costs have been heavily impacted by the invention of new medicines and healthcare technology. Again, information asymmetries come into play. One manifestation is patient adherence – that is, whether the patient follows the prescription and consumes the right medicines at the right time. This is hard to monitor (Martin, et al., 2005).

However, broadly speaking, the usual viewpoints for the research on healthcare and pharmaceutical markets are those relating to economics, policy and medical perspectives. Information and digital technologies have also been studied in relation to these markets, and they have been understood as a key factor bringing productivity gains (Aanestad, et al., 2017b). Some dominant research strands can be identified. One is digital health research, which is approaching the area from the computer science point of view. The current focus is on solutions such as mobile health and wearables (Gray & Gilbert, 2018). Another closely related research area is health informatics, which concerns managing data such as those related to molecular medicine or population health indicators (Gray & Gilbert, 2018). According to a broader definition, "It [health informatics] concerns the use of information and communication technologies (ICTs) for health and in health care" (Bath, 2008, p. 501).

Another point of view is that of information systems (IS) research, in which the health information systems (HIS) arena can be found. Information systems science (ISS) is typically considered a social science field. ISS concerns how organizations and technologies interact and the impact of technology on people. Therefore, the research approach is typically softer than hard science–based computer science.

However, few or none of these research strands touch upon pharmaceutical or medicine supply, and it can be concluded that research combining medicine supply and IS is scarce. One particular area that can be understood to be relevant here is electronic prescription (ePrescription), which has been studied in numerous accounts (e.g. (Abramson, et al., 2011; Caldwell & Power, 2011; Johnson & Lehmann, 2013)). However, research comprehensively exploring the medicine supply and from the IS standpoint is currently lacking.

To illustrate this, if the Finnish national library catalog is searched for doctoral theses (Melinda, https://melinda.kansalliskirjasto.fi) with search terms such as "medicine," "pharmaceutical," "supply" and "delivery," combined with "information systems," and the same in Finnish, no theses can be found, with scarce publications overall. None of these comprehensively examine the medicine supply chain from the IS point of view.

When examining some recent international IS conferences, the results are similar. Investigating articles from the proceedings of the European Conference on Information Systems and Hawaii International Conference on System Sciences (2015 and 2016), 136 HIS articles were identified (Peltoniemi, 2018). Of these, only seven touch upon medicine delivery in some way:

- Five articles are on medication adherence.
- One is on consumer health expressions in terms of ADRs.
- One is on a flu monitoring system based on mining ePrescription data.

The emphasis and themes of other related conferences, such as the World Congress on Medical Informatics (MEDINFO, Global) and Medical Informatics Europe, have been reviewed in studies. For example, a study investigating conference articles between 2007 and 2017 lists various key themes, such as electronic health records, but the medicine supply chain is not one of them (Jia, et al., 2018). This can be verified through examining the MEDINFO 2017 proceedings – one article that discusses medicine supply and data can be identified, but this is restricted to the point of view of clinical systems in a hospital (Lichtner & Cornford, 2017).

Based on this, it can be argued that the medicine supply arena has been sparsely studied from the IS perspective, and there is an opening for novel research. Whereas many other healthcare domains are well studied and there is good coverage of HIS research available, the intersecting arena of medicine supply chain and IS remains blurry. ePrescription-related research may elucidate certain parts of medicine supply, but research on the end-to-end medicine supply chain and how various parts of the chain interconnect is scarce, nor are there studies on current challenges and how this vital concept can be improved. During the present times of pandemics and aging populations, it is of utmost significance to ensure an efficient medicine supply chain. IS and digital technologies, undoubtedly, have a part in this concept; hence, the intersection of the medicine supply chain and digital technologies requires dedicated research.

1.3 Purpose of the thesis and the main research question

To address the current research gap, this study examined the medicine supply chain and identified some major pain points that hinder the efficient delivery of medicines, as well as investigated how IS are used to remediate these pain points. In terms of IS, the emphasis was on digital technology and digitalization. Specifically, those systemic or social innovations that are driven by digital technologies were sought to be identified. It is suggested that healthcare transformation requires systemic change – given it is a vast ecosystem – whereby (ideally) several services are integrated in a patient-centric manner (Virtanen, et al., 2017).

The initial research interest was to understand the digitalization of the medicine supply chain from the eCommerce viewpoint, as a subarea of the wider digitalization of the retail and consumer goods markets. The retail sector has been digitalizing, in the 2010s, at an accelerating pace, which is manifested through the success of online marketplaces such as Amazon and the decline of traditional brick-and-mortar retailing.

As the peculiarities of the market began to become clear, the emphasis of this study was re-aimed at the downstream of the market – that is, the delivery of medicines to patients in pharmacies and hospitals. This choice was made partly due to convenience reasons, as the access to research targets in the downstream is easier. While focusing on the downstream in medicine supply, the aim was, however, to thoroughly understand the supply chain, and the associated original articles also cover the upstream – that is, the pharmaceutical industry.

The research theme can be summarized as follows: *what kind of obstacles and bottlenecks there are in the medicine delivery arena and how those can be remediated with digital technologies*. The goal of this research was to model the delivery chain and study it from this viewpoint.

As shall shortly be seen, the characteristics of the medicine supply chain include that it is pervaded by incomplete and uncertain information, which hinders optimizing the supply chain, and that it is a complex sociotechnical environment. These are the two main perspectives in this thesis and the related research.

1.4 Structure of this dissertation

Based on the four studies conducted in this research, an end-to-end model for medicine supply is suggested. This is depicted in Figure 2. The model illustrates the main actors and entities across the supply chain. The figure also shows how the articles representing the four studies cover the various parts of the model.

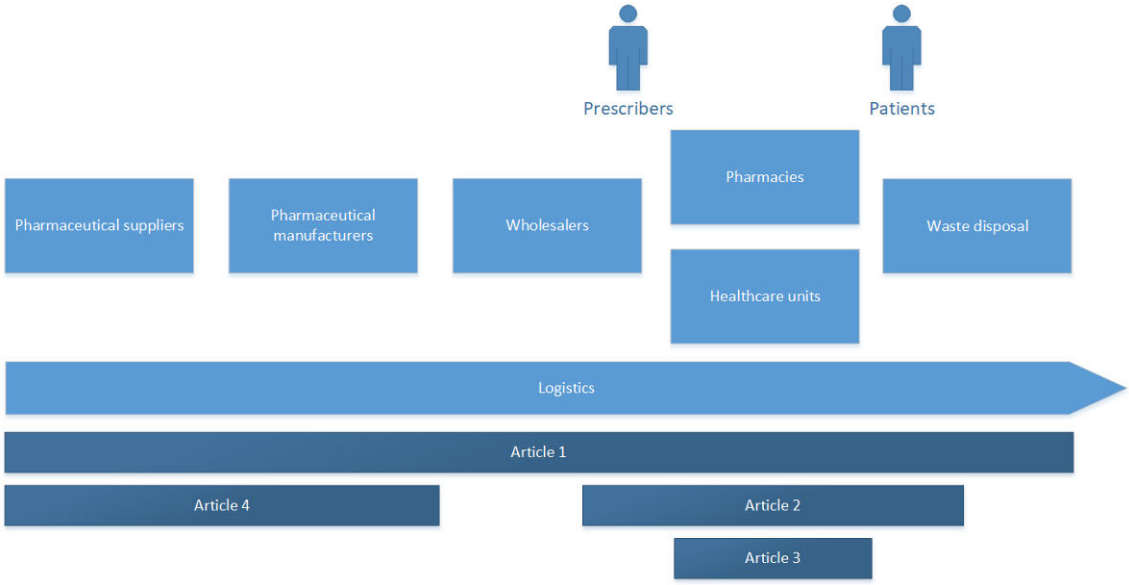

Figure 2. Model for medicine supply and the articles in the dissertation.

Regarding the ever-increasing healthcare expenses and, specifically, medicine expenses, this model can be used to identify bottlenecks and, conversely, areas of improvement.

The research and subsequent articles covered in this thesis consider the two characteristics mentioned above. The research contributes to the field by revealing various challenges in different parts of the supply chain and suggesting solutions and further research topics for these challenges. The articles describe four studies that were researched for this thesis. Given the complexity of the arena, it is impossible to cover the entire supply chain in one thesis; however, the cases still represent several parts of the chain. The focus was on the actual operational level; hence, regulatory and financing processes, for example, were left for subsequent research projects.

Article I: This article lays the foundation for this thesis by outlining the concept and structure of the medicine supply chain and identifying key concepts relating to it. The key challenge it identifies is the information asymmetry that pervades the healthcare and pharmaceutical markets. Through targeted literature reviews, the article identifies several solutions currently used, or planned to be used, to mitigate the information asymmetry problem. For example, from the patient viewpoint, the key solutions include automatic medicine dispensing, ePrescription, electronic patient records, generic substitution, and reference price systems. These are interlinked and often powered by digital technologies. These solutions drive medicine supply today, but it is clear that new means are required going forward, given the occurrence of pandemics and aging populations. Value and evidence-based

approaches, patient empowerment and new technologies such as blockchain can enhance medicine supply through managing the associated information asymmetries.

Article II: Pharmacies are key entities in the medicine supply chain. This article views how the pharmacy sector in Finland has been undergoing a vast transformation in the 2010s due to the launch of ePrescription and related new workflows. The article takes a sociotechnic view and suggests that the changes in the pharmacy dispensing processes are an example of successful digitalization within the medicine supply chain. The research draws on data collected from pharmacy dispensing processes while observing them prior to and after the launch of ePrescription. The article reveals how mandated adoption of the new technology has spawned various streams of other changes in the working processes, whereby the processes have been renewed rather than adapted.

Article III: This study focuses on the medicine supply chain in a hospital. It outlines the related environment of the process, organization and technologies and identifies medicine wastage as one of the key challenges accumulating medicine-related costs in hospitals. This research is based on observations, interviews and a survey and elucidates an uncertain territory whereby hospital staff must cope with inconsistent information and less-than-optimal IT systems. This is an example of a part of the medicine supply chain where digitalization has not happened; the processes remain manual and administratively burdening, causing productivity losses.

Article IV: This article focuses on the upstream of the medicine supply chain, exploring challenges the pharmaceutical industry is facing and suggesting a digital solution. The article specifically investigates the blood plasma market and identifies various risks in the current setting, including ethical and supply chain risks. The suggested solution is based on distributed ledger technology (DLT), illustrating how a digital technology has the capability to transform an established market.

2 Setting the Scene – Previous Literature Review and Conceptual Framework

2.1. Defining key concepts and terms

2.1.1 Medicine as a term

A medicine is defined as "a substance or preparation used in the treatment of illness; a drug; esp. one taken by mouth. Also: such substances generally." (Oxford English Dictionary, 2020). This definition clearly suggests that "medicine" and "drug" are synonymous terms. The same dictionary defines a drug as "a natural or synthetic substance used in the prevention or treatment of disease, a medicine," on the other hand, is "a substance with intoxicating, stimulant, or narcotic effects used for cultural, recreational, or other non-medicinal purposes." To avoid confusion with illegal drugs, the term "medicine" is used in this thesis. "Medicine" is not entirely unambiguous as a term since it can also refer to different things, such as the medical science and methods practiced by physicians. However, this unambiguity is less significant than that related to the term "drug." In Finland, there is no such ambiguity since the word *lääke* refers to medicine as a medicinal product, whereas *lääketiede* refers to medicine as a science or practice.

The terms medicine and drug can, however, be used interchangeably. In the US, the latter seems to be de facto, as can be inferred based on the name of the related authority (FDA). In Finland, the counterpart is named the Finnish Medicines Agency (Fimea). The third related term is "pharmaceutical." This derives originally from the Greek word referring to druggist – that is, it refers to "pharmacy" and, particularly, the sale of medicines (Oxford English Dictionary, 2020).

2.1.2 Definition by authorities

Regulations can be used as a basis for specifying the meaning of medicine. According to the European Commission (Directive 2001/83/EC), a medicinal

product refers to “any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.” Finnish law follows the European Commission directive and includes veterinarian products (Lääkelaki [Medicines Act] 395/1987).

Fimea is responsible for maintaining a catalog that contains formally acknowledged medicines in Finland (Fimea, 2020). The catalog also has a section for herb-based substances that can be used as medicines – which, in these cases, are treated as medicinal products by Finnish law (Lääkealan turvallisuus- ja kehittämiskeskuksen päätös lääkeluettelosta [Finnish Medicines Agency's decision on medicine catalogue] 19.3.2019/415). Furthermore, medically consumed substances whose composition, manufacturing method or mode of action differ from those of traditional medicines are treated as medicines. These include radioactive medicinal products, allergenic products, vaccines, medicinal gases, and blood and blood plasma–based products (Fimea, 2020).

Medicinal products and medical devices are closely related and often get mixed up. The regulation for the latter was introduced more recently than for the former, and many products previously treated as medicines have been transferred to the category of medical devices (Medicines and Healthcare Products Regulatory Agency, 2021). These include wound dressings, surgical materials and irrigation solutions, as well medical imaging equipment. Devices that incorporate a medicine and the instrument used to administer it are treated under the medicine legislation.

The classification between medicinal products and medical devices is not always straightforward. The European Commission has specified a set of regulations for medical devices and argues, “Medical devices and In vitro diagnostic medical devices (IVDs) have a fundamental role in saving lives” (European Commission, 2020). There are, in fact, multiple European Commission directives to regulate this field: Medical Devices, In Vitro Diagnostic Medical Devices and Active Implantable Medical Devices directives (Medicines and Healthcare Products Regulatory Agency, 2021).

Furthermore, terms such as “product” and “use” are often used to mean different things (Langedijk, et al., 2015). A product, for example, can mean a pharmaceutical ingredient or a consumption-ready dosage. Another line of confusion comes from substitutes such as biosimilars; are those biological compositions resembling biological medicines or medicines on their own? In this thesis, however, the review is restricted to top-level ontology and does not address these questions.

2.1.3 What is treated as medicine in a hospital?

The duties of pharmaceutical services in a hospital include the following (Hospital District of Southwest Finland, 2020):

- Pharmaceutical logistics
- Manufacturing medication
- Injections and infusions individually prepared for the treatment of cancer
- The pharmaceutical responsibility of preparing radioactive medication
- The logistics of clinical medicine trials and the preparation of medicine
- Pharmaceutical services in the wards.

The duties of hospital pharmacies are regulated by law in Finland (Fimea, 2018b).

2.2 Medicine supply chain

Supply chain is the end-to-end process from the factory to the customer (Clauson, et al., 2018). The pharmaceutical or medicine supply chain refers to the path a medicine takes when traversing from the manufacturing and packaging plants to be distributed and dispensed to patients. The organizations involved include public and private sector actors at different regional levels (Management Sciences for Health, 2012). Imran, et al. (2017) introduced a two-channel medicine supply chain model whereby one channel goes from manufacturers through pharmacies and clinics to patients and the other through hospitals and hospital pharmacies. Authorities such as health departments come to play in a related integrated healthcare system.

