

MASTER

**An explorative clinical rule engine requirement analysis for a patient-centred clinical decision support system
a system to support patients in the self-management of their chronic disease**

Rutten, M.M.J.

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Eindhoven, August 2018

**An explorative clinical rule
engine requirement analysis for
a patient-centred clinical
decision support system:
A system to support patients in the self-
management of their chronic disease**

by
Marieke Rutten

Student identity number 0982482

in partial fulfilment of the requirements for the degree of

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in Innovation Management**

Supervisors:

Company supervisor: Marcel van Loosbroek, Zorgkluis B.V.

First supervisor: Prof. dr. ir. Uzay Kaymak, TU/e, Information Systems

Second supervisor: dr. Estefanía Serral Asensio, TU/e, Information systems

Third assessor: dr. Maryam Razavian, TU/e, Information systems

TUE. School of Industrial Engineering.
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Management summary

Technology is a driver of change. The internet-, social networking- and mobile connectivity revolution have changed the way people communicate, access information and share information. These three pivot points enabled the digital health revolution, which allows patients to participate in their own health care. To manage all the available data, healthcare professionals get support through a clinical decision support system. In an ideal situation, the health professionals should make optimum, efficient and effective use of their professional judgement, experience and clinical knowledge to make decisions in the interest of the patient. However, in the complex and challenging healthcare environment, clinical errors are sometimes made. Therefore, there is an increased interest in tools which ensure and improve healthcare quality through active participation of the patients themselves.

The rise of patient-centred care impacts the health industry. Patient-centred care is about making clinical decisions based on the patient's preferences, needs and values, to ensure that the patients day-to-day requirements are used to guide these clinical decisions. Key elements of patient-centred care are shared decision-making, communication and self-management, while balancing the clinical and patient responsibilities. Research regarding patient-centred care shows a positive effect on chronic disease outcomes and improvement of the healthcare quality, reducing the financial burden of face-to-face healthcare delivery. By using available information technologies the avoidance of chronic illness hospital readmission and the duration of treatments can be reduced. Especially patients with a chronic condition have an essential role in their own health process and want to be engaged because they make health related decisions and experience challenges on a daily basis. In the Netherlands, 52% of the total population have one or more chronic health conditions. So, with new technologies, the patient is becoming more informed and autonomous and is eager to use these technologies for their own health care.

In response to the developments mentioned above: the internet-, social network- and mobile technologies, the accessibility of health information, the shared decision-making process, the self-management initiatives, the rise of chronic health conditions in the Netherlands and the effects of these developments, Zorgkluis B.V. intends to develop an intelligent healthcare information ecosystem (IHIE) architecture. The IHIE supports the patient in the self-management of their chronic health condition through a patient-centred clinical decision support system (patient-centred CDSS). This study uses an exploratory research to provide a solid basis for the development of a clinical rule engine for a patient-centred CDSS. Therefore, the research purpose of this study is defining the high-level clinical rule engine requirements for a patient-centred CDSS and a clinical rule engine software evaluation to analyse which available software packages and programming languages are fit to develop the clinical rule engine for a patient-centred CDSS. The research design of the thesis is divided into three phases.

- Phase 1: End-users information needs
- Phase 2: Clinical rule engine requirements
- Phase 3: Clinical rule engine software evaluation

It all starts with the analysis of the information needs of the end-users: the patients and the health care professionals. In the first phase of the research, the patient analysis results identify four information needs categories: patient treatment plan, medication use, communication and medication information. The most valuable category for a patient participation self-management patient-centred CDSS is the medication information. Given this result an additional literature review is done regarding medication information. The literature review showed that the patient is most interested in information regarding the medication side effects. The health professional's information needs lie with the increased insight into the patient's day-to-day health status (patient's health parameters and

medication side effects) separate from the medical encounters, receive alerts about the patient conditions and providing insight into the effective clinical rule to prevent day-to-day risks during and after treatment. The overall conclusion of phase 1 is the end-users need, a patient-centred CDSS which supports the individual patient (and their health professionals) with the medication side effects. This gives the opportunity to make health-related decisions based on the patient-specific health data and available health information.

Taking the end-users need into account, the clinical rule engine requirements for the patient-centred CDSS are identified. The input is gathered from the literature review (patient-centred CDSS), interviews and a document analysis of the patient information leaflets. Phase two results in 16 clinical rule engine requirements for a patient-centred CDSS. The requirements are about the reasoning strategies, logic, time reasoning, decision tree reasoning, statistics, fuzzy concepts, machine learning and ontologies of the clinical rule engine. The clinical rule engine requirements contributed to the next phase 'clinical rule engine software evaluation'.

Phase three 'clinical rule engine software evaluation' describes several possible clinical rule engine software packages and programming languages to develop the clinical rule engine of the patient-centred CDSS. The top three of the clinical rule engine software packages: KNIME features 14 requirements, WEKA matches with 12 requirements and RapidMiner 11 requirements. WEKA does not support ontologies and RapidMiner does not support fuzzy concepts, however KNIME supports both. KNIME is a user interface workflow with the needed clinical rule engine functionalities, and provides data analytics, reporting and integration. The top three programming languages are: Python, Java and R, with a shared place one position for Python and Java. Both programming languages benefit from the large online community and open-source developments, leading to extensive packages and libraries. The main differences between these two languages is that Python is dynamically typed and Java statically.

This research gathered the information needs of patients and health care professionals for one chronic disease, focusing on a patient-centered day-to-day and shared health care process. The translation of these needs to clinical rule engine requirements and the match with available software packages and programming language provide a solid starting point for the intended software development process of Zorgkluis B.V to implement a patient-centered CDSS.

Preface

Before you the thesis ‘a clinical rule engine requirement analysis for a patient-centred clinical decision support system’: to support patients in the self-management of their chronic disease’. It has been written to fulfil the graduation requirements of the master study Innovation Management at the Eindhoven University of Technology. A project which creates a starting point for the IHIE project of Zorgkluis B.V., with the future perspective in mind, supporting patients with their chronic disease.

This project is supported by the company Zorgkluis B.V., which develops mobile applications for the patient and is active in the mobile health industry. I would like to thank Marcel van Loosbroek for the feedback and guidance and Onno van Zinderen Bakker for all his input regarding software, data and decision systems. I would also to acknowledge the project supervisors Uzay Kaymak and Estefanía Serral Asensio for the meetings and for answering my questions. I also want to thank all the respondents, participated in the research, without the cooperation I wouldn't have been able to conduct the analysis. Also, I would like to thank my parents, my uncle, brother, and boyfriend for their endless support during the project and for listening to me when I needed it.

I hope you enjoy the reading!

Marieke Rutten

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1. Research introduction

The introductory chapter outlines the background information of the research topic, followed by the problem description and the research question. Last, the system context of the research will be described including a stakeholder analysis.

1.1. Background information

Technology is a driver of change. The internet-, social network- and mobile revolution enabled the digital health industry. The internet and social networks have changed the way people communicate, share information and conduct their daily lives. The social network revolution provided widespread connectivity, weaker group boundaries and increased personal autonomy (Rainie & Wellman, 2012). The mobile revolution has changed the information accessibility (availability, accessibility and affordability of information) and the way people communicate.

These advancements have also entered the healthcare sector. The digital world in the healthcare sector has led to personalisation, connectivity and social networking (Kabene, 2010). The technology enabled innovative initiatives to communicate, translate data into knowledge and exchange data (Ho, 2008; Kabene, 2010; Vitacca, Mazzú, & Scalvini, 2009).

Health professionals work long shifts, are constantly recording patient's data and perform multiple tasks at once (Bouamrane, Rector, & Hurrell, 2011). It is possible for physicians to collect data from various sources. They have access to the general knowledge of the physicians itself, the patient's electronic health record as created by the professionals in the hospital, pharmaceutical information and the latest data of the health professional. The consequence is a clinical decision support system to support the health professional managing these data. In an ideal situation, the health professionals should make optimum, efficient and effective use of their professional judgement, experience and clinical knowledge to make decisions in the interest of the patient. In this complex and challenging environment clinical errors are sometimes made due to for example a lack of concentration or not properly disclosing information at shift handovers (Oyebode, 2013). Therefore, there is an increase interest in tools which ensures and improves healthcare quality through active participation of the patients themselves.

1.2. Problem description

In the Netherlands, 52% of the total population have one or more chronic conditions, which increases every year (NIVEL, 2016). People with chronic health conditions experience challenges daily, such as understanding the impact of the disease and participating in the treatment (H Zheng et al., 2008). Patients with a chronic health condition spend only 2% of their lifetime in the presence of a health professional (European Patient's Forum, 2015). So, 98% of the time the patient needs to deal with the chronic health condition by themselves. People with a chronic health condition, adjust their aspirations, ambitions and goals, because the person adapts to a life with a chronic health condition (Kinney, Kahana, Corbin, & Strauss, 1989). On-going support, acceptance and emotional adaption are factors that influence the success in achieving and retaining the quality of life the patient desires (Agrawal & Mitchell, 2005). Patients with a chronic health condition make medical decisions on a daily basis. By using the available information technologies the avoidance of chronic illness hospital readmission and the duration of treatments can be reduced (Celler, Lovell, & Basilakis, 2003). Self-management initiatives address the patient's need for more patient-centred care and in parallel reducing the financial burden of face-to-face healthcare delivery (H Zheng et al., 2008). People want

to be more engaged in their healthcare process since medical changes and decisions impact the person itself (CDW, 2017).

Health professionals are currently supported by decision support systems in making decisions and managing the data. However, patients deal with their disease every day and to manage the chronic health condition in an organized, coordinated and patient-centred manner, patient-centred self-management systems are needed. The results of patient-centred care research showed improvement in the healthcare quality and positive effects on chronic disease outcomes (Elder et al., 2017; healthinnovationnetwork, 2018; Stuber, Langweiler, Mior, & McCarthy, 2016). The importance of patient-centred care and the increase of chronic health conditions in the total population highlights the increasing need for healthcare systems that allow patients to address their own chronic health conditions. Therefore, a patient-centred clinical decision support system (patient-centred CDSS) is needed to support patients in self-management of their chronic health condition.

1.3. Research question

To develop a patient-centred CDSS a clinical rule engine is needed to monitor and support the patient. The software development methodology is used to develop the software for the clinical rule engine. Figure 1 shows the different phases of the software development life cycle.

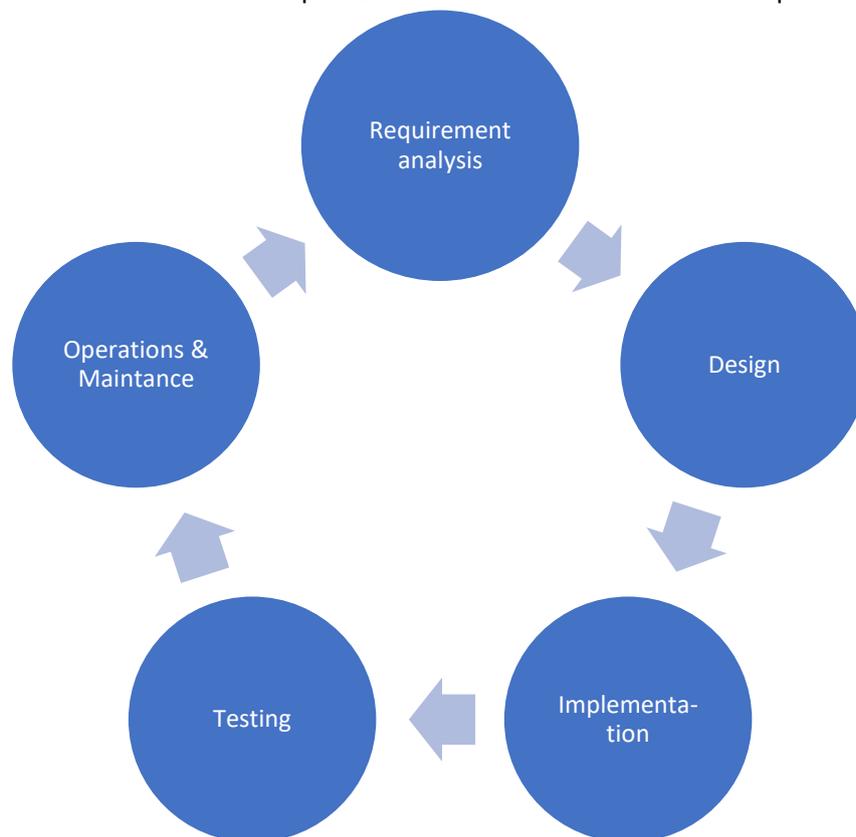


Figure 1. Software development life cycle (Wieggers & Beatty, 2013)

This thesis focuses on the first phase of the software development process. The purpose of the research is to execute a requirement analysis to define high-level requirements of a clinical rule engine for a patient-centred CDSS and an evaluation of software that are fit to develop the required clinical rule engine. With the goal to prove advice for a suitable software to develop the clinical rule engine for the patient-centred CDSS, because there is not yet such advanced and integrated patient-centred CDSS in the market which supports patients in self-management.

Research question:

‘What are the clinical rule engine requirements for a patient-centred clinical decision support system to support patients in the self-management of their chronic health condition?’

The research question identifies three main elements: clinical rule engine, requirements, patient-centred CDSS and chronic health condition. The clinical rule engine refers to the inference engine component of a decision support system in a patient-centred clinical decision support system context. The following definitions are used during the report:

Clinical rule engine/ Inference engine → Definition of Berner (2016) :” *The inference engine is the portion of the CDSS that combines the input and other data according to some logical scheme for output.*”(p.34)

Requirement → Definition of Wiegers and Beatty (2013): “*A requirement is a statement of customer need or objective, or of a condition or capability that a product must possess to satisfy such a need or objective. A property that a product must have to provide value to a stakeholder.*”(p.601)

Patient-centred clinical decision support system → The definition is from the website patient-centred clinical decision support learning network (<https://pccds-ln.org/>): “*Patient-centred CDSS is clinical decision support that supports individual patients and their approved caregivers and/or care teams, in health-related decisions and actions by leveraging information from patient-centred outcome research findings and/or patient-specific information (e.g., patient-generated health data)*”(PCCDS-LN, n.d.).

Chronic health condition → Zheng defines a chronic health conditions as: “*A chronic health conditions are those that a person has over an extended period, or for life.*” (H Zheng et al., 2008, p.1).

1.4. System context

In this paragraph, the system context is described followed by an analysis to identify and understand the stakeholders involved.

To support the patient and the health professional during the process of a chronic health condition, Zorgkluis B.V. started the project Intelligent Healthcare Information Ecosystem (IHIE). The two goals of the IHIE architecture are to support the patient during and after treatment and to support the health professional during the healthcare process. Bergman, Neahauser, and Provost (2011) give a clear overview of the five main stages in the healthcare processes. The healthcare process focuses on the citizen’s point of view. The following five main process stages are: keeping healthy, detecting health problems, diagnosing diseases, treating diseases and providing for a good end of life, see Figure 2 (Bergman, Neuhauser, & Provost, 2011).



Figure 2. Five Main Healthcare Processes. Reprinted from “Five main processes in healthcare”, by B. Bergman, D. Neuhauser & L. Provost, *BMJ Quality and Safety*, 20, p.42. Copyright 2011 by B. Bergman, D. Neuhauser & L. Provost.

The first stage is focused on the prevention of a disease. The citizen is focused on staying healthy by for example physical exercises. Detecting health problems is the next stage. In this stage the patient experiences symptoms. After the diagnosed disease the specialist will determine the treatment. The diagnosed disease indicates which treatment(plan) the patient must follow and the disease is being treated. The last phase is about providing the patient a good end of life. The proposed IHIE project focuses on the last two steps of the healthcare process, treating diseases and providing for a good end of life. Through self-management, the patient can be a significant stakeholder in the healthcare process.

The primary purpose of IHIE is to guide the patient during their healthcare process. It will provide a dynamical set of agreements (care pathway of therapy) between the patient and the healthcare provider(s) about care and self-management. The IHIE project consists of five pre-defined software components:

- The personal health record (PHR) server collects and stores the data of the patient.
- The patient application is an Android/iOS application for the patient's smartphone or tablet. The patient-generated data during the care process is stored in the PHR.
- The dashboard application is a monitor for the health professional to analyse the progress and recovery process of the patient. The specialist-generated data about the patient is also stored in the PHR of the patient.
- The communication infrastructure between the patient and the health professional and it provides the facility to access the system.
- The expert system is a patient-centred CDSS that applies clinical rules and monitors the patients care process.

The focus of this research is on the clinical rule engine of the patient-centred CDSS, also known as the expert system of the IHIE project. The study aims to execute a requirement analysis to define the high-level requirements of a clinical rule engine for the patient-centred CDSS and also a software evaluation to provide advice regarding which software to use to develop the clinical rule engine. In short, IHIE is about guiding the patient during the treatment and care plan and helping the health professional in this process. The pre-proposed system architecture of the IHIE project is illustrated in Figure 3, which consists of three categories, the system users (patient application and health professional monitor) the patient-centred CDSS setting and the healthcare data domain.

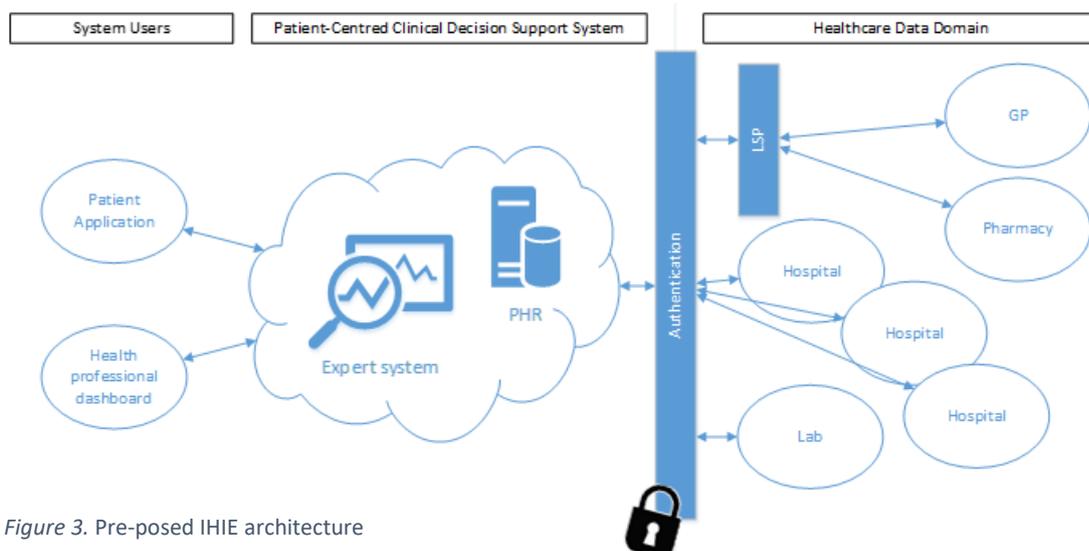


Figure 3. Pre-proposed IHIE architecture

The stakeholders of the system are identified to give insight into their interest and goals. The stakeholders are people, groups or organisations. Sharp and Finkelstein (1999) investigated the stakeholder identification in the requirements engineering process. They identified different definitions. From a strategic management perspective a stakeholder is (Freeman, 1984, p. 46):

“A stakeholder in an organisation is (by definition) any group or individual who can affect or is affected by the achievement of the organisation’s objectives.”

The definition of Freeman (1984) is a widely used definition. However, the description is still vague and may lead to incomplete identification of stakeholders. Therefore, categories are used to better identify the different types of stakeholders. The framework of Sharp, Finkelstein, and Galal (1999) is used to identify the stakeholders. The first stakeholder type is the baseline stakeholders subdivided into the users, developers, legislators, and decision-makers. Below a description of the subdivisions (Sharp et al., 1999, p.3):

- User: *“are the people, groups, or companies who will interact with the software and control it directly, and those who will use the products (information, results, e.g.) of the system.”*
- Developer: *“are stakeholders in the requirement engineering process, but their stake in the final requirements specification, or indeed in the system itself, is different from the users described above.”*
- Legislators: *“Professional bodies, government agencies, trade unions, legal representatives, safety executives, quality assurance auditors and so on may produce guidelines for operation that will affect the development and/or operation of the system”.*
- Decision makers: *“Within the development organisation and the user organisation, there will be decision-making structures/people that relate to the system under development. “*

The baseline stakeholder interacts with the ‘supplier’ -, ‘client’ - and ‘satellite’ stakeholders, which affect the system (Sharp et al., 1999). The baseline stakeholder consists of the four groups mentioned earlier, the users, developers, legislators, and decision-makers. A legislator is for example, government agencies and safety executives and so out of scope.

First, the baseline stakeholders are identified, then the supplier -, client- and satellite stakeholders. The IHIE system consists of different users. The people who will use the system are the patients, through the mobile application and the health professional through the dashboard application. The persons controlling the software directly is the company itself, Zorgkluis B.V. The leading developers of the IHIE system are the organisations involved in the project at this moment, namely hospital Rotterdam Erasmus MC, the software company Digitalis and Zorgkluis. The decision makers of the IHIE project is the director of Zorgkluis.

The subdivisions of the baseline stakeholders are defined, leading to the next type, the supplier stakeholder. The supplier stakeholder is a party that supplies goods or services. There are two suppliers in the IHIE architecture context: the health professional who will be the creators and editors of the clinical rules, and the future system software company (not yet defined). The patient and health professional are the client stakeholders of the IHIE project. The client stakeholders are persons or organizations using the goods or services. Last, the satellite stakeholder is the software company that built a clinical rule engine for the pharmacy. The satellite stakeholder is not a client or supplier, but a stakeholder who interact with the other stakeholders. The company Digitalis focuses on decision support system for the pharmacy in medication safety and optimisation. Concluded the five major

stakeholders regarding the IHIE system are the patients, health professionals, Zorgkluis B.V., the pharmacy of Erasmus MC and Digitalis.

1.5. Thesis outline

The second chapter is an introduction of the digital health literature with the subject's digital health, medical records, patient-centric care trends, decision support systems and the mobile health market. In chapter three the results of the literature review of patient-centred CDSS is presented. The research design and methods are described in chapter four. Followed by the results of phase one 'end-users information needs' in chapter five. The results of phase two 'clinical rule engine requirements' are explained and defined in chapter six. The results of the clinical rule engine software packages and programming language evaluation of phase three is outlined in section seven. Chapter eight describes the conclusion of the research in combination with the research discussion topics.

2. Introduction to digital health

In this chapter a short overview is given of topics related to digital health which are relevant for this research. It will be explained what digital technologies made the digital health revolution possible and how this influenced the position of the patient in the healthcare process. A few notes will be made on how new technologies impact the way medical records are handled, organized, used and shared. Most of these changes are enhancers of the trend to focus the healthcare more around the patient. This will be explained in more detail. The next paragraph is about a Decision Support Systems (DSS) and how these types of systems are used in digital health. Finally, the mobile health market is explained and described.

