Interoperability and machine learning in primary care

A clinical decision support system for low back pain

Wendy Oude Nijeweme - d’Hollosy
INTEROPERABILITY AND MACHINE LEARNING IN PRIMARY CARE
A CLINICAL DECISION SUPPORT SYSTEM FOR LOW BACK PAIN

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Contents

CHAPTER 1
General Introduction

CHAPTER 2
Requirements for and barriers towards interoperable eHealth technology in primary care

CHAPTER 3
Clinical decision support systems for primary care: the identification of promising application areas and an initial design of a CDSS for lower back pain

CHAPTER 4
Design of a web-based clinical decision support system for guiding patients with low back pain to the best next step in primary healthcare

CHAPTER 5
Should I see a healthcare professional or can I perform self-care: self-referral decision support for patients with low back pain

CHAPTER 6
Evaluation of Three Machine Learning Models for Self-Referral Decision Support on Low Back Pain in Primary Care

CHAPTER 7
Using machine learning and patient-reported data to model decision support for physicians on the selection of appropriate treatments for low back pain

CHAPTER 8
Design and Evaluation of an Interoperable eHealth Reference Architecture for Primary Care

CHAPTER 9
General Discussion

& Others

References
Summary
Samenvatting [In Dutch]
Dankwoord [In Dutch]
Curriculum Vitae
List of publications
CHAPTER 1
General Introduction
1.1 eHealth in primary care

eHealth is an umbrella term that has been defined in many different ways\textsuperscript{1,2,3}. The most widely accepted definition, and the definition that I use in this thesis, comes from Eysenbach\textsuperscript{4}:

\textit{“e-Health is an emerging field in the intersection of medical informatics, public health and business, referring to health services and information delivered or enhanced through the Internet and related technologies. In a broader sense, the term characterizes not only a technical development, but also a state-of-mind, a way of thinking, an attitude, and a commitment for networked, global thinking, to improve healthcare locally, regionally, and worldwide by using information and communication technology.”}

eHealth includes many fields, among others telemedicine, mHealth, and clinical decision support systems (CDSS). The application of eHealth technology can benefit the healthcare system within a variety of ways, for example:

- Efficient management of health data and the possibility to share these data among healthcare professionals, informal caregivers, and patients within patient care processes\textsuperscript{5};
- Improvement of the quality and sustainability of healthcare by supporting the self-management of patients\textsuperscript{6,7,8,9};
- Development of big data solutions based on connected digital health data from different sources\textsuperscript{10}, for example clinical decision support systems to tailor treatments based on patient characteristics (personalized medicine)\textsuperscript{11}.

Despite the rapid growth of eHealth technologies, eHealth applications are rarely embedded structurally within primary care. Therefore, little is known about the effects of eHealth on quality of care and costs, and both healthcare providers and patients lack awareness about the possibilities of eHealth in primary care\textsuperscript{12,13,14,15,16}. This is a pity, because especially within primary care, preventive care can be optimized with the support of eHealth, for example to manage modifiable health risk behaviors\textsuperscript{17} or to avoid the development of chronic conditions in patients\textsuperscript{18}. As such, eHealth can help in decreasing the current burden on and rising costs of the healthcare system.

1.2 Clinical decision support systems

A special type of eHealth technology is the Clinical Decision Support System (CDSS). Since the 1960’s, CDSSs have been developed to support the clinical decision process of healthcare professionals\textsuperscript{19,20}. CDSS can be defined as\textsuperscript{19}:

\textit{“Any computer program designed to help healthcare professionals to make clinical decisions”}.
CDDSs can help to manage clinical level of detail and complexity by, for example, alerting professionals, and by providing patient-specific recommendations. Providing patient-specific recommendations covers the assistance in the determination of a diagnosis, providing advice on therapy, or both. Over time, CDSSs have been shown to improve both patient outcomes and costs of care by prompting, reminding and cautioning clinicians whether or not to intervene under specific clinical circumstances. Nowadays, some CDSSs are already used in daily primary care, mainly because they are implemented as functionalities of the healthcare information systems of the healthcare professionals. These functionalities are mainly used for prevention and screening, drug dosing, medical management of acute diagnoses and chronic disease management through the usage of alerts and computerized protocols.

1.3 Interoperability to support health information exchange

One of the key barriers that hinders the implementation of eHealth technologies in primary care is interoperability. Interoperability is defined as the ability of two or more systems or components to exchange information and to use the information that has been exchanged. Interoperability between health systems facilitates health information exchange (HIE). HIE is focused on saving and digitally sharing reliable clinical information among physicians, nurses, pharmacists, other health care providers, and patients across the boundaries of health care institutions, health data repositories, laboratories, public health agencies, and other entities that are not within a distinct organization or among affiliated providers. Interoperability among health organizations, eHealth solutions, IT systems and other entities enables HIE. This facilitates healthcare professionals in working together in the interest of their patients, thereby increasing the quality and continuity of care through shared knowledge, and enabling a more efficient use of that information in the healthcare process.

Unfortunately, the currently available health information systems and digital devices in primary care do not facilitate smooth HIE. Interoperability barriers that hinder smooth HIE are related to technical, organizational, safety, privacy, and security issues. One of the main issues is the usage of standalone systems that store data in different formats and without means for data exchange, despite the existence of available HIE communication standards, like HL7 and terminology standards as SNOMED CT.

1.4 Interoperability and the development of CDSSs

Due to the rise of IT in healthcare, the amount of digitalized healthcare data that have been stored in different repositories of health information systems is exploding. When smooth HIE can be achieved, data from different sources becomes available at the right place at the right time and can be used in clinical decision support for effective medical decision-making. This is also shown in Figure 1.1 by the eHealth pyramid of Rooij et al.
Until now, the most common type of CDSS technology in routine clinical use are knowledge-based systems, also known as expert systems. A knowledge-based approach focuses on the construction and maintenance of a knowledge base and inference engine based on knowledge elicited from literature and experts. This is a very time consuming process, among others because interviews with experts should be planned, conducted, and analyzed. Plus, knowledge can change, based on new insights. With the increasing of computational performance of computers, a data-driven approach with the help of machine learning technologies is increasingly being used in healthcare informatics to extract knowledge from data. By using a data-driven approach with the help of machine learning, I expect this will enlighten the process of building and maintaining the CDSS. This idea is supported by the fact that, when interoperability with other systems can be achieved, the CDSS has access to relevant of digital health data - like the EHR - that can be used to optimize the CDSS usability and performance.

1.5 Outline and scope of this thesis
The aim of this thesis is to contribute in knowledge on how to achieve interoperable eHealth technology for primary care and how to utilize this interoperability for decision support on a data-driven approach with the help of machine learning. The first part of this thesis focuses on the awareness and needs of healthcare professionals when using eHealth technology in primary care. This information was assessed by means of interviews that were held among thirty-three healthcare professionals when using eHealth technology in primary care. This information was assessed by means of interviews that were held among thirty-three healthcare professionals when using eHealth technology in primary care.

Figure 1.1. The eHealth pyramid of Rooij et al.3.
Chapter 1 | General introduction

professionals from seven different Dutch primary care centers. Chapter 2 describes how the results of these interviews have led to the identification of requirements for and barriers towards interoperable eHealth technology in primary care.

Chapter 3 focuses on the needs of healthcare professionals with respect to new eHealth technologies. This has resulted into an overview of promising eHealth application areas in primary care. One of these areas is a CDSS that supports efficient triage and referral of patients to, and within, primary care. Chapter 3 also shows the initial design of a CDSS for the triage and referral of patients with low back pain (LBP). This design can be used as a roadmap for the development of similar systems for all musculoskeletal complaints.

The second part of the thesis focuses on data-driven machine learning in the development of CDSSs, with the development of the CDSS for referral of LBP as application area. Chapter 4 describes the identification of classification factors that are used in care practice to enable an appropriate decision for the triage and referral of LBP complaints. A subset of these classification factors are needed in the self-referral process of a patient with LBP. Based on this subset of classification factors, chapter 5 describes a vignette study that was performed among general practitioners and physiotherapists to collect cases on LBP with a corresponding self-referral advice. This way, I could identify the relationship between the classification factors and the provided self-referral advice. Chapter 6 describes how these cases were used in the training and evaluation of three machine learning algorithms for self-referral decision support on LBP in primary care. Chapter 7 focuses on data-driven machine learning in the development of a CDSS that supports healthcare professionals in their decision for further referral and treatment of patients with LBP.

In Chapter 8, I revisit the issue of interoperability and propose an interoperable eHealth reference architecture for primary care that is optimized for HIE and the use of CDSSs that utilize all available data. Here, the aforementioned CDSS for LBP was used to show how this reference architecture can be used.

Finally, in Chapter 9 I discuss the findings of this thesis and focus on the achievement of interoperable eHealth technology in primary care and how interoperability can benefit the use of machine learning in the development of CDSSs. This chapter also lists directions for future research.
CHAPTER 2
Requirements for and barriers towards interoperable eHealth technology in primary care

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Chapter 2 | Requirements and barriers towards interoperable eHealth in primar care

Abstract
Despite eHealth technology's rapid growth, eHealth applications are rarely embedded within primary care, mostly because systems lack interoperability. This chapter identifies requirements for, and barriers towards, interoperable eHealth technology from healthcare professionals’ perspective — the people who decide when (and which) patients use the technology. After distributing surveys and performing interviews, the authors coded the data and applied thematic analyses. They subdivided results according an interoperability framework to levels of interoperability, as workflow process, information, applications, and IT infrastructure. They found that implementing interoperable eHealth technology in primary care succeeds only when all identified levels of interoperability are taken into account.
2.1 Introduction

EHealth refers to the use of computer based technology within a healthcare environment, and includes many applications, varying from electronic health records (EHRs) to specific telemedicine applications, mobile health, and websites that support patients in self-management. Despite the rapid growth and promises of eHealth, its applications are rarely embedded within primary care. In the literature, one frequently mentioned barrier towards successful implementation of eHealth in healthcare is the lack of interoperability. This barrier also applies to the domain of primary healthcare. With this in mind, we implemented a study to identify the issues involved, while also outlining the requirements for successful interoperability in primary healthcare. We focused on the healthcare providers’ perspective, because they’re the key stakeholders who decide when (and which) patients use eHealth, and they’re the primary drivers to decide about the purchase of eHealth applications. Knowledge on requirements and barriers, elicited from these key stakeholders, can be used to create properly interoperable technologies and implementation strategies for a durable interoperable eHealth infrastructure. Before we delve into the findings of our study, though, first let’s consider some background information.

2.2 The Background Elements of Interoperability

Interoperability is defined as the ability for two or more systems or components to exchange information and use the information that has been exchanged. In recent years, interoperability has become a manifest presence, due to omnipresent connections of databases to the Internet and an increasing need among professionals to share data. In this need for easy and swift data exchange among professionals, the healthcare sector is no exception.