Regarding acquiring medicines in the downstream, over-the-counter (OTC) medicines and prescription medicines can often be separated in terms of financing. For example, in Finland, prescription medicines are largely subsidized for the consumer, whereas OTC medicines are paid for out of pocket (Pharmaceutical Pricing Board, 2020). OTC medicines refer to medicines one can buy without a prescription (FDA, 2018b). Financing in the Finnish pharmaceutical market is discussed more broadly in Section 2.5.

The World Health Organization (WHO) defined the medicines management cycle, which comprises selection, quantification and forecasting, procurement, storage and distribution as main elements (WHO, 2015b). According to the WHO, the medicine supply chain is an integral part of the overall health system, and countries should seek to explore ideal private-public partnerships in this area (WHO, 2015b).

Burns et al. (2002, p. 4) discussed a value chain rather than a supply chain, whereby each step in the chain adds value to the end product provisioned to the customer, i.e. the patient. The main actors include the following:

- Payers: e.g. government, employers and patients.
- Fiscal intermediaries: e.g. insurers.
- Providers: e.g. healthcare service providers, physicians and pharmacies.
- Purchasers: e.g. wholesalers.
- Producers: e.g. medicine manufacturers (also called pharmaceuticals).

Supply chain and value chain are closely related terms and are often used interchangeably (e.g. (Rossetti, Handfield, & Dooley, 2011)). A supply chain concerns a virtual organization producing and distributing goods – in contrast to a vertical organization, which uses end-to-end insourcing (Burns, et al., 2002). It is easy to see that a supply chain can also be a value chain, whereby each of the nodes in the chain contributes (i.e. adds value) to the delivery of the goods. In this thesis, these terms are used interchangeably, and they may also refer to the medicine delivery chain.

Financing is an important aspect of medicine supply, and there are six main models (Management Sciences for Health, 2012, p. 8):

1. Fully public: The state is responsible for the medicine supply in its entirety, including financing, procuring and distributing.
2. Private supply to public health services: Medicines are publicly funded and delivered directly by suppliers to public health service providers.
3. Social health insurance systems: The acquisition of medicines that are dispensed in private pharmacies is subsidized from public funds and social health insurance.
4. Private financing and public supply: Patients pay for medicines supplied and dispensed by public sector service providers.
5. State wholesale monopoly: Public sector monopolized importation and distribution of medicines to private pharmacies.
6. Fully private: Patients pay the entire cost of the medicine they acquire from private pharmacies.

There is country-specific variance in the supply chain approach. The WHO recognizes two models – push and pull (whereby pull is the mainstream way, according to which local-level distribution entities order medicines from higher-

level central distribution centers) (WHO, 2015b). Whereas the pull model requires the lower level to be capable of calculating and forecasting the demand, which according to the WHO is a human task, in the push model, a central entity pushes medicines to the lower level. This can be used, for example, with a limited list of medicines in emergency circumstances or if there is no consumption history data.

The wholesale level of the supply chain can vary as well. For example, the supply chain in Finland has traditionally been dominated by two wholesalers. Whereas there are more than 100 wholesaling organizations in Finland, only two have maintained stocks and downstream distribution channels, while the rest have only imported medicines. Medicine distribution has been carried out through a single wholesale channel, whereby a particular medicine has been solely available for pharmacies from the designated wholesaler rather than multiple wholesalers (Meriluoto, 2018).

This setup is, however, undergoing reconsideration. For example, some pharmaceutical manufacturers have already utilized multiple wholesale channels in cases of supply chain disruptions at the wholesale level (Meriluoto, 2018). The single-channel system is a commonly agreed practice within the industry, which is not based on strict legal requirements (Kilpailu- ja kuluttajavirasto, 2000).

The one-channel distribution concept raises questions about the competitiveness of the market. In other countries, pharmaceutical companies can utilize multiple distributors, and pharmacies and hospitals put medicine orders out to tender. Sweden used to have a one-channel distribution system as well, until it was dismantled as a part of wider deregulation of the pharmaceutical market in 2009 (Rönnback, 2018). Whereas the Finnish Competition and Consumer Authority has assessed the one-channel distribution setup multiple times (e.g. (Kilpailu- ja kuluttajavirasto, 2000), (Kilpailu- ja kuluttajavirasto, 2012)), the agency has, each time, cleared it as compliant with competition regulations. The medicine wholesale sector has seen consolidation in other parts of the EU as well; however, no other member country has a one-channel distribution system (Kanavos, et al., 2011).

The one-channel concept has been justified as an efficient and secure system. It is suggested that the wholesale margins in Finland are among the lowest in Europe (Kanavos, et al., 2011). This can be used to argue for the effectiveness of the distribution system, as the low margins may appear to drive optimizing the supply and warehousing. At the same time, one can also argue that more effective processes and operating models would drive higher margins. Some wholesalers have even admitted that the low margins lead to an unhealthy market (Rapeli, 2007).

The difference from the norm in the EU is also that in Finland, wholesale margins are not regulated (Kanavos, et al., 2011). Whereas the reference prices of those medicines that are subsidized through social insurance are regulated, the wholesale prices are negotiated between the wholesaler and the pharmaceutical manufacturer case by case (Apteekkariliitto, 2020). Because the margins remain low for

medicines, wholesalers seek better profits from other welfare product categories (Rapeli, 2007).

It should be noted that despite the one-channel system, Finland is not immune to disruptions or shortages in global supply chains. For example, as at the time of writing this thesis, the world was undergoing the COVID-19 pandemic, and wholesalers were not able to fulfill the increased demand for certain medical items, such as respirator masks (Kauhanen, 2020). Since the wholesale sector was not able to adapt to the situation, uncommon supply sources were utilized with poor results (Sutinen, 2020). Particularly, the lack of visibility of the distribution channels and product quality caused challenges. Whereas managing those aspects should be among the core competencies of medicine wholesalers, they seemed to struggle to react promptly.

Considering the shortage problem, there can be multiple reasons – a global pandemic or similar disruption is only one potential source. For example, the WHO (2015c) suggests that funding mechanisms and incentives have a role to play. If prices for certain medicines are reduced, the manufacturer ceases to be incentivized to continue producing adequate amounts. Similarly, regulatory processes may slow down or hinder certain medicines from entering the market. What is, however, clear is that there is no upcoming demand visibility. There is also insufficient consistent data to enable proper management and supply chain visibility. Iyengar, et al. (2016) noted that efforts to manage medicine shortages should begin by laying a proper information foundation for the medicine supply chain. This is evident, considering that the reason for the disruption has been identified in only half of the cases (Azghandi, et al., 2018).

Means to manage shortages in the supply chain have been introduced – for example, those relating to inventory management (such as safety stocks) and multisourcing strategies, as well as simulating various scenarios to find an optimal policy (Azghandi, et al., 2018). However, it can be argued that data transparency is the key (Dai, et al., 2020). This refers explicitly to suppliers disclosing information on their capacity levels, which are currently hidden.

With respect to regulations in Finland, the pharmaceutical industry and wholesalers are responsible for importing medicines, and wholesalers for maintaining interim stocks and for distribution (Sosiaali- ja terveysministeriö, 2011). Pharmacies, hospital pharmacies and dispensaries dispense medicines to patients. Dispensaries are authorized medicine distribution services maintained by healthcare service providers, public or private (Fimea, 2018b). Hospital pharmacies, as the name implies, are located in larger healthcare units. Table 1 summarizes the medicine supply chain structure in Finland at the time of writing (Apteekkariliitto, 2017; Fimea, 2018b, 2019a, 2019b, 2019c).

Table 1. Medicine supply chain in Finland.

SUPPLY CHAIN PARTICIPANT	NUMBER
Pharmaceutical manufacturer	34
Wholesaler	102
Wholesaler with warehousing	2
Pharmacy	812
Hospital pharmacy	27
Dispensary	84

Whereas the medicine supply chain is usually highly regulated, whereby authorities grant permits to operate in the market, many European countries have recently deregulated the pharmacy sector, which has increased vertical integration within the supply chain (Fimea, 2017). Vertical integration refers to the merging of various levels of supply chain under the same actors – for example, wholesalers acquiring pharmacies. Horizontal integration is another trend; it denotes the consolidation of the market, such as the pharmaceutical market, under few chains (Kanavos, et al., 2011).

Whereas the medicine supply chain's major role is to make medicines available for patients, it should be noted that not all medicines are consumed as planned. Those not consumed constitute waste – for example, in the UK, the annual cost of prescription medicine waste is estimated at GBP 300 million (Hazell & Robson, 2015). Medicine waste is often hazardous and presents health and environmental risks; therefore, it needs to be treated with appropriate means (WHO, 2015a). This is an important standpoint in the medicine's journey from the manufacturing plant to downstream markets.

It is noteworthy that medicine supply intertwines with the wider healthcare supply chain and is part of the overall care delivery process (Sosiaali- ja terveysministeriö, 2011). In the same vein, it can be argued that the medicine supply chain also includes other parties, such as physicians: prescription drugs can be prescribed only by accredited professionals, and therefore, physicians can be understood as an inherent part of the supply chain. Increasing the granularity at this end, specific solutions and technologies used within the supply chain can be found, including automatic dispensing machines and ePrescription. ePrescription is a key solution integrating the downstream parties of the supply chain. Another view is that of regulators – the field is tightly regulated, and there are various policies in place, including generic substitution and reference price systems. In the next sections, these key concepts are presented in more detail.

The medicine supply arena has been sparsely researched from the IS viewpoint; however, some studies can be identified. For example, Clauson et al. (2018)

suggested that blockchain can play a role in health supply chain management to prevent counterfeit products from entering markets. The other area could be health-related devices, with a focus on investigating how the origin of a product can be verified. Ângelo, et al. (2017) discussed how IS can be utilized in the electronic labeling of medicinal compounds in the related supply chain. The researchers conceptualized an entire ecosystem that increases knowledge on medicinal products and facilitates the cross-supply between pharmacies. The researchers also argued that IS-related studies in this area are scarce. Another viewpoint is that of a single firm operating in the supply chain. Mogdil and Sharma (2017) argued that IS have an impact on the operational performance of a firm in the pharmaceutical supply chain. This happens through improving supply chain practices, which is achieved with IS.

Based on the above, a model of the medicine supply chain is introduced (Figure 3). The model depicts key actors in the supply chain, including the pharmaceutical industry and its suppliers, wholesalers, dispensers (i.e. pharmacies and healthcare units, such as hospitals) and waste disposal facilities, where unused medicines end up. All through the supply chain, logistics is needed to deliver medicines. The model also includes prescribers (i.e. doctors) and patients – as they are, undoubtedly, key actors in the medicine supply. There are other important roles, such as regulators and insurers, but these are not included in this model to maintain a reasonable scope. Furthermore, it can be argued that the supply chain model should focus on concrete medicine flows (e.g. (Imran, et al., 2017)). Actors such as regulators are stakeholders in the related integrated health system, and whereas they undoubtedly influence the process, they do not actively participate in it. This thesis particularly focused on researching how medicines are brought to patients at an operational level; therefore, financing processes, for example, were not addressed.

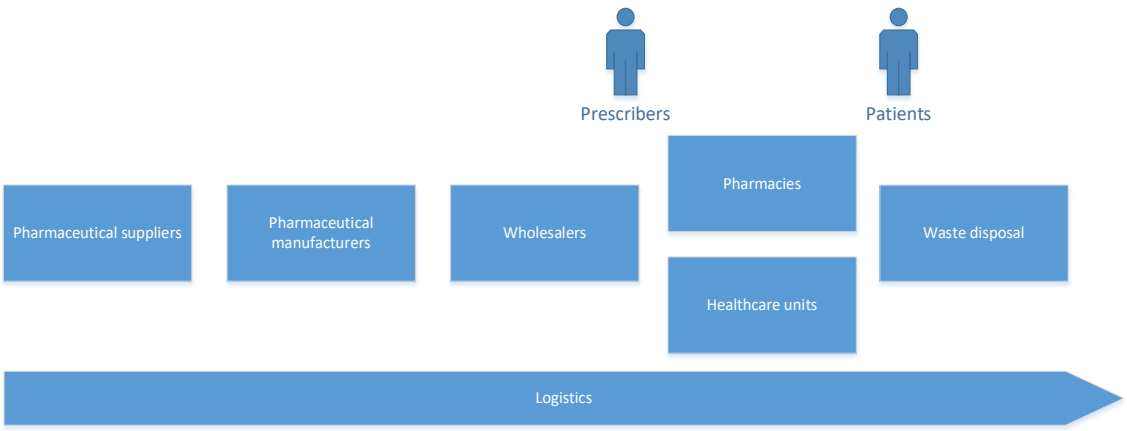

Figure 3. Medicine supply chain.

2.3 ePrescription

ePrescription has been widely studied in different accounts (Abramson, et al., 2011) (Caldwell & Power, 2011) (Clyne, et al., 2012) (Johnson & Lehmann, 2013) (Salmivalli, 2008). The reported key benefits particularly relate to improved risk management and reduced medication errors, as pharmacies or others dispensing medicines do not need to try to interpret handwritten scribbles anymore. Improved communication between pharmacies and prescribers can reduce medication costs, especially for patients with multiple prescriptions (Lizano-Díez, et al., 2014).

eHealth Initiative defines ePrescription as "the use of computing devices to enter, modify, review, and output or communicate drug prescriptions" (2004, p. 7). Whereas this definition reduces ePrescription to a digitized version of a paper prescription, ePrescription can also be understood as a wider concept that connects prescribers, pharmacies and insurers (Aanestad, et al., 2017a). For example, in Finland, the concept is based on a central service – Kanta, which is interfaced by citizens, prescribers and pharmacies (Kansallinen Terveysarkisto, 2020). Kanta hosts databases for personal health records, prescriptions (Prescription Centre), medicine information and medical certificates.

According to Aanestad et al. (2017a, p. 16), ePrescription infrastructure comprises three parts:

- eCapture: the functionality to capture the prescription.
- eTransfer: the associated information flows to share the prescription between required stakeholders.
- eDispensing: the functionality to capture the actual dispensing of medicines.

What is missing from this definition is the integrative component, such as a centralized database, that links the different parts. (One could also argue that a medicine information database is a key part of such architecture.) Nevertheless, from the medicine supply chain perspective, this wider definition of ePrescription is key, as it integrates various stakeholders in the supply chain. ePrescription is considered a factor transforming healthcare delivery, and many governments are trusting it will enable better healthcare spending control through increased visibility (Aanestad, et al., 2017a).

One of the key benefits of this type of comprehensive ePrescription system is the management of the overall medication of a patient. Traditionally, the information may have been dispersed across multiple healthcare service providers, but this can be overcome by a centralized ePrescription system (Kauppinen, et al., 2017). This type of wide-scale ePrescription system is, however, only available in a few EU countries – in 2017, these were Denmark, Sweden, Estonia, Iceland and Finland

(Kauppinen, et al., 2017). It should be noted that these are relatively small nations by population, and for example, in Finland, there is a long tradition of centralized and governmentally managed databases. There is also a unique social security identifier for each citizen – which, one can argue, paves the way for a national centralized database such as ePrescription.

It is self-evident that ePrescription is just one element in a bigger puzzle related to the overall management of medication. ePrescription needs to be linked to electronic patient records of a given patient to obtain the full picture of a patient and their medication history. This is, technically and sociotechnically, a much wider concept. For example, the ownership of this data has been debated, and rather than running a centralized database, distributed solutions have been suggested. This discussion, however, is out of the scope of this thesis.