2.1. Revolution of the digital health

The pivot points enabling the digital health are the social network -, internet - and mobile revolution. Social networks and the internet have changed the way people communicate, share information and conduct their daily lives. The social network defined by Rainie and Wellman as: *“a set of relations among network members whether they are people, organisations or nations”* (Rainie & Wellman, 2012, p.21). The social network changed the digital age because of the widespread enabled connectivity, leading to weaker group boundaries and increased personal autonomy (Rainie & Wellman, 2012). The internet is an unprecedented technological innovation due to the massive adoption rate. In a few years the internet became accessible and affordable. The mobile revolution began separated from the internet but after some years the mobile technology merged with the internet and the social networks. Mobile phones have become ubiquitous, accessible anywhere at any time. The same is true for internet. All these changes and technologies are revolutionizing digital health. According to P. Sonnier digital health revolution is: *“the convergence of the digital and genomic revolutions with health, healthcare, living and society”* (Sonnier, n.d., 2017, para 1). Figure 4 shows the digital health revolution with the current and future results.

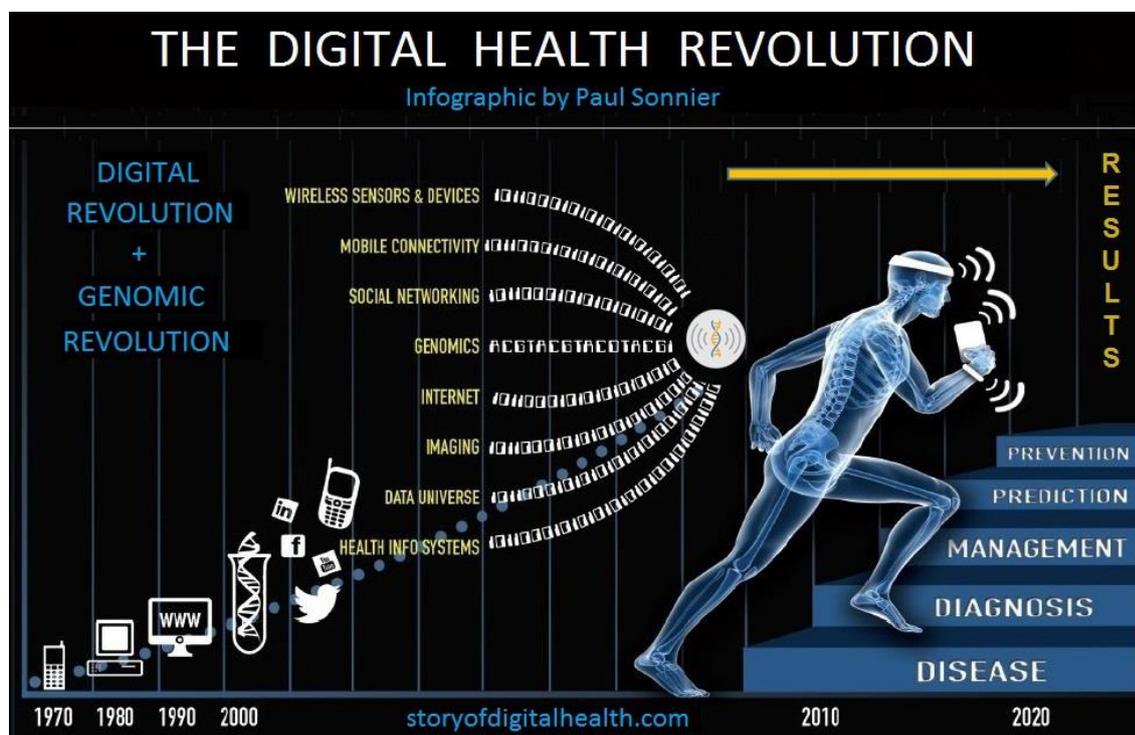


Figure 4. The digital health revolution. Reprinted from *Story of digital health* website, by P. Sonnier, 2017, retrieved from <https://storyofdigitalhealth.com/definition/>. Copyright 2017 by P. Sonnier.

According to the Statistics Portal website around 72% of the Dutch population own a smartphone (Statista, 2016). In 2017 research shows that 98% of the Dutch households have access to the internet (CBS, 2018). The preferred way of people accessing the internet is by mobile devices. 87% of the Dutch population use internet with mobile devices (CBS, 2018). Related to healthcare, research showed that 35% of the U.S. adults search online to figure out which medical condition they may have (Fox & Duggan, 2013). When specifically looking at people with a chronic disease an even higher online searching rate of around 60% is found (Fox & Duggan, 2013). Nowadays the patients are accessing web-based information, especially health information. But that was not always the case. During the last few decades the way health information was received and retrieved has changed dramatically. The figure below explains how these changes took place, see Figure 5.

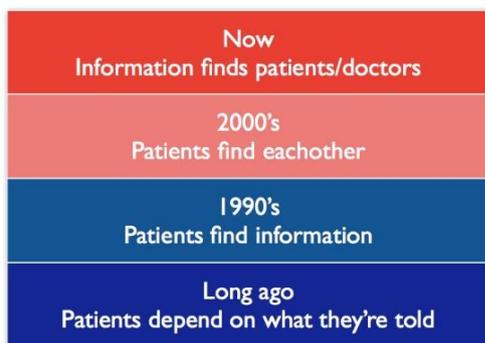


Figure 5. Evolution of Health Information. Reprinted from 33charts website, by B. Vartabedian, 2011, retrieved from <https://33charts.com/physicians-risk-opportunity-social-media/>. Copyright 2011 by B. Vartabedian.

The long-ago category refers to the scenario where patients did what they were told. The patient went to the general practitioner (GP), showed up in the GP office, and the GP told the patient what to do. Most of the time the patient did not ask too many questions and the GP did not explain too much. In 1990 the internet emerged. The patients could find information through static sites and hyperlinks but was not yet able to do active online search (Vartabedian, 2011). This information was sometimes brought to the GP office and resulted in more dialog between GP and patient. When the social network revolution appeared in the 2000's, the patient got the opportunity to get together and have a dialogue with other patients or health professionals through new technologies. The patient was more often well prepared and informed when visiting the GP office but still the GP was in the lead of the health process. The last category is about the current and near future situation where information finds patients and health professionals, through for example the patient's social network. Due to the online information availability, the relationship between patient and doctor is changing. The patient is more in control of his or her health process and is part of the decision making.

2.2. Health informatics and medical records

In 1986, Blum published a paper about clinical information systems and grouped these systems based on the type of objects that the systems processed. The three types Blum identified (Blum, 1986, p.35):

- Data *"are the uninterpreted elements that are given to the problem solver."*
- Information *"is a collection of data that contains meaning"*
- Knowledge *"is the formalisation of the relationships among elements of information and data."*

After this publication in 1989, a model was derived based on those three elements to explain the nursing informatics by Graves and Corcoran Perry. The frame shows the horizontal flow of data and information to knowledge, see Figure 6 (Graves & Corcoran, 1989).

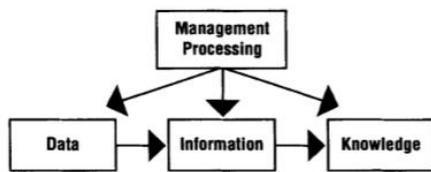


Figure 6. The conceptual framework of nursing information. Adapted from *The study of nursing informatics*, J. Graves & S. Corcoran, 1989, *The Journal of nursing scholarship*, 21, p.228. Copyright 1989 by J. Graves & S. Corcoran.

In 2002, Englebardt and Nelson advanced the ideas of data, information, and knowledge by extending it with wisdom. They positioned the concepts in a model based on the level of complexity and level of interactions and inter-relationships. The result is shown in Figure 7 (Englebardt & Nelson, 2002).

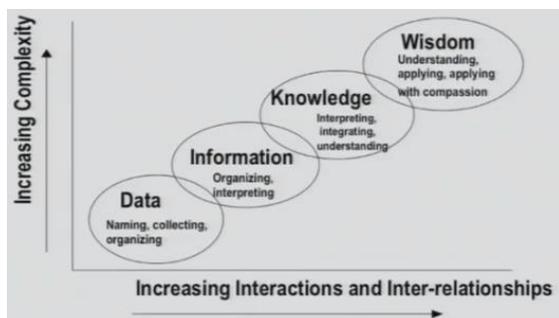


Figure 7. Wisdom continuum. Retrieved from *Healthcare informatics*, p.455, S. Englebardt & R. Nelson, 2002, Mosby. Copyright 2002 by Mosby.

To ensure that the data in the system transforms to knowledge and even wisdom, it is key to understand the transformation from data to knowledge and to understand how the complexity is managed. It starts with a unambiguous definition of the data to ensure that no misconceptions can occur about the meaning of the data (Hoyt & Yoshihashi, 2014). For example, if a patient observation is 64, it should be clear if this is the weight, the age or the temperature and which unit of measurement is used.

To encode meaning into language and logic, semantic tools are developed (Hoyt & Yoshihashi, 2014). In healthcare the standardized classification tools are important semantic tools that help to ensure that data can be used to derive information and knowledge. Examples of such classification tools are the ATC-classification (classification of drug use) and the ICD-9-CM (classification of diseases). By using these classifications research is possible on data from various sources. Ontology is another type of semantic tool focused on capturing domain knowledge and improving the exchange of knowledge between people and systems. The tools are capturing meaning and concepts and showing inter-relationships. In the Oxford dictionary ontology is: "a set of concepts and categories in a subject area or domain that shows their properties and the relationships between them" (Oxford Dictionary, 2018). Another semantic tool that helps in capturing and presenting data is the interface terminologies, defined as "a systematic collection of healthcare-related phrases (terms) that supports clinician's entry of patient-related information into programs" (Rosenbloom, Miller, Johnson, Elkin, & Brown, 2006, p.277). The reference terminologies are used as a common language for comparison and aggregation of data and recorded by multiple people and parties (Spackman, Campbell, & Côté, 1997). The last semantic tools are the interoperability standards. For example, the HL7 standards. The focus of HL7 is

to exchange, integrate, share and retrieve health data (HL7, 2014). All these semantic tools help transfer from data into information to knowledge.

In the overview above the focus was on supporting the healthcare professional in gathering and managing data and information. But there is another source of health data: the patient-generated data. The patient-generated data is also of high value to the specialist concerning the health condition of the patient. The Office of the National Coordinator in the US defines patient-generated health data for health information technology as: *“health-related data created and recorded by or from patients outside of the clinical setting to help address a health concern”* (HealthIT, n.d.). Examples of patient-generated health data (PGHD) are the symptoms or biometric data and medication effects via mobile applications or wearable devices. The use of PGHD generates benefits for the patients and health professionals. It allows the patient to empower and better manage their health and actively participate in their care process (HealthIT, n.d.). For the health professionals, it is beneficial because it allows insight into the patient health data over time in more detail which enables shared information- and decision-making (HealthIT, n.d.).

To have an overview of the patient’s information and have attention for the individual patient, health professionals must collect, retrieve and analyse data in every single healthcare encounter. There are a great variety of terms which are used to describe electronic records. This report uses three terms, namely Electronic Medical Record (EMR), Electronic Health Record (EHR) and Personal Health Record (PHR). The National Alliance for Health Information Technology (2008, p.15) defines the following:

- Electronic Medical Record (**EMR**): “An electronic record of health-related information on an individual that can be created, gathered, managed, and consulted by authorised health professionals and staff within one healthcare organisation.”
- Electronic Health Record (**EHR**): “An electronic record of health-related information on an individual that conforms to nationally recognised interoperability standards and that can be created, managed, and consulted by authorised health professionals and staff across more than one healthcare organisation.”

In the Netherlands known as EPD (Elektronisch Patienten Dossier)

- Personal Health Record (**PHR**): “An electronic record of health-related information on an individual that conforms to nationally recognised interoperability standards and that can be drawn from multiple sources while being managed, shared, and controlled by the individual.”
In the Netherlands known as the PGO (Persoonlijke Gezondheidsomgeving).

For a complete overview of the interaction with each other, see Figure 8.

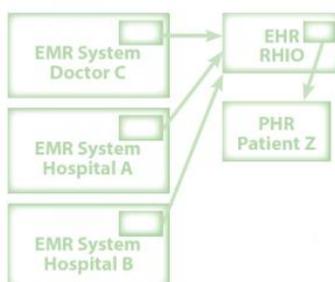


Figure 8. Electronic Health Record Diagram. Reprinted from *ed-informatics*, by creator ed-informatics institution, retrieved from <http://ed-informatics.org/healthcare-it-in-a-nutshell-2/emr-vs-ehr-vs-phr/>. Copyright n.d. by ed-informatics.

The EMR gives information about the patient's health history from a provider point of view. The EMR consists of data created by the health professionals or patient outcomes of clinical orders, for example, prescriptions for medication. The primary objective of an EMR is to provide the doctor with more treatment based information, through the health professional's ability to document observations and findings (National Alliance for Health Information Technology, 2008). The EHR is more patient-focused than the EMR because more provider organisations can give input on behalf of a patient. The primary goal is to have a total longitudinal health history of the patient (National Alliance for Health Information Technology, 2008). However, the EHR is mostly managed and used primarily by the authorised care providers, health professionals who must support the patients care process. The EHR is in the Netherlands known as the electronic patient dossier (EPD). Robert Lowes (2004) showed that an EHR system consists of eight functions:

1. Health information data
2. Result management
3. Order entry
4. Decision Support
5. Electronic communications and connectivity
6. Patient support
7. Administrative processes
8. Reporting and population health management

When the EHR is made available to the individual patient and the patient has control and is able to manage the records, it will become a PHR type system.

When looking at the situation in the Netherlands, there is a national infrastructure for standardised electronic exchange of healthcare data named AORTA. It's a national infrastructure but the data is not stored in a central database. Health professionals have their own information systems and exchange their medical data via the LSP (Landelijk Schakelpunt). AORTA consists of three parts which are the supporting infrastructure for exchanging of medical data:

- LSP (Het landelijk schakelpunt / National Exchange Point)
- ZSP (Zorgserviceproviders/ Healthcare service providers)
- GBZ (Goedbeheerde zorgsystemen/ Well-managed healthcare systems)

These components ensure the secure communication of medical data between health professionals. The Vereniging van Zorgaanbieders voor Zorgcommunicatie (VZVZ) is responsible for the exchange of data via the LSP. In 2011 the VZVZ was established by the healthcare organisations nationwide general practitioners association (LHV, Landelijke Huisartsen Vereniging), General Practitioner (VHN, Vereniging Huisomroepen Nederland), pharmacies (KNMP, Koninklijke Nederlandse Maatschappij ter bevordering der Pharmacie) and hospitals (NVZ, Nederlandse Vereniging van Ziekenhuizen). To make the data available to the connected parties, the patient must authorise the exchange of medical data. Through the LSP, GP practitioners and pharmacies can share medical data from their patients with other care providers connected through the LSP. The LSP makes it able to request medical information of the patient during treatment relationships. The IHIE project of Zorgkluis B.V. uses the LSP to provide the patient-data for the PHR.

2.3. Patient-centred care trends

The patient-centred care trend started from the psychological and psychotherapeutic (medical) perspective. They promoted the idea that a patient not only needs a general practitioner but sometimes also a psychotherapist (Balint, 1969; Holmström & Röing, 2010). This focus opened the patient-centred perspective where the treatment goal must be in line with the patient's life goal(s). Although the phrase 'patient-centred care' was introduced several decades ago the Institute of Medicine named in 2001 patient-centred care as one of the six aims for high-quality health care (Institute of Medicine, 2001). Patient-centred care is about effective communication between the specialist and the patient for optimal health and optimal results. In the paper of the Institute of Medicine patient-centred care is defined as: *"providing care that is respectful of and responsive to individual patient preferences, needs, and values, and ensuring that patient values guide all clinical decisions."* (Institute of Medicine, 2001, p.3).

The level of patient-centred care is depending on the quality of interactions between the health professionals and patients (and sometimes also the patients' family members) and also of the interactions between the health professionals (Epstein, Fiscella, Lesser, & Stange, 2010). Patient-centred care matters because it is the right thing to do based on moral and ethical grounds, and it promotes the well-being of the patient. It is also addressing racial, ethnic and other disparities by actively bridging the differences between patient and health professionals (Epstein et al., 2010). Shared information, shared deliberation and shared mind are key elements of patient-centred care.

When the patient and the health professional are interacting, medical decisions are made in different ways. When looking at patient-centred care and the continuum of decision making a shift is made from the paternalistic way of decision making to shared decision making, see Figure 9.

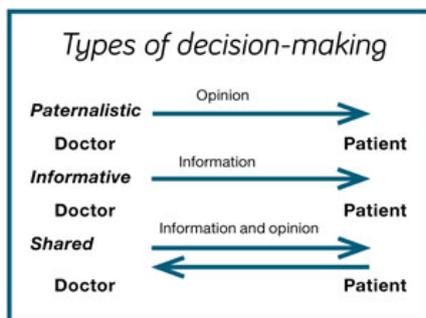


Figure 9. The types of decision-making. Retrieved from Medical Protection, 2015, retrieved from <https://www.medicalprotection.org/hongkong/casebook-resources/mps-connect/articles/articles/hk-shared-decision-making>. Copyright 2015 by Medical Protection.

The shared decision-making process is an interactive process of sharing information and opinions and identifying patient preferences while balancing the health professional and patient responsibilities (Stiggelbout et al., 2012). The IHIE architecture has therefore two different end-users, namely the patient and health professional. Letting the patient participate in the health process results in better informed patients and in improved quality of life (Kaplan, Greenfield, & Ware, 1989; Montori, Gafni, & Charles, 2006). In 1989 the research of Kaplan focused on the doctor-patient relationship and if the relationship influences the patients' health outcomes. The results of the study showed that the relationship may be a significant influencer on patient health outcomes (Kaplan et al., 1989). Another research focuses on the role of the carer in the treatment decision-making process. This study showed that models fail to address the importance of the carer in the treatment decision-making process and it was proposed to include the carer in the models (Hubbard, Illingworth, Rowa-Dewar, Forbat, &

Kearney, 2010). The carer has a vital role in the experience of the patient-carer relationship. The carer has a facilitating role in deliberations and information gathering (Hubbard et al., 2010). The results of the research of Abbott (2017), focusing on patient-centred health care for people with a chronic skin condition, showed that health professionals experience time pressure, which makes the patient-centeredness focus difficult (Abbott, 2017). When the patients with chronic skin condition perceive a lack of personalised care, they experience follow-up appointments as burdensome (Abbott, 2017). Patient-centred care is all about having a voice and being heard. In the medical world, patient empowerment is about the ability to think critically and make informed and autonomous decisions (Anderson & Funnell, 2011). WHO defines empowerment as *“a process through which people gain greater control over decisions and actions affecting their health”* (WHO, 1998, p.6).

Communication is essential to patient-centred care. During the HIMSS 2017 Conference, the CDW company released a patient engagement perspective study, to analyse the challenges and influences for patient engagement care (CDW, 2017). Communication is one of the essential factors for engagement. Both providers and patients see technology as a possibility to give access to the needed information. The care outcomes correlate with patient engagement, patients who are more involved are likely to have more successful results (CDW, 2017). Given the current state of technology it is now possible to access healthcare information, communicate via various tools and access patient portals. When using these information sources and communication tools the patient becomes more knowledgeable about personal medical information. The outcome of CDW's survey¹ on patients engagement confirmed the positive effects of the technological tools and practices. (CDW, 2017). First outcome confirmed that patients feel more knowledgeable when accessing online information. Second, according to the patients and providers, patient portals have a big positive impact on engagement. Another engagement enhancer that was mentioned in the survey, is the use of mobile devices since people are increasingly familiar with these devices. The survey showed that 83% (n=200) of the patient respondents are comfortable with mobile apps and communicating with them. The last finding was that there is still room for improvement. The results showed that 89% would like to have a better user experience when accessing their PHR (CDW, 2017). In contradiction with patient-centric care, empowerment is from origin a movement from social oppression or marginalisation. For example, the history of the emancipation of women.

Another key element of patient-centred care is self-management. Patients have an essential and sometimes active role in their health, for example by taking medication according to the prescription. This is especially true for patients with a chronic health condition. Self-management is essential for patients with a chronic disease because they make health related decisions on a daily basis. Therefore it is promoted to educate these patients to self-managing their disease (Bodenheimer, Lorig, Holman, & Grumbach, 2002). Coping with a chronic condition includes interpreting symptoms, handling functional limitations, living with pain and side effects and all of those issues can be experienced on a physical, psychological and emotional level. In most cases the patients must change their lifestyle. Meaning, people with a chronic health condition try to find a way which allows them to have the best quality of life. Patients with chronic disease must be able to make day-to-day decisions for themselves in their illness. As in the paper of Bodenheimer (2002) stated, self-management *“complements traditional patient education in supporting patients to live the best possible quality of life with their chronic conditions”* (Bodenheimer, Lorig, Holman, & Grumbach, 2002, p.2469). With the increase of

¹ <http://managedhealthcareexecutive.modernmedicine.com/managed-healthcare-executive/news/top-four-patient-engagement-trends-watch>

information technologies a reduction is seen in avoiding chronic illness hospital readmission and in the length of stay (Celler et al., 2003). Research showed that the overall effectiveness of the internet on self-management interventions for adults >50 with chronic disease improves the health behaviour and health status (Stellefson et al., 2013). Also, the significance of IT interventions is positive on the self-management outcomes (Jeddi, Nabovati, & Amirazodi, 2017). So, receiving care through self-management enabled systems affects the patient. Telemedicine is about using information technologies to provide healthcare outside the medical encounter. When patient and care professionals can access the telemedicine data it will result in the patient feeling more secure, knowing they are monitored every day (Barken, Thygesen, & Söderhamn, 2018). Another advantage is that the patient is more aware of the symptoms and ability of the diseased body (Barken et al., 2018). To give the patient an overview of the disease development, the patient will create daily clinical insights and develop knowledge about the health status and progress. The self-reliance of the patient increases when they have access to clinical information, resulting in increased engagement and involvement (Barken et al., 2018). Because of more awareness of their health status, the frequent feedback, and the resulting advice, the patient creates more knowledge about the significance of a measured value. And by that the meaning and representation of the patient's parameters values become more clear and meaningful (Barken et al., 2018).

2.4. Decision support systems

A decision support system (DSS) is a computer-based system with the goal to assist users in making decisions.

The DSS field has gone through an evolution of different focus areas and applications as shown in figure 10 (Arnott, 2008; Arnott, Pervan, Donnell, & Dodson, 2000). The evolution of the DSS field is strongly influenced by technological advances and emergence of new technologies (Arnott & Pervan, 2005). Figure 10 illustrates that the personal decision support system (PDSS) is the oldest type of decision support system (Arnott, 2008; Arnott & Pervan, 2005). The PDSS is a small-scale system developed to help an individual user (often a manager) in making decisions.



Figure 10. Evolution map of decision support system field. Reprinted from "A critical analysis of decision support systems research", D. Arnott & G. Pervan, 2005, 20, p. 69. Copyright 2005 by D. Arnott & G. Pervan.

O’Leary (2008) analysed the different industries in relation to real-time decisions, see Table 1.