Healthcare interoperability applies at different levels. Philip Scott distinguishes two: syntactic (grammatical) and semantic (logical). Syntactic interoperability lets systems process correctly structured information at a technical level, while semantic interoperability lets software systems interpret and validate the exchanged information by a safe reproduction of the contextual meaning of this information. Recently, the European Antilope project for advancing eHealth interoperability presented a model with six interoperability levels (see Figure 2.1), called the eHealth European Interoperability Framework (eELF)-refined interoperability model. This model includes the semantic and syntactic levels, classified under their levels of information, applications, and IT infrastructure. Each level in the model shows the need for close cooperation and agreement by different stakeholders to achieve well-organized information exchange.
Together with this framework, the European Antilope project offers a set of use cases, a glossary of interoperability terms and definitions, and a template for the description of use cases. With these tools, stakeholders can achieve a shared definition of interoperability levels. These use cases are the practical starting points in the realization of interoperability within an eHealth project. Based on these use cases, some corresponding realization scenarios have been established. Where possible, these scenarios have been based on existing interoperability profiles and underlying standards.

The EHR is the specific feature that has boosted the importance of interoperability in healthcare. This digital patient dossier should be linked to all different health information systems (HISs) to inform healthcare professionals at the right time and place, and to ensure correct, up-to-date patient information. Jan Walker and her colleagues calculated that complete interoperability among US HISs could result in saving $77.8 billion a year due to, for example, preventing unnecessary lab tests. Besides cost savings, interoperability can also improve patient safety, as physicians are less likely to make errors when they have a complete and up-to-date dataset during their working processes.

Despite these potential benefits, the actual degree to which we can consider the implementation of an electronic health information exchange (HIE) between interoperable HISs is quite limited. For instance, Denmark, which has one of the most efficient healthcare systems in the world, has a low rate of HIS interoperability, due to the fact that healthcare technologies were developed without coordination.
and a centralized approach. Other countries have similar situations, resulting in large US and European initiatives that have been launched to accelerate HIE’s implementation. One of the most notable initiatives is Health Level Seven International (HL7) that develops standards to facilitate information exchange among healthcare systems.

In reviewing the HIE issue, Patricia Fontaine and her colleagues identified four types of benefits and five types of barriers towards interoperability within primary care. Benefits included improved quality of care and cost savings, while barriers included costs, security and privacy issues, and liability. In the Netherlands, an interview study was carried out regarding healthcare professionals’ views on the benefits and problems associated with the introduction of an interoperable EHR. Benefits mentioned were the availability of up-to-date information and improved quality of care, while potential problems included privacy risks, information overload, and liability issues. None of these studies, however, listed the requirements that healthcare professionals have for implementing interoperable technologies into their daily practice.

2.3 Methods
To better understand the healthcare professionals’ perspective, we identified requirements and barriers by means of a two-step approach. First, we sent online surveys to healthcare professionals at seven primary healthcare centers. In this survey, we questioned participants about demographics, digital skills, technology use within their primary care center, their understanding of the scope and value of eHealth, and their experiences with (and expectations of) such technologies.

Examples of questions we used in the online survey are What is the ideal percentage of your working time in IT usage? and What is the actual percentage of your working time in IT usage? We aimed to find out if there’s a discrepancy between participants’ ideal and actual IT usage. Another question we used is To what extent does the use of computer software facilitate your working processes at this moment? We anticipated that peoples’ current experiences with IT would predict their acceptance of new technologies, and might serve as a trigger for them to discuss possible barriers towards eHealth’s implementation.

After completing the online survey, we interviewed most of the participants. These interviews were semi-structured: a first set of questions was adapted or supplemented by questions brought forth by each completed survey. For example, a general practitioner addressed in the online survey that online triage before online scheduling by a patient is a crucial functionality, which resulted in the interview questions What is the reason why this is important, as this can also be done by the assistant? and Can you describe this online triage scenario you have in mind? To encourage participants to talk about certain topics and identify where new technologies can benefit working processes, we started each interview with asking the participant to describe his or her normal working day.
Chapter 2 | Requirements and barriers towards interoperable eHealth in primary care

The basic interview setup addressed the following topics:

- describing the schedule of a typical day at work;
- describing the process of a specific task that could be facilitated by means of eHealth;
- specific characteristics of the primary healthcare center that possibly influence the deployment of new technology;
- the center’s technical infrastructure (addressed if the participant was knowledgeable on this topic);
- characteristics of the patient population (percentages of patients with a chronic disease, socio-economic state, educational level, and so on);
- IT skills of colleagues;
- decision making concerning IT and eHealth purchases;
- positive and negative work-related experiences with IT; and
- future expectations of eHealth implementation.

We audio recorded and transcribed all of the interviews. We imported these texts, along with the participants’ responses to the online survey items, into Atlas.ti, which is a software package for performing qualitative data analysis.

Figure 2.2. Final thematic map, showing the main themes. The themes are related to each other, as indicated by the lines used in the thematic analysis. For example, a primary care center may already use technology with certain functionalities and issues. Also, the healthcare professionals in this center have requirements on (new) technologies. The found data on this center are then labeled according to these themes.
Next, we applied thematic analysis using Virginia Braun and Virginia Clarke’s guidelines. We created a first coding scheme based on the interview scheme and aimed at describing the interviewees’ technical infrastructure, and wishes for and problems with eHealth technology. During the data analysis, we derived new codes from the data, in which case we added them to the code scheme and reconsidered all previously assigned codes. After the thematic analysis, we linked and visualized all the themes in a thematic map (see Figure 2.2).

2.4 Results
Now that we detailed the methods used, let’s review the results.

2.4.1 Participant Characteristics
In total, 33 healthcare professionals, working in seven different Dutch primary care centers, participated in our study. Twenty-seven of the participants are healthcare professionals: nine general practitioners, eight nurse practitioners, nine physiotherapists, and one district nurse. This was the main target group of this study. The other six participants support some of these healthcare professionals during their working processes, namely five doctor’s assistants and one pharmacy assistant. From these 33 participants, 25 people (76 percent) both filled in the online survey and were questioned during an interview; three (5 percent) only filled in the online survey, and five (9 percent) were interviewed only. Most of the participants were between the ages of 40–49 (30 percent), with slightly more than half of the participants being women (54 percent), and most participants being highly educated (78 percent completed degrees at a university or college).

![Figure 2.3. Functional requirements brought forth by general practitioners (GP), nurse practitioners (NP), physiotherapists (PT), doctor’s assistants (DA), and other professions.](image-url)
Chapter 2 | Requirements and barriers towards interoperable eHealth in primary care

Figure 2.4. Nonfunctional requirements brought forth by GP, NP, PT, DA, and other professions.

Figure 2.5. Barriers brought forth by GP, NP, PT, DA, and other professions.
2.4.2 Requirements and Barriers
Figure 2.3 presents the functional requirements identified by participants. Figure 2.4 presents the nonfunctional requirements, and Figure 2.5 presents the barriers.

2.4.2.1 Functional requirements
The analyses resulted in 21 functional requirements. The functional requirement identified most was “patient monitoring.” This implies self-monitoring of health parameters by the patient (such as blood values, heart rate, electrocardiogram, and spirometry) with automatic HIE from patients’ homes to the primary healthcare center. Nurse practitioners were especially interested in these requirements, as they guide patients with a chronic disease and thereby the general practitioners. Based on the measured values, the healthcare professional can decide to see a patient earlier or later than planned.

The top five functional requirements also show “patient coaching,” and “patient training.” These terms are often used interchangeably. The term “coaching” here refers to the activity that the patient is coached in, such as smoking cessation or weight loss. “Training,” on the other hand, concerns the availability of an online training program that provides physical or mental exercises by means of movies, pictures, or just text. Physiotherapists identified both “coaching” and “training” as the most important functional requirements.

Finally, the list contains the functional requirements “booking of appointment,” “prescription refills,” and “eConsult.” These are often part of a patient portal that’s integrated with websites of primary care centers. Although these functionalities are already available in most centers, often these functionalities weren’t integrated yet in the current IT infrastructure. This means that data obtained from a portal still must be imported manually into other systems, leading to extra actions in working processes, and therefore interviewees indicated these functional requirements in the context of interoperability.

2.4.2.2 Nonfunctional requirements
Besides 21 functional requirements, the analyses also resulted in 14 nonfunctional requirements. Figure 2.4 shows that the requirement “easy to use” is clearly first place in the list and named by all professions. Participants mentioned such terms as “user-friendliness,” “clarity of the technology,” and “as few as possible steps on the screen to perform a task” in this context. The list also shows the nonfunctional requirements added value of technology on workflow efficiency and added value of technology on quality of care. “Added value of technology on workflow efficiency” means that the technology should improve the working processes by, for example, decreasing the amount of necessary steps taken during a working procedure. “Added value of technology on quality of care” means, for example, providing the healthcare professional with timely up-to-date health information of patients to improve patient care.
Chapter 2 | Requirements and barriers towards interoperable eHealth in primary care

2.4.2.3 Identified barriers

Our analysis resulted in identifying 20 barriers. The barrier identified most was users’ technological illiteracy. The participants used words such as “computer skills of end users,” “time needed to learn new technology,” and “unaccustomed end user” in this context. The participants indicated that a lack of skills in using technology leads to ineffective usage, or even nonusage. Close to the barrier of users’ technological illiteracy is the barrier of the end user’s attitude. One often-mentioned factor with regard to the end user’s attitude was that the end user explicitly must see the benefits of the technology’s use — otherwise, he or she won’t use it.

Participants also mentioned “technology failure” as a barrier. Some of them had negative experiences with IT solutions, due to technological failures. In most cases, they didn’t try this IT solution again. When the use of said technology was imposed, they were reluctant to use these IT solutions. Another important barrier found was costs. It appears that in each visited primary care center, there’s no clarity regarding the reimbursement by patients’ medical insurers. This restricts healthcare professionals in implementing new technologies. One participant put it this way: “If financing was not a problem, we would have been many steps further with the implementation of eHealth technologies.” None of the respondents had mentioned cost savings as a nonfunctional requirement. Probably, the participants were more focused on the investments that must be made, not realizing that this, on the other hand, might also lead to cost savings — for example, by reducing paper-based workflow processes.

2.4.2.4 Requirements, barriers, and interoperability levels

We can subdivide the identified requirement and barriers to the interoperability model’s various levels (see Figure 2.1). Table 2.1 shows the results. The indicated levels specify with which goal a close cooperation among different stakeholders is needed to achieve the implementation of interoperable eHealth technologies that meets these requirements and overcomes these barriers.