Figure 4 illustrates the ePrescription domain within the medicine supply chain. ePrescription particularly integrates the downstream arena of the chain, where prescribers, dispensers and patients operate.

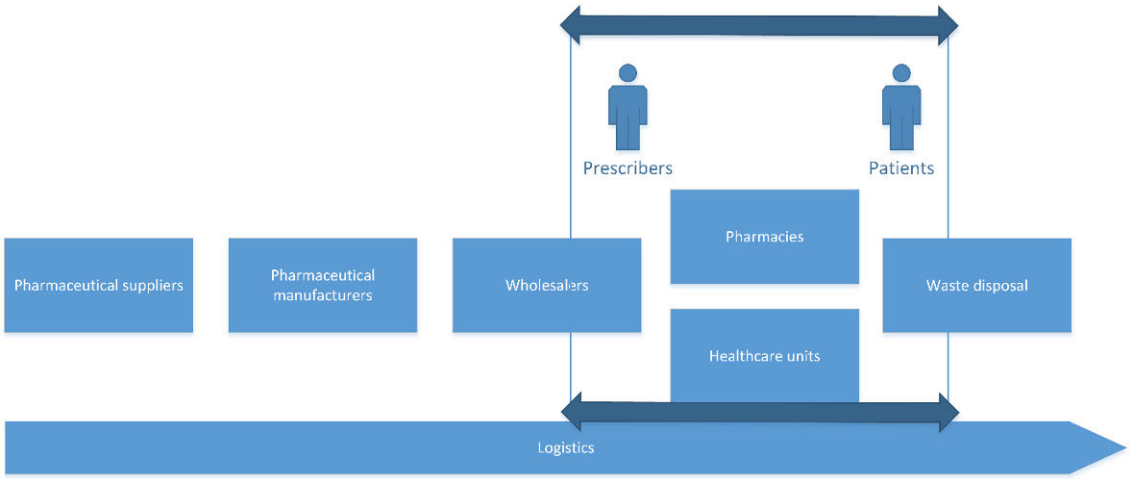

Figure 4. ePrescription in the medicine supply chain.

Typically, ePrescription deployments are lengthy projects in which existing information infrastructures, such as IS used by healthcare service providers and pharmacies, must be considered (Hanseth & Bygstad, 2017). An example of this is from Finland, where the Finnish healthcare and pharmacy sector went through the deployment of ePrescription in the period 2012–2016 (Mäkinen, Rautava, Forsström, & Äärimaa, 2011) (Kansallinen Terveysarkisto, 2020). The adoption and use of ePrescription was enforced through legislation (Laki sähköisestä lääkemääräyksestä [Electronic Prescription Act] 61/2007). The Finnish Patient Data

Repository (Kanta) is a database containing personal healthcare records (including prescriptions, however in a separate partition) collected from healthcare service providers' patient IS (Kansallinen Terveysarkisto, 2021). The first steps in the development project were taken in 2001, so it has been a lengthy project (Jormanainen, et al., 2018). However, it is estimated that the annual productivity gains amount to EUR 50 million through saving time used for the manual processing of prescriptions (Parviainen, Kääriäinen, Honkatukia, & Federley, 2017).

2.4 Prescription adherence and automatic dispensing solutions

The WHO defines adherence as "the extent to which a person's behaviour – taking medication, following a diet, and/or executing lifestyle changes – corresponds with agreed recommendations from a health care provider" (WHO, 2003, p. 3). Adherence is one of the key concepts in medicine delivery; nonadherence (i.e. failing to follow prescribed treatment) may lead to adverse effects and, ultimately, increased mortality (Chisholm-Burns & Spivey, 2012). Nonadherence is costly as well – as it leads to an increased need for health services, such as outpatient visits or inpatient treatment (Kane & Shaya, 2008). For example, in the US, nonadherence costs USD 300 billion every year (Foo, et al., 2011). This is not surprising, given that according to WHO's estimates, adherence is typically at 50% among patients with chronic conditions (WHO, 2003) – in other words, only half of patients actually follow prescriptions.

The reason for non-adherence can be intentional or unintentional, whereby the patient may either actively or passively discard the prescription (Gadkari & McHorney, 2012). Passive, unintentional nonadherence can be about forgetting to take the dose at the right time. Particularly, those with polypharmacy (i.e. having multiple medications at the same time) are in the danger zone (Marcum & Gellad, 2012). These are often elderly people with lowered cognition capabilities, which worsen the problem. According to Sorensen et al. (2005), problems are caused by a large number of prescribers and dispensers for medications found in the home, hoarding, multiple storage locations for medication, the lack of medication administration routines, discontinued medication repeats retained and a mix-up of names of medicines.

Often, however, nonadherence is intentional, whereby the patient actively decides not to comply with the prescription. This can be due to the patient's beliefs in terms of the treatment and their condition (Gadkari & McHorney, 2012). In fact, it has been suggested that the so-called unintentional nonadherence is not completely passive; rather, beliefs about medicines may steer toward nonadherent behaviors such as forgetfulness (Unni & Farris, 2011).

In any case, interventions are required to tackle the issues. Various solutions have been proposed – for example, ingestible biosensors emitting a radiofrequency signal when encountering a certain pH value (Chai, et al., 2016), electronic pillboxes (Hayes, et al., 2006), blister packaging (Connor, et al., 2004) and phone reminders (Unni & Farris, 2011). One of the key solutions is, however, the automatic medicine dispenser. Automatic dispensers were introduced in the 1960s to offload the medicine administration burden from nurses (Balka, et al., 2007). Modern automatic dispensers intend to provide an end-to-end solution, with functionality spanning from the physician order entry to the sorting of medicines and distribution to either nursing staff or patients.

Typically, medicines come out from the automatic dispensers in plastic packs, guiding and facilitating that the right dose is taken at the right time (Van Den Bemt, et al., 2009). A common type is blister packaging, which is illustrated as Exhibit A in Figure 5; however, other types exist, such as strip packing, which is based on heat-sealable coated films, and aluminum foil packaging (Choundary, 2015). In blister packs, medicines are sorted and packed in separate blisters in the order they should be consumed. Some also prefer pouches and sachets (Exhibit B in Figure 5), which contain one or multiple medications that need to be consumed at the same time (Clews, 2017). The traditional manual pill dispenser is also illustrated in Figure 5 as Exhibit C.

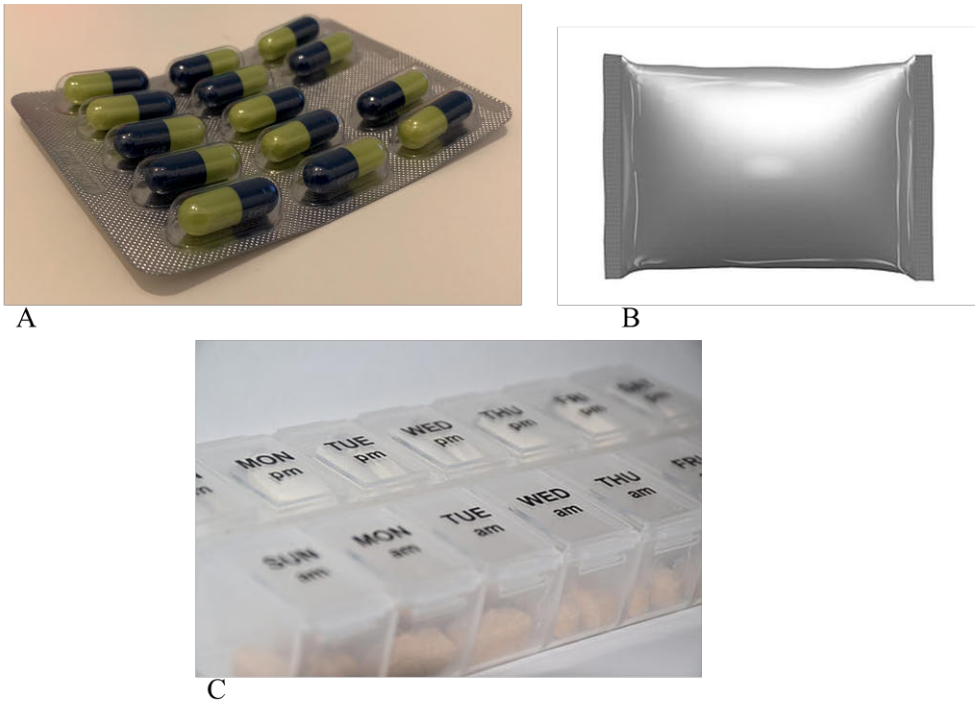

Figure 5. Different medicine packaging types (A: https://commons.wikimedia.org/wiki/File: Pharmaceutical_Blister_Pack.png, B: https://www.pxfuel.com/, C: https://www.piqsels.com/).

Automating the dispensing process can reduce medication errors relating to medicine administration; this is common sense, as a robot will not make the so-called human errors. Furthermore, automatic dispensing can contribute to adherence, as medicines become available at the right time. Some automatic dispensers are connected devices with functionality to notify in case of deviations, and this way further tackles the adherence problem (Suomi, et al., 2016). In addition to enforcing adherence, dispensers are also commonly understood to facilitate efficiencies, as they reduce the administrative burden and remove manual tasks in the medicine delivery process.

From the medicine supply chain perspective, automatic dispensing integrates actors in the downstream. One related service is automated dose dispensing (ADD). ADD connects the pharmacy, physicians and caregivers: prescriptions are sent from a pharmacy to ADD service providers – who package medicines according to the prescription (taking into account doses, dispensing times and so forth), which are then inserted into automatic dispensers (Suomi, et al., 2016).

There are also critics of automatic dispensers. For example, in some cases, they can increase the risk of a medication error. If, for instance, the dispensed medicine

requires additional manipulation, such as crushing, this typically remains a manual task, which is error-prone (Van Den Bemt, et al., 2009).

The reasons for nonadoption have been studied in Finland, and they include costs and regulations (Suomi & Li, 2014). Dispensers are typically expensive, and they are not fully covered as part of standard health plans. Dispensers also need to incorporate failsafes and assurance mechanisms, which makes them expensive to build. Regulations also hinder adoption since the fulfillment and validation process requires pharmacy visits. Figure 6 depicts which parts of the medicine delivery chain automatic dispensing covers.

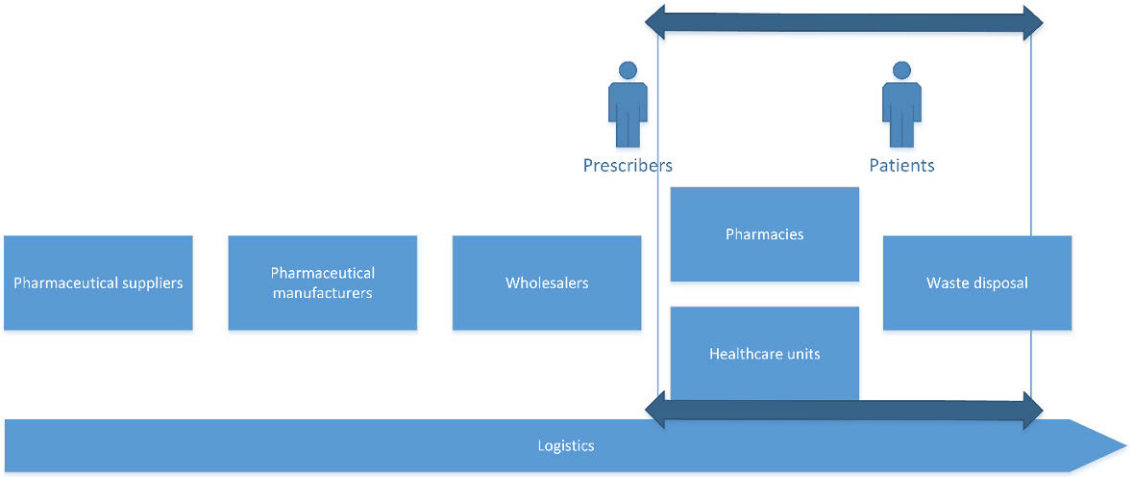

Figure 6. Automatic dispensing in the medicine supply chain.

2.5 Regulatory perspective

The area of medication is highly regulated. For example, it is commonly regulated that only accredited professionals can prescribe medicines. Moreover, it is regulated that only accredited pharmacies can dispense these medicines and that the development and manufacturing of medicines must follow strict guidelines. Separating prescription and dispensing originates from medieval times when states began to seek to regulate this and forbid a single party from diagnosing and dispensing (Liaw & Peterson, 2009). However, there are differences between regions on how strict these regulations are.

The introduction of regulated prescriptions dates to the 1930s (Flanigan, 2012). Not all countries are, however, enforcing strict prescription laws. Particularly in low- and middle-income countries, it is typical that pharmacies act as the first and only interface to health services for many, and pharmacies dispense medicines without requiring a prescription (Abdelaziz, et al., 2019). Whereas one can argue that this

may contribute to the misuse of medicines such as antibiotics, leading to more resistant bacteria, many do not have access to a physician and need to rely on pharmacists and self-medication. There are also ethical questions regarding whether the prescription system is violating one's right to self-medicate and is a manifestation of paternalism (Flanigan, 2012).

The right to prescribe medication in Finland is regulated so that only physicians, dentists and nurses who are specifically authorized to prescribe certain medicines are entitled to prescribe medication to patients (Sosiaali- ja terveysministeriön asetus lääkkeen määräämisestä [Decree on medicine prescribing] 2010/1088). After the prescription is made and the patient fetches it from a pharmacy, another regulatory tool comes to play: the generic substitution system.

The purpose of generic substitution is to replace higher-priced brand products with lower-priced generic products. In Finland, for example, pharmacies are mandated to substitute brand-based prescriptions with generic products if a generic equivalent is available and it is at a lower price (Lääkelaki [Medicines Act] 395/1987). The equivalent product needs to, of course, contain the same active ingredients as the brand product.

The generic substitution system is a key mechanism in managing medicine costs, whether paid for out of pocket by consumers or subsidized by the state. As supporting evidence, in Finland, medicine expenditure slowed after the introduction of generic substitution in the 2000s (Fimea and Kela, 2015). There are, however, countries regulating less in this area – for example, in the US, the lack of generic substitution is estimated to cost USD 9 billion annually in outpatient care (Stenner, et al., 2010).

Another related regulatory component is the reference price system, which mandates prices for medicines in a jurisdiction. In Finland, this is built into the legislation (Lääkelaki [Medicines Act] 395/1987). Countries negotiate the prices individually for various medicines with related pharmaceutical manufacturers and typically utilize some benchmarking pricing information from similar countries (Kalo, et al., 2013).

The pharmaceutical defines an ex-factory price for a medicine, which is used as a basis for price negotiations. The ex-factory prices are different, depending on the market, and therefore, the reference prices can differ by country. It is also suggested that new medicines become available to higher-income countries with higher price levels (Vogler, et al., 2019). It is suggested that ex-factory prices are relatively low in Finland (Kanavos, et al., 2011).