Industry	Real-time data	Object identification	Visualization	System/process integration	Intelligent agents	Event managers
Electric power	X		X			
Electronic markets	X				X	
Health care	X	X		X	X	
Nuclear power	X					X
Telemarketing						X
Transportation	X				X	X
Supply chain		X		X	X	X

Table 1. Matrices of industry and real-time decisions. Reprinted from “Supporting decisions in real-time enterprises”, D. O’Leary, 2008, 6, p.244. Copyright 2008 by D. O’Leary.

The healthcare research, Table 1, focuses on real-time data, object identification, system integration and intelligent agents (O’Leary, 2008).

The decision support system for a health professional is called a clinical decision support system (CDSS). The systems are designed to help the health professional with decision making about the patient. The definition of a computer-based clinical decision support system by Robert A. Greenes: “The use of information and communication technologies to bring relevant knowledge to bear on the healthcare and well-being of a patient” (Robert A. Greenes, 2014, p.8). The computer-based component of the clinical decision support system definition refers to information and communication technologies (ICT). So, computer-based is about using ICT to provide the CDSS. The terminology focuses on aiding instead of making the decisions (Greenes, 2014). The goal of a CDSS is to make the patient data accessible and apparent for a person. A user of a CDSS can be a nurse, physician, patient, caregiver etcetera. A CDSS is not only used for decision support but also to assist in administrative tasks, in managing clinical complexity and in the area of cost control. (Perreault & Metzger, 1999). A CDSS is composed of various functional components that are identified by Greens as can be seen in Figure 11 (Greenes, 2014b). The CDS module obtains the data through an interface application, where the data is entered by the users or retrieved from the HER (Greenes, 2014b). Whereas the module applies the knowledge (e.g. clinical rules or algorithms). The module is transforming the input parameters and knowledge in a decision model to generate patient-specific output (Greenes, 2014b).

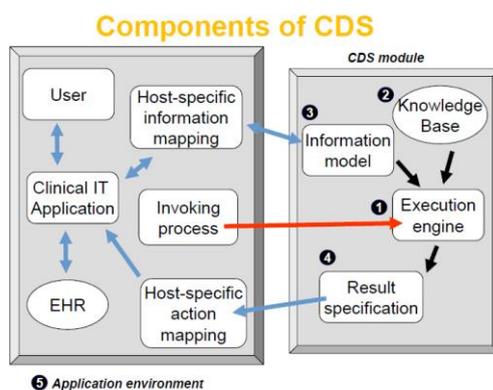


Figure 11. CDS Components. Reprinted from *Clinical decision support* (p.128), by R. A. Greenes, 2014. Copyright 2014 by Elsevier.

There are two types of CDSS systems. The first one is knowledge-based clinical decision support systems and the other type is non-knowledge based clinical decision support systems (Berner, 2016;

Greenes, 2014b). A knowledge-based CDSS consists of three parts: the knowledge base, the inference engine and the mechanism to communicate the results to the user (Berner, 2016; Greenes, 2014b). The knowledge base is the 'brain' of the CDSS, the fuel for running the CDSS. The knowledge base stores the rules and guidelines, also known as the knowledge artefacts. The knowledge artefacts could include decision support rules, clinical guidelines, care pathways, documentation templates and order sets. If new knowledge comes available, the knowledge base (knowledge artefact) must be updated. Most of the time the knowledge base consists of, if-then rules (Berner, 2016). The inference engine combines the information of the knowledge base with the electronic health record (EHR) data, in this thesis known as the clinical rule engine. After this, the system will transfer the result data out of the system and present it to the user in a way it helps the user in making a decision (Berner, 2016). The non-knowledge based CDSS has an additional function namely the use of artificial intelligence, also called machine learning. By using machine learning, the system learns from past experiences (data) and defines patterns. The focus of the patient-centred CDSS in the IHIE architecture is a knowledge-based CDSS.

A general model of the CDSS and possible features created by El-Sappagh and El-Masri (2014). It displays the EMR, medical knowledge base and inference engine relation, see Figure 12 (El-Sappagh & El-Masri, 2014).

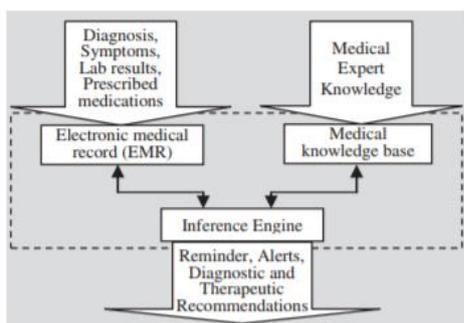


Figure 12. Clinical decision support system framework. Retrieved from "A distributed clinical decision support architecture," S. El-Sappagh & S. El-Masri, 2014, *Journal of Computer and Information Sciences*, 26, p.71. Copyright 2014 by Elsevier.

The communication between the inference engine, EMR and medical knowledge base, results in reminders, alerts, diagnostic and therapeutic recommendations. The EMR data is about diagnosis, symptoms, lab results and prescribed medications. The medical knowledge base is the medical expert knowledge data (evidence-based).

CDSS are also implemented in mobile apps. Research shows that the percentage of usage of apps by intended users is 48,44% specialists, 33,85% physicians, 6,77% nurses, 5,73% paediatricians and 5,21% emergency staff (Martínez-Pérez et al., 2014). An analysis about the development and implementation of a smartphone application for the process of Imperial Antimicrobial Prescribing Application shows that 81% of the participants find the app useful and helpful (Charani et al., 2013). The target group of the study were junior doctors and pharmacists to assist with clinical calculations and in decision support (Charani et al., 2013).

2.5. Mobile health market

The development of mobile applications in the healthcare sector is increasing. A study by the institute Research2Guidance, done in 2017 with 2400 experts in mobile and digital health, found around 300.000 health apps available in the Apple App Store and Google Play Store (Research2Guidance,

2017). In 2016, there were around 230.000 mHealth apps, which shows a growth of 70.000 applications in the Google Play and Apple App stores combined. As can be seen in Figure 13, the growth rate of the Google Play Store was 50%.



Figure 13. Number of mHealth apps per app store. Retrieved from “mHealth app economics 2017”, Research2Guidance, p.10, 2017. Copyright 2017 by Research2Guidance.

In another study by IMS Institute for Healthcare informatics done in 2015 there was an increase measured of more than 100% for the number of mobile health apps in the iOS ecosystem when comparing 2013 and 2015 (IMS Institute for Healthcare Informatics, 2015). When the existing mobile ecosystems are combined, there were over 165.000 healthcare apps in 2015 (IMS Institute for Healthcare Informatics, 2015). When categorizing the most relevant apps (almost 27.000) the distribution of the apps over the identified categories is shown in Figure 14.

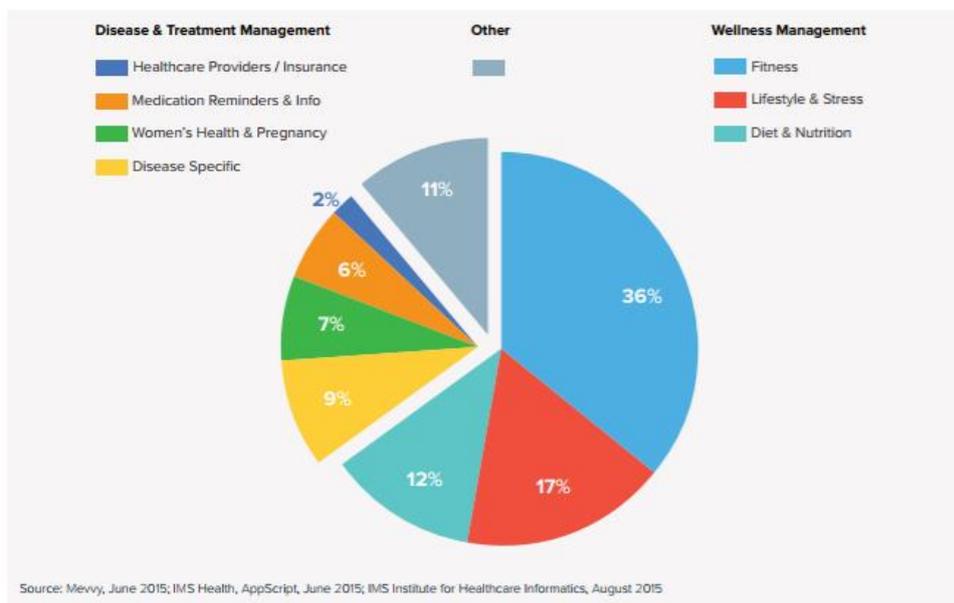


Figure 14. Categorising of mHealth apps. Adapted from “Patient adoption of mHealth”, IMS Institute for healthcare informatics, p.4, 2015. Copyright 2015 by IMS Institute for Healthcare informatics.

The study by IMS differentiated the apps in two main categories. Apps focusing on self-management of overall wellness and apps focusing on disease management and disease prevention (IMS Institute for Healthcare Informatics, 2015). The growth of the mobile applications is because the consumer is

taking a more active role in health in combination with smartphone usage. The total distribution of the healthcare applications shows that two-thirds are in the category of wellness management. The wellness management focusses on fitness, lifestyle & stress and diet & nutrition. An estimated quarter is for disease and treatment management. More than a third of the apps within that quarter is disease-specific. When looking in more detail to the disease-specific apps it is found that the main part of these apps focusses on self-management of chronic conditions. While the availability of mHealth apps is still growing, the capabilities of most of the applications are limited to delivering information alone. When the applications are grouped based on the functional dimensions inform, instruct, record, display, guide, remind/alert, communicate the result of the distribution is shown in Figure 15.

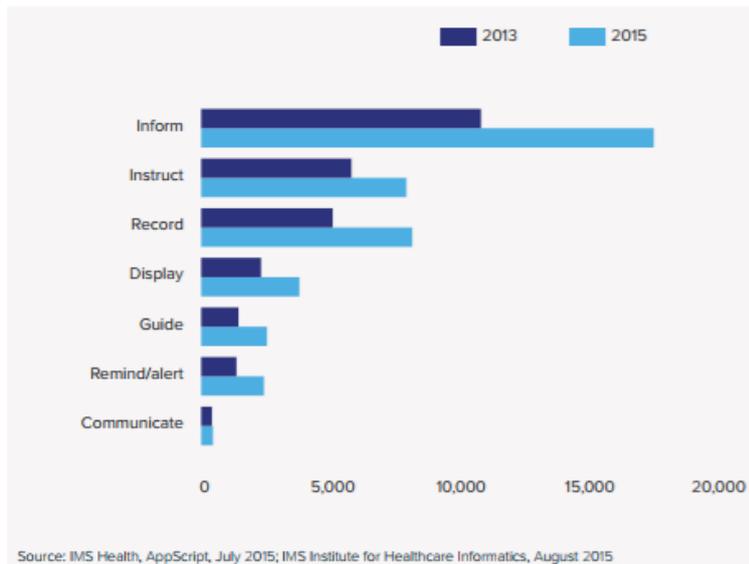


Figure 15. App functionality distribution. Adapted from "Patient adaption of mHealth", IMS Institute for healthcare informatics, p.8, 2015. Copyright 2015 by IMS Institute for Healthcare informatics.

The functional dimension in which most of the applications are categorized is the inform functionality. And most of the apps support only one functional dimension. These apps are essential and give a value to the patient, but the applications are not integrated with patient-generated data and healthcare systems (IMS Institute for Healthcare Informatics, 2015). Only when applications have broader functional scope, integration capabilities and are able to connect with healthcare systems the full value of mobile health will be recognized (IMS Institute for Healthcare Informatics, 2015).

2.6. Conclusion

The development of social network-, internet- and mobile technologies are the pivot points which enable the digital health revolution. These technologies have changed the way people communicate, share information and conduct their daily lives. People search online to figure out which medical condition they may have and access other medical web-based information. Nowadays, it is possible to unlock and integrate medical health data from (different) medical institutions to support patients (and health professionals) in their healthcare process. Data is increasingly mobile and patients use the information to search and manage their chronic health condition. The information revolution resulted into shared data and information for decision making regarding the healthcare process. The increase in data availability and accessibility led to decision support systems. The CDSS are designed to support the health professional in decision making and are extremely valuable for patients with a chronic condition who deal with their disease every day.

Patient-centred care is about making clinical decisions based on the patient's preferences, needs and values, to ensure that the patients values are used to guide these clinical decisions. Shared decision-making is a key element of patient-centred care. The shared decision-making process is an interactive process of sharing information and opinions and identifying patient's preferences while balancing the clinical and patient responsibilities. Communication is another valuable element of patient-centred care, because of the possibility to access health information and communicate through various tools so patients are more involved (patient engagement) throughout the healthcare process. The next key element is self-management. Patients have an essential and sometimes active role in their own health process, this is especially true for patients with a chronic health condition. Patients with a chronic health condition make health related decision on a daily basis, therefore the IHIE project is focused on patients with a chronic health condition. Research about self-management initiatives showed that the health behaviour and health status improved and has a positive effect on the awareness of symptoms and ability of the diseased body. Due to the self-management initiatives the patient creates more knowledge, and health information becomes more clear and meaningful. Patients with a chronic disease deal with their disease every day and to manage the chronic health condition in an organized, coordinated and patient-centred manner, patient-centred self-management systems are needed. Therefore the pre-defined IHIE architecture is introduced by Zorgkluis B.V.

3. Literature review patient-centred clinical decision support systems

In this chapter the results are described of the literature review study concerning patient-centred CDSS. Details on the search strategy for the literature review, see Appendix A.

3.1. Patient-centred clinical decision support literature review

The website pccds-ln.org is a learning network that focuses on patient-centred clinical decision support.

The site defines PCCDS as (PCCDS-LN, n.d.-a):

“CDS that supports individual patients and their approved care givers and/or care teams in health-related decisions and actions by leveraging information from PCOR findings and/or patient-specific information (e.g. patient-generated health data)”

The key elements of this definition is the involvement of both patient and caregivers, the use of knowledge as available in Patient-Centered Outcomes Research and the use of patient-specific data which is not only the patient-generated health data but also the patient-specific social, cultural and genetic factors.

In 2010, Basilakis designed a decision support architecture for management of remotely monitored patients, see Figure 16 (Basilakis, Lovell, Redmond, & Celler, 2010).

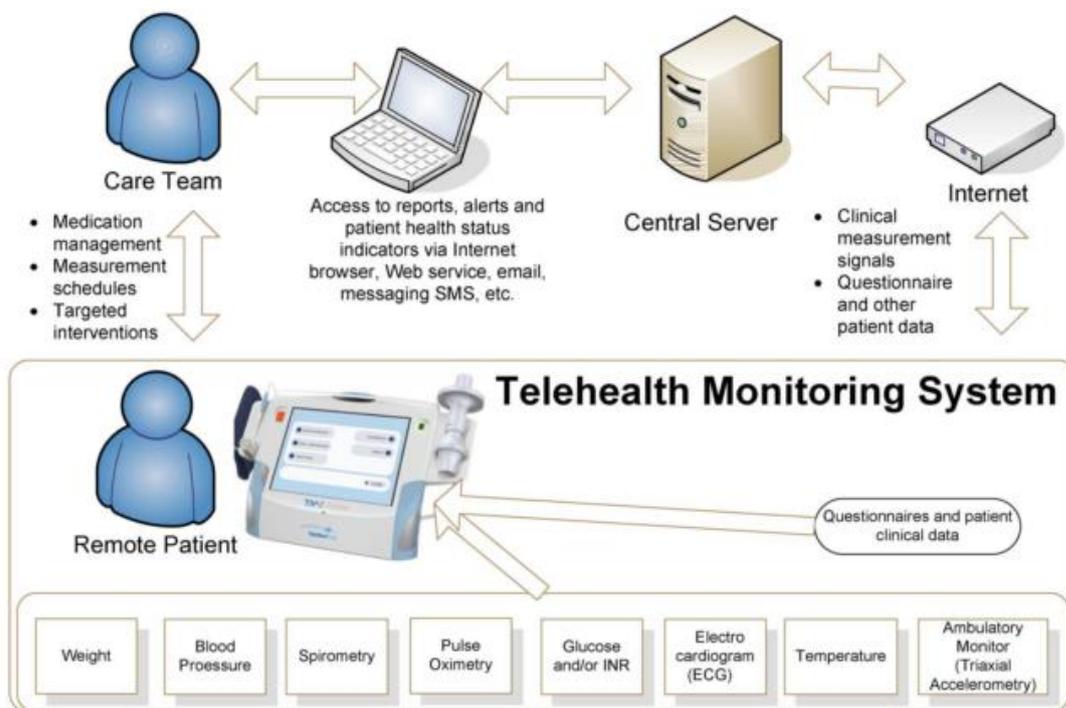


Figure 16. Decision support system architecture. Reprinted from “Design of a decision-support architecture for management of remotely monitored patients”, J. Basilakis, N. Lovell, S. Redmond and B. Celler, 2010, 14, p.1218, Copyright 2010 by J. Basilakis, N. Lovell, S. Redmond and B. Celler.

The primary role of the DSS is to reduce the data overload and stratify the health risks of the patients. The decision support system analysis the data based on threshold values or on statistical analysis of trends and averages. The rule-engine gives alerts, reports, health risk stratification and workflow modifications outputs. The system is based on a workflow management system and monitors patients

remotely using patient information gathered from questionnaires and records of physiological measurements in a home setting.

In 2010 Zheng et al., developed a personalised self-management system for patients with chronic conditions. The research describes the infrastructure of the personalised self-management system, see Figure 17. The results of the study show that telecare is feasible to support self-management for chronic diseases (Huiru Zheng et al., 2010).

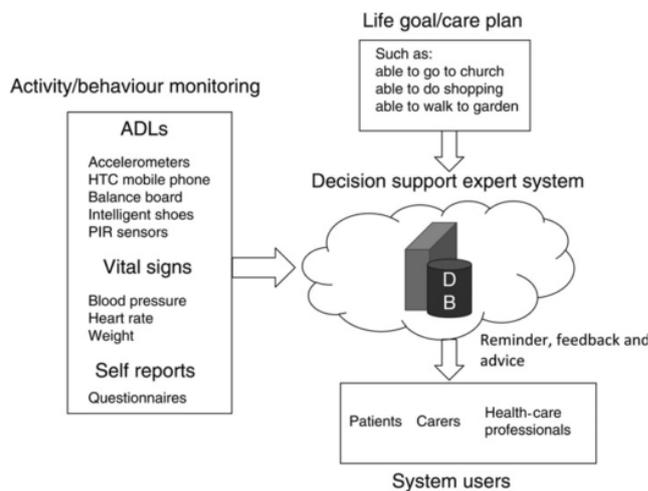


Figure 17. Infrastructure of the personalised self-management system. from "Smart self-management: assistive technology to support people with chronic disease", H. Zheng, C. Nugent, P. McCullagh, Y. Huang, S. Zhang, W. Burns, R. Davies, N. Black, P. Wright, S. Mawson, C. Eccleston, M. Hawley and G. Mountain , 2010, 16, p.2258, Copyright 2010 by H. Zheng.

In the article by Seto et al. (2012) the developed rule-based expert system for telemonitoring heart failure patients showed significantly increased self-care. The research demonstrated that the developed rule-set could be used as a first step for further development and validation. Heart failure health professionals defined the rule-sets and a matrix of outcome states created from possible combination of measurements.

The study by Davis et al. (2014) executed qualitative research of rural primary care health professional views on remote monitoring technologies. In 2015, Sanchez-Morillo et al. (2015) published an article about a mobile health system to detect COPD exacerbations early on a day-to-day basis. The findings are that the electronic questionnaire could help early COPD detection using k-means clustering (Sanchez-Morillo et al., 2015).

The input data the systems use are patient-generated data. For example: questionnaire answers and health parameters (Basilakis et al., 2010; Minutolo, Esposito, & De Pietro, 2015; Sanchez-Morillo et al., 2015; Seto et al., 2012a; Huiru Zheng et al., 2010). Some only created by the patient, other also by the health professional during a consult or appointment. The input is analysed using rule-based reasoning with descriptive statistics (Basilakis et al., 2010; Davis et al., 2014), statistical trend analysis (Basilakis et al., 2010), statistical threshold analysis (Basilakis et al., 2010; Huiru Zheng et al., 2010), matrix of outcome states (Seto et al., 2012a) and a k-means clustering algorithm (Sanchez-Morillo et al., 2015). The rule engine of Zheng et al., (2010) is used to compare the data collected from a smartphone, for example, steps, related to the target steps created by the patient and specialist. Another use is to create a matrix with all possible combinations of measurements to define the rule set for the expert system (Seto et al., 2012a). The output of these systems are alerts, reports, instructions, messages, reminders, and advice (Basilakis et al., 2010; Sanchez-Morillo et al., 2015; Seto et al., 2012a; Huiru Zheng et al., 2010).

Because of the complexity and challenges of achieving patient-centred care the research of Ogden, Barr, and Greenfield (2017) mapped the required organisational actions to achieve patient-centred care. The requirements are divided into 13 different categories, see Figure 18 (Ogden, Barr, & Greenfield, 2017).

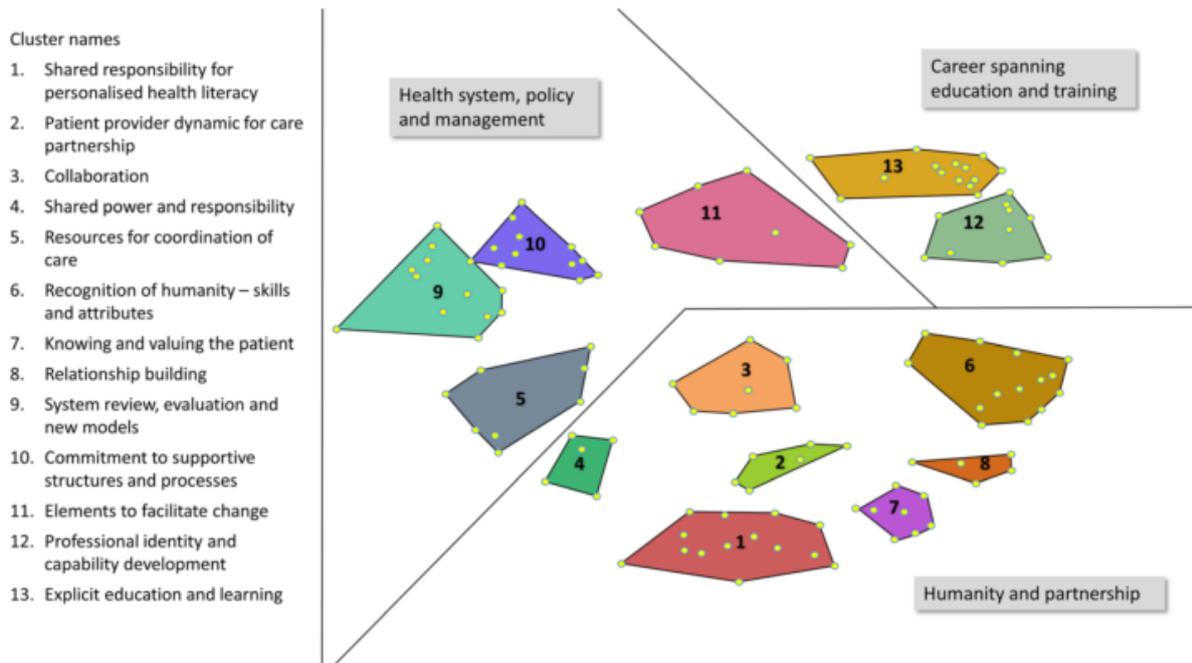


Figure 18. The requirements of Patient-centred care systems. Reprinted from “Determining requirements for patient-centred care”, K. Ogden, J. Barr & D. Greenfield, 2017, BMC Health services research, 17, p.5. Copyright 2017 by K. Ogden, J. Barr & D. Greenfield.