During the interviews, not all the processes mentioned by the interviewees were care processes. For example, the requirement “Easily accessible helpdesk” refers to the handling of a helpdesk procedure in case of a technical problem. Therefore, we translated the level “care process” in the model into “workflow process.”
Table 2.1. Requirements and barriers related to interoperability levels.

<table>
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<tr>
<th>Interoperability level</th>
<th>Functional requirements</th>
<th>Nonfunctional requirements</th>
<th>Barriers</th>
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<td>Speed of technological development</td>
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<td>Workflow process</td>
<td>Patient monitoring</td>
<td>Added value of technology on workflow efficiency</td>
<td>Users’ technological illiteracy</td>
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<td>Patient education</td>
<td>Added value of technology on quality of care</td>
<td>Anxiousness for extra work</td>
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<td>Patient coaching</td>
<td>Education in technology usage</td>
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<td>Patient training</td>
<td>Fast problem solution</td>
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<td>consultation</td>
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<td>Information</td>
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<td>Interpretable data</td>
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<td>Applications</td>
<td>Video consult</td>
<td>Easy to use</td>
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2.5 Discussion
This study identified functional and nonfunctional requirements for, and barriers towards, interoperable eHealth technology from the perspective of healthcare professionals in primary care. Most barriers we identified were of a legal, literacy, financial, or technical nature and are similar to those found when implementing the electronic HIE$^{12,43}$.

Based on these legal, literacy, financial, and technical issues, we related the identified requirements and barriers to the interoperability framework, developed within the European Antilope project$^{36}$. This framework has six interoperability levels, namely legal and regulatory, policy, care process, information, applications, and IT infrastructure. Each one represents a level in which different stakeholders must cooperate on agreements to achieve a well-organized information exchange. (These stakeholders are also shown in the gray part of Figure 2.1.) The different interoperability levels, however, strongly affect each other, and some stakeholders are involved at different interoperability levels. Consider, for example, the following scenario:

A nurse practitioner wants to monitor the blood pressure of a patient at home as part of her care process (the workflow process level). This blood pressure should be expressed according to a semantic standard (the information level), so this information can be used in an unambiguous way in different systems. An application for monitoring patients’ blood pressure at home (the application level) sends its data automatically to the center through the Internet (the IT infrastructure level).

In this example, agreements on standards between different stakeholders are needed at all levels. At the level of the working process, healthcare professionals must adopt workflow directives in the care process. These workflow directives must ensure a standardized working process on remotely monitoring patients’ blood pressure and describe the units in which these blood pressure values should be expressed.

At the information level, these blood pressure values should be expressed in an unambiguous way and in a certain context based on the agreements made at the workflow process level to achieve semantic interoperability. Stakeholders involved in semantic interoperability are information architects and business analysts, together with healthcare professionals. In healthcare, a commonly used terminology standard to achieve semantic interoperability is SNOMED CT$^{45}$.

An application that enables remote monitoring of patients’ blood pressure at home must be able to process information as defined at the information level. Therefore, at the application level decisions are made about setting up technology that meets the requirements for information processing (as defined at the information level). Stakeholders involved in achieving interoperability at the application level are information analysts, coders, system architects, and system engineers.
Finally, at the IT infrastructure level, there should be an agreement on the standard used for electronic data exchange. In healthcare, HL7 is an organization that provides a comprehensive framework and related standards for the exchange, integration, sharing, and retrieval of electronic health information that supports clinical practice and the management, delivery, and evaluation of health services.

The example scenario shows interaction between stakeholders at the following interoperability levels: workflow process, information, application, and IT infrastructure. Table 2.1 shows that the largest part of the identified functional and nonfunctional requirements and barriers found in our study are related to these levels, and are in control of the healthcare professionals, together with IT professionals. However, Table 2.1 also shows one nonfunctional requirement and four barriers at the legal and regulatory and policy interoperability levels. These levels are beyond the control of healthcare professionals and must be addressed by policymakers, regulators, advisors, and healthcare managers.

When comparing our results to the literature, we see some similar results. Fontaine\textsuperscript{12} and Marieke Zwaanswijk and her colleagues\textsuperscript{43} both identified benefits and barriers. In our study, we used the term ”nonfunctional requirement” instead of “benefit,” because we also identified functional requirements. We didn’t find literature on functional requirements on eHealth technology from the viewpoint of healthcare professionals. Nonfunctional requirements that we identified, that were also found previously, are the added value of technology on workflow efficiency and quality of care\textsuperscript{12,43}, and the importance of the availability of useful workflow directives\textsuperscript{43}. Barriers that were previously identified, and which are reconfirmed in this study, are costs and a lack of instruction on technology usage by a lack of IT training and support\textsuperscript{12}, and the limited speed of the network for electronic information exchange\textsuperscript{43}.

Fontaine\textsuperscript{12} also mentions the benefit of cost savings. Surprisingly, the respondents in our research didn’t mention this, probably because (as we mentioned previously) our participants were more focused on the investments needed to purchase new technology, and not realizing that conversely this also might lead to cost savings by reducing paper-based workflow processes. Zwaanswijk\textsuperscript{43} also mentioned barriers we didn’t identify — namely, the possibility of information overload, and the unclear regulation regarding liability of the healthcare professional for information from outside sources. We can only conclude that such concerns (which are valid) don’t live among healthcare professionals in primary care. This can be due to the fact that they’re unfamiliar with these issues, or don’t consider them important. A new, previously unidentified, barrier we found is the concern about the speed with which new technology develops. Often, once purchased, technology is soon overtaken by new solutions, making it difficult for healthcare professionals to decide which technologies to purchase and at what time.
Chapter 2 | Requirements and barriers towards interoperable eHealth in primary care

As we mentioned, we performed our study in Dutch primary healthcare centers. And although the organization of healthcare differs from one country to the next, we firmly believe that the requirements and barriers we identified can be generalized to other countries. The problems that healthcare systems in the Western world face are similar: They must deal with an aging population and an increasing number of patients with a chronic disease. Although worldwide eHealth technology has been named often as a possible solution for coping with the growing demand on healthcare at reasonable costs, societal issues that hinder or increase the success of interoperability are alike. Applications are developed as silos and don’t communicate. The policies that are developed to integrate these technologies (such as those developed by the Ministry of Health in the Netherlands and that of the National Health Service in the UK) are similar. An important note that this research adds is that such policies should incorporate solutions to satisfy the needs and take away the barriers at all the different levels (legal, organizational, semantic, and technical). Only then will healthcare professionals adopt eHealth in their daily work, so that we can reap the envisioned benefits of eHealth technology.
CHAPTER 3
Clinical decision support systems for primary care: the identification of promising application areas and an initial design of a CDSS for lower back pain

Published:
Oude Nijeweme - d’Hollosy W, van Velsen L, Swinkels I C, Hermens H.
Abstract
Decision support technology has the potential to change the way professionals treat patients for the better. We questioned thirty-three healthcare professionals on their view about the usage of eHealth technology within their daily practice, and areas in which decision support can play a role, to lower healthcare professionals’ workload. Qualitative analysis resulted in an overview of desired eHealth functionalities and promising areas for decision support technology within primary care. Based on these results, we discuss future work in which we will focus on the development, and evaluation of a clinical decision support system (CDSS) for advising patients with physical complaints on whether they should see a healthcare professional or can perform self-care. Next, the CDSS should advise healthcare professionals in selecting relevant training exercises for a specific patient. In first instance, this CDSS is focused on diagnostic triaging and selection of training exercises for patients with nonspecific lower back pain.
3.1 Introduction
In the last decades, the focus of healthcare has shifted from providing intramural and curative care, towards offering extramural care, self-care, and prevention. This shift of healthcare delivery from secondary towards a primary care setting is the result of the World Health Organisation Alma-Ata Declaration \(^{46}\). This states that the need for care has to be centered within the primary care setting \(^{47}\). As a consequence, the role of primary care professionals (such as general practitioners, nurse practitioners and physical therapists) has changed: They have to deal with a wider range of chronic conditions and an increasing number of patients.

Simultaneously, we are witnessing the rise of eHealth technology. eHealth can be defined as “Health services and information delivered or enhanced through the Internet and related technologies” \(^{44}\). Primary care professionals may use eHealth technology to cope with their increasing workload. eHealth technology can, for example, support care professionals in the care of patients with a chronic condition. Remote monitoring in combination with alerting for action when needed can help to reduce the number of standard consults that are normally scheduled to monitor a patient’s condition. Another, more generic, example is that eHealth technology can facilitate video consults or e-consults with patients. Finally, eHealth technology can support patients in their independence and self-management \(^{6}\), for example by showing them relevant exercises for the day or giving recommendations on how to stop smoking.

Next to the support of daily care, eHealth technology can also be used to support primary care professionals in expanding their expertise. This is becoming a prerequisite now that a great amount of care is moving from a specialized, secondary setting to primary care. Online information sources with evidence-based medical information and clinical decision support systems (CDSSs) can be very valuable here \(^{48}\).

In this chapter, we describe a study that sought to identify application areas within primary care in which CDSSs may enlighten the workload as seen from the viewpoint of healthcare professionals. Literature shows that a close cooperation with the intended end-users is an important step in the design and development of fit-for-purpose-technologies \(^{49}\). It is important to understand the end-users opinions, perspectives and work processes, as also shown by a study of general practitioners’ perspectives on electronic medical records systems \(^{50}\), to improve user adoption of the new technology, and to ensure that the system functionalities will fit into the working processes of the end-users. This certainly also applies to the development of CDSSs.

To find the intended CDSS application areas, we performed in-depth semi-structured interviews with 33 key players in primary care, including general practitioners, nurse practitioners, and physical therapists. From the wishes the interviewees voiced on eHealth functionalities, we deduced the most promising application areas for a CDSS.
3.2 Related Work
Since the 1960's CDSSs have been developed to support the clinical decision process of healthcare professionals. Musen et al.\textsuperscript{19} define a CDSS as “any computer program designed to help healthcare professionals to make clinical decisions”. From this perspective, key decision support functions are information management, managing clinical complexity and details by alerting, cost control, and decision support by providing patient-specific recommendations\textsuperscript{19,21}. Providing patient-specific recommendations covers the assistance in the determination of a diagnosis, providing advice on therapy, or both diagnostic assistance and therapy advice.

Famous examples of early CDSSs on providing patient-specific recommendations are INTERNIST-1\textsuperscript{51}, MYCIN\textsuperscript{52}, and ONCOCIN\textsuperscript{53}. These systems were experimental and intended for use by internists and oncologists. Later, the development of CDSSs has evolved to CDSSs to be used in daily care\textsuperscript{54}, such as the paediatric clinical decision support system ISABEL\textsuperscript{35}. Over time, CDSSs have been shown to improve both patient outcomes and cost of care by prompting, reminding and cautioning clinicians whether or not to do certain things under specific clinical circumstances\textsuperscript{22}.