Each wholesaler in Finland negotiates the purchase price for medicines it distributes (Apteekkariliitto, 2020). The reference prices for wholesale prices are regulated by the Pharmaceutical Pricing Board for those medicines that are reimbursable through social insurance and are included in the generic substitution

system (Pharmaceutical Pricing Board, 2020). The board defines reference price groups, wherein similar medicines (i.e. medicinal products with the same active ingredients, dosages and package sizes) are grouped, and determines a reference price for the given group. Pharmaceutical companies then confirm their wholesale prices, which cannot exceed the reference prices. Reference prices are valid for three-month periods, and wholesalers are required to notify the new wholesale prices before the beginning of each period. (Pharmaceutical Pricing Board, 2020)

The retail price of a prescription medicine in Finland is the sum of the wholesale price – which, if applicable, can be up to the reference price – the pharmacy margin and 10% value-added tax (Apteekkariliitto, 2020). The pharmacy margin is regulated by law in Finland, and it depends on the wholesale price of the medicine; the more expensive the wholesale price, the lesser the margin (Valtioneuvoston asetus lääketaksasta [Decree on drug tariffs] 713/2013, 2013).

The combination of generic substitution and reference pricing systems is an effective mechanism to manage medicine costs. From the pharmaceutical industry point of view, this is, however, challenging, as pharmaceutical manufacturers need to maintain the profitability of the business. Investments required to develop a new medicine are often counted in billions; should the profits decrease, there may be less investments in pharmaceutical research and development. Another implication could be that the ex-factory prices are raised, making medicines less accessible in lower-income jurisdictions (Kalo, et al., 2013). This requires careful balancing from the regulator, as new medicines can lower healthcare costs and even mortality rates. However, the prices of medicines are typically high, and the market needs to be adequately attractive for the pharmaceutical industry to invest.

Another noteworthy policy topic is copayment, which is another instrument for managing medicine costs. Potential policies include cap policies, whereby the amount of prescriptions (which is reimbursed to the patient through, for example, social insurance) is restricted (i.e. capped); ceiling policies, whereby the reimbursed fees are restricted to certain amounts; and coinsurance, whereby the patient covers a certain part and the insurer the remaining part (Luiza, et al., 2015). For example, in Finland, prescription medicines are reimbursed, after an initial EUR 50 fee, at 40%, 65% or 100%, depending on the medicine (KELA, 2020). There is also a cap for out-of-pocket costs; if the cap is met, an additional reimbursement is introduced (KELA, 2020).

It has been shown that changes to the reimbursement rates of a medicine have an impact on the consumption of that particular medicine (Garcia-Gomez, et al., 2018). This has been reported to have varying implications. Introducing copayment and cap policies may have adverse health and economic effects since medicines prescribed for chronic conditions, for example, may become less available for those who need them (Luiza, et al., 2015). This may increase the need for treatment and hospital

stays. Conversely, it has also been reported that introducing even a minor, nominal payment reduces consumption (Garcia-Gomez, et al., 2018). This may have a positive impact if the reduced consumption is due to reconsidering the given prescription with a relevant professional.

There are regulations to protect the industry as well. It is particularly the counterfeiting that regulators are trying to curb through new legislation. Currently, intellectual property relating to pharmaceutical products can be protected with patents. The World Trade Organization requires a 20-year protection period, which has been mandated under the Trade-Related Aspects of Intellectual Property Rights Agreement (WHO, 2021). However, the medicine counterfeit market is estimated to have risen to USD 200 billion, and it is clearly a global issue (Janvier, et al., 2018). The EU defines two types of counterfeiting: First, a falsified medicine is made to resemble the original product but may not contain the right active ingredients (European Medicines Agency, 2018a). Second, counterfeit medicines are those breaching intellectual property rights – that is, made using a patented formula without a license.

To stop counterfeiting, the EU has introduced multiple regulatory measures. These include a two-dimensional barcode and an antitampering device in the medicine package, which have been mandatory for prescription medicines and some OTC medicines as of the first part of 2019 (European Medicines Agency, 2018a). The pharmaceutical manufacturer is required to upload the unique identifier, reflected by the barcode, to a centrally managed EU database, which is then queried in the different phases of the supply chain to verify the authenticity of the medicine. Good Distribution Practice requires supply chain parties, such as wholesalers, to verify the incoming consignments (Guidelines on Good Distribution Practice of medicinal products for human use, 2013). The EU's Good Manufacturing Practice governs the manufacturing process itself, stipulating that any suppliers used to provide, for example, raw materials and ingredients are of an adequate standard (Standard l) (European Medicines Agency, 2018b).

Similar initiatives have been launched in the US. The FDA introduced the Drug Supply Chain Security Act in 2013 (FDA, 2018a). The act mandates the traceability of medicines through the supply chain as well; however, it is less prescriptive and not based on a centralized state-led database. Nevertheless, it mandates serialization of medicine packages and traceability across the supply chain. Other jurisdictions are taking similar actions to stop counterfeiting (e.g. (Tseng, et al., 2018)).

Turning attention to the end of the supply chain model – that is, waste disposal – this area is varyingly regulated around the globe. This topic is discussed in Section 2.6.

The key regulations and their domains in the supply chain are depicted in Figure 7. It should be noted that there are also many other regulations in the area of

medication and healthcare, such as those relating to the clinical testing or the marketing of medicines. Further discussion on those areas in this thesis is omitted for the sake of brevity and considering the focus on the supply chain.

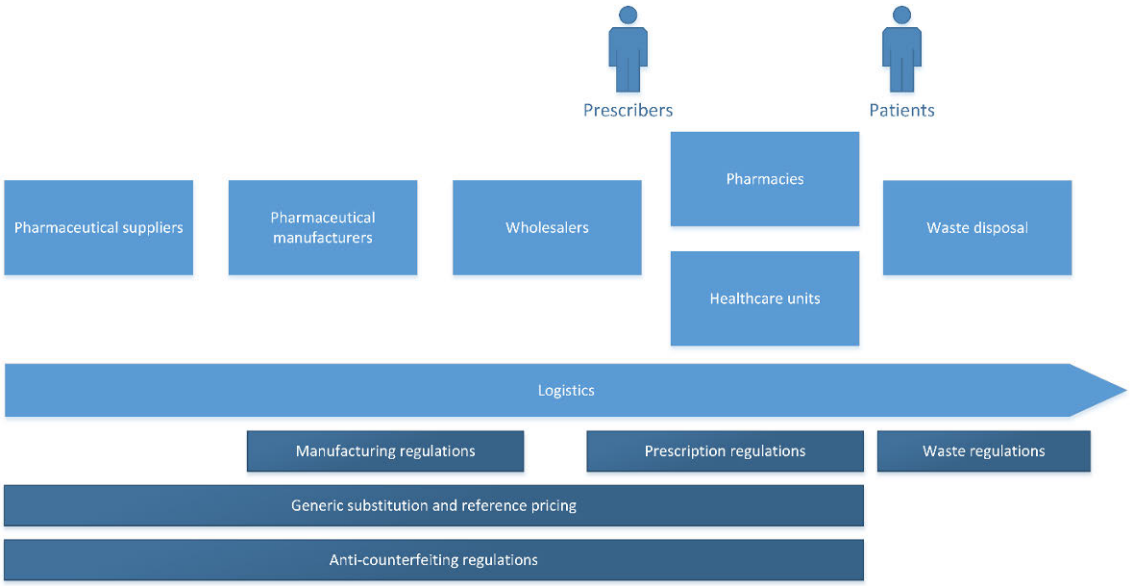

Figure 7. Some central regulations across the medicine supply chain.

2.6 Medicine waste disposal

Medicine waste disposal can be approached from two perspectives: first, how it is carried out in institutions, such as hospitals, and second, how it is conducted in households and homes. Medicine waste comprises unused, expired and contaminated medicines. It is part of healthcare waste, which also covers other types of waste generated in the course of healthcare delivery, such as pathological waste and syringes (WHO, 2015a). Furthermore, consumed medicines can be argued to generate waste; this is simply because consumed medicines tend to end up in the public sewage system through natural ways (Rogowska, et al., 2019).

Medicine waste can cause many problems if not properly processed. For example, it can contaminate drinking water and, therefore, cause health problems (WHO, 2015a). Unprocessed medicine waste from landfills can be propagated to ground water – for example, in Germany 156 pharmaceuticals were detected in drinking water (Kuster & Adler, 2014). Furthermore, it has been shown that water treatment plants are unable to filter all the pharmaceutical waste from sewage wastewater (Rogowska, et al., 2019).

The environmental risk is acknowledged, and there have been attempts to regulate it. For example, in the US, the arena is heavily regulated through the Medical Waste Tracking Act, which governs the collection and processing of medical waste (Winfield & Brooks, 2015). Medical waste here refers particularly to that generated by healthcare facilities, rather than households (U.S. Environmental Protection Agency [EPA], 2017).

The EU has established the Directory of Hazardous Waste, which is mandated for each member country (Winfield & Brooks, 2015). The issue, however, is that it is only a directive rather than actual legislation, leaving leeway for interpretation and adoption across the union. This is a global issue: there is no unified definition for medical waste, although it is evidently a significant health and environment hazard.

Furthermore, the aforementioned regulations govern medicine disposal in healthcare units only. A lot of waste is also generated in households. According to Finnish legislation, municipalities are responsible for arranging waste collection for households – including hazardous waste, such as medicine waste (Jätelaki [Waste Act] 646/2011, 2011). Finnish municipalities tend to do this without charge in order to attract citizens to dispose of hazardous waste in a proper way (Suomen Kuntaliitto ry, Suomen Kiertovoima ry [KIVO] & Suomen Apteekkariliitto ry, 2019).

In Finland, the disposal of medicine waste is carried out through pharmacies, where people can return their unused medicines and other medicine waste without cost. Municipalities have agreed to this arrangement with the Association of Finnish Pharmacies (Suomen Kuntaliitto ry, Suomen Kiertovoima ry [KIVO] & Suomen Apteekkariliitto ry, 2019). The role of the pharmacy in the medicine waste disposal process is not peculiar only to Finland; many other European countries have a similar system whereby pharmacies accept unused medicines from households (Rogowska, et al., 2019). EU Directives 2001/83/EC and 2001/82/EC mandate member countries to arrange for the collection of expired medicines (Rogowska, et al., 2019). Again, since this is a directive, it leaves room for each of the member countries to interpret and implement it as it wishes.

The extent of household medicine waste should not be underestimated. Many medicines are available without prescription, and they contribute to the increasing wastage. For example, the consumption of ibuprofen, a common pain reliever, amounted to 975 tons in Germany in 2012, whereas it was 250 tons in 2002 (Kuster & Adler, 2014). It is common sense that this will have consequences for the environment.

Medicine waste from pharmacies and healthcare units is usually incinerated. Other methods include autoclaving and microwaving (Messerle, et al., 2018). For example, in Finland, the waste disposal plant processes 400 tons of medicine waste annually (Hyvönen, 2016). Medicine waste is delivered to the plant in large containers, which are incinerated at a high temperature. The incineration temperature

is usually between 900°C–1200°C. Whereas this certainly disinfects the medical waste, it may release hazardous substances such as dioxins into the environment (Messerle, et al., 2018). The bottom ash may also remain toxic (Hossain, et al., 2012). The problem is also more significant in developing countries, which may lack relevant regulatory and waste disposal mechanisms.

To conclude this section, one more viewpoint is introduced. In this thesis, the medicine supply chain is discussed from the perspective of human medicines. However, livestock are medicated as well, and their manure is used for fertilization, releasing more medicines to the environment. All effects of the pharmaceutical exposure to the environment, people, livestock and wildlife are yet to be seen (Arnold, et al., 2014).

3 Theoretical Foundation

3.1 Summary of theoretical background in this thesis

This thesis draws from information asymmetry theory, and it is used to explain bottlenecks in a given domain. In terms of related articles, Article I specifically refers to this theory in the course of building the initial model for this thesis. The scarce and unequal information is revisited in the following articles.

Furthermore, the sociotechnical systems model is utilized when examining the transformation in the domain, as well as inefficiencies across the medicine supply area. Article II views the transformation in the pharmacy sector through this theoretical lens. Article III utilizes the model as well when examining the management of medicine waste in a hospital. In this chapter, these two theories and their applicability in the healthcare and medicine supply arenas are discussed.

3.2 Information asymmetry

3.2.1 Information asymmetry as a concept in the healthcare and pharmaceutical markets

The healthcare market is pervaded by unequal information. In this thesis, a model of the medicine supply chain has been introduced, and it will be demonstrated that there are multiple disconnections between the various actors, leaving the entire ecosystem across the supply chain to operate largely in the dark.

If attention is turned to the healthcare market as a wider concept, expanding the discussion in Section 1.2, the consideration can begin with the physician-patient relationship. As described by Arrow (1963), the asymmetry derives from the fact that physicians are accredited professionals with years' worth of education, usually having a deep understanding and knowledge of their field. Conversely, patients are often laymen without extensive knowledge of treatments or the capability to evaluate recommendations they receive from healthcare professionals. By default, patients do not understand the economic impact of their treatment, either.

The consequences can be severe, especially for patients with polypharmacy (i.e. those with multiple medications). The risks relating to polypharmacy include ADRs, increased hospital stays and mortality (Masnoon, et al., 2017). The situation becomes especially risky when there are multiple prescribers without visibility to all prescriptions. One way to mitigate this is through making adequate information available with ePrescription and electronic health record systems, which intend to maintain a unified view of the medication regimen for the given patient. (Please see Section 2.3 for more discussion on this.)

One of the implications of information asymmetry is the moral hazard. This occurs when party A must bear the risk for party B's actions but has no means to control party B's intentions or how they behave. Party B then exploits this information asymmetry and transfers the risk to party A. This is typically an issue in the insurance industry, whereby the insurer cannot evaluate how the insured acts or manages the risk after the insurance agreement has been signed (Arrow, 1963).

In the context of medication, nonadherence is susceptible to moral hazard. This is especially true if the patient does not directly cover the cost themselves but it is covered by an insurance arrangement. This drives increased insurance fees, and in the case of national health insurance taxpayers, the patient eventually bears the cost.

It should be noted that an asymmetric position as such is not a problem directly. Actually, it is a norm in business: firms have confidential information they use to gain a competitive edge, people have their personal data they want to keep to themselves, and so on. This inequality can have adverse effects on the market; however, when exploitation goes too far – as was proven by Akerlof (1970), who studied the used cars market (which later made him a Nobel Laureate). He showed that car sellers selling the so-called lemons (i.e. cars in poor condition) while hiding information about the defects eventually led to market failure. As buyers usually have no means to verify the condition, defective cars can be sold at the same price as nondefective cars. This leads to better cars disappearing from the market, leaving only defective cars (i.e. lemons), which eventually erodes the trust from the market. This is also called adverse selection.

The healthcare and medicine supply markets are prone to similar failures and are therefore protected through strict regulations. A failure would have grave consequences and could entail higher mortality. For example, if falsified or contaminated medicines were propagated to the market and people could not trust the medicine dispensed in the pharmacy is what it is supposed to be, and, therefore, cease to consume prescribed medicines, the entire basis for the healthcare system would collapse. This is, of course, an unlikely scenario in the developed world, where medicine supply is highly regulated. In markets where regulations are less developed, however, this can be a real risk. In many emerging regions where healthcare services are scarcely available, pharmacies are the first and perhaps only

channel for treatment. According to the WHO, one in 10 medicines is falsified or otherwise substandard in low- and middle-income countries (WHO, 2017).