The research by Davis (2014) provided insight into the health professional's view of remote monitoring technologies (Davis et al., 2014). The health professional finds remote monitoring technologies useful and effective because of the possibility to analyse the patient's behaviour outside the medical encounter. Also, it improves the communication and coordination with other medical professionals. The health professionals emphasised that the remote monitoring technology has potential benefit for patients with a need or specific disease, by analysing the patient with a chronic illness and to support and facilitate rapid interventions. The quantity of the data is a difficult aspect, the health professional wants enough information at the right time, to get a clear view of the patient's situation, but there is a fine line between enough information and getting too much information. They preferred that the data is automatically imported into the EHR and to be accessible in the care setting. The presentation of the data must be available in multiple display formats depending on the audience and context. Sometimes the individual values are important and needed but sometimes the values need to be displayed in trend graphs.

3.2. Conclusion

In the last decade, multiple DSS implementations show to be effective in decision support. Despite the (architectural) variances between these implementations, the positive effects of the rule-based support, the statistical analysis and the remote monitoring facilities over time are mentioned in all/most studies. But the required organisational actions to achieve patient-centred care must not be forgotten.

4. Research design

This chapter describes the research design approach of the thesis.

4.1. Software development life cycle

The software development life cycle (SDLC) is a process with distinct steps to develop, alter, maintain a software system. Wiegers and Beatty (2013) in five distinct steps: requirement engineering (analysis), design, implementation, testing and operations & maintenance. This thesis uses the waterfall model, in line with the system development approach of Zorgkluis B.V. As Figure 19 shows the linear sequential design of a waterfall software development life cycle.

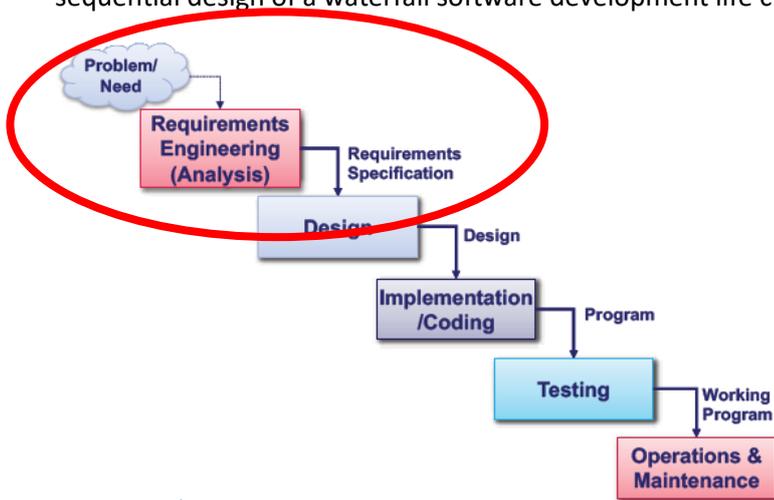


Figure 19. Software development life cycle: waterfall. Turetken, 2016/2017, 'Software Development Paradigms Revisited'[PowerPoint presentation], 1BM20: innovation management.

Since the purpose of this research is to identify the requirements for a clinical rule engine of a patient-centred clinical decision support system, the step 'requirement engineering' is the main focus here. The input for the requirement engineering step is the 'problem/need' of the end-users. Without understanding the user, the risk might occur to create a well-functioning system that no one wants to use. Therefore, it is important to have first an understanding of the end-users information needs. Because the main goal of the IHIE project is to support the patient during his/her healthcare process, the end-users information needs are in this case the desires or needs of the patient with a chronic disease. Noted that the health professional must be willing to support the patient in his/her information needs. Hence, a patient- and health professional analysis is done to identify the end-users information needs.

After the 'problem/need' is identified the requirement engineering process is executed. The output of the analysis (requirements engineering) are the requirements to design the clinical rule engine for a patient-centred CDSS. Figure 20 shows the nature of the requirements development cycle.

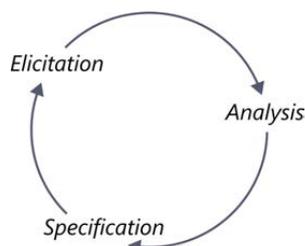


Figure 20. Requirement development cycle. Reprinted from *Software requirements*, K. Wiegers & J. Beatty (p.120), 2013. Copyright 2013 by K. Wiegers and Seilevel.

The requirement development process is an iterative, analytical and collaborative process to collect, discover, extract and define requirements (Wieggers & Beatty, 2013). It starts with elicitation, which is about identifying and understanding the different needs by various stakeholders. This is done by elicitation techniques, for example interviews and document analysis (Hans van, 2007; Wieggers & Beatty, 2013). The main objective of the analysis phase is gathering more information to reach a richer and more precise understanding of the collected requirements in the elicitation phase. Requirement specification identifies and documents the requirements for the future system (Wieggers & Beatty, 2013). Requirement development engineering is an iterative process, it requires iteration since you learn through the process, writing down requirements and determining missing information and performing additional elicitation techniques.

4.2. Research approach

The research design of the thesis is divided into three main phases, see Figure 21. As mentioned before this thesis focuses on the pre-step the end-users information needs and the first step of the SDLC: requirement engineering.

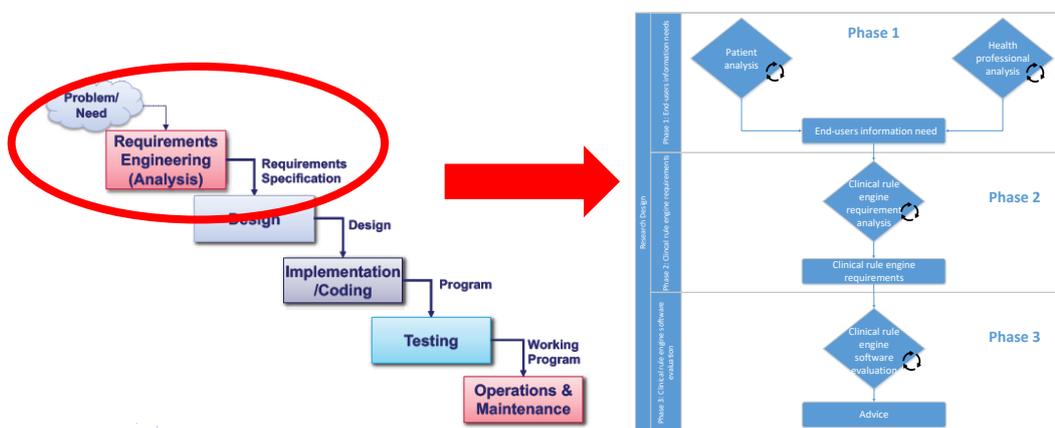


Figure 21. Software development life cycle -> Research design thesis

The research process of this thesis is therefore divided into three main phases, see Figure 22.

- Phase 1: End-users information needs
- Phase 2: Clinical rule engine requirements
- Phase 3: Clinical rule engine software evaluation

The first phase focuses on the end-users information needs to identify the most valuable focus areas. Using patients and health professionals (the end-users) as the main source for gathering the needs. The input results in a defined end-user information need for the patient-centred CDSS to generate the greatest benefit for the company Zorgkluis B.V. and the end-users. Phase two is about specifying and determining the clinical rule engine requirements, step 1 of the software development life cycle. The input for phase two are based on the needs of the end-users (patient and health professional analysis), literature review (patient-centred CDSS), additional interviews and document analysis technique. Phase three is a clinical rule engine software evaluation of the currently available software packages and programming languages for the development of the clinical rule engine for a patient-centred CDSS.

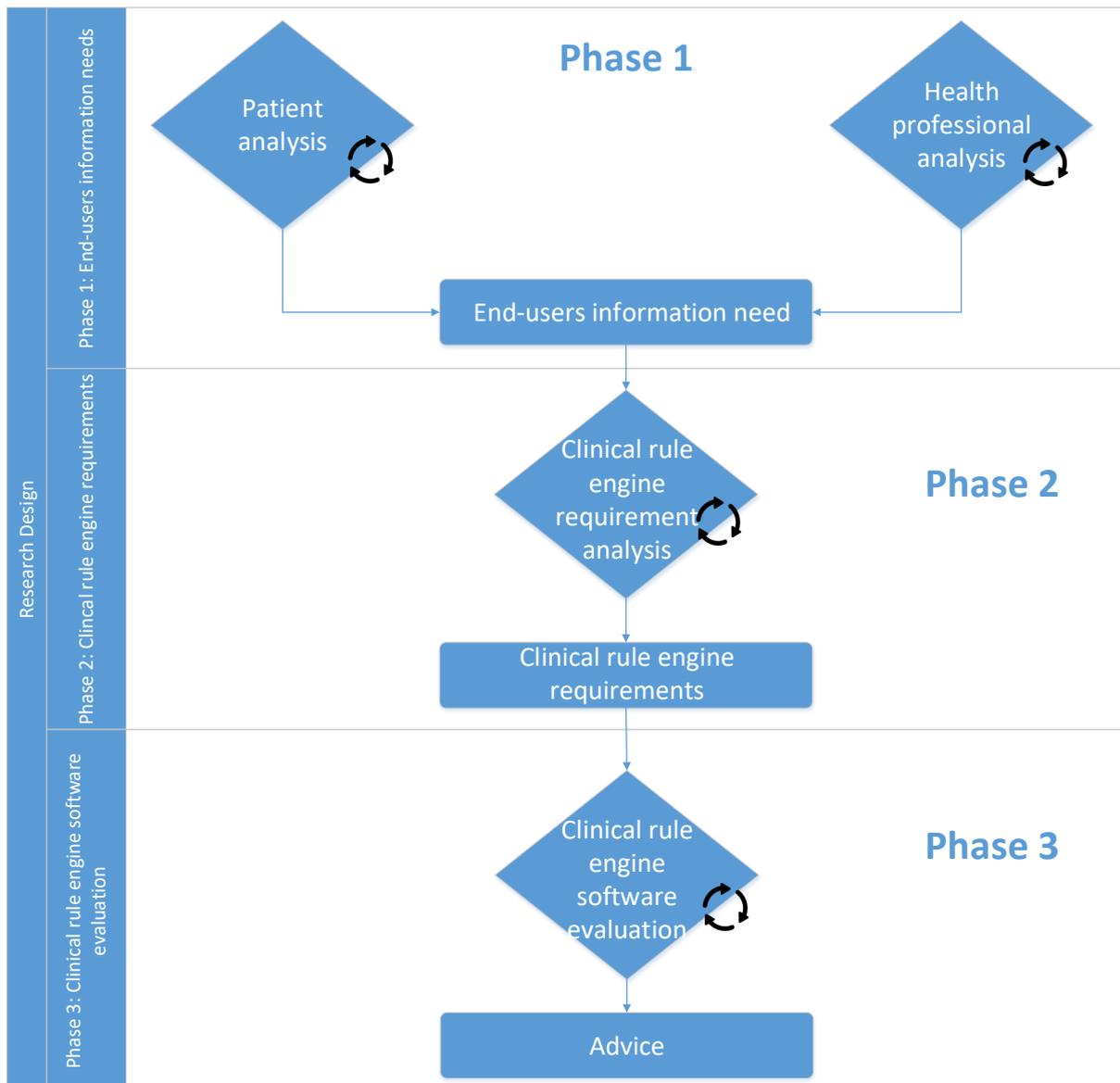


Figure 22. Research design thesis

The diamonds represent the diverging and converging processes. Diverging is about expanding, exploring and generating. Converging is about making, selecting and refining choices. The rectangles indicate the outcome of the diamonds. The iteration icon refers to the cycle of Wiegiers and Beatty (2013) and is used with different techniques.

4.2.1. Phase 1: End-users information needs

The patient analysis focuses on the patient perspective. Hence, the information needs of the patient regarding the mobile application and the IHIE architecture in self-management of their chronic disease. Figure 23 shows the techniques used in the patient analysis. In the first iteration, interviewing two patients, it became clear that they found it hard to imagine what a system, not yet existing, can do to support their chronic health care process. Therefore, the choice is made to use an observation technique to analyse the patient in relation to the healthcare process. The observation technique is experienced as a valuable methodology for clinical setting research. Based on the observations, a questionnaire is composed to validate the patients' needs in addition to gain more in-depth

information in the second iteration. The interviews, observations, and questionnaire led to the conclusion of the patient analysis. For the results of the interview, questionnaire and observation of phase one, see Appendix E ‘Results phase one: patient analysis’.

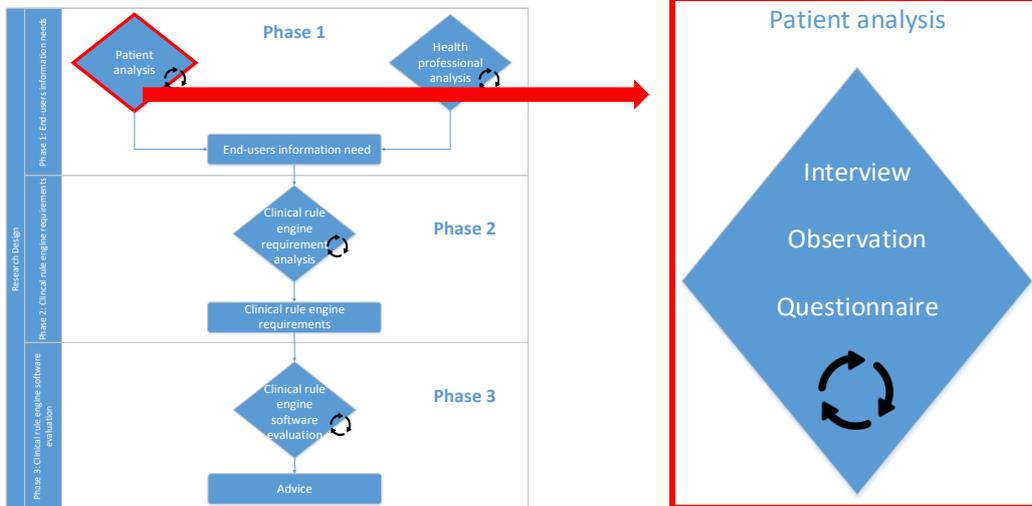


Figure 23. Research design thesis --> Patient analysis

In parallel the health professional analysis is performed because the health professional must be able and willing to support the patient in his or her needs. The IHIE architecture benefits most if both parties are interested in the same focus area. At first, interviews are done with health professionals, to identify the needs. To analyse the needs in a clinical setting, the observation technique is used. After the observations, a second series of interviews is executed to identify new needs and to validate the needs explored and analysed during the first interview and the observations, see Figure 24. For the results of the interviews and observations of the health professional analysis of phase one, see Appendix F ‘Results phase one: health professional analysis’.

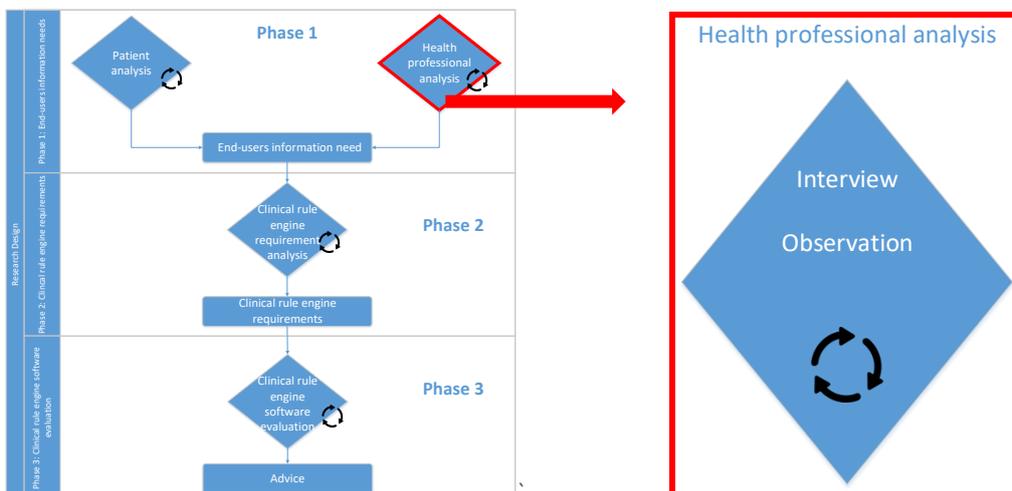


Figure 24. Research design thesis --> Health professional analysis

After both analysis, the most valuable end-user need is identified resulting in an end-user information definition.

Interview-, observation- and questionnaire techniques

The interview technique is the first technique used in phase one ‘End-users information needs’. Interviewing is one of the primary methods used in an information systems project and requirement

engineering. Talking with people who are directly or indirectly involved is one way to get information from different perspectives. Guidelines for effective interviewing are: to plan the interview, listen and take notes and to be neutral and seek for diverse views. There are three different types of interviews: structured, non-structured and semi-structured interviews (Wieggers & Beatty, 2013). The first one is a structured interview. The interviewer has prepared and predetermined questions for the candidate. An interview could also be unstructured, whereas the questions are not prepared in advance. Most of the time unstructured interviews are informal and free-flowing, questions arise spontaneously. With regard to semi-structured interviews, the interviewer formulated a few questions upfront while other questions arise during the interview itself. This thesis uses the semi structured interview technique for the patient analysis and the health professional analysis, also known as phase one. The project uses the semi-structured type for all the interviews held in phase one of the thesis. The choice for semi-structured interview methodology is because of the unfamiliarity of end-users with the possibilities of information systems and mobile applications and the unfamiliarity with the analysis of meaningful recordable data to improve the health process. That is why semi-structured interviews lends itself. The semi-structured interviews are explorative of character and it is possible to ask additional, in-depth and validating questions. The goal of a semi-structured interview is to keep the interview unstructured enough to successfully handle and discover all the knowledge of the participant, but structured enough to not deviate too far from the subjects. All questions were open-ended, which result in more detailed information than if the interview were fully structured. The semi-structured interview started with a fact question, the 'what'-question, which allowed the interviewer to ask the opinionated 'why'-question (if applicable). Interviews were held with oncology patients and oncology specialists, see Appendix B 'Interviews'.

The observation technique is chosen to verify the needs and obtain valuable requirements and the information need which is fundamental for carrying out their jobs. The method could be done passively or actively (Hoffer, George, & Valacich, 2008). When the analyst is passive, the analyst has no interaction with the actor. The active observation technique allows the analyst to ask questions during the observation session. The major advantage of the observation technique is extracting information from the real-life physical environment in which the health care process takes place. The end-users involved in the project find it hard to explain what they do in detail and what they want, so the observation technique is executed in the patient- and health professional analysis. The passive observation method is chosen for this project because the goal is to get a clear view of the as-is situation during a consultation session between the patient and health professional. The observation is done unstructured because the focus is on analysing the behaviour without interruption of the observer to analyse a real situation and gather as much information as possible and to be able to observe the actors in detail. For the detailed information of the observation, see Appendix C 'Observation method'.

The third technique used in the patient analysis is a questionnaire, to collect information in a structured and measurable form. There are two types of questionnaires, open-ended and closed questions (Hans van, 2007; Wieggers & Beatty, 2013). An open-ended question gives the respondent the opportunity to formulate his/her answer, whereas the closed questions do not allow the respondent to draft a response but instead must pick a reply from the given answers. These options can be exhaustive or/and mutually exclusive. The closed questions distinguish four types of level of measurement response scales, namely: nominal, ordinal, interval and ratio. The goal of the questionnaire is to obtain and validate information about the needs of the patient to support self-

management of their chronic health condition. Therefore the questions are closed and based on the Likert-scale measurement system. The Likert-scale is an interval level of measurement and used to measure opinions. To use the Likert-scale it is possible to measure the importance of the discovered patients' needs. Only the last question is open-ended, this is done to check if there is a certain need that is not included in the closed questions. The target group of the questionnaire consists of patients who are a member of the patient association Olijf (n=20). Olijf is a network for women with gynaecological cancer. For the results see Appendix D 'Questionnaire'.

4.2.2. Phase 2: Clinical rule engine requirements

The analysis of the clinical rule engine requirements is the first step of the software development process.

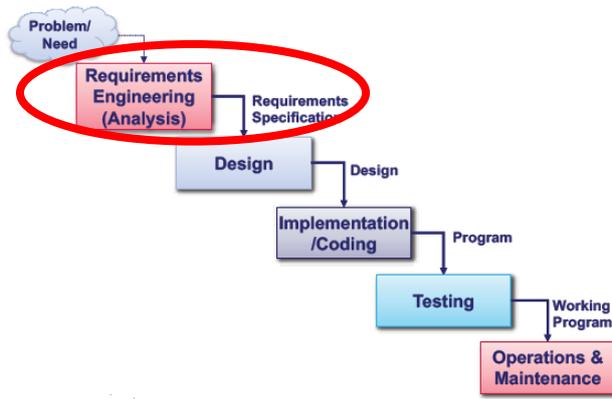


Figure 25. Waterfall software development process

Through the literature review, about patient-centred CDSS and the iteration between interviews and document analysis, the requirements are elicited, analysed and specified as is illustrated in Figure 26.