Nowadays, CDSSs are also used in daily primary care. In the Netherlands, 89 percent of the general practitioners have some form of clinical decision support on their systems\textsuperscript{24}. CDSSs in primary care are mainly used for prevention and screening, drug dosing, medical management of acute diagnoses and chronic disease management\textsuperscript{23,24}, through the usage of alerts and computerized protocols.

The possibilities of CDSSs will improve when all necessary information is available at the right place at the right time for a specific task. However, at this moment information in primary care is mainly available as data stored in isolated IT systems. Therefore, interoperability among these systems is a must. Interoperability is defined as the ability for two, or more, systems or components to exchange information and to use the information that has been exchanged\textsuperscript{25}. Interoperable systems in primary care further enlarge the possibilities for new application areas for CDSSs. Therefore, several large projects have recently started with the aim of achieving interoperability among Healthcare Information Systems, such as ANTILOPE\textsuperscript{36} or eLabEL\textsuperscript{56}.

3.3 Methods
We held in-depth, semi-structured interviews with professionals working in primary care to identify promising applications for eHealth that may enlighten the workload as seen from the viewpoint of these healthcare professionals. Before each interview, an interviewee received a link to an online survey. This survey contained questions about demographics, self-esteemed digital skills, use of technology within their primary care center, their understanding of the scope and value of eHealth technology, and their current experiences with, and future expectations of, eHealth technologies, including CDSSs.
During the interviews, the following subjects were addressed:

- A typical day at work;
- Characteristics of the patient population, such as percentages of typical chronical illnesses, social economic status, educational level;
- Describing the process of a specific task that appeared to be suitable for eHealth or CDSS support;
- Positive and negative work-related experiences with IT.
- Future expectations of eHealth at their workplace.

All interviews were audio-recorded, transcribed, and coded and analyzed in Atlas. ti. Next, thematic analysis was applied, using the guidelines by Braun and Clarke. A first coding scheme was created based on the interview scheme. During this thematic analysis, new codes could be derived from the data, in which case they were added to the code scheme, and all previous codes were reconsidered.

### 3.4 Results

#### 3.4.1 Interviewee Demographics

Thirty-three healthcare professionals, working in primary care, participated. They worked in seven different primary care centers spread around the Netherlands. The group of respondents included nine general practitioners, eight nurse practitioners, nine physiotherapists, and one district nurse. The other six participants were doctor's assistants (five) and one pharmacy assistant that support these healthcare professionals during their work processes.

#### 3.4.2 Promising CDSS Areas as identified by the Interviewees

The interviews led to nine application areas for CDSSs in primary care, which are shown in Figure 3.1.

![Figure 3.1](image_url)  
*Figure 3.1. Identified CDSS application areas brought forth by general practitioners (GP), nurse practitioners (NP), physiotherapists (PT), doctor's assistants (DA), and other professions (Other).*

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*Clinical decision support systems for primary care | Chapter 3*
Chapter 3 | Clinical decision support systems for primary care

The identified CDSS application areas can be related to different levels of patient care: general patient care and care for patients with a chronic condition. General patient care comprises visits to the primary care center with acute problems, such as a sprained ankle or a persistent cough. Patients with a chronic condition are patients that are seen regularly by a nurse practitioner (e.g., every three months) and once a year, or in the case of an exacerbation, by a general practitioner. Therefore, it is not surprising that ´patient monitoring´ in combination with an ´alert system´ is mainly preferred by nurse practitioners. One interviewee mentioned this as follows:

“If the possibility of automatic patient monitoring exists, it would be most ideal when a system also provides an alert as “this lady has these monitored blood sugars and this average is too high.” Furthermore, it would be nice to have a list of patients within our own information system that works with colors, with on top the patients with red and orange states. Then you know at once which patients need the most attention.”

Another application area in which a CDSS can play a critical role is ‘Patient education’. Patients can be provided with relevant information, for example, to perform self-care. A well-informed patient is in a better position to perform self-management when confronted with health problems. In the Netherlands, general practitioners, nurse practitioners, and doctor's assistants often encourage patients in self-care by referring to http://www.thuisarts.nl, a website with reliable and independent information about health and disease based on clinical protocols. This website was developed, and is managed, by The Dutch College of General Practitioners (NHG). The NHG is the scientific society of Dutch general practitioners with the mission to improve and to support evidence-based general practice. An English equivalent of thuisarts.nl is http://www.webmd.com/. A CDSS that automatically shows webpages containing relevant information, based on already known health data of a patient will aid patients’ online information-seeking behaviour in a more intelligent and safe manner.

The functionalities ‘patient coaching’, and ‘patient training’ are often mixed. The term ‘coaching’ refers to the activity that the patient is coached in, like smoking cessation or improving one’s lifestyle. The term ‘training’ refers to online training programs that provide and guide patients through a scheme of physical or mental exercises by means of movies, pictures, and text. These training exercises are prescribed by the healthcare professional and patients should perform these exercises at home to improve their physical or mental condition. However, in practice, these schemes are often not adhered to by patients. During the interviews, ‘patient training’ was mainly mentioned in the context of care of patients with musculoskeletal/sports problems within primary care. For example, the following comment was given by a general practitioner during an interview:

“I now have a print-out with pictures of some exercises for low back pain and neck pain, sore shoulder, knee problems. These are the most common complaints. People are happy to be guided in this. It would be nice to have our own physical therapist, or
a website of physical therapy, that supports the selection of proper training exercises for a specific patient. A website with physical therapy exercises that people can already perform or can be searched. And yes, thuisarts.nl also provides information on back pain and related exercises, but there are no pictures, only text. That is not enough support for people”.

A CDSS on training advice can support healthcare professionals in selecting suitable exercises for a patient. These exercises help the patient with a given complaint and can be executed at home in a safe manner. Such a personalized advice can improve patients’ adherence to such schemes, which is currently low to very low. Next, a website with exercise movies is better equipped in explaining how patients should perform their exercises correctly and safely.

The application areas ‘triage’ and ‘the preselection of the relevant health care professional’ are related to actions prior to the visit of a patient to a primary care center. In this context we can also take into account the application area ‘questionnaires as pre-consult’. During the interviews, all physiotherapists indicated that they ask patients to fill in a questionnaire about their complaints prior to the first visit as pre-consult. During the consult, information gathered through these questionnaires helps the physiotherapist in setting the right diagnosis. A CDSS that helps a patient through a triage process, and that also involves the relevant pre-consult questionnaires during this process, will save time during the first consult. Next, the outcome of the triage process can also give advice whether to perform self-care, as described in the context of ‘patient education’, or give advice which healthcare professional in the primary care center can best be consulted based on his or her expertise.

Figure 3.1, finally, also lists ‘prescription refills’ as a CDSS application area. CDSSs on drug dosing already have quite a tradition and are described in detail in the literature.

3.5 Discussion

By means of an interview study, we identified a set of application areas in which Clinical Decision Support Systems (CDSSs) can aid healthcare professionals within primary care. In literature, CDSS applications described most are focused on diagnostic assistance, managing clinical complexity and details by alerting, and providing advice on therapy. However, the application areas ‘triage’ and ‘patient training’ have little or no existence in primary care at this moment.

With ‘triage’ we see promising possibilities for web-based triaging by patients themselves. In fact, this may also be a supplement on diagnostic assistance. An online triage CDSS can give a patient advice whether to see a healthcare professional, or to perform self-care, in an intelligent and safe manner. This advice is then based on answers given by the patient on triage questions. Subsequently, information gathered during the triage process can be used by the healthcare professional to
have a more efficient consultation. Avoiding unnecessary visits to the centre, by providing the patient with self-care information when applicable, will reduce healthcare costs and unnecessary burden for the patient. Next to ‘triage’, we also see ‘patient training’ as a promising CDSS application area in primary care in the context of patient rehabilitation. A CDSS that informs patient training can support healthcare professionals in the selection of the exercises that match the situation of an individual patient best.

A CDSS can be a stand-alone system. However, decision support by a CDSS can be made more efficient and easy to use when it becomes integrated with current available information systems. In other words, when different systems become interoperable and can exchange data, computerized decision support becomes more powerful. For example, when a CDSS becomes interoperable with information systems that contain a patients’ electronic health record (EHR), EHR information can then be used as additional information to improve the CDSS advice. Despite the fact that interoperability in healthcare is still a challenge, it is important to take into account the future possibilities of interoperability in healthcare when developing a new CDSS application. Also a close cooperation with the intended end-users has still be important in selecting what systems have to be connected to exchange data in relation to working processes.

3.5.1 Future Work
Driven by the findings of our interview study, we will develop a CDSS that consists of a triage part and a training-recommender-and-rehabilitation-part for matching patients to a suitable healthcare professional or self-care advice, and for selecting a personalized rehabilitation scheme for the domain of musculoskeletal/sports problems. Within primary care, such problems are commonly dealt with by a general practitioner or a physiotherapist. And in the Netherlands patients can see a physiotherapist for a complaint without a referral from their general practitioner (so-called self-referral). This certainly has improved the choice of care for the patient, but this also requires from a patient that he or she exactly knows when it is best to visit a general practitioner, to visit physiotherapist, or to perform self-care. An online web-based triaging CDSS will be helpful for patients in making this decision.

Next to triage, the CDSS will, subsequently, support healthcare professionals in the selection of the rehabilitation training exercises that are most suitable for a specific patient, and support patients in the individual rehabilitation process at home. We expect that personalized treatment schemes, and a system that encourages patients to perform exercises at home, will improve patient adherence.

The domain of musculoskeletal/sports problems is still a large domain. Therefore, we initially will focus the CDSS on the domain of lower back pain (LBP). On this topic, evidence-based clinical guidelines regarding diagnosis and treatment exist. These guidelines will form a solid starting point in the design of the triage part of the CDSS. Another reason for developing a CDSS for lower back pain is because
literature on CDSS for diagnostic triaging on LBP is sparingly\textsuperscript{62,63}, although more than 80 percent of the people will have significant LBP at some point in their life. About 20 percent of the LBP patients develop a chronic problem, which is debilitating for the patient and costly for society\textsuperscript{64}. Therefore we want to avoid the development of acute LBP to chronic LBP as much as possible, a process that starts in primary care by identifying those acute LBP patients that are susceptible to develop chronic LBP. Furthermore, the guidelines on LBP also indicate that most patients with acute problems and a normal course of LBP can be helped by information to perform self-care at home by keeping active. This can also be guided by the CDSS rehabilitation part. From this all, it can be concluded that using LBP as a case in the development of our CDSS has a high relevance for improving healthcare.