It is especially generic products that are susceptible to falsification since there may not be adequate testing facilities and policies to verify that the given generic medicine contains the required active ingredients (Silverman & Glassman, 2019). This leads people to avoid the generic products and choose the brand product; it is the market of generic medicines that fails in this case. As described in this thesis, generic substitution is a critical element to manage medicine expenses and contributes to a sustainable healthcare system. Information asymmetry is a particularly problematic situation for most vulnerable people in the world.

Some authors have even further suggested that the entire medicine market is largely a lemon market. Light and Lexchin (2021) discussed how new medicines are developed and marketed as superior to existing medicines; however, if risks such as ADRs are weighed, the benefit is questionable. According to the authors, there are multiple layers of mechanisms smoke screening those with lesser information, including unreliable clinical trials, biased scientific literature and hidden adverse effects. The authors back their findings through presenting several statistics on how ADRs have increased over the past few decades. The difference to Akerlof's (1970) used cars market is that new lemon medicines cost more and there is no trend for lower price levels in the market.

3.2.2 Uncertainty and information asymmetry as a supply chain problem

Whereas the patient-centered downstream is usually emphasized, information asymmetries also exist in other parts of the medicine supply chain. One example is pricing information: it can be considered a normal business practice to hide pricing information between markets. Pharmaceutical manufacturers negotiate prices with each country and do not disclose information widely on their ex-factory prices (Vogler, et al., 2019). Another example relates to shortages: information on disruptions have not been adequately available from pharmaceutical manufacturers (Rees, 2020). This information asymmetry, whether due to the upstream actors hiding information on disruptions or due to a general lack of transparency, can be understood as one of the root causes for medicine shortages. Given the disruption would be known earlier, precautionary actions such as ordering a substitute medicine could be taken.

Global supply chains may have single points of failures that are not fully understood in the downstream, and downstream parties are left to react to sudden changes and operate in uncertainty. Considering the medicine supply area, this is a significant issue.

To manage medicine shortages, an EU regulation for mandating pharmaceuticals to submit information on supply disruptions is underway (Rees, 2020). This has been accelerated by the COVID-19 pandemic. Finnish law already requires the importer, as well as the wholesaler, to inform authorities in case of a disruption (Laki lääkelain muuttamisesta [Amendment to Medicines Act] 553/2020).

Sometimes no supply chain party deliberately hides information, but rather the signals are not collected and interpreted. Data that could reveal an upcoming disruption might be available through various datasets, news feeds and such, but those are not utilized. Again, in the context of medicine supply, if the supply chain is not fully understood, transparency is not demanded or created, and predictive models creating more information are not developed. Those who do it gain a more powerful position, as they can prepare for disruptions and recover from those faster. At higher levels, these kind of information asymmetries could exist between competing countries and regions. Overall, considering medicine supply, the focus should be aimed at the upstream when considering the data, and data are often the key when creating or removing information asymmetries – it is clear that those who master it benefit.

3.2.3 Patient empowerment as a concept to manage information asymmetries and incomplete information

The information asymmetry between the physician and patient exists the other way around as well; one example is prescription nonadherence. A patient may choose to not follow a prescription and hide information on this. To tackle this, the options include monitoring and enforcing adherence. There are ways to do this, such as using automatic dispensers; however, this may be problematic from, for example, the privacy viewpoint. Patient empowerment, however, is suggested to be a cost-efficient and ethical means to manage the moral hazard.

Patient empowerment can be defined as "patient management that, through health education and the promotion of health-friendly behaviors, provides the person with the critical tools to make better decisions for their well-being, reducing cultural and social inequalities" (Ippolito, et al., 2019, p. 93). It is often the patient themselves who is the best expert in their condition, as they are the one experiencing it.

Patient empowerment can be understood as an instrument to manage the information asymmetry inherent in the healthcare market. The empowerment is both a process and an outcome in such that it entails actions required to enable a patient to take better control of their treatment – which, as the outcome, results in better understanding regarding own well-being and therefore better health results (Ippolito, et al., 2019). This is beneficial not just in terms of individuals' rights and self-efficacy but also from the cost perspective.

Self-management is particularly important in terms of chronic conditions, whereby treatment is a lengthy and continuous process (Ippolito, et al., 2019). If the patient misses the treatment, the condition may worsen and require more treatment. This, of course, increases costs. It is, therefore, self-evident that patient empowerment is an important element to manage costs with aging populations. Patient-physician information asymmetry is problematic since health is a personal and sensitive topic; introducing a monitoring framework to reduce the information asymmetry can be deemed surveillance and breaching one's privacy. Patient empowerment is not invasive. It does not remove the asymmetry but helps to cope with it.

Information as such plays a crucial role in patient empowerment, as it is based on information sharing and information availability (Loukanova, et al., 2007). The patient needs to understand their condition and the treatment, including the related medication. This increased information is an antecedent to the motivation required to better engagement with the treatment. Pharmaceutical prescription is, however, a problematic area, as despite the improved adherence, the patient may not be able to judge the effect of the prescription during or even after consumption. Hence, patient empowerment is not an adequate solution on its own.

3.2.4 Regulation as a controlling tool

Regulations are key instruments for managing information asymmetries. One example is generic substitution. Usually, a patient does not have the ability to assess prescribed treatment. To combat medicine costs, whether out of pocket or subsidized, the system reduces the asymmetry, as it mandates the prescription to be evaluated by a professional (i.e. the pharmacist) while dispensing and be replaced if necessary. Furthermore, separating prescribing and dispensing prevents the moral hazard relating to prescribers lobbying certain pharmaceutical brands or treatments (Liaw & Peterson, 2009).

Another policy intervention is copayment. The reimbursement of medicine costs presents the risk of moral hazard, whereby the consumption of medicines is not considerate. It has been reported that introducing even a minor out-of-pocket cost for a medicine reduces its consumption (Luiza, et al., 2015) (Garcia-Gomez, et al., 2018). Finding the right balance with copayment is a key question for medicine supply. The policy needs to combat the moral hazard while keeping medicines affordable and accessible for those who need them.

To understand some further information asymmetries in the pharmaceutical market, the works of Spence (1973) and Stiglitz (1975) need to be considered. In addition to Akerlof, they were rewarded the Nobel Prize for Economic Sciences in 2001 on the works they conducted on asymmetric information (Nobel Media AB,

2001). According to Spence's signaling theory, actors in a market reduce information asymmetry through signaling the information to less-informed parties (Spence, 1973). Conversely, Stiglitz viewed the phenomenon from the perspective of the less-informed party and suggested they undertake screening actions to reduce asymmetry and adverse selection (Stiglitz, 1975).

The regulation governing clinical trials protects consumers who cannot evaluate how a pharmaceutical manufacturer assures the safety of its products. In this case, the pharmaceutical manufacturer does not need to pay for signaling in terms of the safety of the product, as consumers can expect all pharmaceutical products in the market to have been adequately tested (this is not to say that they would not need to advertise to differentiate). Conversely, consumers do not need to screen products to find a safe one.

In low- and middle-income countries, where regulations and testing practices are scarce, signaling is more important. This is where a brand product – a brand is a signal – may be the only option for a buyer, as they cannot trust generic products, as described above.

Whereas a regulation may reduce signaling or screening costs, it has a price, as it typically requires heavy monitoring and enforcing. Another problem with regulations is that they are typically behind technological innovations (Koskinen, 2016). This blocks innovations and causes economical inefficiency. Considering the clinical R&D case, the massive regulatory framework effectively blocks new entrants entering the market. Spence (2015) suggested that digital technologies and platforms in particular are changing this landscape, as they are introducing new kinds of trust mechanisms. Digital platforms such as AirBnB and Uber equalize information about buyers and sellers through user ratings, and there is no requirement for a third party. Fraudulent and malign actors are removed quickly from the platform. Noteworthy here is that the monitoring and enforcing costs are small.

How this would work in the healthcare and medicine supply domain remains to be seen. The patient empowerment requires information on treatments and conditions to be available; however, this information must be valid to avoid, again, eroding trust in the market. In other respects, health is such a topic that deregulating seems far-fetched in terms of, for example, testing and verifying products. It is, however, a question how these regulations can be implemented in a cost-efficient manner so that emerging markets could also deploy and benefit from them.

Another discussion is the one relating to privacy and control over own data. Digital technologies and technological solutions can be used to collect data in real time to monitor behavior. In the health insurance market, utilizing wearables and monitoring, for example, health records can be used to calculate personal premium levels. Mobile applications monitoring activity levels are already present (e.g. (Fjuul, 2020)). This, however, is objected by many authors. For example, Zuboff (2019)

introduced the term surveillance capitalism, which is an economic system driven by personal data collected through various digital channels creating significant power inequality for the benefit of big businesses. Hence, whereas removing the information asymmetry through digital means might seem a good solution from the market viewpoint, it might lead to an unequal power structure.

3.2.5 The concept of asymmetric information in this thesis

In addition to the few examples outlined in this section, there are also many other asymmetries in the medicine supply. Article I identifies these asymmetries and investigates potential solutions, especially based on digital technologies. The article models the medicine delivery value chain and identifies problem areas in the chain, including those relating to prescribing and patient adherence. Article III also explores information asymmetries while reviewing the medicine delivery process in a hospital. In this article, it is demonstrated that incomplete and poor information is one of the reasons for an inefficient delivery process.

The reason this thesis utilizes the concept of information asymmetry is that the intention is to identify bottlenecks in the medicine supply chain and suggest solutions. The medicine supply is a highly information intensive arena whereby incomplete or unequal information causes friction in the chain. The general thesis based on Article I is that reduced information asymmetry is, in fact, one of the key benefits of digitalization and an indicator of the wider impact of digital technologies and digitalization on an economy.

Conversely, Article IV suggests a solution to manage asymmetric information with DLT; the article specifically discusses that actors seek to hide their critical business information in a competitive market. To tackle this problem, a DLT-based solution can be utilized to remove the need for a centralized database and reduce the amount of information various parties in the business network need to know about each other. It should be noted that hiding information may have ethical and severe health-related impacts, and therefore, it is important to manage it.

Various information asymmetries across the medicine supply chain have been compiled in Table 2, along with their implications, related literature and potential solutions.

Table 2. Asymmetric information across the medicine supply chain.

ASYMMETRIC PARTIES	IMPLICATIONS	LITERATURE	POTENTIAL SOLUTION
Physician-patient	Patient less aware of treatments and their effects	(Arrow, 1963) (Liaw & Peterson, 2009)	Prescribing and dispensing separated
Patient-physician	Patient may hide information on adherence	(Ippolito, et al., 2019) (Loukanova, et al., 2007)	Patient empowerment
Patient-insurer	Patient may hide information on behavior. Moral hazard with medicine consumption	(Arrow, 1963) (Akerlof, 1970) (Zuboff, 2019) (Luiza, et al., 2015) (Garcia-Gomez, et al., 2018)	Copayment policies. Solutions to monitor the behavior, such as wearables
Pharmacy-patient	Pharmacy may hide information on the most cost-effective treatment	(Fimea and Kela, 2015) (Lääkelaki [Medicines Act] 395/1987, 1987)	Regulations such as reference price and generic substitution
Pharmaceutical manufacturer-distribution party	Pharmaceutical manufacturer may hide information on supply disruptions	(Rees, 2020)	Regulations to enforce information sharing
Pharmaceutical manufacturer-dispensing party	Pharmaceutical manufacturer may hide information on the quality and effectiveness of a medicine	(Light & Lexchin, 2021)	Regulatory framework for clinical trials, adequate testing and monitoring of pharmaceuticals

3.3 Sociotechnical systems model

The sociotechnical systems model is a widely used concept in IS research. The theory examines IS from the point of view of both social and technical subsystems (Bostrom & Heinen, 1977). The theory is based on the assumption that these subsystems must fit to enable the successful adoption of IS in organizations. Too often, the changes introduced by a new system are not understood, especially because technical and social variables are interdependent and the relationships are not resolved in the design phase (Bostrom & Heinen, 1977). This can lead to problems and resistance from users toward the new system. This eventually causes the rollout to fail – although, technically, the system would be fully viable. In fact, it is reported that only 10% of IS projects fail due to technical reasons, whereas 90% fail due to social reasons (Dohert & King, 1998).

The roots of the theory derive from the 1950s, when it was introduced at London Tavistock Institute (Mumford, 2006). The approach advocated for better working conditions and worker democracy in factories and coal mines. According to the theory, when technology becomes deterministic, task structures are built around them without considering people. This deteriorates working conditions, making them routinized, less humane and degrading. Whereas the problem was evident in conveyor belt assembly lines, the theory's heyday was especially in the 1970s and 1980s, when it was applied to office surroundings. These were the early days of computerization, when the rollout of new information technology profoundly changed working practices and task structures. This caused friction at workplaces. Sociotechnical systems design practices intended to combat this through incorporating organizational and people aspects in the design of a new system.

Sociotechnical factors have been studied in healthcare IS research in various accounts (e.g. (May, et al., 2001), (Aarts, 2012)). The sociotechnical approach is lucrative in healthcare environments – as they are often labor-heavy and complex, yet dependent on IT (Coiera, 2007). However, it is not rare that a failed healthcare IT project is reported in the media. It seems new systems are implemented without considering the impact on workflow and staff, which causes chaos and disorder (e.g. (Allen, 2019)). Often, the new system is only partially used, and parallel shadow practices remain. Furthermore, health systems are different, and one size rarely fits all, which should be considered when integrating a new IT system. Arguably, sociotechnical analysis has a role to play in all this.

Relating to the medicine supply domain, ePrescription has been especially studied from the sociotechnical perspective. For example, pharmacists might demonstrate resistance toward the new prescription system (Clauson, et al., 2011). ePrescription may also lead to changing jurisdictions of professionals across the prescription process – as pharmacists, for example, may have access to information that was available for only physicians before (Motulsky, et al., 2011). This may lead to friction between these professional groups.

Another area of discussion is how new digital systems, such as ePrescription, contribute to deskilling or reskilling. According to Petrakaki et al. (2012) ePrescription contributes simultaneously to both. The deprofessionalization may occur through replacing manual processes, which required a higher degree of professionalism, with automated processes. A higher degree of automation transforms the process more piecemeal to human workers, something one can associate with a conveyor belt assembly work. The authors also argue that ePrescription can depersonalize the process leading to losing interoccupational personal relationships – for example, those between physicians and pharmacists. On the beneficial side, Petrakaki et al. (2012) argued that ePrescription can

reprofessionalize pharmacy staff, as automating mundane processes frees time for more challenging tasks.

In another study, Petrakaki et al. (2014) discussed how ePrescription impacts the jurisdiction of pharmacists and pharmacy staff. According to the researchers, responsibilities, for example, may be displaced, leading to the jurisdiction of the technical pharmacy becoming wider. This may then entail blame shifting and other similar consequences. This may not be the original intended use of the system but rather a novel affordance ePrescription provides. The affordance concept changes the discussion about reskilling/deskilling – which has traditionally assumed a deterministic view to technology, whereby technology dominantly leads to reskilling or deskilling (Hutchby, 2001). Conversely, affordance mixes the materiality of a technological artifact and the social processes, whereby technology provides affordances (i.e. opportunities and risks) and it is up to the users to adopt those.