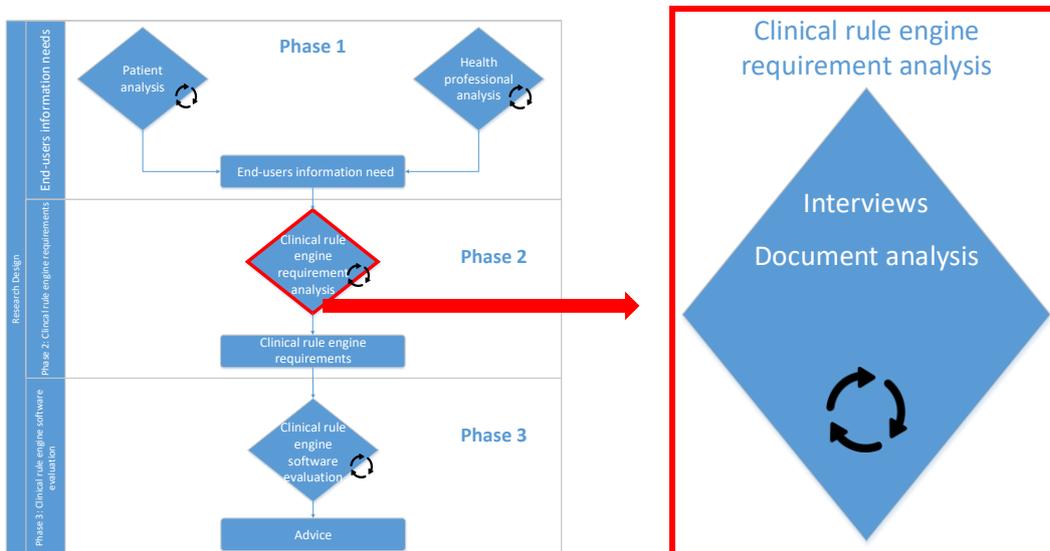


Figure 26. Research design thesis --> Clinical rule engine requirement analysis

The literature review, see chapter three, is done to gain insight into the current patient-centred CDSS studies and as input for the interview questions executed in phase two. The structure and set-up of the interviews are the same as explained in the previous paragraph. The reason for semi-structured questions in this phase is because of the unfamiliarity with the IHIE architecture. Also, to have the

opportunity to discuss the as-is situation (general topics, what is already known), to better specify insights (reason for the answer) and to address their own vision. It is about exploring and gathering in-depth knowledge as input for the clinical rule engine requirements. The interviews were face-to-face meetings, telephone calls and e-mail exchanges to execute the elicitation technique. Interviews were held with oncology patients, oncology specialists, pharmacists, health IT consultants, and software developers, see Appendix B 'Interviews'.

Another qualitative research method used during the requirements analysis is a document analysis. The goal is to examine existing medical documentation for potential requirements. This method is chosen because of the existing in-depth information and the possibility to convert this medical information to requirements for the patient-centred CDSS. Patient information leaflets are used to analyse existing information regarding medication information to the patient. First different kind of medication information leaflets are examined, based on the most common chronic conditions and used medications. For the medication analysed list, see Appendix G 'patient information leaflets'.

An overview has been created to make a clear representation of which technique has provided input per clinical rule engine requirement. In Appendix H 'Techniques and derived clinical rule engine requirements' show per requirement the related source of the derived requirements.

4.2.3. Phase 3: Clinical rule engine software evaluation

The clinical rule engine requirements analysis of phase two results in the requirements for a clinical rule engine software for the patient-centred CDSS. The clinical rule engine requirements are used as input for phase three, the clinical rule engine software evaluation. Figure 27 illustrates the 'Clinical rule engine software evaluation' approach. The evaluation analysis the currently available software languages and clinical rule engine software packages based on their characteristics. The output of phase three will be used to advise the company Zorgkluis.

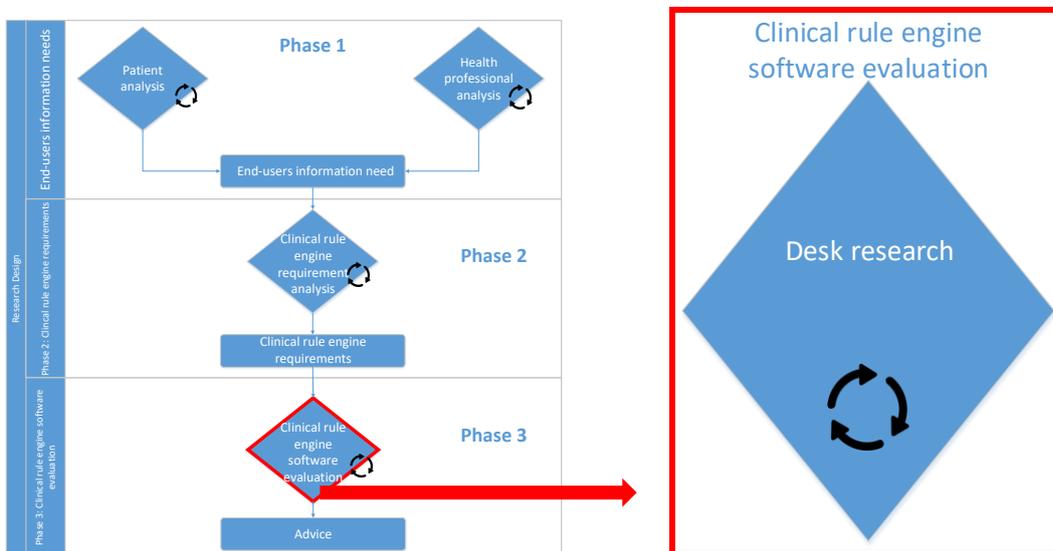


Figure 27. Research design thesis --> Clinical rule engine software evaluation

The desk research technique is used to provide insight into and evaluate the software packages and programming languages. The desk research method analysis existing information. It is about gathering and analysing information found on the internet or information in printed format.

5. Results phase 1: End-users information needs

In this chapter, the results of phase one are presented. The information needs of the patients and health professionals are analysed using different techniques (interviews, observation and questionnaire), leading to one defined end-user information need definition. As mentioned before this phase has an explorative character. Due to the small group of end-users available a combination of several different techniques has been carried out.

5.1. Patient analysis

The patient analysis logically revolves around the patients' information needs. The patient needs are derived from interviews, observations, questionnaire and an additional literature review. To identify the information needs, the interviews (n=3) and observation technique (n=10) are applied. In order to validate the patient's information needs a questionnaire (n=20) is carried out. For the results of the interview, questionnaire and observation of phase one, see Appendix E 'Results phase one: patient analysis'.

The questionnaire is based on the Likert-scale measurement with the indications: 1= not important | 2= somewhat important | 3= neutral | 4= important | 5= very important. The respondents of the questionnaire showed most interest (defined as a score of at least 65% with a 5=very important) in the categories: medication information and communication.

In the observation the patients' information needs in 13 medical situations are mapped to 5 information categories, resulting in a ranking of, first the medication information category, second the medication use and third the patient treatment plan.

The interview results are scored using the following point system (see Appendix E): 0 points for if the category is not mentioned, 1 point if the category is mentioned briefly and 2 points if it is mentioned as most important. The top three important interview categories are: first the medication information, second the communication and third the medication use.

The combined outcomes of the questionnaire, observation plus interviews suggest the following four areas of attention (indicated with high, medium and low importance):

- Patient treatment plan (low)
- Medication use (medium)
- Communication (high)
- Medication information (high)

Table 2 provides insight into the ranking per analysis technique in relation to the four areas of information. The lower the score, the better. Because this indicates that it was high in the ranking per analysis technique. The analysis is indicative and a check is required in the future.

Areas of attention/ analysis techniques	Medication information	Communication	Medication use	Patient treatment plan
Interview	1	2	3	4
Observation	2	1	3	4
Questionnaire	1	Unknown	2	3
Total score	4	3	8	11
Level of importance:	High	High	Medium	Low

Table 2. Level of importance

Patient treatment plan

The patient treatment plan splits into two categories, information and appointments. The information category is about being able to access information concerning the patient's treatment plan from a trustworthy party. The appointment sub-category is about registration information, reminders of actions and the appointments from your personal treatment plan. Patients find it convenient to have an overview of the different healthcare providers and information about the appointments during their healthcare process. The trustworthy party is mentioned in two interviews and also the observations show the importance of the trustworthy party. The information from a trustworthy party is important, because patients want to know if the information is reliable and applicable. The results of the questionnaire showed that 55% (question 5) find it very important to get reminders and information about actions and appointments of their personal treatment plan. And 25% (question 9) find it very important to get information about the treatment and chronic condition. The interviews show an importance of only one point (out of 6), which indicates that the patients who were interviewed find this less important than the other categories. The observation showed limited interest for the patient treatment plan category. The patient treatment plan category has occurred 4 times and mentioned 11 times during the observation. So, the patient treatment plan is in ranking of the categories, has finished twice in the last spot of importance (place 4 by interview and observation) and with the questionnaire in third place. Therefore, this category is classified as low, see Table 2.

Medication use

This category is about the medication intake during the patient's treatment, an overview of the medication as well as the intake schedule of the medication. All participants of the interviews (n=3) mentioned the medication use category, with total points of 3. Results of the questionnaire showed that 55% of the respondents find this 'very important' to register their medication intake during treatment. During the observation three situations (total of 13 situations) referred to the medication use category. Times patients mentioned the situations is a total of 14 times (total of 30 possible). The category has finished twice in third place (interview and observation), and once in second place (questionnaire). This indicate a medium interest in the medication use category.

Communication

This category is about retrieving and accessibility to medical data and the communication between patient and health professional. For instance, the possibility to send the doctor or nurse a message. Quoted from the interview, 'When I am at home, I want to communicate with the doctor to ask questions that came to my mind later.' The possibility to send a message to a healthcare professional who is aware of the patient's situation is very important (as indicated by 65% of the questionnaire respondents). The communication category is with 5 points (out of 6) considered as important according to the participants of the interviews. The observation technique showed no interest in the communication category, this is explained due the observation setting, because the observation is itself already a conversation between the healthcare professional and the patient. Concluded, the communication category is of high value based on the questionnaire and interviews (despite no information is available from the observation technique).

Medication information

The medication information refers to the effect of the medication on the body and the procedures of the medication. Due to side effects, patients are not always able to function 'normally.' In this case, normally is defined as if the patient is being able to do the activities of daily routine. Quoted from an interview with a patient: "I want to have insight into the pattern to get more grip, control, and security". The participants of the interviews see the medication information as most important, with 6 points (out of 6). Hence, 65% of the respondents find it very important to register the daily side

effects and 50% find it important to register pain. Also, the observation showed highly interest in the category medication information. It is the number one in ranking of the observation technique. There are 5 situations which refer to the medication information category. The number of times patient mentioned the situation is 32 times (out of 50). Therefore is the medication information category labelled with a high interest.

So the different categories are analysed and specified, which resulted into two important categories with high interest: communication and medication information. In consultation with the company it is decided to focus on the medication information category, because of the patient participation aspect of the patient-centred CDSS architecture. Given these results and the chosen category, an additional in-depth literature review is done regarding medication information.

Literature review

A patient-centred system is able to provide information and to make choices and decisions as a patient and health care professional together. The literature and the patient- and healthcare professional analysis indicate that patients want reliable, comprehensible and exhaustive information about their medication (Victoor, Friele, Delnoij, & Rademakers, 2012). In 2014 the NPCF (patient federation) investigated the topic 'shared decision making'. They mostly talked about the advantages and disadvantages of the different treatment plan risks (Haastert & Lekkerkerk, 2013). The key to shared decision-making is therefore information, most importantly: medication information. Literature showed the importance of medical information both before and after the pre-determined treatment plan (Van Dijk, Hendriks, Zwikker, De Jong, & Vervloet, 2016). New questions may arise when a patient starts with a new medication, for example, if the patient experiences side effects. When experiencing side effects, providing valuable information to the patient is also very important. In 2016 a research by Nivel investigated the information needs of Dutch patients regarding medication. The top five mentioned subjects are (Van Dijk et al., 2016):

1. Side effects (69%) (also known as 'Drug reaction')
2. Chance of side effects (55%)
3. Driving while taking the medication (53%)
4. What to do with occurring side effects (53%)
5. What to do if they forgot their medicine (52%)

The subjects mentioned above are based on written and digital information sources. Another information dimension is oral sources. The themes discussed during oral sources revolved mostly around the duration of medication intake (59%), the goal of the medication (57%), the dose of the drug (54%) and the drug-drug interaction (53%) (Van Dijk et al., 2016). The patient wants to receive the information before they will take the medication and consequently after possible health issues occur because of the consumption of the medication (Van Dijk et al., 2016). The most used source of information is the patient information leaflet, requiring that the information is accurate, complete, reliable and up-to-date.

5.2. Health professional analysis

The health professional must be willing to support the patient in his or her information needs. The IHIE architecture is of most value if both parties show the same interest. To discover if this is true the health professional analysis focuses on the needs of the health professional. At first, interviews are done with health professionals, to identify the needs. The health professional will be the user of the dashboard in the IHIE architecture and the creator of clinical rules. Therefore the health professional's viewpoint and needs are analysed using interviews (n=4) and observation (n=10). For the results of the interviews and observation of the health professional analysis of phase one, see Appendix F 'Results phase one:

health professional analysis'. From a health professional viewpoint, self-management systems can reduce hospital admissions (Davis et al., 2014). The observation and interview techniques provided the essential information to analyse the health professional's information needs. The interview results are based on the same scoring system as the interviews of the patient analysis: 0 points for if the category is not mentioned, 1 point if the category is mentioned briefly and 2 points if it is mentioned as most important (with a maximum of 8 points: 4 interviews x maximum 2 points). The top three categories regarding patient information is shown in Table 3.

Health professional	Health parameters	Side effects	Pain
Interview 1	2	2	1
Interview 2	2	2	1
Interview 3	0	2	2
Interview 4	2	1	1
Total points	6	7	5

Table 3. Outcome top three categories: interviews health professionals

The observations are scored based on the frequency a category have been occurred during a consultation session with the patient (with a maximum of 10 sessions), see Table 4 of the top four categories.

Patient consultation session/ Category	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	Total
Health parameters	X		X		X	X	X	X	X	X	8
Medication Use	X		X		X	X	X	X	X		7
Side effects	X	X		X	X	X	X	X	X		8
Pain		X	X	X	X	X		X			6

Table 4. Outcome top four categories: observations health professional

The most interesting for the health professional is to monitor and analyse the patient's health outside the medical encounter. The information needs of the health professional are the patient's health parameter and the side effects. The interviews showed with 7 points, interest in the side effects and with 6 points interest in the health parameters. The results of the observations indicate an information need for the patient's side effects (observation: occurred 8 times, interviews: 7 points) and health parameter (observation: occurred 8 times, interviews: 6 points). The different types of side effects or health parameters depend on the patient's chronic health condition. Also, the information needs of medication use is seen as interested by the health professional during the observation (observation: occurred 7 times), but experienced as less important during the interviews (total of 4 points).

Apart from the information about the patient's health, the health specialist wants to get alerts based on the patient's information. The challenge of the clinical alerts is finding the balance in number of alerts and alert priorities. The health professionals agree (3 interviewers) that there must be different levels of alerts because of the urgency and severity of the clinical rule fired in the patient-centred CDSS. Also, the content, frequency and timing of the alerts differ per chronic health condition and healthcare professional. Lastly, the healthcare professional specialist wants information regarding the clinical rule fired by the clinical rule engine of the patient-centred CDSS to identify and analyse what is going on with the patient and to validate the decision made by the patient.

So, the overall conclusion is that the information needs lie with the increased insight into the patient's day-to-day health status (health parameters and side effects) separate from the medical encounters, and the effective clinical rules to prevent day-to-day risks during and after treatment. In addition, the health care professional values the use of alerts.

5.3. Conclusion

In conclusion, with the information needs gathered from the patient- and health professional analysis and the literature regarding medication information, the most valuable information need for the development of a patient-centred CDSS is the medication side effects. In consultation with the company and taking into account the results of the patient-, health professional- and literature analysis, the end-users information need definition is: a patient-centred CDSS, which supports the individual patient (and their health professionals) with the medication side effects. Thus, giving the opportunity to make health-related decisions based on the patient-specific health data and available health information.

6. Results phase 2: Clinical rule engine requirements

The result of phase one leads to the following end-user information need definition: a patient-centred CDSS, which supports the individual patient (and their health professionals) with the medication side effects. Taking this end-users need into account, the clinical rule engine requirements for the patient-centred CDSS are identified. The input is gathered from the literature review (see chapter three), interviews and the document analysis of the patient information leaflets (n=10) in the current phase.

For tracking purposes, an overview has been created to make a clear representation of which technique has provided input per clinical rule engine requirement. In Appendix H 'Techniques and derived clinical rule engine requirements' show per clinical rule engine requirement the related source of the derived requirements. The clinical rule engine requirements serve as a purpose for input of phase three 'clinical rule engine software evaluation'. Noted that the *must* requirements refer to required requirements and *may* requirements refer to optional requirements for the future. This prioritization is done in consultation with the company Zorgkluis B.V.

6.1. Clinical rule engine requirements

The clinical rule engine of the patient-centred CDSS uses clinical rules as the knowledge representation. By the different data types and functionalities, the following requirements are defined for the clinical rules engine of a patient-centred CDSS, see Table 5. The requirements are derived from the observations, interviews, document analysis and the literature review. For the additional requirements gathered through the requirement analysis, see Appendix I.

Topic	Number	Clinical rule engine requirements
Reasoning strategies	CRER-1	The system <i>must</i> be able to execute forward chaining.
	CRER-2	The system <i>may</i> be able to execute backward chaining.
Logic	CRER-3	The system <i>must</i> be able to manage Boolean logic.
Time	CRER-4	The system <i>must</i> be able to manage time reasoning.
Decision tree	CRER-5	The system <i>must</i> be able to execute decision tree reasoning.
Statistics	CRER-6	The system <i>must</i> be able to execute descriptive statistics.
	CRER-7	The system <i>must</i> be able to execute Bayesian statistics.
	CRER-8	The system <i>must</i> be able to execute a linear regression.
	CRER-9	The system <i>may</i> be able to execute nonlinear regression.
	CRER-10	The system <i>may</i> be able to execute statistical hypothesis testing.
	CRER-11	The system <i>must</i> be able to insert a data input into a mathematical calculation.
Fuzzy	CRER-12	The system <i>must</i> be able to execute mathematical calculations.
	CRER-13	The system <i>must</i> be able to manage a fuzzy concept.
	CRER-14	The system <i>must</i> be able to execute fuzzy reasoning.
Machine learning	CRER-15	The system <i>may</i> be able to execute machine learning methods.
Ontology	CRER-16	The system <i>must</i> be able to manage ontologies.

Table 5. Clinical rule engine requirements

Forward and backward chaining are two methods of reasoning of a rule-based system (requirement CRER-1 and 2), using the conditional computer programming statements (if-then-else). Both functionalities are of value for the IHIE system, because of the extraction until a goal is reached or the working backward from the goal. For example:

Forward (data-driven): IF patient experiences the side effect pain THEN contact doctor for Diclofenac

Backward (goal-driven): The patient registers the intake of Diclofenac. The system knows that Diclofenac is a painkiller, which indicates that the patient experiences pain. The system asks where and how intense the pain is, based on the system knowledge (Diclofenac = painkiller = pain). So the action of the system is triggered by the registration of Diclofenac)

The system analysed the medication side effect pain. Based on the forward reasoning method the system provides feedback with the advice to contact the doctor for a prescription Diclofenac. If the system uses backward chaining, the system will gain more insight into the patient's health. In the example above the patient registers the intake of medication Diclofenac. Based on this patient-generated registration the system analysis that Diclofenac is a painkiller and therefore the patient must have some pain. So the outcome of the backward reasoning method is that the system asks more information about the patient's pain.

The justification of the requirements concerning logical reasoning (CRER-3) is the need for sequence of deduction, the presentation of the clinical rules and analysing if the variable is true or false. For example:

Example 1: Piet is 55 years old and has high blood pressure. He takes his medication Amlodipine daily and registers the medication intake in the mobile application. After one day of using his medication, he experiences some abdominal pain. He takes his mobile phone and records his side effect in the mobile app. Piet has the rest of the week heavy abdominal pain, after seven days the DSS sends a message to the app advising to take action and consult a doctor or nurse and also advising the doctor in the clinical dashboard.

In this example Piet experiences a medication side effect: abdominal pain. The system must be able to analyse if the experienced side effect is related to time and the message send, is true or false. Therefore the system must also be able to manage time reasoning (CRER-4). The patient-generated data about the side effects and the clinical rules of the system can be related to time. Therefore the time requirement is included. For example:

Example 2: Anna is 65 years old and uses the medicine Zopiclone, Acetylsalicylzuur, and Omeprazole. Yesterday she started with Amlodipine. The mobile application will ask her on day 3, 9 and 14 if she experiences any side effects. On day nine she registers dizziness. The advice given by the system is, at the beginning of the treatment (start with medication Amlodipine) it is common to have dizziness. Also, it may help to take medicine before bedtime. After two weeks the side effect should decrease. The system asks Anna after two weeks if the dizziness had stopped. She answers 'no', the system advice is to take action and go to the doctor.

The example is about Anne who has started a new medication treatment. The system analyses the medication side effects of Anna in the next few days/weeks. The time aspect is important, because the system must be able to know when it is day 3, 9 and 14. Also the moment in time when the side effect occurred, and to analyse over time when the side effect has decreased.

The next clinical rule engine requirement is about the decision tree requirement (CRER-5). The decision tree supports the presentation of the alternatives, choices and consequences of a decision. Also it visualizes the decisions made by the system and enables to report the decisions made by the system. The statistics functionalities (CRER-6, 7, 8, 9, 10, 11, 12) refer to the possibility to analyse the data generated by the patient, healthcare professional and system itself or test with the generated data a certain assumption/condition. For example:

Example 3: Wim is 46 years old and has high blood pressure. The prescribed doses are once a day 10mg Amlodipine. Wim registers his blood pressure when he is sitting down for a half hour, twice a day. The expert system detects an increasing trend over the last two weeks. Because his blood pressure is too high, but not high enough for a hypertensive crisis interval, the application shows a prediction of the future. The forecast is for the next days. Wim's blood pressure range is pre-high, and Wim is warned by the application to be very careful, and the healthcare specialist is informed. If applicable, the specialist gives Wim advice or feedback.

In the example above, Wim has high blood pressure. When using the medication Amlodipine, it is known that the patient should be extra careful if he/she has a strong increase in blood pressure. The increase in blood pressure is a medication side effect. Therefore the system analyses using statistics, the blood pressure over time. Also, a prediction can be made to have insight in the future. To visualize the blood pressure over time, descriptive statistics is needed.

The next required functionality is about crisp and fuzzy concepts (CRER-13 and 14). The analysis showed the need to manage fuzzy concepts. The 'vague' definitions of concepts described in the patient information leaflets led as input for the functionality to manage fuzzy and crisp concepts. The examples show an indication of the information in the patient information leaflet. For example:

When to use this medicine → You have very low blood pressure.

When you need to be extra careful with this medicine → Too little potassium in the blood.

Possible side effects → Reduced white blood cells

The examples above show the fuzzy concepts in a patient information leaflet. The system must be able to analyse these fuzzy concepts to provide valuable feedback to the patient and healthcare professional, without any uncertainty or confusion.

The machine learning requirement (CRER-15) refers to the possibility to execute machine learning methods to learn from datasets to create patterns and processes. For example:

Example 5: Pim is 32 years old has overweight and type 2 diabetes. He tried dieting and exercising to regulate his blood sugar level sufficiently, but the blood sugar level was still too high. Therefore he also takes the medication, to control his blood sugar levels. Pim takes an additional medicine to assuage the side effects of the treatment. He prefers to take the side effect medication in the morning because it helps him to wake-up. The system analyses the dataset to create patterns and processes the rule. The system analysis 80% support for the relation between the medicine to assuage the side effect and the period of time taking the medication (morning). So the system suggests taking the side effect medication at the same time as the blood sugar medication (controlled medicine).

The example above illustrates a possible scenario of using an association rule learning method, which is a rule-based machine learning technique. The system analyses the situation of Pim experiencing side effects using the machine learning technique. The system provides feedback on the possible related reasons of the occurring side effects.