The next sections describe both the CDSS triage part and a training-recommender-and-rehabilitation-part, that are also subsequently shown in Figure 3.2 and 3.3.

3.5.1.1 The CDSS triage part

The CDSS triage part (Figure 3.2) will guide patients through a decision process that has one of the following three outcomes:

1. To see a general practitioner, or
2. To see a physiotherapist, or
3. To perform self-care.

The primary end-users for the CDSS triage part will therefore be patients. Patients use the CDSS triage part before the first visit on acute LBP. In order to achieve one of the three possible outcomes, the CDSS triage part will use

- Answers on triage questions,
- Information about a patient from the EHR in the Medical Information System (MIS) when the CDSS and the MIS are interoperable, and
- General knowledge on specific and non-specific LBP.

When the patient is visiting a healthcare professional, this healthcare professional has access to the answers of the patient, given during the triage process. This information will enable a more in-depth, and efficient, consult with the patient, because basic questions on the problem have already been posed by the CDSS.

The usage of this CDSS part should lead to a decreasing number of visits of patients with LBP in primary care, because patients that can handle their LBP with self-care will be filtered beforehand. However, patients with serious underlying conditions or suffering from psychosocial factors must be detected and referred to the most suitable healthcare professional for further examination.
Figure 3.2. Visualization of the CDSS triage-part. In this figure, the HIS is the medical information system of the general practitioner, and the FIS is the medical information system of the physiotherapist.
Figure 3.3. Visualization of the CDSS training-recommender-and-rehabilitation-part. In this figure, the HIS is the medical information system of the general practitioner, the FIS is the medical information system of the physiotherapist, and RRD COCO web service the external training and exercise coaching program.
3.5.1.2 The CDSS training-recommender-and-rehabilitation-part

Based on the diagnosis made by the healthcare professional, the CDSS training-recommendation-part (Figure 3.3) will provide the healthcare professional with a recommendation on a personalized training scheme with exercises for a given patient. Therefore the primary end-user of this CDSS part is the healthcare professional.

Normally, general knowledge on LBP is used to relate to appropriate exercises as specified in guidelines on LBP. Worldwide, general practitioners and physiotherapists use guidelines in the clinical evaluation and classification, and management of LBP. However, literature shows that guideline adherence by professionals is not always the case due to various barriers these professionals met when they try to incorporate these clinical guidelines into their care practice. The adherence varies between general practitioners and between guideline recommendations. Therefore, this CDSS might also help to improve guideline adherence by health care professionals.

The given recommendation of the CDSS training-recommendation-part is based on

- Information retrieved by the CDSS triage part (when available), and
- Information provided by the healthcare professional which is retrieved during the consult with the patient, and
- Already available information on this patient as stored in the EHR in the medical information system (MIS) when the CDSS and the MIS are interoperable, and
- General knowledge on specific and non-specific LBP.

In this list of information sources, the input of information retrieved by the CDSS triage part is optional. When this information is available, the treatment advice can be more precise, but it should also be possible to use the CDSS training-recommendation-part as a single component, independent from the CDSS triage-part. On the other hand, when the CDSS triage part advises a patient in self-care, the CDSS training-recommendation-part can be used to provide the patient the most-suited exercises. Although the CDSS provides an advice for a treatment scheme, the healthcare professional should always have the possibility to adapt a recommended scheme of exercises. This is because, ultimately, it is the healthcare professional that stays responsible for a patient’s treatment. Furthermore, there can always be extern reasons, not known by the CDSS, why an advised treatment scheme has to be adapted for a patient by the healthcare professional. Finally, the achieved training scheme of exercises can serve as input for the support of individual rehabilitation of patients at home by an external training and exercise coaching program. In Figure 3.3 this system is called RRD COCO, an already available system. With this extension of the CDSS, secondary end-users of this CDSS part will be patients who perform exercises at home.
3.5.2 Development and evaluation of the CDSS

The development of a CDSS exists of various steps. Prior to the actual development of the CDSS the following parts have to be designed: 1. A knowledge base, 2. An inference engine, and 3. A communication mechanism that defines the human-machine-interaction.

An ontology forms the basis of the design of the knowledge base and the inference engine. An ontology is "a description of the concepts and relationships that can exist for an agent or a community of agents"\(^68\) and defines the vocabulary for a domain and the relations among concepts. During the definition the ontology, we will investigate whether we can make use of available terminology systems to define the ontology. A very suitable candidate for a terminology system will be SNOMED CT as it facilitates semantic interoperability with other Medical Information Systems\(^65\).

The storage and access of knowledge will be determined by the knowledge base, which will be built upon the ontology. We will use Protégé\(^69\) to create the ontology for our application.

A challenge in our future research is that we have to find the optimal knowledge representation format for our CDSS. Knowledge representation formats are, for example, logic-based knowledge representation, procedural knowledge representation, networks (such as Bayesian belief networks), decisions trees, and artificial neural networks. As healthcare is not a static domain and also utilizes casual and temporal knowledge, we will also have to look at formats for representing these kinds of knowledge, taking into account that all of this knowledge will change over time. The latter is known as the “frame of reference” problem\(^70\).

We will start the design of the CDSS by defining an ontology. In this, it is important to know the domain and the end-users. Furthermore, a key issue in building an ontology is term selection. Therefore, we will interview general practitioners and physiotherapists on their approach to the treatment of LBP patients, and the use of guidelines in the clinical evaluation and classification, and management of LBP. Themes in these interviews will include:

- Demographics of the interviewee;
- Expertise of the interviewee on LBP (e.g., how often this health care professional sees a LBP patient, how knowledge on LBP is kept up to date);
- Steps in the clinical evaluation and classification, and management of LBP, by asking out the healthcare professional on specific patient cases;
- Definitions on LBP concepts;
- Future expectations of a CDSS that supports healthcare professionals and patients in the evaluation and classification, and management of LBP.
We will use case descriptions of fictitious patients as a means to identify steps in the clinical evaluation and classification, and management of LBP. These cases will be based on clinical guidelines on LBP. The patients’ cases will differ in a way that the steps in analyzing these cases lead to different outcomes on the clinical evaluation and classification, and management of LBP. This differentiation is made by using so-called red flags and yellow flags in these cases. Red flags indicate LBP problems that are caused by serious underlying conditions and yellow flags indicate psychosocial factors are associated with a poor prognosis of LBP. Next, the cases include differences for demographics, social-economic status, and medical history to elicit tacit knowledge, because we also want to find out if healthcare professionals make decisions not documented in the guidelines, but which are based on personal experience.

Based on these interviews, we will build an ontology. We first will design, develop and implement the CDSS triage part in the near future. The design and development of the CDSS training-recommender-and-rehabilitation-part is planned at a later stage, namely at the moment when exactly is known what kind of information is retrieved by the CDSS triage that can serve as input for the second part of the CDSS. Therefore, this first ontology will define the concepts and inference steps important in the triage process of acute lower back pain.

To evaluate this first ontology, we will present the result to the interviewed healthcare professionals. Based on new patient cases on LBP, these professionals will test this ontology on completeness and consistency. When needed, the ontology will be adjusted, and this process is repeated until a constant ontology has been achieved. Subsequently, the CDSS triage part will be developed, based on this ontology, and then evaluated.

In literature, several systematic reviews can be found on studies that evaluate CDSS on practitioner performance and patient outcomes by means of controlled clinical trials. However, health informatics still lacks well-established instruments and outcome variables to measure efficacy and effectiveness of CDSSs. Because no evaluation instruments are available, our intention is to start the evaluation of our CDSS triage part in a Turing-test setting with healthcare professionals as well as patients. In this way, it becomes possible to compare the CDSS outcomes with the current ways of acute LBP classification as performed by healthcare professionals or doctor assistants. Based on the evaluation results, we will decide when we will start the real implementation of the CDSS triage part in daily primary care.
3.6 Closing Remarks
The interviews we held with thirty-three health care professionals in primary care resulted in a number of promising CDSS application areas. This resulted in a plan for our future work. We will develop a CDSS on the triage, and the recommendation of training exercises, for patients with lower back pain (LBP). The objectives of this CDSS is to provide patients with the advice to see a healthcare professional or to perform self-care. Next, the system will advise healthcare professionals on a personalized treatment scheme with exercises for a patient, and support patients in their rehabilitation process at home (via a web service that includes exercise videos). The objective of such a system is to decrease the number of LBP consults in primary care and to increase treatment adherence. Another important objective is to detect those patients who have problems that are caused by serious underlying conditions, or that are associated with a poor prognosis because of psychosocial factors, in an as early state as possible. This should limit the number of patients developing chronic LBP.
CHAPTER 4
Design of a web-based clinical decision support system for guiding patients with low back pain to the best next step in primary healthcare

Published:
Abstract
Low back pain (LBP) is the most common cause for activity limitation and has a tremendous socioeconomic impact in Western society. In primary care, LBP is commonly treated by general practitioners (GPs) and physiotherapists. In the Netherlands, patients can opt to see a physiotherapist without referral from their GP (so called ‘self-referral’). Although self-referral has improved the choice of care for patients, this also requires that a patient knows exactly how to select the best next step in care for his or her situation, which is not always evident. This chapter describes the design of a web-based clinical decision support system (CDSS) that guides patients with LBP in making efficient choices on self-referral. We studied literature and guidelines on LBP and used semi-structured interviews to question 3 general practitioners and 5 physiotherapists on the classification of LBP with respect to the best next step in care: GP, physiotherapist or self-care. The interview results were validated by means of an online survey, which resulted in a select group of key classification factors. Based on the found results, we developed an ontology and a decision tree that models the decision making process of the CDSS.
4.1 Introduction

Low back pain (LBP) is the most common cause for activity limitation in people, and has a tremendous socioeconomic impact\textsuperscript{75,76}. More than 80% of all persons experience low back pain in their lifetime\textsuperscript{77}. A distinction is made between specific low back pain and non-specific low back pain. Most cases of low back pain are non-specific\textsuperscript{78}. Non-specific low back pain is defined as “pain symptoms anywhere in the lower back between the twelfth rib and the top of the legs, with no recognizable, specific pathology such as infection, tumour, osteoporosis, fracture, radicular syndrome, or cauda equina syndrome that is attributable to the pain sensations”\textsuperscript{79}.

Most people who suffer from non-specific low back pain recover within six weeks, but about 10-15% develop chronic symptoms\textsuperscript{77}. It is not always clear why some people with non-specific low back pain develop chronic low back pain. In literature, multiple risk factors have been identified including abnormal course of the low back pain, patients’ belief and expectations about recovery, anxiety, distress and depression\textsuperscript{64}. Patients with increased risk to develop chronic low back pain should be identified and supported by the most relevant healthcare professional at the earliest possible stage of non-specific low back pain, thereby reducing the development of a chronic condition\textsuperscript{80}, while patients who do not have increased risk profiles, may do well by self-management.