Harvey, Avery, Waring and Barber (2012) studied the sociotechnical impact of ePrescription in community pharmacies in relation to the upcoming new release of the national ePrescription service in the UK. The researchers particularly investigated how ePrescription affects work practices and discovered that pharmacies can be divided into three categories based on the sociotechnical orientation: technically oriented, improvising and socially oriented. These categories are characterized by different levels of utilization of technology, dispensing process governance and strictness of workflow methodology. Harvey et al. (2012) found significant distinctions in the dispensing procedures and lead times (i.e. the time between accepting the prescription and dispensing it to the customer) between these different categories.

Sociotechnical systems theory was chosen to be used in this thesis since it suits the research domain well, as it can be concluded when investigating the extant literature. The intention is to understand the complex domain of the medicine supply chain – which is labor-intensive, especially in the downstream (consisting of various stakeholders and technologies). The sociotechnical systems model can arguably be used to illuminate this interface, and the theory is particularly used in Articles II and III.

4 Methodological Background

4.1 Summary of the methodological background used in this thesis

This research follows the qualitative, descriptive IS research approach, whereby Articles I–III are firmly descriptive. Article IV is more prescriptive by nature, having design science research elements. Descriptive emphasis is unavoidable, given that the research concerns elucidating a novel area. Descriptive research intends to answer "what" questions (de Vaus, 2001), and this is the aim. The main research theme is studying what is going on in the medicine supply chain arena and the role IS play in this. This could not be answered with a fully prescriptive study.

Whereas Article IV is a pilot study describing a high-level, however concrete, solution, a wider design science and prescriptive research could follow this initial research – investigating, for instance, a problematic part of the supply chain and proposing a solution. As the field is novel, a descriptive model is needed to set the scene. This lays the foundation for future prescriptive studies and design science, as well as action research projects.

The purpose of this research calls for using qualitative methods and an exploratory approach. The purpose is not to confirm a theory but rather explore and create the basis for theorizing within the area of medicine supply chain and IS. The research is based on multiple qualitative studies, including a targeted literature review, an observational study, a case study and a design science-based study examining the area from different perspectives. This enabled building an overview of the complex phenomenon and allows some theory proving along the way. It was anticipated that the research questions would be refined in the course of the research; hence, the objective was not to test the same detailed hypothesis with multiple cases but rather to accumulate knowledge and understanding through various studies and enable building detailed hypotheses at a later stage.

The main methodological approaches that steered this research are in this chapter: descriptive qualitative research, IS research, IS case study research and design science research.

4.2 Qualitative methods in IS research

According to Galliers and Huang (2012), although being not uncommon, qualitative research is not dominant or even equivalent to the volume of quantitative research in IS research if measured by the number of articles in top journals. The reasons for this are many, including the lack of education (there are more quantitative courses available) and the rejection and negative attitude toward qualitative articles (Conboy, et al., 2012). One aspect is the difficulty of qualitative research. It is based on tacit skills difficult to train to novice researchers, which leads to a vicious circle with less qualitative practitioners and more rejection toward qualitative research (Galliers & Huang, 2012).

According to Crabtree and Miller (1999), the aim of scientific research is identification, description, explanation generation, explanation testing or control. The first three are exploratory by nature and often researched inductively using qualitative methods, while the last two are often quantitative research–driven. It is common sense that the last two are based on deductive approach, whereby data are evaluated utilizing a general theory. This contrasts with inductive approach, whereby generalization and theory follow the data.

Whether induction can be a truly objective task can be argued. Some argue that induction cannot take place in isolation to the researcher's background, previous knowledge, aims and so forth (Srivastava & Hopwood, 2009). It is rather subjectively contextualized, whereby the researcher's knowledge, skills and experience heavily affect the reasoning (Ketokivi & Mantere, 2010). Qualitative approach does, however, not necessitate an interpretive position (Conboy, et al., 2012). There are, for instance, positivist case studies.

Qualitative research often follows an iterative process, whereby analysis, data collection and explanation are repeatedly revisited. More than a feature of qualitative methods, this relates to the interpretive approach. In contrast to positivist research, which is usually waterfall-like and progresses linearly from the problem statement to the hypothesis, the interpretive approach requires a more reflective position, whereby the knowledge is accumulated incrementally. In the course of iterations, while receiving more information and interpreting it, even the research question may be refined to be more relevant (Crabtree & Miller, 1999). Practically, when analyzing the data, the researcher needs to ask themselves what the data are telling, what is it that is required to be known and how these two are linked (Srivastava & Hopwood, 2009). Answering the last question may lead to refining the focus and research questions.

This is also the approach in this thesis. The research theme was iteratively refined and clarified during the project after more knowledge on the arena was gained. Data were collected in multiple ways, including interviews, observations, questionnaire, extant literature and other documentation (including annual reports), and the work

progressed inductively. It can be argued that a novel area, such as the intersection of medicine supply and IS, gains from the inductive approach. Since the aim is to outline and explore a wide area, one cannot restrict oneself to nor tie oneself too tight to a predefined theory. This is not to say that there would not be any theoretical basis but, rather, a theoretical frame – that is, the sociotechnical systems and information asymmetry concepts have been utilized when interpreting the data collected in multiple exploratory cases.

Rather than a fully interpretive, the approach could be called aparadigmatic, whereby one is not strictly restricted to certain methods and research settings. Perhaps functionalism, as defined by Burrell & Morgan (1979), would be close in some respects – such as a status quo–seeking approach, with an emphasis on management viewpoint and the deterministic standpoint. The differences are in the idiographic and interpretive approaches adopted throughout the study. This thesis also utilizes design science.

According to Goldkuhl (2012), the pragmatist paradigm suits the needs of design science. Pragmatism values actions in its ontology, and its priority is to help local practices through practical interventions. The pragmatist researcher assumes a participatory role, and pragmatism can be understood to be located between the positivist and interpretivist positions, which would also describe the approach assumed in this thesis.

4.3 Descriptive and prescriptive approaches and design science in IS research

According to March and Smith (1995), IS have been studied from two perspectives: descriptive and prescriptive. The former aims at creating understanding about IT and its usage. The latter aims at giving guidelines for IT practice. Whereas descriptive research is typically associated with traditional sciences, prescriptive research is associated with design science. March and Smith (1995) argued that the descriptive approach has traditionally been conceived as “real science,” and the prescriptive approach as “less scientific.” Design science has, however, had its place in IS research – given the special nature of the research domain: an area studying technology, organizations, governance and individuals, as well as heavily emerging, only having begun some decades ago and now adopted ubiquitously.

This thesis is descriptive by nature, as it intends to map out medicine supply and the IS area. The intention is not to provide a set of blueprints for implementation but rather to understand the wider concept and its main features. It is the follow up work that can be more prescriptive. Some prescriptive features, however, can be found in the thesis: Article IV utilizes the design science approach when introducing a

concept for managing scarce information and risks in the plasma derivatives supply chain.

According to van Aken (2004), design science is an acknowledged form of science in the fields of engineering and medicine, whereas it is not so in social sciences. In the social science arena, explanatory approach is still conceived as a more rigorous science. According to the critique, the problem with explanatory approach – as compared to, for example, design science research – is its objective to create predictive and general theories. This can lead to banal theories with no real-world use.

Design science aims at creating general-purpose constructs and models, where the researcher's position is less interpretive and external to the research topic at hand (Iivari & Venable, 2009). Design science contains evaluative actions for examining the context, the construction of artifacts and, finally, actions to evaluate the artifacts. The value of the research is determined based on the value it produces to those adopting and using the artifacts in real life. According to the design science position, creating new knowledge is considered futile if it does not generate any practical benefit. The design also must be innovative and new (March & Smith, 1995). The concept introduced in Article IV matches these criteria.

4.4 Case studies within IS research

It can be argued that the IS field is pervaded by fast-paced technological development that often keeps practitioners ahead of academic researchers. This has led researchers to examine current practices instead of identify future directions that would be implemented by practitioners (Benbasat, et al., 1987). Idiographic research strategy (i.e. one that seeks to understand phenomenon in its own settings) seems to be suitable for this kind of problem area (Benbasat, et al., 1987). This is the reason Bensabat et al. (1987) suggested that case study is a viable method in IS research.

Case studies allow researchers to answer "how" questions, which are typical when exploring novel and emerging research topics with limited prior knowledge (this is not to say that "what" questions cannot be answered with case studies). Typical research topics in ISS examine the interfaces between humans, organizations and technology (Dube & Pare, 2003). Understanding these complex and emerging environments – such as the intersection of medicine supply chain and IS areas, which is investigated in this thesis – require interpreting rich and varying data.

Bensabat et al. (1987, p. 371) summarized common characteristics for case research, including the following:

1. Phenomenon is examined in a natural setting.
2. Data are collected by multiple means.

3. One or few entities (person, group, or organization) are examined.
4. The complexity of the unit is studied intensively.
5. Case studies are more suitable for the exploration, classification and hypothesis development stages of the knowledge building process; the investigator should have a receptive attitude towards exploration.
6. No experimental controls or manipulation are involved.
7. The investigator may not specify the set of independent and dependent variables in advance.
8. The results derived depend heavily on the integrative powers of the investigator.
9. Changes in site selection and data collection methods could take place as the investigator develops new hypotheses.
10. Case research is useful in the study of "why" and "how" questions because these deal with operational links to be traced over time rather than with frequency or incidence.

These are quite well aligned with those specified by Dube and Pare (2003). For example, the research target is a contemporary phenomenon related to an entity such as an organization, person or technology, which is researched in its complexity in real-life circumstances and integrated into its context with no controlled observation involved.

When considering this thesis, many of these characteristics match. This research studies a contemporary phenomenon in natural settings; data are collected from multiple sources and integrated and then interpreted by the author, building a new concept. There are no experimental controls or independent variables in play.

Case research can be categorized according to the paradigm (Dube & Pare, 2003). In other words, case studies can be conducted from the positivist or interpretive perspective or critical perspective – which could, for instance, be that of critical realism. Another categorization is explanatory vs. descriptive. According to Dube and Pare (2003), the former is theoretically grounded, whereas the latter aims at merely describing a phenomenon. Explanatory case research takes a positivist stance, with hypothesis testing as a priority. Conversely, descriptive case research explores a phenomenon – the case, aiming to create an interpretation. The emphasis in case research has traditionally been on the latter.

The third category Dube and Pare (2003) introduced is exploratory case study. This resembles the descriptive approach but has a clear theoretical foundation, whereas descriptive case study often has none. The categorization follows that of Yin (1994), which is a highly influential and cited source. Exploratory case studies

often answer to "what" type research questions (Tellis, 1997) and suits therefore the requirements of this research, which intends to explore *what* the impact of digitalization on the medical supply chain is. According to Dube and Pare (2003), single case study is dominant in IS research. Whereas explanatory case research would require a multiple case approach due to reliability and validity questions, in cases of exploratory and descriptive case studies, it can be argued that a single case approach suffices.

4.5 Reliability and validity

Reliability and validity are attributes labeling the quality of scientific research but coined in association with positivist quantitative research. According to Koskinen, I. et al. (2005), traditional means for assessing reliability and validity are not applicable in qualitative research in the same way they are applied in quantitative research. Eikeland (2006) argued that validity as a concept in social sciences does not have a sound foundation and can be philosophically questioned from many aspects. According to him, demanding validity is especially problematic since it assumes there is a natural state the organization under research operates in and which may become disrupted by the research group. Furthermore, it assumes that the operation is structured around controllable causes and effects. Validity also assumes complete objectiveness from researchers, and finally, it should not be regarded as a problem that research subjects – humans – are treated as external objects.

Although this is an interpretive and qualitative study, these questions require discussion. To answer the reliability question, various actions were taken. Article I is based on multiple literature sources, whereby each of the explanations given as the result of the study are based on multiple sources. Through this, the researched topics are examined from multiple perspectives, and none is based on a single source that could be easily conflicted by other sources. Article II is based on data collected from multiple pharmacies and therefore relies on one case only. Article III is based on semi-structured interviews and a survey – whereby the same questions and themes are, again, asked from multiple respondents. This is backed up by data sources such as annual reports. Conversely, Article IV relies on multiple sources.

In terms of validity, the question is harder. As per Eikeland (2006), an entire sociotechnical concept with various stakeholders, interfacing entities and underlying structures is examined, and therefore, isolating the research target from its surroundings, and one as a researcher from the research target, is challenging, if not impossible. Rather than proving a hypothesis based on natural science criteria and units in a controlled environment, in this study, the researcher interprets the knowledge accumulated through the process. However, one form of validity can be enforced: content validity. According to de Vaus (2001, p. 30), "Content validity

evaluates how well the measures tap the different aspects of the concept as we have defined it." The concept – that is, the medicine supply chain – was investigated from several aspects; hence, it can be argued that content validity was achieved.

5 Summary of Research Articles

5.1 Summary of data strategies

In this research, multiple data collection methods were utilized in each of the studies. Article I is based on extant literature, and it aims at building a concept. Article II utilizes quantitative data collected through observing the dispensing process in pharmacies. This is combined with extant literature. Article III is based on multiple interviews, a survey and background documentation study. Article IV is again based heavily on extant literature, while the concept is built using the design science approach.

This research follows explanation building strategy – which, according to Yin (1994), is one of the main analysis strategies in case studies. This is an iterative process whereby an initial theoretical proposition is compared to findings. This often leads to revising the proposition and involves multiple cases – which are, subsequently, compared to the revision. In Article I, an initial model was created based on the information asymmetry concept, and the extant literature was analyzed to explore this model. Article II built an overview and explanation of how pharmacies have digitalized after ePrescription, basing on the theoretical frame of sociotechnical systems. In Article III, knowledge on the medicine waste area was accumulated iteratively, and this was then used to answer the thematic questions raised at the beginning of the study. Article IV is slightly different, given its design science approach; the analysis of the extant literature culminates in a concrete model.

Overall, this thesis investigates the medicine delivery from various aspects through the four studies. This assures an adequate coverage. Considering the specific articles, Article I is based on a targeted literature review, covering a multitude of sources used to investigate the research topic from various aspects. Article II utilized data collected from multiple pharmacies. For Article III, again, a multitude of sources were utilized, whereby the research arena and themes were outlined through multiple open interviews and observation in the first place. Article IV was coauthored with an industry subject matter expert that supports ensuring the relevance of the designed artifact.

5.2 Article I: Information asymmetry as a key problem in medicine delivery

Article I is titled *The digitalization of the Medical Value Network – How Information Asymmetries Can Be Managed with Digital Innovations*. The aim of the article was to conceptualize the medicine supply chain through building a model for the chain and investigating it based on extant literature. The article studied how technology is used in the supply chain and how it specifically mitigates the problem of asymmetric information. Another theoretical basis it utilized is the value network theory. It was published in the *International Journal of Telemedicine and Clinical Practices* (Vol. 2, No. 4) in 2017. The summary of Article I is presented in Table 3.