Last the requirement regarding ontology (CRER-16) is justified due to the complexity of the entity and relations between medical categories. For example, the existing classification for medicine, the ATC-classification. The possibility to integrate ontologies and to create ontologies is of value for the system, because of the translation complexity of the patient's generated health information and the medical science information into clinical rules.

6.2. Conclusion

The requirement analysis techniques led to the specified clinical rule engine requirements in collaboration with the software development team of Zorgkluis B.V. The clinical rule engine requirements are based on the scenarios of a patient-centred CDSS, which supports the individual patient (and their health professionals) with the medication side effects. Thus giving the opportunity to make health-related decisions based on the patient-specific health data and available health information translated into clinical rules. The clinical rule engine requirements are about: reasoning strategies, logic, time, decision tree, statistics, fuzzy, machine learning and ontology. In the future, the more detailed requirements must be defined and analysed to operate the clinical rule engine into a valuable system which supports the patient in handling the medication side effects.

represented guidelines (de Clercq, Hasman, Blom, & Korsten, 2001). Last, the Gaston software is a rule execution engine. Gaston uses the ontology software Protégé editor to create ontologies, providing the steps taking by the healthcare provider (Li, Superceanu, & Zheng, 2014). The software provides four types of icons: action, decision, branching, and synchronisation. The Catharina hospital in the Netherlands uses Gaston to gather the necessary information at the right time in a structured manner (Van Berkel, Wasylewicz, Kreeftenberg, & Boer, 2015).

KNIME

KNIME is a data analytics, reporting, and integration platform using a graphical user interface workflow (Analytics Vidhya content team, 2017). Written in Java and built on Eclipse and a broad range community for questions and topics (Reifer, 2015). The software is among others used to predict disease using classification techniques and big data problems in healthcare (Hashi, Zaman, & Hasan, 2017; Mathew & Pillai, 2015; P. Mazanetz, J. Marmon, B. T. Reisser, & Morao, 2012; Wang, Tang, Nguyen, & Altintas, 2014). The functionalities of KNIME are: input and output functionalities, database, data manipulation, data views, statistics, mining, distance matrix, image processing, meta (for example feature elimination), loop support, time series and mining (KNIME, n.d.-b). The data views are, for instance, boxplot, histogram, an interactive table, line plot, etc. The software provides regression analysis and linear regression statistics methods. The data mining techniques KNIME supports are association rules, Bayes, clustering, rule induction, neural network, decision tree, multidimensional scaling, principal component analysis, support vector machine, and scoring. It is possible to integrate KNIME with Python, R or WEKA (KNIME, n.d.-b). Due to the possibility to integrate with WEKA, it is possible to execute the classification algorithms, for example, k-nearest neighbours classifier and cluster algorithms, and association rules. Regarding machine learning, KNIME integrates with the H2O machine learning library (KNIME, 2017b). Also, KNIME provides active learning, meta-learning and deep learning (KNIME, n.d.-a). Research showed that KNIME offers a solid basis for fuzzy learning and visualisation and disposes of nodes to deal with fuzzy sets and systems (Berthold, Wiswedel, & Gabriel, 2013; Pancho, Alonso, Kotter, Berthold, & Magdalena, 2014).

RapidMiner

RapidMiner is a data science software platform, used for data preparation, machine learning, and predictive analytics (RapidMiner, n.d.-b). The software is also a powerful visual programming environment like KNIME. The data exploration category provides descriptive statistics, for example, univariate statistics and plots, transition matrix and graph (RapidMiner, n.d.-a). RapidMiner has extensions to integrate Python and R scripting (RapidMiner, n.d.-d). The language does not support fuzzy logic. RapidMiner is good with other data analysis techniques, such as decision trees and segmentation analysis and a diverse in data preparation techniques (Meijs, 2017). The data science workflow design RapidMiner is an application with an interface, data access, data exploration, data preparation, modelling, validation, scoring and automation features. The data exploration divides into descriptive statistics and graphs and information (RapidMiner, n.d.-a). The modelling capabilities and machine learning algorithms for supervised and unsupervised learning, similarity calculation, rule induction, Bayesian modelling, regression, clustering, neural networks, market basket analysis, support vector machines, decision trees, memory-based reasoning, and model ensembles (RapidMiner, n.d.-c). The big difference between KNIME and RapidMiner is that KNIME can run edits individual and supports fuzzy logic, while RapidMiner runs the whole flow and does not support fuzzy logic (Meijs, 2017).

WEKA

WEKA is a collection of machine learning algorithms in Java, executing data mining tasks (WEKA, n.d.-b). WEKA's main features are pre-processing data, classification and regression algorithms, clustering

algorithms, feature selection algorithms, association rule algorithms and graphical user interface using exploratory, experimental, and process model techniques (Ian H. Witten & Eibe Frank, 2005). It contains a graphical user interface with the possibility to compare learning algorithms. In 2013 a method for fuzzy decisions and fuzzy rule generation called the FRG algorithm was developed (Mala, Akhtar, Javid Ali, & Saood Zia, 2013). Another application of WEKA is in the medical domain for a heart dataset using the J48 classification (C4.5 algorithm).

Conclusion

The five-different clinical rule engine software packages have been analysed. Table 6 shows an overview of the clinical rule engine requirements. The software package company get zero points if the requirement is not included, one point if the requirement is included and a *may* requirement and second points if the clinical rule engine requirement is included and a *must* requirement. If it is unknown whether the requirement is possible with the software package the question mark icon is inserted.

Subject	Number	Clinical rule engine requirements	Digitalis	Gaston	KNIME	RapidMiner	WEKA
Reasoning strategies	CRER-1	forward chaining	2	2	2	2	2
	CRER-2	backward chaining (<i>May</i>)	0	0	0	0	0
Logic	CRER-3	Boolean logic	2	2	2	?	2
Time	CRER-4	time reasoning	0	0	?	?	?
Decision tree	CRER-5	decision tree reasoning	2	2	2	2	2
Statistics	CRER-6	descriptive statistics	2	0	2	2	2
	CRER-7	Bayesian statistics	0	0	2	2	2
	CRER-8	linear regression	0	0	2	2	2
	CRER-9	nonlinear regression	0	0	2	2	0
	CRER-10	hypothesis testing (<i>May</i>)	0	0	1	1	1
	CRER-11	insert a data input into a mathematical calculation.	0	2	2	2	2
Fuzzy	CRER-12	execute mathematical calculations.	0	2	2	2	2
	CRER-13	manage fuzzy concepts	0	0	2	0	2
	CRER-14	execute fuzzy reasoning	0	0	2	0	2
Machine learning	CRER-15	machine learning methods (<i>May</i>)	0	0	1	1	1
Ontology	CRER-16	ontologies	0	2	2	2	0
Total			8	12	26	20	22

Table 6. Outcome clinical rule engine software package analysis

The outcome of the clinical rule engine software package analysis illustrates that KNIME is the best option, with 26 points. The main differences with the second (WEKA) and third (RapidMiner) is that WEKA does not support ontologies and RapidMiner does not support fuzzy concepts, whether KNIME supports both. But there is no backward chaining possible and it is unknown how KNIME is managing time reasoning (this is also the case by RapidMiner and WEKA). Since the time reasoning requirement is of high value for the clinical rule engine of the patient-centred CDSS, further research is recommended.

7.2. Clinical rule engine programming languages

The programming languages analysed are the top four data science programming language of 2018: Python, Java, R and Julia, plus the programming languages Prolog chosen by Zorgkluis B.V. (Deoras, 2018). For the mapping of the clinical rule engine requirements versus the programming languages, see Appendix K 'Clinical rule engine programming languages analysis'.

Python

Python is a programming language developed in the 90s (Python, 2015). The purpose of Python is to work quickly and integrate systems more effectively (Johnson, 2018). Python is mostly used by data scientists, to analyse data or apply statistical techniques. An advantage of Python is the flexibility and the possibility to use it for developing websites or other applications. Another possibility is to run R code from within Python, using the RPy2 library (Johnson, 2018; Python, 2015). It is open-source software and free to download for everyone. Python ecosystem is loaded with packages and libraries of scientific computing and data science (third-party packages). Python's fan base has built on Python by creating additional libraries, over the years. Also the discussions by the fans, for any purpose, keeps Python relevant (Recchione, 2018). The number one programming languages for data scientists is Python (Deoras, 2018). Another application of Python, besides data analysis, is the ability to use it as an integration language (van Rossum, 1998). So Python is an easy to read code program, with useful libraries such as artificial intelligence, statistics and machine learning and indentation feature to shorten coding (Scriptol, 2014).

Java

Java is a readable and relatively simple programming language (Deoras, 2018). Java is an object-oriented language. The best option for using machine learning techniques in Java code, is to integrate with WEKA (WEKA, n.d.-a). Creating ontologies in Java is possible among others with Jena or JavaBeans (Jena, n.d.; Knublauch, n.d.). The advantage of Java is that modern systems and applications are based on Java back-ends. Which allows integration with data science methods directly (Gleeson, 2017). For dedicated statistical applications, R and Python are more productive than Java (Gleeson, 2017). The visualisations of R and Python are stronger and provide more descriptive statistical analysis. Both Python and Java benefit from the online community and open-source development (Henney, 2017). Implementing Python scrips in Java is possible using the designated library Jython (Jython, n.d.).

R

R is a programming language for statistics and graphs (R Core Team, 2016). It is mostly used by statisticians and data miners to analyse data (R Core Team, 2016). R is ranked third on the list of 'top 10 programming language for data scientists to learn in 2018' (Deoras, 2018). The tool is useful in data manipulation, calculation and graphical display (r-project, n.d.). R is an object-oriented, imperative, procedural, functional and reflective programming language. The community of R is continually adding new libraries and features. R is about mastering data manipulation, data visualisation, and machine learning. R contains machine learning packages, but it is also possible to integrate WEKA into R using the R/WEKA interface (Hornik, 2018). However R is strong in statistics, R is less suitable for general purpose programming (Gleeson, 2017).

Julia

Julia is a programming language for numerical computing, with extensive mathematical functions. It is possible to integrate open source C and Fortran libraries (for example linear algebra) into Julia. Also, the integration with Python is possible, to call Python functions into Julia using the PyCall package (Johnson, 2018). Julia uses a diverse range of statistical packages and supports parallel execution, and powerful type inference (Rohit, 2016). Julia is still a young company (established in 2010), in

comparison with the other programming languages. Therefore there are less third-party packages, because of the small community (Yegulalp, 2017). The data visualisation packages are lacking in the core system of Julia (Joshi, 2016). Hence, the integration with the packages PyPlot, Unicodeplots, Vega, and Gadfly is often used (Joshi, 2016). Julia is capable to execute data mining, machine learning and parallel computing. The advantage of Julia is the speed can be compared with C and the dynamics of Ruby (Recchione, 2018). Overall Julia offering simplicity and dynamic typing with integration capabilities like Python, however, the maturity of the packages and the number of available packages is limited due to the duration of the company existence.

Prolog

Prolog is a logic-based programming language used to model and support in making decisions (Prolog, n.d.). It involves deterministic searching and performs complex searches over a database. Prolog is strong in symbolic rule-based systems encoded in first-order logic (Prolog, n.d., 'Prolog features'). It is a declarative and logical programming language. The declarative programming characteristic is about defining the data and relationships between the data items. Hence the Prolog programming is complex, this is due to the logic-based characteristic. The rules must be near to perfectly defined to prevent errors.

Conclusion

The programming languages Python, Java, R, Julia and Prolog are analysed. The analysis of the programming languages differ from the software packages analysis, because of the possibilities to integrate packages or applications into the basis of the programming language. Therefore in Appendix K 'Clinical rule engine programming language analysis' examples are given of the needed additional packages. For an overview of the clinical rule engine requirements, see Table 7. The scoring system is the same as in the software package analysis of the previous section: zero points if the requirement is not included, one point if the requirement is included and a *may* requirement and second points if the clinical rule engine requirement is included and a *must* requirement. If it is unknown whether the requirement is possible with the programming language the question mark icon is inserted.

Subject	Number	Clinical rule engine requirements	Python	Java	R	Julia	Prolog
Reasoning strategies	CRER-1	forward chaining	2	2	2	2	2
	CRER-2	backward chaining (<i>May</i>)	1	1	0	0	0
Logic	CRER-3	Boolean logic	2	2	2	2	2
Time	CRER-4	time reasoning	2	2	2	2	?
Decision tree	CRER-5	decision tree reasoning	2	2	2	2	2
Statistics	CRER-6	descriptive statistics	2	2	2	2	0
	CRER-7	Bayesian statistics	2	2	2	2	0
	CRER-8	linear regression	2	2	2	2	0
	CRER-9	nonlinear regression	2	2	2	2	0
	CRER-10	hypothesis testing (<i>May</i>)	1	1	1	1	0
	CRER-11	insert a data input into a mathematical calculation.	2	2	2	2	0
	CRER-12	execute mathematical calculations.	2	2	2	2	0
Fuzzy	CRER-13	manage fuzzy concepts	2	2	2	2	2

	CRER-14	execute fuzzy reasoning	2	2	2	2	2
Machine learning	CRER-15	machine learning methods (<i>May</i>)	1	1	1	1	0
Ontology	CRER-16	ontologies	2	2	2	0	2
Total			29	29	28	26	12

Table 7. Outcome clinical rule engine programming languages analysis

The programming languages Python and Java have the highest score with 29 points. The high score of the programming languages R is due to the possibilities to integrate with other packages of, for example WEKA and Python. Be aware, the integration of different packages from different programming languages/ software packages, the complexity increases. Also R is mainly used for statistical analysis and Python for general approaches to data science. Therefore the programming languages Python and Java show more value due to the extensive packages provided by the programming languages itself. The visualisation possibilities in Python are stronger than in Java, and provide more descriptive statistical analysis. Both Python and Java benefit from the online community and open-source developments. The main difference between these two languages is that Python is dynamically typed and Java is statically typed. This means that if the Java code contains any error, it will not run until the error(s) are fixed.

7.3. Conclusion and advice

The software of Digitalis is a software package that focuses on the lab-medication perspective and is a rule-based system. The Gaston software focuses on providing a framework for decision making, handling data, rule-based representation and ontologies to represent the guidelines. The KNIME software offers the user to create data flows with the graphical user interface and is easy to use with a variety of functionals. In KNIME mining algorithms, data manipulation and visualisations are available to understand the data better. RapidMiner is a Java-based system for machine learning, data mining and predictive analysis. Compared with KNIME, RapidMiner does not support fuzzy logic concepts. WEKA is also built in Java and is a data-mining software with extensive machine learning algorithm techniques and integrable with KNIME. The visualisation of WEKA is limited in comparison with KNIME and RapidMiner. The programming language Python is understandable, flexible with a large community. The Java programming language supports only one programming paradigm namely object-oriented. Python supports object-oriented, functional and imperative programming. R is an object-oriented, imperative, procedural, functional and reflective programming language and differs from the other languages in the statistical packages. Julia is the newest programming language and therefore limited in packages availability. The last software programming language analysed is Prolog. The programming language is formal logic and limited in fuzzy logic, Bayesian and machine learning techniques.

The analysis provided insight into the characteristics of the available clinical rule engine software packages and the programming languages. Based on the clinical rule engine software packages analysis the good choice is to use KNIME. KNIME is a graphic user interface-based program and offers a solid basis for fuzzy learning and visualisation and disposes of nodes to deal with fuzzy sets. Noted that future research is recommended to investigate the time-requirement before choosing for KNIME. In the previous chapter, the importance of time is illustrated, see the examples. Also, to execute machine learning techniques WEKA or Python must be integrated into KNIME. So future research is recommended to which extent Python can be integrated into KNIME.

The conclusion of the clinical rule engine programming language analysis is a tie, all the defined clinical rule requirements are available. Python and Java are both interesting for the patient-centred CDSS. The programming languages Python and Java show value due to the extensive packages provided by the programming languages itself. As mentioned before it depends if the software programmer wants to type dynamically (Python) or statically (Java). It is recommended to execute further research to check in detail which packages and/or programming languages are most relevant for Zorgkluis B.V.

8. Conclusion and discussion

In this chapter, the main findings of the research question are summarised, the strengths and limitations are identified, and suggestions for further research are presented.

Conclusion

The studies' aim is an exploratory research regarding the clinical rule engine for a patient-centred decision support system. The study was executed based on the first step of the software development cycle: requirement engineering. The research design of the thesis is divided into three phases:

- Phase 1: End-users information needs
- Phase 2: Clinical rule engine requirements
- Phase 3: Clinical rule engine software evaluation

Phase one analysed the information needs of the patient and healthcare professionals. The patient analysis identified four information needs categories: the patient treatment plan, medication use, communication and medication information. The most interesting information need category is about the medication information. In addition, the literature review showed that the patient is most interested in information regarding the medication side effects. The conclusion of the health professional analysis illustrated interest in the patient's health parameters and the side effects, alert system and insight in the clinical rules fired. So, the health professional's information needs lie with the increased insight into the patient's day-to-day health status separate from the medical encounters, and the effective clinical rules to prevent day-to-day risks during and after treatment. Therefore, the conclusion of phase 1 is the definition of the most important end-users information needs, namely: a patient-centred CDSS which supports the individual patient (and their health professionals) with the medication side effects. This makes it possible to make health-related decisions based on the patient-specific health data and available health information. To give the patient an overview of the disease development, the patient must create daily clinical inputs to develop knowledge about their own health status and progress. It makes it possible for the patient and healthcare specialist to get insight into the daily measurements and the symptoms of the patient outside the medical encounter.

Concerning the end-users' information needs definition of phase one, the high-level clinical rule engine requirements are specified in phase two. The requirements are elicited, analysed and specified using different techniques. Phase two resulted into 16 clinical rule engine requirements, shown in Table 8.

Topic	Number	Clinical rule engine requirements
Reasoning strategies	CRER-1	The system <i>must</i> be able to execute forward chaining.
	CRER-2	The system <i>may</i> be able to execute backward chaining.
Logic	CRER-3	The system <i>must</i> be able to manage Boolean logic.
Time	CRER-4	The system <i>must</i> be able to manage time reasoning.
Decision tree	CRER-5	The system <i>must</i> be able to execute decision tree reasoning.
Statistics	CRER-6	The system <i>must</i> be able to execute descriptive statistics.
	CRER-7	The system <i>must</i> be able to execute Bayesian statistics.
	CRER-8	The system <i>must</i> be able to execute a linear regression.
	CRER-9	The system <i>may</i> be able to execute nonlinear regression.
	CRER-10	The system <i>may</i> be able to execute statistical hypothesis testing.
	CRER-11	The system <i>must</i> be able to insert a data input into a mathematical calculation.
	CRER-12	The system <i>must</i> be able to execute mathematical calculations.

Fuzzy	CRER-13	The system <i>must</i> be able to manage a fuzzy concept.
	CRER-14	The system must be able to execute fuzzy reasoning.
Machine learning	CRER-15	The system <i>may</i> be able to execute machine learning methods.
Ontology	CRER-16	The system <i>must</i> be able to manage ontologies.

Table 8. Outcome phase 2 'Clinical rule engine requirements'

The clinical rule engine requirements are based on the scenarios of a patient-centred CDSS, which supports the individual patient (and their health professionals) with the information about the medication side effects. The clinical rule engine requirements categories are: reasoning strategy, logic, time, decision tree, statistics, fuzzy, machine learning and ontology. The clinical rule engine requirements are used in phase three to evaluate possible clinical rule engine software packages Digitalis, Gaston, KNIME, RapidMiner and WEKA, and the programming languages Python, Java, R, Julia and Prolog. The software packages and programming languages are analysed to provide insight into the characteristics and advice the company. The clinical rule engine software evaluation specifies and analyses each software tool based on the characteristics and clinical rule engine requirements of phase two. The top three of the clinical rule engine software packages: KNIME features 15 requirements, WEKA has 13 requirements and RapidMiner 12 requirements. WEKA does not support ontologies and RapidMiner does not support fuzzy concepts, whereas KNIME supports both. The top three programming languages are: Python, Java and R, with a sharedplace one position for Python and Java. Both programming languages benefit from the large online community and open-source developments, leading to extensive packages and libraries. This results in the availability of all the 16 clinical rule engine requirements in both programming languages. The main differences between these two languages is that Python is dynamically types and Java statically (not a requirement).

Strengths

The several analysis techniques used during the research increased the understanding of the clinical rule engine of a patient-centred CDSS. The exploratory research facilitated the increase in knowledge on the topic, in this case the understanding of the end-users' information needs, clinical rule engine requirements and software/programming languages for the clinical rule engine of a patient-centred CDSS. The use of different techniques to define the software requirements for the patient-centred CDSS is also experienced as valuable, because of the different perspectives and different information gathered. The observation technique has been of high relevance for the research. The observations showed the needs of the health professionals and patients, without both parties being fully aware. While observing the dialog during the consultation between the patient and health professionals, relevant information about the needs of the patient and health professional could be analysed. Analysing the observation brought insight in what the health professional wanted to know from the patient and what the patient expected from the health professional. The observation technique was experienced as a valuable technique for requirements research in a clinical setting. In conclusion, a few iterations were done during the functional requirements specification phase and proved to be valuable and essential in validating the gathered information.

Limitations and barriers

A drawback of the exploratory character of this research is the lack of statistical strength, but at this stage of information gathering it helps in determining and understanding the end-users information needs and requirements to be able to develop a clinical rule engine for a patient-centred CDSS in the future.

At the beginning of the study, the investigation focused only on the chronic disease: cancer/oncology. After the analysis of the patient's and the health professional's information needs, the document

analysis of the patient information leaflets was generalised to other chronic diseases, for example, COPD and arthritis. Nonetheless, when exploring other chronic diseases, other clinical rule engine requirements might be discovered.

Due to the limited number of end-users (patients) participating in the research the questionnaire has been based on the Likert scale which involves no parametric statistics but relies on the non-parametric statistics and the ordinal nature of the data because of the individual questions. The limitation of the interview technique is that a single researcher evaluated the interviews, and therefore the possibility of bias exists. Another limitation is the fact that the selection process on software packages and programming languages has exclusively focused on the clinical rule engine requirements.

A barrier to the project is the accessibility of registered patient data in different systems. It must be possible to access and integrate the patient's data as recorded by the hospital, GP, lab and pharmacy to make it possible to analyse the data. And, last but not least, the patient must be willing to register his/her personal data on a day-to-day basis.

The project is also dependent on the legal regulations regarding patient data safety. The government maintains the security laws and rules for patient information exchange, the law 'Wet Bescherming Persoonsgegevens' (wbp) and the GDPR 'General data protection regulation'. All involved parties must comply to these laws and regulations. Also, to create and develop the IHIE architecture, parties such as hospitals must be willing and/or allowed to collaborate with the IHIE system of Zorgkluis B.V. Not only to make the system more valuable and usable but also to gather medical information and clinical rules. Another barrier is the willingness of the patient to store the medical data at Zorgkluis B.V.