In the Netherlands, patients with musculoskeletal disorders can make use of so-called ‘self-referral’. Patients’ self-referral, or direct access, means that patients can be examined, evaluated and/or treated by a physiotherapist without the requirement of a physician referral\textsuperscript{81,82}. Although self-referral has improved the freedom of choice of care for patients with musculoskeletal problems, it also requires that a patient knows exactly what is the best care for his or her current situation. This, however, is not always evident, especially for those patients new to musculoskeletal complaints.

Swinkels et al\textsuperscript{82} also showed that people who self-refer to physiotherapy receive treatment less often than referred patients and that their mean number of visits is lower. Next to this, Bornhöft, Larsson and Thorn\textsuperscript{83} concluded that patients referred to physiotherapists required fewer GP visits or received fewer musculoskeletal disorders-related referrals to specialists/external examinations, sick-leave recommendations or prescriptions during the following year, compared to patients that were referred to GPs.

Although it may seem that a patient with a musculoskeletal complain is best served by referral to a physiotherapist, there are also situations, in which a patient should indeed go to the GP, or it is sufficient to perform self-care. For example, in case of the presence of so-called ‘Red Flags’, indicating a serious condition, the patient should contact his or her GP\textsuperscript{84}. Therefore, a correct referral for patients with low back pain is essential for effective treatment of patients, leading to decreased chronic conditions. Moreover, efficient treatment alleviates the burden on healthcare. In this
Chapter 4 | Design of a CDSS for patients with low back pain

chapter, we describe a study that identifies key classification factors to be used as the basis for the development of a web-based clinical decision support system (CDSS) that guides patients with low back pain to the best next step in healthcare by advising the patient to 1) see a GP, 2) see a physiotherapist, or 3) perform self-care.

4.2 Related work
4.2.1 Classification of patients with low back pain
In order to enable an appropriate decision for the next step in the care of low back pain complaints, the nature of the pain should first be classified correctly\(^{59,75}\). Classifying patients is, however, a difficult task due to the high degree of diversity of patients and risk factors.

Literature on the classification of low back pain is extensive. This has, for example, resulted in guidelines for GPs as well as physiotherapists for the classification and treatment of patients with low back pain\(^{84,85}\). In all guidelines, patients are classified and stratified into groups for further treatment. A recent study showed that stratified care for back pain implemented in family practice leads to significant improvements in patient disability outcomes and a halving in time off work, without increasing health care costs\(^{75,86}\).

Basically, literature shows that the classification of patients with low back pain is mainly based on looking for the presence of so-called “Red Flags” and “Yellow Flags”. “Red Flags” are considered to be serious conditions, such as trauma, cancer, and herniated discs. “Yellow Flags” are psychosocial factors complicating the condition as anxiety, distress and depression. Some papers categorize “Yellow Flags” into further detail calling these “Blue Flags” (factors about work that may lead to prolonged disability)\(^{66}\), “Orange Flags” (psychiatric factors), and “Black Flags” (contextual factors as a compensation system under which workplace injuries are managed)\(^{87}\).

Flags can be used as decision factors in the decision process for further referral, also called ‘triage’, to determine whether the patient has to go to the GP or to the physiotherapist, or can perform self-care. Furthermore, flags can also be used as decision factors at a later stage in the healthcare process, for example, after anamnesis and physical examination of the patient with low back pain to determine the further treatment path.

4.2.2 Clinical decision support systems for healthcare professionals as well as patients
Over almost half a century, clinical decision support system (CDSSs) have been developed to support healthcare professionals during the clinical decision process. The term CDSS is defined as “any computer program designed to help healthcare professionals to make clinical decisions”\(^{19}\). One of the key decision support functions is to provide patient-specific recommendations that cover assistance in making a diagnosis, providing advice on therapy, or both diagnostic assistance and therapy advice\(^{21}\).
CDSSs on the management of low back pain have also been developed. These CDSSs were mainly developed to improve uptake of guideline recommendations on low back pain by healthcare professionals. Next to this, CDSSs were developed to assist healthcare professionals in making a diagnosis on low back pain as, for example, detecting chronic low back pain by the evaluation of MRI images of the brain, classifying low back pain when dealing with uncertainty, and stratifying patients in risk groups on the development of a chronic condition based on questionnaires (StarTBack and Örebro).

Besides systems for healthcare professionals, systems have also been developed to aid patients in decision support. These computerized patient decision aids range from general home healthcare reference information to symptom management and diagnostic decision support. For low back pain, computerized patients decision aids have been found for patients facing a surgical treatment decision. No systems have been identified in literature that support patients in the classification of their own low back pain prior to contacting a primary healthcare professional. However, such a system will be very helpful to support patients in the determination of a correct self-referral, an essential prerequisite for an effective treatment of patients with low back pain.

### 4.3 Methods

The first steps in the development of a web-based clinical decision support system that guides low back pain patients to the most relevant healthcare professional is finding those factors that can classify these patients for further referral. To find these factors, the following steps were taken:

1. Studying physiotherapist and general practitioner guidelines on the classification and treatment of patients with low back pain;
2. Performing in-depth, semi-structured interviews with an group of 3 general practitioners and 5 physiotherapists;
3. Performing a thematic analyses on the interview transcriptions;
4. Validation of the results gathered thus far by means of an online survey among the interviewees.

#### 4.3.1 Studying guidelines on low back pain

During this step, the Dutch physiotherapist guideline on low back pain and the Dutch GP guideline on low back pain have been studied. The main goal of this step was to gain an good understanding of the low back pain domain, the terminologies used in this domain by GPs as well as by physiotherapists, and the methods used to stratify patients with low back pain into profiles for further treatment.
4.3.2 Setting up and analysis of the interviews
Knowledge gained from the previous step was used to set-up the interviews. These were semi-structured interviews, based on the following themes:

- Demographics of the interviewee (e.g., age, specialization);
- Expertise of the interviewee on classifying and treating low back pain (e.g., how often the healthcare professional sees a patient with low back pain, how knowledge on low back pain is kept up-to-date);
- Steps in the clinical evaluation and classification, and management of low back pain by asking out the healthcare professional on specific patient cases on self-referral (see "Appendix");
- Definitions on low back pain concepts (e.g., the differences between specific and nonspecific low back pain, description of concepts on possible serious disorders);
- Future expectations of a CDSS that supports healthcare professionals and patients in the classification, treatment and management of low back pain.

The interviews were held among 3 GPs and 5 physiotherapists. These interviewees were selected based on reachability related to distance as well as via contacts. The number of interviews was kept low, because interviews are labor-intensive, and because of the expected low variance in the answers on the interview questions. Afterwards, the interviews were transcribed verbatim and analysed by means of thematic analysis.

4.3.3 Validation of the identified decision factors for classifying low back pain by means of an online survey
The previous steps resulted into a large number of decision factors for classifying low back pain related to further referral in care (GP, physiotherapist, or self-care). These factors were resubmitted to the interviewees to be validated by means of an online survey, and by evaluating these factors on the following two aspects:

1. The importance of being questioned during initial triage to determine whether the patient has to see a GP or a physiotherapist, or can perform self-care;
2. The importance to be included into the decision for further treatment interventions.
4.4 Results

Studying literature and guidelines, resulted in a clear global overview of possible classes of patients with low back pain, and the possible prognosis and potential risks these patients face according to these classes. The focus of the guidelines was mainly placed on nonspecific low back pain, but factors related to specific low back pain were also found. We made a visual overview of the knowledge, gained during this step. This overview is shown as an ontology in Figure 4.1.

In Figure 4.1 the yellow blocks refer to knowledge classes that are general to knowledge concepts in the health care domain, the blue blocks refer to knowledge classes that are needed to describe the knowledge classes needed to classify patients with low back pain. This figure also shows three patient profiles to stratify patients with non-specific low back pain. Profile 1 is a patient with non-specific low back pain (no “Red Flags”) with a normal course. Profile 2 is a patient with non-specific low back pain with an abnormal course, but no psychosocial factors (“Yellow Flags”). Profile 3 is a patient with non-specific low back pain with an abnormal course and psychosocial factors.
Chapter 4 | Design of a CDSS for patients with low back pain

Table 4.1: Classification factors for patients with low back pain, based on literature, guidelines and the interviews. Divided in the groups ‘general’, ‘psychosomatic’, and ‘serious’.

<table>
<thead>
<tr>
<th>General factors</th>
<th>Psychosomatic factors (&quot;Yellow Flags&quot;)</th>
<th>Serious factors (&quot;Red Flags&quot;)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Patients’ request for help</td>
<td>• Depression</td>
<td>• Start LBP before age of 20</td>
</tr>
<tr>
<td>• Well-being as experienced by patient</td>
<td>• Extremely nervous</td>
<td>• Start LBP after age of 50</td>
</tr>
<tr>
<td>• Course of the LBP</td>
<td>• Extremely worried</td>
<td>• Response on analgesics</td>
</tr>
<tr>
<td>• Sick leave</td>
<td>• Stress (e.g., caused by family or relational problems)</td>
<td>• Prolonged use of corticosteroids</td>
</tr>
<tr>
<td>• Earlier hospitalization on LBP</td>
<td>• Relationship with colleagues</td>
<td>• Serious diseases, such as cancer, in patient history</td>
</tr>
<tr>
<td>• Working environment</td>
<td>• Irrational thoughts about LBP</td>
<td>• Neurogenic signals</td>
</tr>
<tr>
<td>• Family history of LBP</td>
<td>• Problems with employers occupational insurance</td>
<td>• Specific pathologies</td>
</tr>
<tr>
<td>• Working ergonomics</td>
<td>• Dysfunctional cognition</td>
<td>• Problems with moving, shortly after waking up</td>
</tr>
<tr>
<td></td>
<td>• Anxiety disorder</td>
<td>• Decreased mobility</td>
</tr>
<tr>
<td></td>
<td>• Patients’ coping strategy</td>
<td>• Radiation in the leg below the knee</td>
</tr>
<tr>
<td></td>
<td>• An ongoing investigation on personal injury</td>
<td>• Nocturnal pain</td>
</tr>
<tr>
<td></td>
<td>• Kinesiophobia</td>
<td>• Rapid weight loss, &gt; 5 kg per month</td>
</tr>
<tr>
<td></td>
<td>• Personality disorder</td>
<td>• Loss of muscle strength</td>
</tr>
<tr>
<td></td>
<td>• Borderline disorder</td>
<td>• No biomechanical pattern</td>
</tr>
</tbody>
</table>

Figure 4.1 shows that the main determining factors in classifying patients are the course of the low back pain (normal, abnormal), the presence or absence of serious factors (“Red Flags”) as specific underlying serious conditions, and the presence or absence of psychosocial factors (“Yellow Flags”). These observations were also supported by the results of the interviews. The analysis of the interviews resulted in 43 identified factors for classifying low back pain. These factors are shown in Table 4.1.