Table 3. Article I.

TITLE	The Digitalization of the Medical Value Network – How Information Asymmetries Can Be Managed with Digital Innovations
PUBLICATION DATA	Peltoniemi, T., 2017. *International Journal of Telemedicine and Clinical Practices*, 2(4), pp. 298–317
THEORETICAL BASIS	Information asymmetry, value network
METHOD	Targeted literature review and interview
RESEARCH THEMES	How can incomplete information and information asymmetries in the medical value network be managed? How can digital tools support this?
RESULTS	Based on multiple examples across the value network, including ePrescription, electronic health records, generic substitution, automatic dispenser technology, outcomes-based methods, online medical information and medicine demand management, it can be argued that technology and digital tools can play an important role in managing information asymmetries, and equalizing information between value network actors is one of the key benefits of digitalization.

The purpose of the article was to set the scene in terms of building the concept of medicine delivery chain – forming the basis for the model, as illustrated in Figure 3, and mapping out challenges. Therefore, the article was largely based on studying extant literature. The study discusses key sources (e.g. (Akerlof, 1970), (Arrow, 1963)) in information asymmetry and how the medical market is especially subject to it. Conversely, the value network is used as a theoretical basis to model the supply chain.

The value network is a network of parties producing a service or a product (i.e. value) for a customer (Stabell & Fjeldstad, 1998), and information flows are the lifeblood of the network (Sherer, 2005). Information is an asset, and those having

more of it have been powerful actors in the network. Digitalization can, however, change this, as it makes information available at low cost through digital networks (Spence, 2015). This changes the dynamics in various industries and related value networks.

A model of the medicine supply value network is outlined in Figure 8. Whereas this is a simplified view to the network, it contains the main pharmaceutical actors – that is, from the medicine manufacturing industry to the customer (i.e. patient) – and should illustrate the idea.

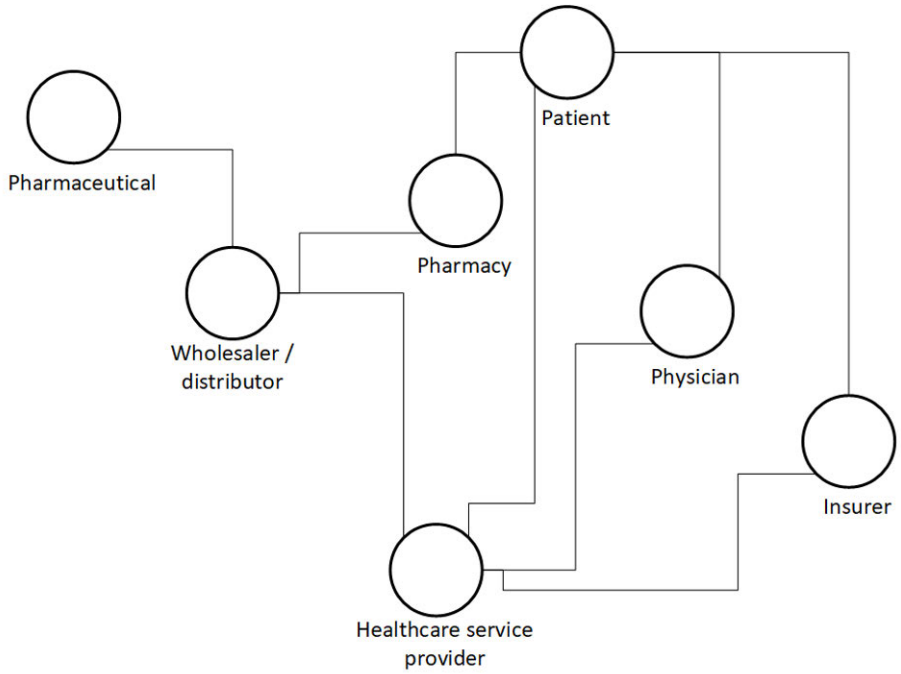

Figure 8. Medical value network.

Several possible unequal information positions can be identified in this network (it is worth noting that these are risks that may or may not realize). For example, the medical market is subject to supplier-induced demand, whereby physicians may prescribe treatments that are not really needed and the patient has no means of evaluating this. The physician's prior performance is also unknown to the patient. At the same time, neither the physician nor the insurance company can be sure that the patient will follow the prescription. A major asymmetry is the one inherent in the entire health concept – the patient themselves is the expert in their condition, as they are the one experiencing it.

Moving up the stream, the service providers are uncertain of their medicine stock levels and keep ordering medicines – which, given incomplete expiry information at the wholesalers' end, become rapidly expiring stocks and waste. Wholesalers' information on their stock levels, however, may also be inaccurate, leading to pharmacies ordering expiring products.

An entirely different discussion is demand management. There are currently several challenges in predicting the demand, which leads to shortages. For example, during the time of writing, the world was facing the COVID-19 pandemic. This led to shortage of respirator masks, for example, and a surge of substandard products entering the market (Yu, 2020). Although predicting the pandemic a year ahead would have been impossible, the medicine supply chain organizations failed to read the signals when the virus outbreak began, which would have allowed them more time to prepare.

There also are many other uncertainties, as well as information asymmetries, in the supply chain. For example, it is beneficial for a pharmaceutical manufacturer to hide information on ex-factory prices, as it increases their negotiation power in different markets. For counterfeit product vendors, it is beneficial to hide information on the origins of products. Not all problems are information asymmetries per se but rather uncertainties and a lack of transparency.

What can be argued here is that this incomplete and unequal information creates significant inefficiencies in the market and burdens the economy. For example, annual expenses relating to prescription noncompliance to the US economy are estimated at USD 300 billion (Foo, et al., 2011) and relating to the lack of generic substitution is estimated at USD 9 billion (Stenner, et al., 2010). Wasted prescription medicines burden the UK economy with GBP 300 million annually (Hazell & Robson, 2015).

Regarding other markets, it can be observed that digital platforms have equalized information between buyers and sellers through new kinds of trust mechanisms (Spence, 2015). Uber and AirBnB users rate each other, for example, and microloans markets are based on self-policing rather than mediators and regulations. Traditionally, regulations have mitigated information asymmetries, whereby regulators act as mediators preventing any one side from exploiting their power position. It can be argued that digital technologies can smoothen transaction costs through increased monitoring capabilities (Varian, 2010). Table 4 summarizes various technologies that are or can be used to manage information asymmetries in the medicine delivery domain.

Table 4. Technologies to manage information asymmetries in the medicine supply chain.

CATEGORY	SUBCATEGORIES
ePrescription	ePrescription
Electronic health records	Electronic Health records Blockchain
Generic substitution	Generic substitution system Reference pricing system Online medicine information Medicine pricing databases
Automatic dispensing technology	Automatic medicine dispenser
Outcomes-based methods	Outcomes-based methods Evidence-based medicine Wearables
Online medical information	Healthcare information sources Healthcare applications Social media
Medicine demand management	Just-in-time processes Simulation Big Data Electronic communication Automatic medicine dispenser

The contribution of this article to the thesis is twofold: First, this article sets the scene through outlining the medicine delivery supply chain model (Figure 3). Second, the article investigates the model through the lens of information asymmetry to highlight challenges and potential solutions. The knowledge gained in this study is utilized in later phases of the thesis through taking the investigation to a more granular level.

5.3 Article II: The digitalization pattern in pharmacies

Article II considers how Finnish community pharmacies have digitally transformed in the past decade. The trigger for the digitalization was ePrescription, which was rolled out in Finland from 2012 onward and regulated by law. The research especially focuses on the sociotechnical impact of the digitalization. The article has been submitted to *BMC Health Services Research*, and the details are outlined in Table 5.

Table 5. Article II.

TITLE	The Electronic Prescription as a Driver for Digitalization in Finnish Pharmacies
PUBLICATION DATA	Peltoniemi, T., Suomi, R., Lähteenoja, M. & Peura, S. Submitted to *BMC Health Services Research*
THEORETICAL BASIS	Sociotechnical systems model
METHOD	Observation
RESEARCH THEMES	What is the impact of ePrescription to the dispensing process? How does digital transformation impact pharmacy practice?
RESULTS	The dispensing process has significantly changed as a consequence of the ePrescription, which has been one of the main triggers for the digital transformation in pharmacies. Sociotechnically, this new technology is shaping the working practices and tasks to more prescribed and regulated from workers' point of view.

The study was based on observing the dispensing process before and after the deployment of ePrescription. Pharmacy practices have been disrupted by not only ePrescription but also the so-called direct dispensing model, which has also been rolled out in pharmacies. This entails that the medicine is dispensed to the customer immediately in the customer service event, rather than the pharmacist preparing the delivery and calling the customer to pick it up.

According to the study, these changes have made the dispensing process faster. In addition, the digitalized process seems more predictable and more tightly governed. Sociotechnically, this implies there is less freedom to improvise, which changes the work environment of the pharmacy staff. Regulations form a significant factor – as ePrescription, which is based on laws and regulations in Finland (Laki sähköisestä lääkemääräyksestä [Electronic Prescription Act] 61/2007), is the trigger for the digital transformation.

One of the drivers of ePrescription is the increased visibility and understanding of a patient's overall medication regimen and the increased role a pharmacy can take in the treatment. Therefore, one would consider that counseling time would increase in the pharmacy, but this is not visible in the results. However, the research implies that digitalization can increase efficiency in terms of the working processes across the medicine supply chain and that these may have sociotechnical implications, such as bringing tighter structures to work processes.

5.4 Article III: The consequences of poor information in medicine delivery in practice

Article III focuses on medicine waste management and is titled *Eliminating Medicine Waste in a Finnish University Hospital – A Qualitative Study*. The study investigated, at a more granular level, one of the challenges identified in Article I. The article was published in *Journal of Pharmaceutical Policy and Practice* on 2 October 2019. The details of the article are presented in Table 6.

Table 6. Article III.

TITLE	Eliminating Medicine Waste in a Finnish University Hospital – A Qualitative Study
PUBLICATION DATA	Peltoniemi, T. & Suomi, R, 2019. *Journal of Pharmaceutical Policy and Practice*, 12, 27.
THEORETICAL BASIS	Sociotechnical systems model
METHOD	Interviews and survey
RESEARCH THEMES	How is medicine waste managed in hospital settings? How do social and technical subsystems support it?
RESULTS	The bottlenecks in the technical system include poor quality of data across the medicine delivery chain, covering wholesalers, pharmacy and wards, and weak support of information systems, which reduce the ability to efficiently manage the waste. The pharmacy staff seeks to compensate this with informal practices.

This article highlights, again, how incomplete information accumulates through the medicine delivery chain. In a ward, inventory is often maintained manually and inaccurate. This leads to ordering approximate quantities of medicines from the central pharmacy. The central pharmacy combines orders and the inaccurate information received from wards when ordering from wholesalers, which often leads to expiring stocks of medicines that are not needed. The information of medicines in wholesalers' stocks is also inaccurate, and they may dispatch medicines that will expire in a few days. Also, prescription recommendations and medication preferences may change, which is not communicated to wards or the pharmacy; this leads to the pharmacy stocking up with obsolete medicines.

From the sociotechnical viewpoint, the IS support for work routines is inadequate. In addition to the poor quality of information, usability is often poor, and hospital staff try to avoid the cumbersome applications used across the medicine delivery chain. The processes are, hence, manual and reliant on the knowledge and skills of individuals. The main findings are summarized in Table 7.

Table 7. Main findings from Article III.

FINDING	DESCRIPTION
Inconsistent expiry information	The medicine inventory in wards is maintained manually, and there is no accurate information on expiry dates. The expiry information on the wholesaler's ordering system may be incorrect.
Lack of integration	As the IT systems are not fully integrated, staff need to manually cross-check information from various applications when estimating medicine demand and placing orders. Staff often avoid this manual task and base their estimations on previous orders and common sense.
Lack of an official recycling scheme	Recycling is not a managed process, and it is based on voluntary action and an unofficial email list.
Poor usability of IT applications	Applications appear unintuitive and onerous to use, which leads to further avoidance of their use.
Infrequent ordering process	As the ordering process is a rather heavy, manual operation, it is more economical to order infrequently and in larger quantities than needed.
Inaccurate metrics	Accurate figures on medicine waste are unavailable, given that only medicines returned to the pharmacy are counted as waste. This leads to more confusion in terms of managing and reducing waste.

To cope with the shortcomings in the technical subsystem, the social system is emphasized. There are informal structures in place to facilitate recycling, for example. This is facilitated by an unofficial email list and such. Moreover, the pharmacy staff forms an inner circle for information sharing; those outside the inner circle may not be aware of these unofficial structures.

It can be argued that the related IS are inadequate and unaligned with the needs of the work processes and the delivery organization. This is despite the decades-long research tradition, especially in the healthcare domain. Surely, sociotechnical viewpoint must have been part of the design practices of these systems; few IS are designed without considering users and their requirements.

The issue seems to relate to the silo organization, whereby the end-to-end view of the process diminishes. Individuals across the supply chain execute what is expected in relation to their role, disconnected from each other. Not understanding the big picture or the economic impact of their actions, many may be tempted to work with estimates. This, combined with the poor availability of accurate data, leads to results with questionable integrity.

Therefore, sociotechnically, the focus should be on the big picture, understanding the entire supply chain process both from technical and social perspectives in the hospital and surrounding organizations. Traditionally, sociotechnicality entails bottom-up style user-centricity, which is clearly inadequate

in many healthcare projects in which politically and organizationally complex networks are present.

5.5 Article IV: How to manage information asymmetry with novel digital solutions

Article IV's focus is on the upstream of the medicine delivery chain, examining the blood plasma industry through investigating extant literature on distributed ledger usage in the healthcare and logistics domains. It identifies multiple risks relating to the plasma supply chain and suggests distributed ledger–based solutions. This article was published in *Blockchain in Healthcare Today* (Vol. 2) in 2019, and the details are presented in Table 8.

Table 8. Article IV.

TITLE	Evaluating Blockchain for the Governance of the Plasma Derivatives Supply Chain: How Distributed Ledger Technology Can Mitigate Plasma Supply Chain Risks
PUBLICATION DATA	Peltoniemi, T. & Ihalainen, J, 2019. *Blockchain in Healthcare Today*, 2.
THEORETICAL BASIS	Design science
METHOD	Extant literature, design science
RESEARCH THEMES	How is distributed ledger technology, such as blockchain, utilized in the healthcare domain? What are the risks in the plasma supply chain? How can blockchain be utilized to mitigate these risks?
RESULTS	The plasma supply chain is pervaded by incomplete data across the chain, which presents several risks. Blockchain and zero-knowledge proof technologies allow the reduction of the requirement for complete information between the supply chain partners and, hence, can be used to mitigate the risks.

Plasma is used in the pharmaceutical industry to produce certain medicines (International Council for Commonality in Blood Banking Automation [ICCBBA], 2018). Globally, it is a major industry, whereby the US is the biggest exporter (Transparency Market Research, 2018). The shortage of plasma has grave consequences, as several critical medicines cannot be produced without it.