Future work

The findings show an exploratory study of the requirements for a patient-centred CDSS to support patient chronic disease self-management. This research can be used as a guide in creating a patient-centred CDSS. The end-users information needs regarding a patient-centred CDSS has been analysed. Future research is necessary to investigate the exact patient profiles (gender, age etc.) in relation to the information needs regarding a patient-centred CDSS.

Another future research could be done regarding the clinical rule requirements per chronic disease. The detailed requirements must be defined and analysed to operate the clinical rule engine into a valuable system which supports the patient concerning the medication side effects. To define these detailed functional clinical rule engine requirements for a patient-centred CDSS system further research is necessary. The advice is to choose a specific type of cancer as chronic health condition and decide which information about the medication side effects and patient's health parameters are most relevant in supporting the patient. The additional research regarding the detailed functional clinical rule engine requirements must give insight into the input (for example analytical methods) and the output (for example trend graph) of the patient-centred CDSS.

Future research is also necessary to investigate the software packages tools integrating with the programming languages and how the software packages and programming languages deal with time reasoning. The time reasoning is an essential aspect of the patient-decision support system and therefore future research is needed to define the best options regarding the time aspects of the data items.

The patients showed interest in the IHIE architecture through the patient analysis, however detailed information and further research is needed concerning the functional and non-functional requirements of the mobile application. This also applies to the health professional's dashboard. Additional research is also needed about measuring the effect of the IHIE architecture. Research on

what the impact is of using an expert system such as the IHIE system, and the effect of the patient application on the patient. Research showed that self-management tools are effective and useful, see also literature review chapter two. But research is needed to validate the IHIE system. The primary objective of the additional study must be to detect and analyse the effect of the IHIE architecture on the patient because of the patient-centred focus of the IHIE architecture ecosystem. Also after the first implementation of the patient-centred CDSS and a certain production period, a re-evaluation must take place to validate the end-users information need, clinical rule engine requirements and the clinical rule software packages and programming languages evaluation.

This research gathered the information needs of patients and health care professionals for one chronic disease, focusing on a patient-centered day-to-day and shared health care process. The translation of these needs to clinical rule engine requirements and the match with available software packages and programming language delivers a solid starting point for the intended software development process of Zorgkluis B.V to implement a patient-centered CDSS.

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Appendix A: Search strategy literature review

The search strategy describes the databases used for the literature review of patient-centred clinical decision support systems. Also, the database search query's and selection criteria are defined.

The database that is used to search for relevant articles is the 'library search' of the Eindhoven University of Technology. Note that the facts are per 17-1-2018.

Database	Facts
WorldCat	412.132.068 bibliographic records (as of December 2017)
Web of Science	2486 Journals 21147 Books
Medline	5600 Journals
Springer link	2900 Journals 250.000 Books

Table 9. Database overview

A review is done to present the state-of-art characteristics properties and requirements for a successful patient-centred decision support system. Using the following inclusion criteria:

- Patients with a chronic condition,
- Self-management component,
- Decision support component and,
- Application in a home environment

The selection criteria for the articles are that the articles must be written in English, full-text accessible, completed papers and articles published between 2008-2018. The search terms in WorldCat: decision support, self-management, chronic disease, 'home' or 'smart', 'tele' or 'telecare', telemedicine, telemonitoring. This resulted in 38 articles, from which the abstract is analysed with regard to the inclusion criteria's. The abstract analysis led to an inclusion of 13 relevant articles, these articles are fully reviewed, including articles found in references. The articles analysed in detail N=6.

Author(s)	Title
Basilakis, Lovell, Redmond, & Celler, (2010)	Design of a decision-support architecture for management of remotely monitored patients
Zheng et al., (2010)	Smart self-management: assistive technology to support people with chronic disease.
Seto et al., (2012)	Developing healthcare rule-based expert systems
Davis et al., (2014)	A qualitative study of rural primary care health professional views on remote monitoring technologies
Sanchez-Morillo, Fernandez-Granero, & Jiménez, (2015)	Detecting COPD exacerbations early using daily telemonitoring of symptoms and k-means clustering
Ogden, Barr, & Greenfield, (2017)	Determining requirements for patient-centred care: A participatory concept mapping study

Table 10. Articles literature review

Appendix B: Interviews

The interviews are done with (n=15): 5 oncology healthcare specialists, 3 oncology patients, 3 software developers, 2 e-health consultants, 1 pharmacists and 1 clinical computer scientist

Name	Function	Company	Input phase	
			Phase 1	Phase 2
Lia van Zuylen	Doctor oncology	Hospital Erasmus MC	X	X
Lieke Simkens	Doctor oncology	Hospital Maxima Medical Centrum	X	X
Gertrud Krekels	Dermatologist → skin cancer	MohsA		X
Hugo van der Kuy	Head of clinical pharmacy	Hospital Erasmus MC		X
Bob van de Loo	Project manager Digitalis (developer of clinical rule engine)	Digitalis/Clinical Rules		X
Onno van Zinderen Bakkeren	Software Developer (clinical decision support system)	Zorgkluis B.V.		X
Thomas Timmers	Software Developer e-Health (award 2017)	Patient Journey App		X
Patrick Eliasar	Consult: e-health and self-management	Zorgbelang brabant/zeeland		X
Jeroen Kwak	Senior Consult: e-health and self-management	Zorgbelang brabant/zeeland		X
Lonneke Vermeulen	Clinical computer scientist	IKNL		X
Wendy Oldenmenger	Nursing researcher oncology	Erasmus MC	X	X
Diana Lüring	Nursing Specialist GE carcinomas	Hospital Maxima Medical Centrum	X	X
Patient 1	Oncology patient	/	X	X
Patient 2	Oncology patient	/	X	X
Patient 3	Oncology patient	/	X	X

Table 11. Participants interviews

The characteristics of the patients interviewed:

Patient/ characteristic	Gender	Age	Disease stable or fluctuating
Patient 1	Female	37	Stable
Patient 2	Female	42	Fluctuating
Patient 3	Female	53	Stable

Table 12. Patient characteristics

Appendix C: Observation method

The observation method is used in phase one and as input for phase two of the research.

Set-up

The observation is done in the Erasmus MC hospital department oncology with special attention to ovarian cancer and palliative care. The persons who were observed are the oncology specialist and the oncology patients. The patients are adults and are in different stadiums of their personal treatment plan. Participants are n=10.

Procedure

The observation is conducted from a one-day session end of March 2017. The information is recorded through notes during the observation, since it was not clear what to expect the following set up was used.

The first hour of the observation day, special attention was given to the interaction between the patient and specialist. After the first hour, the analyser (the writer of this thesis) made a high-level structure to make notes for the future sessions of that day. The notes were described first with the goal of the consult, which questions were asked by the specialist as well as the patient and last the information that was given without asking. For every conversation between patient and specialist, the information is captured through notes.

Results

The health professional's information needs are analysed. The information needs have three different components:

- Subject: refers to the main subject of the information need
- Need: refers to the information health professional needs.
- Patient: refers to the amount of consult sessions the subject is discussed.

1. Subject: Health parameters

Need: The health professional wants insight into trends of heart rate, weight, side effects, blood pressure, performance (ADL, algemene dagelijkse levensverrichtingen).

Patient: 8/10

2. Subject: Medication use

Need: The health professional wants insight in medication usage of patients.

Patient: 7/10

3. Subject: Personal details

Need: The health professional wants to have contact details of patients.

Patient: 3/10

4. Subject: Personal details

Need: The health professional wants information about the home-situation to get more insight into the patient's daily life activities.

Patient: 3/10

5. Subject: Quality of life

Need: The health professional wants insight into the quality of life of a patient.

Patient: 7/10

6. Subject: Side effects

Need: The health professional wants insight in the medication side effects of the patient.

Patient: 8/10

7. Subject: Pain

Need: The health professional wants insight in the patient's pain level.

Patient: 6/10

8. Subject: Information about the treatment

Need: The health professional wants to inform the patient about the treatment.

Patient: 3/10

9. Subject: Information about the medication

Need: The health professional wants to inform the patient about the medication.

Patient: 4/10

The patients' information needs are identified during the observations. The information needs have four different components:

- **Situation:** refers to the scenario the patient/care provider experiences.
- **Need:** refers to something the patient/care provider needs or wants.
- **Goal:** refers to what the patient wants to achieve.
- **Patients:** refer to the how many patients refer to the need.

1. Situation: The oncology patient will receive chemotherapy.

Need: The patient wants to know more about the purposes, uses, side effects and procedures of chemotherapy.

Goal: To know what they can expect regarding clinical problems during the therapy.

Patients: 3/10

2. Situation: The patient has appointments with different care providers.

Need: The patient wants insight into dates, names and purposes of appointments with care providers.

Goal: Give complete information to their doctor.

Patients: 1/10

3. Situation: The patient uses medication X and experiences side effects.

Need: The patient wants insight into when the side effects have started, the time span of side effects, if it is 'normal' to feel and the severity of side effects.

Goal: To inform their doctor correctly, to feel 'normal' and confident.

Patients: 9/10

4. Situation: The patient is being treated at hospital X, but finds an alternative treatment outside hospital X.

Need: The patient wants an opinion of their doctor about their treatment and information on why hospital X is not providing this alternative treatment.

Goal: Receive information from their doctor's perspective to make a decision to continue the current

treatment or to take an alternative treatment from a different hospital.

Patients: 4/10

5. Situation: The patient is insecure before a consult with the doctor.

Need: The patient wants information about the status of their treatment and insights about their lab values.

Goal: To be informed before consult and feel secure.

Patients: 6/10

6. Situation: The patient is going on holiday with medication(s).

Need: The patient wants a medication passport and information of what is not allowed to do (for example: lying in the sun).

Goal: To be prepared before going on a holiday and avoid doing something that is not allowed during their care pathway.

Patients: 1/10

7. Situation: The patient is interested in becoming a donor.

Need: The patient wants information if it is possible to be a donor and which type of donor is possible.

Goal: Informed to make the decision.

Patients: 2/10

8. Situation: The patient uses medication X from their doctor, but also uses medication Z from the general practitioner.

Need: The patient wants to inform the doctor, so the doctor will have an accurate overview of which medication the patient uses (in case something goes wrong).

Goal: To have an up to date overview of medication usage.

Patients: 7/10

9. Situation: The patient had a physical examination to check if they have breast cancer.

Need: The patient wants to know the current status of the examination results and wants to check if the waiting time deviates from a normal procedure.

Goal: No fear that something is wrong.

Patients: 1/10

10. Situation: The patient's medication supply is running low.

Need: The patient wants a repeat prescription.

Goal: Preventing from being without medication.

Patients: 3/10

11. Situation: A physical examination is done during a consult. The patient tells the doctor that the circumstances, for example on the leg, was very different two weeks ago.

Need: The patient wants to show the doctor how the circumstances (leg) were two weeks ago.

Goal: Insight in changing circumstances of physical treatment.

Patients: 8/10

12. Situation: The patient has side effects during and after chemotherapy.

Need: The patient wants insight into patterns of side effects.

Goal: To plan personal activities and reassurance.

Patients: 10/10

13. Situation: The patient uses medication X, but forgot to take in the medication.

Need: The patient wants to remember their medication intake schedule.

Goal: Take medication on right time.

Patients: 4/10

Appendix D: Questionnaire

The aim of the questionnaire is to gain insight into the wishes and needs of oncology patients for a mobile application that supports the patient during and after the treatment. With n=20 respondents.

The questions asked:

1. Retrieve medical data from the general practitioner, pharmacy, and hospital.
2. Registration of medication intake during treatment
3. Registration of weight, blood pressure or other physical data
4. Diary in which you record side effects (such as pain) and other data
5. Reminders of actions/appointments from your personal treatment plan
6. A system that reports possible problems to you and the doctor, so that immediate action can be taken
7. The ability to send a message to the doctor or nurse
8. Video calling on an appointment with the doctor or nurse
9. Information about your chronic condition and the treatment (text or/and videos)
10. What would you like to see in the mobile application? → control question

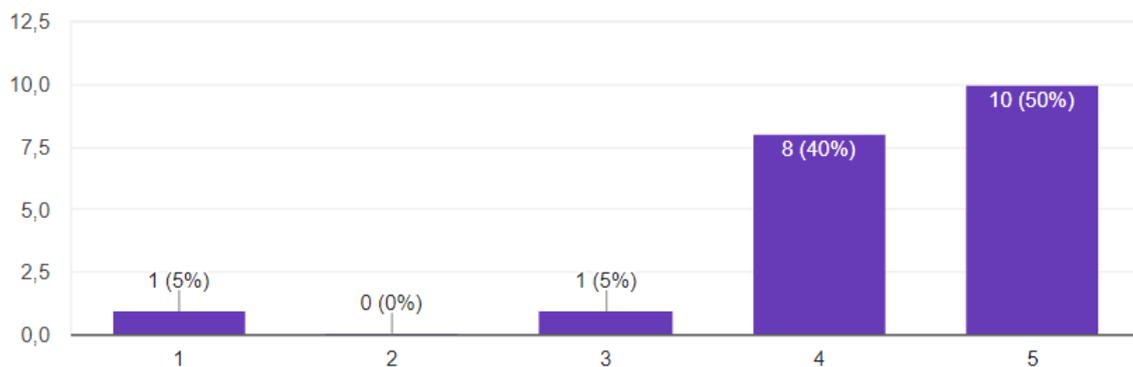
Likert scale:

- 1= not important
- 2= somewhat important
- 3= neutral
- 4= important
- 5= very important

1. Ophalen van medische gegevens bij de huisarts, apotheek en ziekenhuis



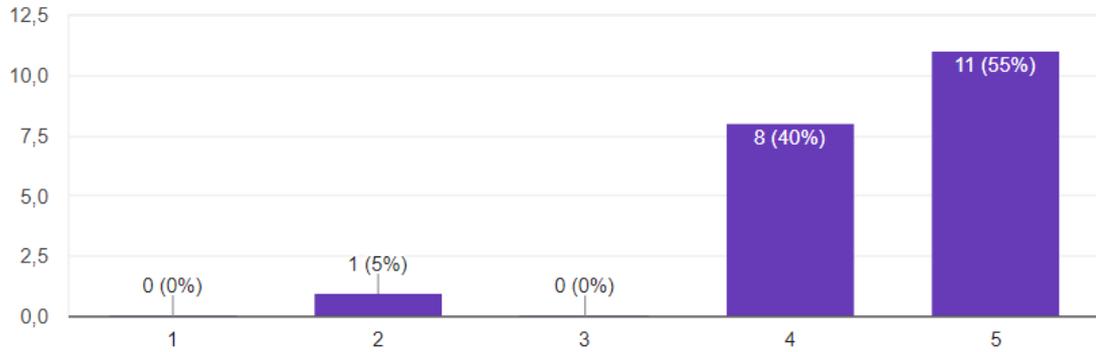
20 reacties



2. Registratie van medicatie- inname gedurende de behandeling



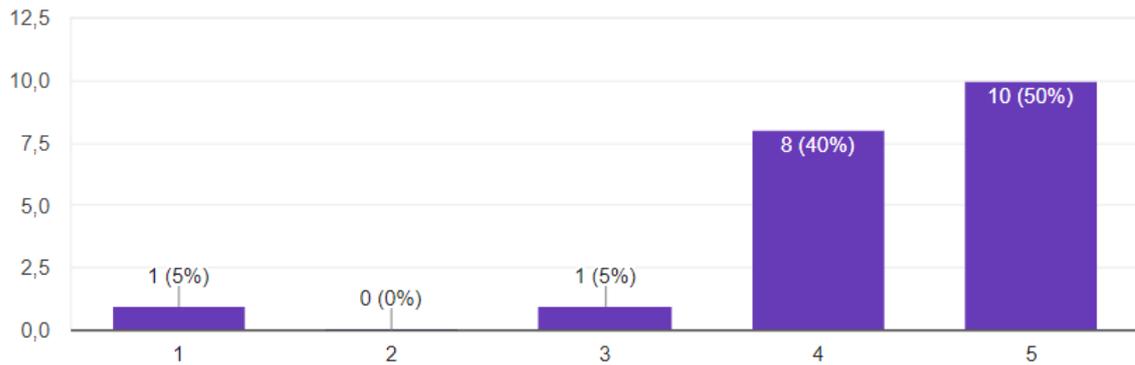
20 reacties



3. Registratie van gewicht, bloeddruk of andere lichamelijke gegevens



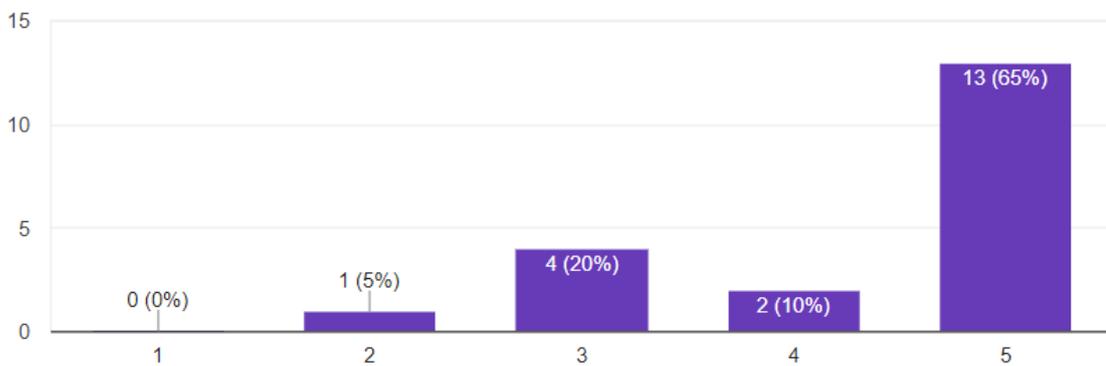
20 reacties



4. Dagboek waarin u bijwerkingen (zoals pijn) en andere gegevens registreert

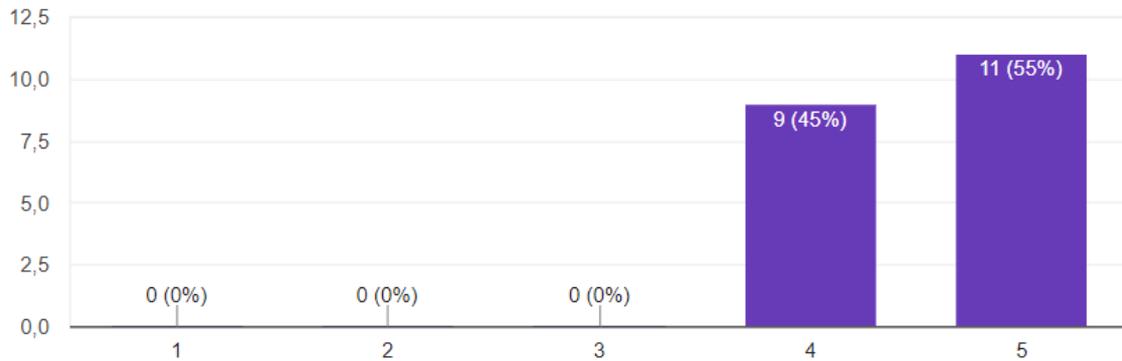


20 reacties



5. Herinneringen aan acties/afspraken uit uw persoonlijke behandelplan

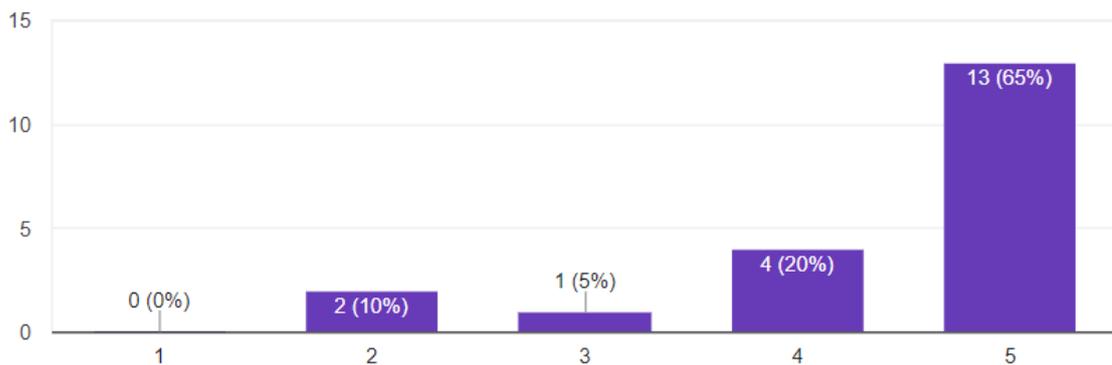
20 reacties



6. Een systeem dat mogelijke problemen aan u en de dokter meldt, zodat onmiddellijk actie kan worden ondernomen



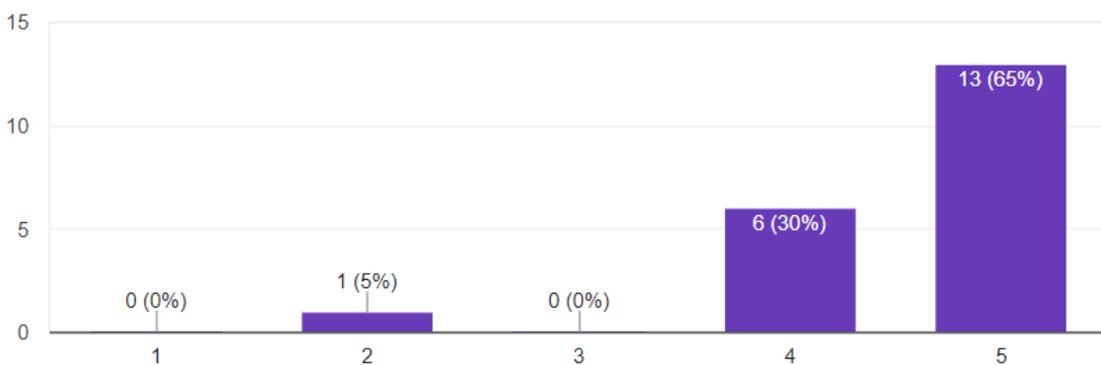
20 reacties



7. Mogelijkheid om een bericht te sturen naar de dokter of verpleegkundige

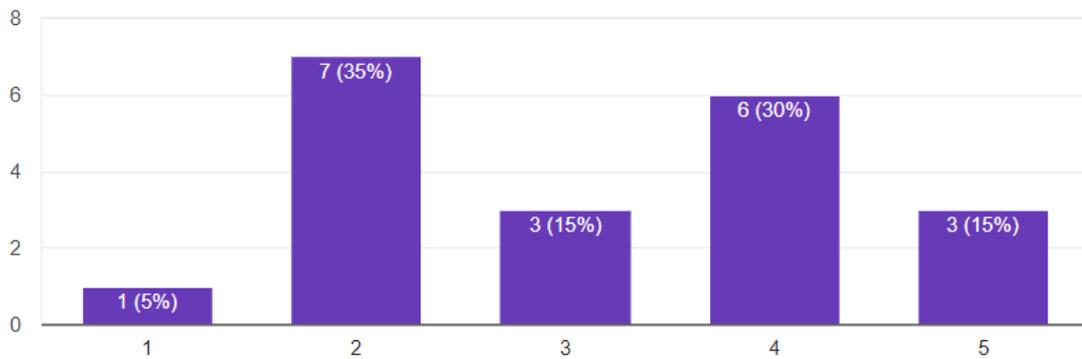


20 reacties



8. Op afspraak met de dokter of verpleegkundige beeldbellen

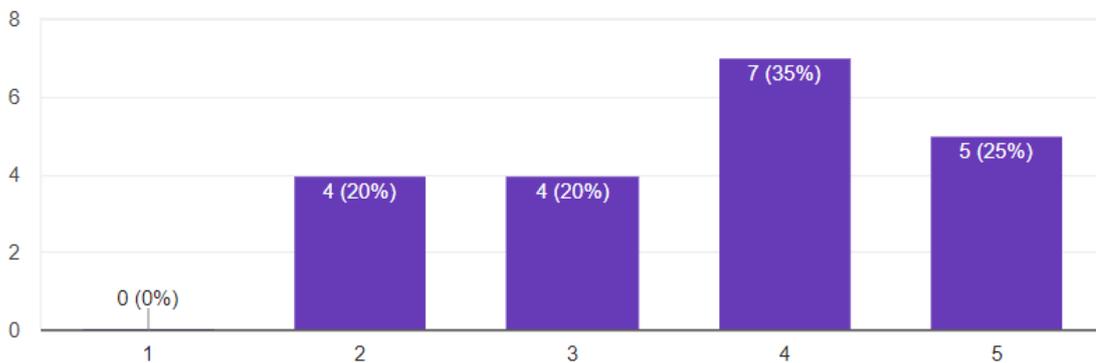
20 reacties



9. Informatie over uw ziekte en de behandeling d.m.v. filmpjes of teksten



20 reacties



10. What would you like to see in the mobile application?

(open-end question)

Subject	Respondents
Functionalities mentioned in previous questions	14
I don't know	1
Olijf specific	1
No need for an application at all	1
Transparency	1
Save sound recordings	1
Message support groups	1

Table 13. Answers open-end question 10

Appendix E: Results phase one: Patient analysis

The results of the interview, questionnaire and observation are shown below.