The interviewees indicated that in case of the presence of a serious factor (“Red Flag”), the patients should be sent to a GP. Next, the interviewees indicated that in case of the presence of a psychosocial factor (“Yellow Flag”), the patient has a risk
on the development of an abnormal course on low back pain, possible resulting in chronic low back pain. In order to avoid the development of a chronic condition, these patients should see the right healthcare professional as early as possible who can guide the patient during his or her rehabilitation process. In most cases, this will be a physiotherapist, sometimes working in a multi-disciplinary setting with other healthcare professionals as, for example, a psychologist, with the physiotherapist as head therapist.

For the CDSS, we want to use the lowest number of classification factors for providing the best self-referral advice. This in order to minimize the workload for the patient in answering questions, asked by the CDSS. Therefore, we resubmitted the 43 identified classification factors (Table 4.1) to the interviewees so that these factors could be validated on two aspects: 1) their importance during initial triage to determine a self-referral advice for the patient, and 2) their importance for the decision process to determine further treatment interventions, also after the first anamnesis and physical examination of the patient with low back pain by the healthcare professional. Six of the 8 interviewees (3 physiotherapists and 3 GPs) responded on the Internet survey. This resulted in an overview of the most important classification factors to determine the advice for self-referral (Figure 4.2) and the most important classification factors for determining a treatment plan (Figure 4.3).

Figure 4.2. An overview of the identified factors to classify patients with low back pain, and their importance related to initial triage of patients with low back pain.
Figure 4.3. An overview of the identified factors to classify patients with low back pain, and their importance to determine further treatment plans.

Figure 4.4. The retrieved model of the triage process to provide advice on further referral of patients with low back pain.
Both figures show the results in radar charts. The identified factors are labelled around the circle. The number of times an interviewee marked the factor as important for triage, and for determining a treatment plan (Figure 4.2 and Figure 4.3 respectively), is plotted for each factor as a point along a separate axis that starts in the centre of the chart (0 marks, no interviewee marked the factor as important) and ends on the outer ring (all 6 interviewees marked the factor as important). Connecting these different points results in a quick overview of the most important factors for triage and treatment assessment. For better visibility, we also divided the circle into three pie slices: white represents the “general factors”, grey checked represents the “psychosocial factors (Yellow Flags)”, and dark grey represents the “serious factors (Red Flags)”.

Figure 4.2 shows that only general and serious factors (“Red Flags”) are pointed at the 5th and 6th rings, fifteen factors in total. Subsequently, we used these fifteen factors to model the inference process of the CDSS, presented as a decision tree in Figure 4.4. This decision tree models the process to determine the referral advice, i.e. see a GP, see a physiotherapist, or perform self-care. Figure 4.2 shows twelve serious factors on the 5th and 6th rings: Start LBP after age of 50, prolonged use of corticosteroids, serious diseases (e.g., cancer) in patient’s history, neurogenic signals, continuous pain, regardless of posture and movement, radiation in the leg below the knee, nocturnal pain, rapid weight loss (more than 5 kg per month), loss of muscle strength, trauma, and failure symptoms during increased pressure (e.g., coughing, straining, lifting gives extra pain). In Figure 4.4, these serious factors are taken together in one block to keep it as simple as possible: “# Red flags >= 1” means the presence of one or more serious factors.

Next, we decided that the factor “Asking patients’ request” cannot be used in the decision process itself, because it is no indication of patients’ condition. Therefore, the block “Asking patients’ request” is not a part of the decision tree. However, the healthcare professionals certainly want to know the patient’s request for help, therefore “Asking patients’ request” is at least part of the triage process, and will be sent to the healthcare professional to be used during the first anamnesis, when the patient is referred to a healthcare professional.

4.5 Discussion
By means of studying literature, and interviews and an online survey among 3 GPs and 5 physiotherapists, we identified 43 decision factors to classify low back pain for determining the best next step in primary healthcare. Fifteen of these identified factors have been used to model the triage process as the basis in the design of a web-based clinical decision support system (CDSS) that supports patients with low back pain in making a decision on self-referral. That is advising the patient 1) to see a GP, 2) to see a physiotherapist, or 3) to perform self-care. A correct self-referral is an essential prerequisite for an effective treatment of patients with low back pain.
Chapter 4 | Design of a CDSS for patients with low back pain

The identified classification factors correspond to classifications factors also found in literature\(^\text{59,64,75,78}\). In our study, one new identified factor emerged compared to factors found in literature, namely the general factor “Patients’ request for help” (Table 4.1). Almost all study participants indicated the importance of this factor in triage, because healthcare professionals want to know the wishes of the patient in respect to the management of his or her low back pain complaints. Therefore, although the factor “Patients’ request for help” is not an indication of patients’ condition needed for determining the advice for further referral, we included this factor into model of the triage process (Figure 4.4).

The identified classification factors appear to be evidence-based, which is supported by the great correspondence of our study results to the factors found in literature. This means that the identified factors can be used in the decision process to determine a self-referral advice for patients suffering from low back pain. As no other systems have been found in literature to support patients in the classification of their own low back pain before contacting a primary healthcare professional, we cannot compare our found identified factors to other similar studies.

Looking at the classification process itself, there are CDSSs that stratify patients in risk groups on the development of a chronic condition based on questionnaires as the StarTBack screening tool\(^\text{75}\) and the Örebro tool\(^\text{88}\). These CDSSs, however, are intended for use by healthcare professionals and are not used to triage a patient for further referral, but for further treatment.

This difference in usage compared to our CDSS probably also explains the difference in classification factors used. For example, the StarTBack screening uses 8 prognostic factors for low back pain as 2 items on function, and items on radiating leg pain, pain elsewhere, depression, anxiety, fear avoidance, catastrophizing, and bothersomeness\(^\text{86}\). These are mainly psychosocial factors, so called “Yellow Flags”, while the identified factors in our study for usage during initial triage are only general and serious factors (“Red Flags”)(Figure 4.2). However, the results in our study also show the importance of psychosocial factors (“Yellow Flags”) in the classification process of patients with low back pain for assessing further treatment, thus after initial triage (Figure 4.3). In this, our study identifies the factors “Irrational thoughts about LBP” and “Dysfunctional cognition” as most important.

4.5.1 Study limitations
In our study, we used the Dutch physiotherapist guideline on low back pain\(^\text{84}\) and the Dutch GP guideline on low back pain\(^\text{85}\). This may seem a limitation of our study, especially because of the unique situation of self-referral in the Netherlands. However, Koes et al.\(^\text{59}\) compared international clinical guidelines for the management of low back pain. This study showed that there are some differences between international guidelines, which may be due to a lack of strong evidence regarding these topics or due to differences in local health care systems. But, in general, diagnostic as
well as therapeutic recommendations are similar among these guidelines. This indicates that using only Dutch guidelines will not substantially affect the results as presented in this chapter.

Next to this, the interviews and the online survey were held among a small group of GPs and physiotherapists. However, the number of interviews was kept low, because interviews are labor-intensive, and because of the expected low variance in the answers on the interview questions as the participants all work according to the same guidelines. Next to this, all interviewees were experienced healthcare professionals on low back pain. That is four of the five interviewed physiotherapists had also a background as chiropractor, and all GPs had more than 10 year experience in primary care.

4.5.2 Future work

4.5.2.1 Next steps in the evaluation and further refinement of the process model

In future research we aim to evaluate the process model, as shown in Figure 4.4, in more detail. By means of a vignette survey, also called factorial survey92, we will present cases (vignettes) to a group of more than 500 GPs and physiotherapists. This vignette survey will evaluate the importance of the presence or absence of the 15 classification factors as identified most relevant for initial triage as described in this chapter. The outcome of the vignette survey should lead to a smaller set of classification factors that is an optimum between the factors necessary to determine a correct referral advice, while minimizing the workload for patients in answering questions.

Finally, we will relate the remaining factors to questions to be posed to the patients by the CDSS. For most of the identified classification factors in our study, validated questionnaires exist that also can be used in the CDSS. Commonly used questionnaires in low back pain research are, for example, the Visual Analog Scale (VAS) for Pain93, and the Oswestry Low Back Pain Disability Questionnaire94.

Based on the results of the vignette survey, and the usage of validated questionnaires that determine the presence or absence of a factor, the CDSS will be developed. Subsequently the CDSS will be evaluated with patients in primary healthcare.

In our study, we focused on low back pain, because the musculoskeletal disorder domain is a large domain95. However, we used general approaches to design the CDSS as building an ontology and a decision tree are common used methods in the development of CDSSs. Therefore, we expect these same approaches are also applicable to extend the CDSS for other musculoskeletal disorders. To explore this, we will also start new studies on the development of CDSSs that advice patients with other musculoskeletal disorders in self-referral, by using the same approaches as described in this chapter.
Chapter 4 | Design of a CDSS for patients with low back pain

4.6 Appendix Chapter 4
During the semi-structured interviews, the following four patient cases were presented to the interviewees. For each case, the interviewee was asked about the clinical evaluation and classification, management of low back pain, and the ultimate advice on self-referral: see a GP, see a physiotherapist, or perform self-care.

Case 1
• Male, 53 years, bus driver, married;
• Tennis: 2 times a week;
• Since three weeks;
• He has a burden of the spine with radiation just above the right knee;
• Also low back pain problems in the past;
• Six years ago, some X-rays were made not showing any causes to explain the symptoms;
• On sick leave at the moment;
• Worried that something has been broken in his back;
• He avoids pain;
• No pain during lying and sitting down.

Case 2
• Female, 69 years old, divorced;
• Low body weight;
• Sleeps poorly
• Worrying a lot and feeling nervous;
• Has low back pain complaints since several weeks;
• Continuous pain, independent of posture and movement;
• Walks crooked.

Case 3
• Male, 39 years, bricklayer;
• Wants to visit primary healthcare for the 2nd time in 3 months, because of no improvement in low back pain complaints despite medication and advice;
• Otherwise a healthy person;
• No symptoms below the knee;
• Moves slowly, because of pain presence;
• Only walks short distances.
• Believes that the low back pain will never end;
• 100% sick leave.