The supply chain is, however, vulnerable, as it is reliant on few exporters. Moreover, there are ethical questions to be considered since plasma-exporting jurisdictions often remunerate donors and this attracts addicts and other vulnerable individuals (The Economist, 2018). The effect of frequent donation to health is unknown. To mitigate these risks, it would be good to have more exporters of

plasma. However, there is a risk of falsification – whereby, for example, the origin of the plasma is blurred. Testing and disinfecting the blood is costly, and there may be a temptation to bypass this process.

To mitigate these risks, an ability to govern the plasma supply chain is needed. Again, the information in the supply chain needs to be equalized to bring adequate transparency to the downstream of the delivery chain. However, it is often not in a commercial organization's interest to openly disclose information on its business operations, so there should be a way to verify the key element – that is, the origin of the plasma – through disclosing the minimum amount of information.

Article IV and the related study examines the role of a distributed ledger to tackle this problem. A distributed ledger is used in logistical operations and the medicine supply arena (e.g. (Center for Supply Chain Studies, 2017)). The key concept is zero-knowledge proof, which enables verifying transactions with the least amount of information (Radocchia, 2018). This concept turns the question of information asymmetry upside down; rather than increasing the information, it removes the need for information. In the healthcare domain, this can be useful – as the related information is often of a sensitive nature and sharing it exposes various risks, such as those relating to information security, and sharing this data is therefore often restricted by law.

6 Findings and Discussion

6.1 Main findings

This doctoral thesis investigated the medicine supply arena through modeling it conceptually, examining problems and bottlenecks across the delivery chain and suggesting some solutions to mitigate these problems. The main problems relate to the incomplete information and uncertainty, as well as asymmetric information, in the supply chain. This applies to specific parts of the supply chain, as well as the entire chain. For the latter, it is specifically the lack of an end-to-end view of the process, which generates uncertainty.

The medicine supply chain can be modeled considering the pharmaceutical industry in the upstream and the patient as the end user in the downstream. The supply chain comprises many participants, including logistics providers, wholesalers, insurers, regulators, hospitals, pharmacies, healthcare service providers and so forth. The information is highly asymmetric between the participants, whereas the efficient supply of medicines would require more transparency across the chain. Some of the information asymmetries are illustrated in Figure 9

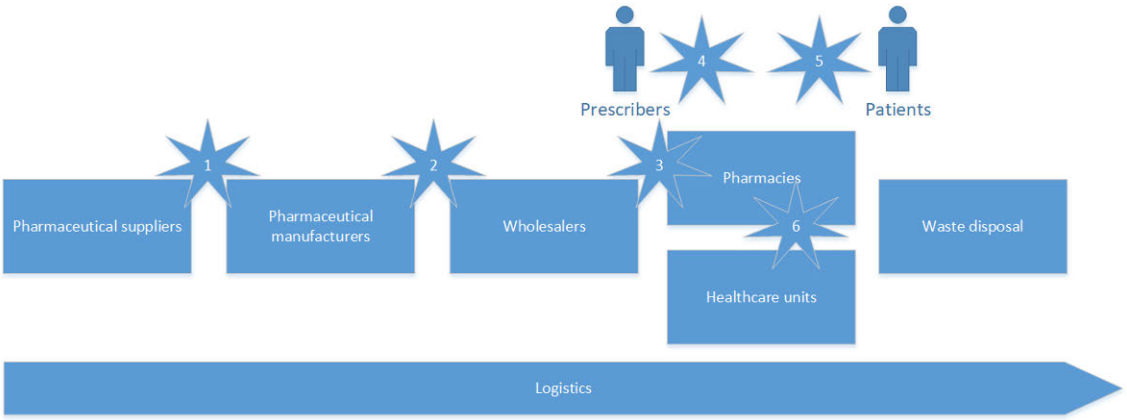

Figure 9. Asymmetric information across the medicine supply chain.

In Figure 9, the problematic areas are identified with numbered asterisks:

1. Pharmaceutical suppliers may seek to hide the origin of the supply or attempt to falsify it somehow. For example, the suppliers of plasma derivatives may seek to falsify testing practices.
2. Pharmaceutical manufacturers may seek to hide information on pricing and product availability (Breen & Yaroson, 2018). For the former, the intention is to maintain profitable pricing in varying markets. For the latter, this may be carried out to create demand in the downstream of the supply chain. The incomplete information is propagated through the supply chain – creating supply chain disruptions, such as medicine shortage. The EU is currently deploying a regulation to mandate more accurate reporting of shortages and, therefore, increase the predictability of medicine supply disruptions (Milmo, 2019). Another information asymmetry risk relates to product falsification and counterfeiting. There are illicit manufacturers attempting to introduce counterfeit products into the supply chain, and they naturally aspire to hide the origin of the medicine.
3. The data disclosed by wholesaler can be outdated or otherwise inaccurate – which may lead to pharmacies ordering medicines that expire shortly, leading in turn to wastage. Medicine wastage is a significant cost at the societal level – for example, in the UK, the annual cost of prescription medicine waste is GBP 300 million (Hazell & Robson, 2015). The wastage also has a grim environmental impact. Furthermore, incomplete or hidden information in upper parts of the supply chain can be propagated downward to wholesalers to drive prices up.
4. Prescribers know more about treatments than laymen. Furthermore, usually, they solely hold the power to prescribe medicines. If there is scarcity of a prescribed medicine, the customer (i.e. the patient) needs to consult the physician to change the prescription. The customer is rarely in the position to assess the prescription and potential lower-cost alternatives. It is also challenging to estimate the past performance of the prescribed treatment to the given symptom.
5. Patients may seek to hide their adherence to a prescription. This may be intentional or unintentional. Both are affected by attitudes toward treatment. The cost of nonadherence is high – for example, it is estimated to cost USD 300 billion annually in the US (Foo, et al., 2011). In the same way, patients may seek to hide information about their behavior from

insurers and other stakeholders. At the same time, the patient is always the best expert in their condition.

6. In hospital settings, medicine delivery is often pervaded by incomplete and inaccurate information. To name just a few issues, the inventory of stocks is often inaccurate, there is no visibility of future demand of medicines and the medicine ordering staff may not know about preferred treatments, which all lead to ordering wrong quantities of potentially wrong medicines. This leads to both wastage of some medicines and shortage of others.

Based on the above, the issues can be categorized as *upstream challenges*, involving the pharmaceutical industry–related stages; *supply chain challenges*, involving the logistics and wholesaler stages; and *prescriber challenges, patient challenges* and *downstream challenges*, involving healthcare units and pharmacies. Various tools can be used to manage these challenges – for example, regulations are required in this field to manage the adverse effects of information asymmetries. However, if the focus is on digital solutions, some upcoming or current solutions to ease these challenges are listed in Table 9. The key is better data transparency, as also demanded by other authors more recently due to the COVID-19 pandemic (Dai, et al., 2020).

Table 9. Digital solutions in the medicine delivery arena.

THE PROBLEM AREA	SOLUTIONS
Upstream challenges	Blockchain and zero-knowledge proof Better quality information on pricing
Supply chain challenges	Better quality information on stocks and inventories Better quality information shared on disruptions
Prescriber challenges	Outcomes-based medicine and solutions to facilitate it More information available on treatments and physician performance
Patient challenges	Automatic dispenser ePrescription Wearables and similar solutions to monitor prescription adherence
Downstream challenges	Automatic inventories in hospital units

Another viewpoint is how to obtain a situational view to the entire process, producing visibility of each of the problem domains, from upstream to downstream. Considering wider issues such as medicine shortage, they may relate to, and be caused by, many problem areas across the supply chain.

For example, according to Heiskanen et al. (2017), medicine shortage in Finland is usually caused by multiple issues, such as the small size of the pharmaceutical market, fluctuating demand, small stock sizes, long delivery times and complex supply chains. Therefore, to manage the shortage, a situational view of the entire chain, rather than just one part of it, is required. Situational awareness concerns observing the environment, understanding the situation, projecting the future situation, deciding the course of actions and performing those actions (Endsley, 1995). In terms of the medicine supply chain, this means understanding the demand, as well as supply, to the level where failing supply chain nodes, such as manufacturing plants and distribution entities, can be identified in a timely manner, allowing precautionary actions to be taken. If the current situation is not understood and predictions cannot be made, researchers are left reacting to events that have already occurred, with no control of the situation whatsoever.

In a wider domain, such as the supply chain, it has been difficult to obtain the situational view due to the lack of sophisticated analytical tools, and it has been hard to predict the demand or the disruptions in the production chain. However, predictive solutions have emerged and allow managing supply chain risks. Predictive solutions can involve multiple data sources, such as news feeds, device data, social media and data sources of global institutions, incorporated with production data and alerts on potential disruptions along the production chain (e.g. (KPMG, 2019)).

Data and analytics-based tools have also been introduced to increase visibility and simulate processes. It has been suggested, for example, that process mining – a technique for discovering and analyzing business processes based on data, rather than manually – is a useful tool in healthcare settings due to the complexity and variability of the process environment (Erdogan & Tarhan, 2018). Medicine supply processes are equally complex and, hence, could benefit from process mining.

6.2 Discussion

Turning attention to the sociotechnical perspective, many discussion points can be identified. A key question is as follows: Why do many healthcare digitalization projects keep failing despite the strong footprint and long tradition of the sociotechnical approach? If the challenges introduced in this thesis are especially observed, they have not been solved to date. Many sociotechnically viable solutions seem to require more data and more information available in real life.

A key issue with the medicine delivery domain is that it is siloed. Some actors in the network benefit from this – for example, firms and businesses tend to maximize their profits, and this may entail hiding information, such as that relating to pricing or product availability. Conversely, if sociotechnically optimal solutions in intersecting organizations require this information to be available, this results in an problem that cannot be solved with any design, no matter how user-centric.

Another viewpoint here is more philosophical. Idealistically, to maximize the efficiency of the medicine delivery, individuals' behavior and, for example, how they follow prescriptions need to be monitored. This is also called surveillance, and this word has a negative connotation to many. Mandating people to continuously disclose data of their behavior would seriously jeopardize their privacy. This is where care is required since it is likely that people would consent to the use of their data with no objection without realizing all the potential outcomes of this action.

One could also challenge the pervading emphasis on protecting current practices. If researchers always consider existing structures and how they need to accommodate those in new developments, there is a danger that they are tied to an old practice and cannot deliver impactful change. Transformation programs are deemed to remain meek digitization exercises rather than being truly transformational digitalization. In domains such as healthcare and medicine delivery, this is a risk, as solving the dilemma of sustainability in aging societies requires exponential change.

It may not be the aim of the sociotechnical systems approach to hinder innovation, but there is a risk it becomes such. Emphasizing the social system in the design should not become a structure to maintain status quo. Those new practices needed to transform industries require drastic changes in organizations, roles and ways of working, and researchers cannot adhere to old ways by using the excuse of sociotechnical designs.

One of the viewpoints is that researchers need to consider solutions that require less information rather than increasing the information in the design of a new system. A good example is the zero-knowledge proof concept. This allows verifying transactions without revealing data about it, undoubtedly a useful concept in a domain with sensitive data. This kind of design is difficult to come by if the design is based on user-centricity. Zero-knowledge proof is based on DLT, a technology that is mainly invisible for the everyday user, and many uses of the technology have been suggested in the healthcare domain (e.g. (Chawdhuri, 2019)).

Electronic Health Record (EHR) systems have existed for decades, and standardization work has been carried out also for a long time – for example, HL7, the global healthcare data exchange standard was initiated in 1987 (Oemig & Snelick, 2016). However, researchers still struggle with designing a computerized

prescribing system that can support pharmacies and physicians in finding the right medicine and help pass the prescription safely to the pharmacy (Schiff, et al., 2016).

The siloed nature of the healthcare domain is hard to overcome; it is a complex network. First, it is required to regulate across the supply chain to manage the information asymmetries. Second, it is required to innovate new digital solutions that reduce the impact of asymmetric information through identifying potential data sources across the supply chain and facilitating information sharing. Where this is challenging due to confidentiality and data privacy reasons, it is required to learn to make use of scarce and scattered data across the supply chain in innovative ways and reduce the need for complete information.

6.3 Theoretical and practical implications

In this thesis, it was described that the medicine supply chain operates with scarce and incoherent data, which hamper the efficient operation of the supply chain. Expanding medicine costs, especially in countries with aging populations and because of global pandemics, are likely. The medicine supply chain is prone to disruptions, and there is no control or transparency to efficiently manage it.

For the practical implications, first, there is an urgent requirement to increase transparency across the supply chain. This entails identifying what data are available from across the supply chain and utilizing them to simulate the supply chain. This allows identifying and analyzing bottlenecks, improving the process and intervening where applicable. The regulatory work needs to continue and ensure that the data become increasingly available in a timely manner across the supply chain. The policy work should focus on the upstream of the global supply chain; this requires a thorough mapping out of the chain and associated risks and aiming the regulatory work to where it will have the most impact. Whereas the emphasis in the regulatory discussion may have been around patient and personal data, it is imperative that the data across the chain, covering the upstream and distribution, become more open. This cannot happen unless determined global regulation work is performed.

Second, predictive models need to be deployed to allow better preparation for disruptions in the supply chain. This, again, requires data availability. It is nationally and regionally important that researchers can utilize global data sources – which are increasingly available – and form predictive models to be better prepared for disruptions. It is clear that the discussion on complex and fragile supply chains with single points of failures will take place and the global medicine supply chain in its current shape will be reconsidered.

Whereas the priority needs to be in taking better control of the entire supply chain, multiple digital solutions can continue to be utilized to facilitate specific parts of the medicine supply chain – contributing to patient experience and empowerment,

for example. However, the impact on the bigger picture remains cosmetic unless the entire supply chain is fully understood and continued to be regulated strictly.

Theoretically, it has been described how information asymmetry forms a major hindrance to the medicine supply chain and how digital solutions can contribute to overcoming it. Managing the incomplete information is, undoubtedly, one of the main drivers of the digital transformation in this domain.

The applicability of the sociotechnical systems model in the design of new digital solutions is, however, questionable, as the user-centric approach often leads to status quo–seeking solutions, whereas it is imperative to discover radical new ways of working. It should, however, be noted that the sociotechnical viewpoint can be beneficial to understanding wider and complex environments with many, sometimes conflicting, interests and regulations and a domain that is, eventually, quite personal and sensitive. This view certainly cannot be obtained through researching a miniscule phenomenon.

6.4 Future research

There is an opening for a design science-oriented research piece in which the mechanisms for improving transparency and predictability of the supply chain are designed and piloted. These could be based on identifying stakeholders and data points across the chain and designing predictive models based on those. This study should approach the topic in an out-of-the-box manner, whereby current practices are significantly questioned. This also applies to the user-centricity that many traditional systems design methods overemphasize. The user-centricity should be transformed to customer-centricity – whereby the outcome of the system matters, rather than the process to achieve it. Whereas this may seem like a harsh way of viewing the world, it is the way that enables discovering radical solutions for pressing problems. The shift should involve understanding what outcome is required and then investigating what inputs and processes are required. This may be entirely different from the current state.

From the sociotechnical systems perspective, more research is required to adapt the model to better suit a modern, rapidly changing world. Current status quo–seeking tradition may well not be suited to finding radical solutions required to manage disrupted environments and business areas.

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