Interview

Focus area of interviews:

Patient/ needs	Communication	Medication information	Medication use	Patient treatment plan
Patient 1	1	2	1	0
Patient 2	2	2	1	0
Patient 3	2	2	2	1
Total	5	6	3	1

Table 14. Patient interviews outcomes

0 = Not mentioned | 1 = Mentioned | 2 = Mentioned as most important

Questionnaire

The questions asked:

1. Retrieve medical data from the general practitioner, pharmacy, and hospital.
2. Registration of medication intake during treatment
3. Registration of weight, blood pressure or other physical data
4. Diary in which you record side effects (such as pain) and other data
5. Reminders of actions/appointments from your personal treatment plan
6. A system that reports possible problems to you and the doctor, so that immediate action can be taken
7. The ability to send a message to the doctor or nurse
8. Video calling on an appointment with the doctor or nurse
9. Information about your chronic condition and the treatment (text or/and videos)
10. What would you like to see in the mobile application? → control question

Below a table with the overview per question, of the questionnaire, and the related category of the patient analysis.

Question	Category			
	Communication	Medication information	Medication use	Patient treatment plan
1	X			
2			X	
3		X		
4		X		
5				X
6	X			
7	X			
8	X			
9				X

Table 15. Question per category

A series of individual questions that have a Likert response is used. Therefore to analyse the Likert-type items the average, modes, medians and frequency are defined (the University of St-Andrews, n.d.).

Likert scale: 1= not important | 2= somewhat important | 3= neutral | 4= important | 5= very important

Question	Average	Modes	Median	Respondents frequency (%)					
				Likert scale	1	2	3	4	5
1	4,3	5	4,5		5%	0%	5%	40%	50%
2	4,45	5	5		0%	5%	0%	40%	55%
3	4,3	5	4,5		5%	0%	5%	40%	50%
4	4,35	5	5		0%	5%	20%	10%	65%
5	4,55	5	5		0%	0%	0%	45%	55%
6	4,4	5	5		0%	10%	5%	20%	65%
7	4,55	5	5		0%	5%	0%	30%	65%
8	3,15	2	3		5%	35%	15%	30%	15%
9	3,65	4	4		0%	20%	20%	35%	25%

Table 16. Questionnaire outcome

Observation

The results of the observation are shown in Table 17 below.

Situation	Patients (n=10)	Category				
		Communication	Medication information	Medication use	Patient treatment plan	Other
1	3			X		
2	1				X	
3	9		X			
4	4		X			
5	6				X	
6	1		X			
7	2					X
8	7			X		
9	1				X	
10	3				X	
11	8		X			
12	10		X			
13	4			X		
Total situations*		Unknown	5 (38,46%)	3 (23,07%)	4 (30,77%)	1 (7,70%)
Times mentioned**		Unknown	32 (64%)	14 (47%)	11 (28%)	2 (20%)
Ranking		Unknown	1	2	3	4

Table 17. Outcome patient observation

*The total situations refer to the total situations mentioned in the category: The percentage is the situation in relation to the total situations possible.

** Times mentioned refer to the total amount of patients mentioned the category: The percentage is the number patients mentioned the category in relation to the number of patients possible in this category.

Appendix F: Results phase one: Health professional analysis

In this Appendix the results of the interviews and observations are presented.

Interview

In total four interviews are executed. Table 18 gives an overview per interview and the health professional's information needs. The points are divided based on:

0 = Not mentioned

1 = Mentioned

2 = Mentioned as most important

Health professional	Patient information						System information	
	Health parameters	Side effects	Quality of life	Medication use	Home situation	Pain	Alerts	Clinical rules
Interview 1	2	2	0	1	0	1	1	1
Interview 2	2	2	1	0	1	1	1	1
Interview 3	0	2	0	1	0	2	1	1
Interview 4	2	1	0	2	0	1	1	1
Total points	6	7	1	4	1	5	4	4

Table 18. Outcome interviews patient information by the health professionals

Observation

The results of the observation are shown in Table 19. The health professional has a consult session with a patient. In total 10 consult sessions have been observed. For each session, the information needs of the health professional are analysed.

Patient/Category	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	Total
Health parameters	X		X		X	X	X	X	X	X	8
Medication Use	X		X		X	X	X	X	X		7
Personal details				X	X					X	3
Quality of life	X	X					X	X			4
Side effects	X	X		X	X	X	X	X	X		8
Pain		X	X	X	X	X		X			6
Inform about the medication			X			X			X		3
Inform about the treatment	X			X				X		X	4

Table 19. Outcome health professional information needs

Appendix G: Patient information leaflets

The patient information leaflets analysed in detail:

- Salbutamol (COPD)
- Metformin (Diabetic)
- Amlodipine (Blood pressure)
- Rosuvastatin (Cholesterol)
- Diclofenac atrium Aurobindo (Arthrosis)
- Xarelto (Anticoagulation)
- Pantoprazole (Heartburn)
- Casodex (Cancer)
- Tamoxifen (Cancer)
- Myleran (Cancer)

Appendix H: Techniques and derived clinical rule engine requirements

Topic	Number	Clinical rule engine requirements	Interviews	Document analysis	Literature review
Reasoning strategies	CRER-1	The system <i>must</i> be able to execute forward chaining.	5 oncology healthcare specialists 1 pharmacists 1 clinical computer scientist	X	Celler et al., (2003); Huiru Zheng et al., (2010)
	CRER-2	The system <i>may</i> be able to execute backward chaining.	1 oncology healthcare specialists 2 software developers 1 clinical computer scientist	X	
Logic	CRER-3	The system <i>must</i> be able to manage Boolean logic.	3 oncology healthcare specialists 3 software developers 1 pharmacists 1 clinical computer scientist	X	Celler et al., (2003); Davis et al., (2014); Seto et al., (2012b); Huiru Zheng et al., (2010)
Time	CRER-4	The system <i>must</i> be able to manage time reasoning.	5 oncology healthcare specialists 3 software developers 2 e-health consultants 1 pharmacists 1 clinical computer scientist	X	Celler et al., (2003); Davis et al., (2014); Sanchez-Morillo et al., (2015); Seto et al., (2012b); Huiru Zheng et al., (2010)
Decision tree	CRER-5	The system <i>must</i> be able to execute decision tree reasoning.	5 oncology healthcare specialists 3 software developers 2 e-health consultants 1 pharmacists 1 clinical computer scientist	X	

Statistics	CRER-6	The system <i>must</i> be able to execute descriptive statistics.	5 oncology healthcare specialists 3 software developers 2 e-health consultants 1 pharmacists 1 clinical computer scientist	X	Celler et al., (2003); Davis et al., (2014); Ogden et al., (2017); Sanchez-Morillo et al., (2015); Seto et al., (2012b); Huiru Zheng et al., (2010)
	CRER-7	The system <i>must</i> be able to execute Bayesian statistics.	2 oncology healthcare specialists 2 software developers 1 pharmacists 1 clinical computer scientist	X	
	CRER-8	The system <i>must</i> be able to execute a linear regression.	2 oncology healthcare specialists 2 software developers 1 pharmacists 1 clinical computer scientist	X	
	CRER-9	The system <i>may</i> be able to execute nonlinear regression.	2 oncology healthcare specialists 2 software developers 1 pharmacists 1 clinical computer scientist		
	CRER-10	The system <i>may</i> be able to execute statistical hypothesis testing.	1 oncology healthcare specialists 1 software developers 1 pharmacists		
	CRER-11	The system <i>must</i> be able to insert a data input into a mathematical calculation.	5 oncology healthcare specialists 3 software developers 2 e-health consultants	X	

			1 pharmacists 1 clinical computer scientist		
	CRER-12	The system <i>must</i> be able to execute mathematical calculations.	5 oncology healthcare specialists 3 software developers 2 e-health consultants 1 pharmacists 1 clinical computer scientist	X	
Crisp and fuzzy	CRER-13	The system <i>must</i> be able to manage a fuzzy concept.	2 software developers 1 pharmacists 1 clinical computer scientist	X	
	CRER-14	The system <i>must</i> be able to execute fuzzy reasoning.	2 software developers 1 pharmacists 1 clinical computer scientist	X	
Machine learning	CRER-15	The system <i>may</i> be able to execute machine learning methods.	1 oncology healthcare specialists 3 software developers 2 e-health consultants 1 clinical computer scientist		X
Ontology	CRER-16	The system <i>must</i> be able to manage ontologies.	2 oncology healthcare specialists 2 software developers 1 clinical computer scientist	X	Sanchez-Morillo et al., (2015)

Table 20. Clinical rule engine requirements and the elicitation techniques

Appendix I: additional requirements

Additional requirements are derived during the research. Below the system architecture – and system output requirements.

System architecture requirements	Number	Requirements
Location of DSS component	SAR-1	The location of the DSS <i>must</i> be in the cloud.
	SAR-2	The users <i>must</i> be able to access the system from various locations.
Autonomy of DSS component	SAR-3	The system <i>must</i> provide real-time response and control of the patient's input.
	SAR-4	The decision component of the patient-centred CDSS <i>must</i> be able to make autonomous decisions.
Integration	SAR-5	The system <i>may</i> have the possibility to retrieve medical data from a medical device.
	SAR-6	The patient-centred CDSS <i>may</i> be integrated with the health professional's systems.
Database component	SAR-7	The system <i>must</i> be able to retrieve the clinical data from the database to analyse the data.
	SAR-8	The system <i>must</i> be able to store the clinical data retrieved.
	SAR-9	The system <i>must</i> be able to store the (historical) clinical rule fired per patient.
Filtering clinical data	SAR-10	The system <i>must</i> be able to filter clinical data based on the health professionals and patients information needs.

Table 21. System architecture requirements

System architecture requirements	Number	Requirements	Interviews	Document analysis	Literature review
Location of DSS component	SAR-1	The location of the DSS <i>must</i> be in the cloud.	3 software developers		
	SAR-2	The users <i>must</i> be able to access the system from various locations.	1 oncology healthcare professional 3 software developers 2 patients 2 e-health professionals		Basilakis et al., (2010); Huiru Zheng et al., (2010)
Autonomy of DSS component	SAR-3	The system <i>must</i> provide real-time response and control of the patient's input.	5 oncology healthcare specialists 3 oncology patients 3 software developers 2 e-health consultants		Basilakis et al., (2010)

			1 pharmacists		
	SAR-4	The decision component of the patient-centred CDSS <i>must</i> be able to make autonomous decisions.	5 oncology healthcare specialists 3 oncology patients 3 software developers 2 e-health consultants 1 pharmacists 1 clinical computer scientist		
Integration	SAR-5	The system <i>may</i> have the possibility to retrieve medical data from the medical device.	2 oncology healthcare specialists 1 oncology patients 1 software developers 2 e-health consultants		Celler et al., (2003); Davis et al., (2014); Sanchez-Morillo et al., (2015); Seto et al., (2012b); Huiru Zheng et al., (2010)
	SAR-6	The patient-centred CDSS <i>may</i> be integrated with the health professional's systems.	5 oncology healthcare specialists 1 pharmacists 1 clinical computer scientist		Davis et al., (2014); Ogden et al., (2017)
Database component	SAR-7	The system <i>must</i> be able to retrieve the clinical data from the database to analyse the data.	3 software developers		Celler et al., (2003); Davis et al., (2014); Ogden et al., (2017); Sanchez-Morillo et al., (2015); Seto et al., (2012b); Huiru Zheng et al., (2010)
	SAR-8	The system <i>must</i> be able to store the clinical data retrieved.	3 software developers		Celler et al., (2003); Davis et al., (2014); Ogden et al., (2017); Sanchez-Morillo et al., (2015); Seto et al., (2012b); Huiru Zheng et al., (2010)
	SAR-9	The system <i>must</i> be able to store the (historical) clinical rule fired per patient.	5 oncology healthcare specialists 1 software developer		

Filtering clinical data	SAR-10	The system <i>must</i> be able to filter clinical data based on the health professionals and patients information needs.	5 oncology healthcare specialists		(Davis et al., 2014)
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Table 22. System architecture requirements and the elicitation techniques

The system output requirements are about the different types of information output, see Table 23.

System output requirements	Number	Requirements
Alerts	SOR-1	The system <i>must</i> be able to prioritise the output alerts.
	SOR-2	The system <i>must</i> be able to provide alerts.
Visualisation	SOR-3	The system <i>must</i> be able to visualise the clinical data.
Reports	SOR-4	The system <i>must</i> be able to create reports.
	SOR-5	The system <i>must</i> be able to send reports.

Table 23. System output requirements

System output requirements	Number	Requirements	Interviews	Document analysis	Literature review
Alerts	SOR-1	The system <i>must</i> be able to prioritise the output alerts.	4 oncology healthcare specialists 2 oncology patients 3 software developers 1 pharmacists 1 clinical computer scientist	X	Celler et al., (2003); Davis et al., (2014); Sanchez-Morillo et al., (2015); Seto et al., (2012b); Huiru Zheng et al., (2010)
	SOR-2	The system <i>must</i> be able to provide alerts.	5 oncology healthcare specialists 3 software developers 2 e-health consultants 1 pharmacists 1 clinical computer scientist		Celler et al., (2003); Davis et al., (2014); Ogden et al., (2017); Sanchez-Morillo et al., (2015); Seto et al., (2012b); Huiru Zheng et al., (2010)
Visualization	SOR-3	The system <i>must</i> be able to visualise the clinical data.	5 oncology healthcare specialists 3 software developers		Celler et al., (2003); Davis et al., (2014); Ogden et al., (2017); Sanchez-Morillo et al.,

			2 e-health consultants 1 clinical computer scientist		(2015); Seto et al., (2012b); Huiru Zheng et al., (2010)
Reports	SOR-4	The system <i>must</i> be able to create reports.	1 oncology healthcare specialists 2 software developers		Celler et al., (2003); Davis et al., (2014); Sanchez-Morillo et al., (2015); Huiru Zheng et al., (2010)
	SOR-5	The system <i>must</i> be able to send reports.	1 oncology healthcare specialists 2 software developers		

Table 24. System output requirements and the elicitation techniques

Appendix J: Clinical rule engine software packages analysis

Topic	Clinical rule engine requirements	Digitalis	Gaston	KNIME	RapidMiner	WEKA
Reasoning strategies	The system <i>must</i> be able to execute forward chaining.	Yes	Yes	Yes	Yes	Yes
	The system <i>may</i> be able to execute backward chaining.	No	No	No	No	No
Logic	The system <i>must</i> be able to manage Boolean logic.	Yes	Yes	Yes, Boolean operators	?	Yes
Time	The system <i>must</i> be able to manage time reasoning.	No	No	?	?	?
Decision tree	The system <i>must</i> be able to execute decision tree reasoning.	Yes	Yes	Yes, PMML decision tree model (KNIME, 2017a)	Yes	Yes
Statistics	The system <i>must</i> be able to execute descriptive statistics.	Yes	No	Yes, Boxplot Histogram	Yes, Distribution plot Rainflow matrix (RapidMiner, n.d.-a)	Yes*, Histograms *limited
	The system <i>must</i> be able to execute Bayesian statistics.	No	No	Yes, Naïve Bayes	Yes, Bayesian modelling	Yes,
	The system <i>must</i> be able to execute a linear regression.	No	No	Yes	Yes	Yes
	The system <i>may</i> be able to execute nonlinear regression.	No	No	Yes, BfROpenLab (Thoens et al., n.d.)	Yes, Polynomic (LibSVMlearner)	No
	The system <i>may</i> be able to execute statistical hypothesis testing.	No	No	Yes, t-test	Yes, t-test ANOVA	No

	The system <i>must</i> be able to insert a data input into a mathematical calculation.	No	Yes	Yes	Yes	Yes
	The system <i>must</i> be able to execute mathematical calculations.	No	Yes	Yes, Feature Calculator	Yes, Create formula	No
Fuzzy	The system <i>must</i> be able to manage a fuzzy concept.	No	No	Yes, Fuzzy queries	No	Yes
	The system <i>must</i> be able to execute fuzzy reasoning.	No	No	Yes, FuzzyNumberValue FuzzyIntervalValue Fuzzy c-means algorithm	No	Yes, FuzzyWEKA Fuzzy Lattice Reasoning Classifier
Machine learning	The system <i>may</i> be able to execute machine learning methods.	No	No	Yes, Deep neural networks (H20) Decision trees	Yes, Deep learning (H20) Support vector machines	Yes, Association rules Neural network
Ontology	The system <i>must</i> be able to manage ontologies.	No	Yes	Yes, RDF, OWL, SKOS, SPARQL (Vicenzo, 2016)	Yes, RMonto (Potoniec & Lawrynowicz, 2011)	No

Table 25. Software packages vs software requirement analysis

Appendix K: Clinical rule engine programming languages analysis

Topic	Clinical rule engine requirements	Python	Java	R	Julia	Prolog
Reasoning strategies	The system <i>must</i> be able to execute forward chaining.	Yes, PyKE (PyKE, n.d.)	Yes, Jess Drools (Andres, 2017; Jess, n.d.)	Yes	Yes	Yes, Pfc package (Prolog, n.d.-a)
	The system <i>may</i> be able to execute backward chaining.	Yes, PyKE (PyKE, n.d.)	Yes, Drools	No	No	Yes
Logic	The system <i>must</i> be able to manage Boolean logic.	Yes	Yes	Yes	Yes	Yes
Time	The system <i>must</i> be able to manage time reasoning.	Yes, Time module TimeTuple (Tutorials Point, n.d.-b)	Yes, Boolean before (Tutorials Point, n.d.-a)	Yes, POSIXIt package POSIXct package (Beck, 2012; Hiemstra, n.d.)	Yes, See chapter Working with dates and times (GitHub, n.d.-a)	??
Decision tree	The system <i>must</i> be able to execute decision tree reasoning.	Yes, Using Scikit-learn is easier (Mayo, n.d.)	Yes, Drools (JBoss, n.d.)	Yes, Party package (Tutorials Point, n.d.-c)	Yes	Yes

Statistics	The system <i>must</i> be able to execute descriptive statistics.	Yes Plotly (boxplot, histogram) (Plotly, n.d.)	Yes, JavaFX charts (pie charts, bar chart, line chart)	Yes, Ggplot2 (boxplot, line segments)	Yes, Integration with Pyplot package Unicodeplots (Joshi, 2016)	No
	The system <i>must</i> be able to execute Bayesian statistics.	Yes Bayesian statistics (Downey, 2013; Github, n.d.)	Yes JavaBayes (Cozman, n.d.)	Yes, JAGS OpenBUGS	Yes, Naive Bayes package	No
	The system <i>must</i> be able to execute a linear regression.	Yes, Panda library NumPy library (Bronshstein, 2017)	Yes	Yes, Bolstad package (Park, 2018)	Yes	No
	The system <i>may</i> be able to execute nonlinear regression.	Yes, SciPy package	Yes	Yes, Nlstoools package	Yes, NLreg package (GitHub, n.d.-c)	No
	The system <i>may</i> be able to execute statistical hypothesis testing.	Yes, SciPy package (SciPy, n.d.) Hypothesis library (Hypothesis, n.d.)	Yes, TTest package (The Apache Software Foundation, n.d.)	Yes, t.test (DF Team, 2017)	Yes, t-test (Joshi, 2016)	No
	The system <i>must</i> be able to insert a data input into a mathematical calculation.	Yes	Yes	Yes	Yes	No
	The system <i>must</i> be able to execute mathematical calculations.	Yes	Yes	Yes	Yes	No
	Fuzzy	The system <i>must</i> be able to manage a fuzzy concept.	Yes	Yes	Yes	Yes
The system <i>must</i> be able to execute fuzzy reasoning.		Yes, Scikit-fuzzy toolkit for SciPy	Yes, jFuzzyLogic (jFuzzyLogic, n.d.)	Yes, FuzzyR package Fbrs package	Yes, Fuzzy.jl package (GitHub, n.d.-b)	Yes, Fuzzy Prolog extension

		(Scikit-Fuzzy, n.d.)		(Garibaldi, Chen, & Razak, 2017; Riza, Bergmeir, Herrera, & Benitez, 2015)		(Vaucheret, Guadarrama, & Bueno, n.d.)
Machine learning	The system <i>may</i> be able to execute machine learning methods.	Yes, Scikit-learn library Keras Library (deep learning)	Yes, WEKA jBNC Toolkit Deeplearning4j	Yes, RWEKA E1071 package Nnet package (Peddibhotla & KDnuggets, 2015)	Yes, MXNet package deep learnig (Joshi, 2016; JuliaML, n.d.)	No
Ontology	The system <i>must</i> be able to manage ontologies.	Yes, Owlready2 library SETH integrate Python with Web Ontology Language (Lamy, 2017; Seth, n.d.)	Yes, Jena Ontology (Jena, n.d.)	Yes, OntologyX package (Greene, 2017a, 2017b)	No	Yes, OWL ontologies (Prolog, n.d.-d)

Table 26. Programming languages vs software requirement analysis