Case 4
• Female, 15 years old, follows 4th grade high school education;
• Suffers from low back pain since 6 months;
• Unclear start and cause of the low back pain;
• Plays handball;
• Otherwise a healthy person;
• Little pain when lying and sitting;
• Stiffness in the morning.
CHAPTER 5

Should I see a healthcare professional or can I perform self-care: self-referral decision support for patients with low back pain

Published:
Chapter 5 | Should I see a healthcare professional or can I perform self-care

Abstract
When people get low back pain (LBP), it is not always evident when to see a general practitioner (GP) or physiotherapist, or to perform self-care. A direct correct referral is essential for effective treatment to prevent the development of chronic LBP the utmost. In the context of designing a tool that is able to provide a referral advice to a patient, 63 healthcare professionals (GPs and physiotherapists) participated in a vignette study. They had to judge 32 LBP cases on 1. See a general practitioner, 2. See a physiotherapist, and 3. Perform self-care. In total, 1288 vignettes were judged. Multinomial regression analysis showed that Weight Loss, Trauma, and Nocturnal Pain are the three most significant predictive variables. A decision tree was generated that showed the same conclusion. This decision tree is the basis to build a tool that provides personalized referral advice to patients with LBP from the very beginning.
5.1 Introduction
Almost 80 percent of the people experience low back pain once in their lifetime\textsuperscript{77,78}, and about ten percent of patients with (acute) low back pain develop chronicity\textsuperscript{77,96}. Response of individual patients on interventions is highly variable: from great benefits to worsening of the problem. Therefore, methods for selecting the optimal interventions for individual patients should be improved\textsuperscript{97}. The common way for determining the clinical pathway for a patient is first to classify this patient\textsuperscript{98}. This classification can for example be used for diagnosing the healthcare problem and to refer the patient to the most relevant healthcare professional for his or her healthcare problem. An optimal referral is essential to ensure optimal interventions in tackling a healthcare problem\textsuperscript{99}. In literature relevant studies can be found on the classification of patients with musculoskeletal disorders, and low back pain in particular\textsuperscript{75,88,99}. The applications of these classification studies are focused on the usage by healthcare professionals to identify patients at an early stage that have risk to develop a chronic condition and to select appropriate treatment plans for these patients.

In case of patients with a new episode of low back pain there is a wide acceptance that the management of this healthcare problem should start in primary care\textsuperscript{59}, thus by treatment of a GP or a physiotherapist. In an increasing number of countries, including the Netherlands, patients with musculoskeletal disorders can decide themselves whether to see a GP or a physiotherapist, or not\textsuperscript{82,100}. This is also called “direct access” or “patient self-referral”\textsuperscript{100}. However, from the viewpoint of the patient, it is often unclear whether it is best to see a GP, a physiotherapist, or even to perform self-care\textsuperscript{101} (as a third option). Self-care helps to reduce back-related worry and fear-avoidance beliefs\textsuperscript{102}, and in case of acute low back pain, continuing ordinary activities within the limits permitted by the pain leads to more rapid recovery than either bed rest or back-mobilizing exercises\textsuperscript{100}. No optimal referral at the first time means time lost for both the patient as the healthcare professional thereby increasing changes on chronicity of the disorder, because no optimal interventions were used at the earliest possible stage. Therefore, an online service that is able to provide an optimal referral advice to a patient is desired to guide the patient directly to the best next step in dealing with the healthcare problem and to avoid unnecessary consults in primary care.

It is known that clinical decision support systems (CDSSs) can be very helpful in assisting healthcare professionals to make clinical decisions for the benefit of their patients\textsuperscript{11,103}. A CDSS is defined as “any computer program designed to help healthcare professionals to make clinical decisions”\textsuperscript{19}. In most cases, these are clinical decisions related to making a diagnosis, selecting a treatment plan, or improving adherence to guideline recommendations\textsuperscript{21,63,104}. Besides CDSSs for healthcare providers also decision support systems for patients exist. Examples of this kind of systems are systems that reference to home healthcare information to support self-care, or systems that provide an advise to patients facing a surgical treatment decision\textsuperscript{89,91}. Although websites and apps can be found that help patients
with the question "When to see a doctor?"\textsuperscript{105,106}, no decision support systems have been found in literature that supports patients with low back pain in determining when to see a doctor, when to see a physiotherapist, or when to perform self-care.

Also no literature was found that deals with the classification of patients with low back pain for the context of self-referral in primary care. As this is the general aim of our research, namely the design of a CDSS for self-referral as an online service for patients, we started with a study on the classification of patients with low back pain in 2015\textsuperscript{107}. This study has resulted in the identification of 43 factors to classify patients with low back pain, of which 15 factors seemed to be important in the referral process of patients with low back pain. These factors were: start of low back pain after age of 50, prolonged use of corticosteroids, serious diseases (e.g., cancer) in patient’s history, neurogenic signals, continuous pain, regardless of posture and movement, radiation in the leg below the knee, nocturnal pain, rapid weight loss (more than 5 kg per month), loss of muscle strength, trauma, and failure symptoms during increased pressure (e.g., coughing, straining, lifting gives extra pain)\textsuperscript{107}.

The aim of the study described in this chapter was to generate a decision tree that models the self-referral process for patients with low back pain. Before generating this decision tree, first the actual importance for each of the 15 identified factors was assessed to determine whether a factor really has to be included into the model or not. The underlying idea is that when the number of factors can be decreased, the referral advice can be determined by asking the patient an efficient as possible number of questions. The finally included factors were used to generate the decision tree as the next step in our research in the design of a tool for self-referral decision support to the optimal primary healthcare intervention for patients with low back pain.

### 5.2 Methods

#### 5.2.1 Design

A vignette study was used to obtain the most important factors that determine the choice of referral to the optimal primary healthcare intervention for a low back pain patient. In this study a vignette was defined as a brief narrative text presentation of the situation of a patient with low back pain. This text included a text representation of each of the 15 factors described in Table 5.1. The values of these factors varied among these vignettes leading to different cases of patients with low back pain. The possible values of these factors were categorical and are shown in the third column in Table 5.1.
Table 5.1. Classification factors important in the decision of referral of patients with low back pain to primary care.

<table>
<thead>
<tr>
<th>#</th>
<th>Short description</th>
<th>Text values per factor inserted into the vignette text</th>
</tr>
</thead>
</table>
| 1  | Preference for help                           | 0: "wants to go to the GP"  
1: "wants to go to the physiotherapist"  
2: "only wants advice and information on low back pain" |
| 2  | Well-being as experienced by patient          | 0: "bad"  
1: "medium"  
2: "good" |
| 3  | Course of the low back pain                   | 0: "less than 2 weeks"  
1: "more than 2 weeks" |
| 4  | Start of the low back pain after age of 50    | 0: "younger than 50"  
1: "older than 50" |
| 5  | Response on analgesics                        | 0: "does not respond"  
1: "responds" |
| 6  | Prolonged use of corticosteroids              | 0: "not"  
1: "" |
| 7  | Serious diseases, such as cancer, in patient history | 0: "had no"  
1: "did have" |
| 8  | Neurogenic signals                            | 0: "no"  
1: "" |
| 9  | Continuous pain, regardless of posture and movement | 0: "not"  
1: "" |
| 10 | Radiation in the leg below the knee           | 0: "not"  
1: "" |
| 11 | Nocturnal pain                                | 0: "no"  
1: "" |
| 12 | Rapid weight loss, more than 5 kg per month   | 0: "less"  
1: "more" |
| 13 | Loss of muscle strength                       | 0: "does not suffer"  
1: "suffers" |
| 14 | Trauma                                       | 0: "not"  
1: "" |
| 15 | Failure symptoms during increased pressure    | 0: "does not suffer"  
1: "suffers" |
Chapter 5 | Should I see a healthcare professional or can I perform self-care

Figure 5.1. Overview of the general vignette text, and the possible judgements on a vignette. In a generated vignette, the <> boxes were replaced by the text values of the randomly selected factor values.
The vignettes were judged by independent physiotherapists and GPs. Three 5-point Likert scales were used to judge a vignette on the referral decisions to go to the GP, the physiotherapist, and to perform self-care (Figure 5.1) separately. Next to this, a participant could provide open comments on a vignette when preferred.

In total we distinguished 32 different factor values. As shown in Table 5.1, 13 factors had two possible values and two factors had three possible values. This means that in principal $3^2 \times 2^{13} = 73728$ different vignettes were possible. Figure 5.1 shows the vignette text in the grey box where the factor values between the $<$ > have been left open. The text between the ‘‘”’, shown in Table 5.1, was the text that appeared in the vignette between the $<$> for the concerning factor value. For example, in case of the factor Radiation (“The patient does <radiation> have radiation below the knee”), the vignette text could either be “The patient does not have radiation below the knee.” (radiation=0, text value=“not”’) or “The patient does have radiation below the knee.” (radiation=1, text value=“”’).

Because 32 different factor values could be distinguished, we wanted a participant to judge 32 vignettes. To be able to show 32 random developed vignettes, in which all 32 values were at least once showed to a participant, we developed a web-application in php/mysql. The general description of the algorithm to obtain a sample of vignettes without replacement of all possible vignettes used in this application is given by the following pseudo code. In this pseudo code, “fv” in the variable name $selected_fv$ is acronym for “factor value”:

1. Put all 32 factor values in random order in an array.
2. $selected_fv =$ First factor value (fv) in this array.
3. Create the vignette around $selected_fv$:
   a. $selected_fv$ is a value that belongs to 1 of the 15 factors. Select the values for the other 14 factors randomly out of the possible values for each factor.
   b. Check if a vignette with exact the same factor value combination already exists in the database.
   c. If yes, reject the just created vignette and perform step a) and b) again around $selected_fv$.
   d. If not, show the vignette to the participant.
4. Store the vignette and the judgement into the database.
5. Select the next factor value in the array as $selected_fv$, and repeat step 3 and 4 until all 32 factor values have been used.
5.2.2 Obtaining participants
The intended participants of this study were GPs and physiotherapists as these are the common primary healthcare professionals treating patients with low back pain in primary care. To gain participants for this study, we used a convenience sample by sending an invitation mail to GPs, physiotherapists, and primary health care centers out of our network. We also used social media by posting on Twitter and weblogs. Next to this, a message was posted in the newsletter of the Royal Dutch Society for Physical Therapy (KNGF).

5.2.3 Used methods for statistical analysis
The outcome scale of the judgements was ordinal. As the referral decisions were judged on three 5-point Likert scales, the values of a judged advice type were distributed on the scale of 1 (totally disagree) to 5 (totally agree). Therefore, the data was analyzed in the following ways:

1. First the data was checked visually by using bubble charts whether the judgements show a course as could be expected beforehand. These bubble plots showed the joint distribution of the value of two of the three judged advice types (GP, physiotherapist, and self-care) on a fixed value of the third, in which the size of a bubble in a plot was related to the frequency of this value combination of judgements.

2. A participant could judge a case on three dimensions (GP, Physiotherapy, and self-care) on a 5-points scale. These judgements in de vignette study were combined to be able to form one advice. The following algorithm was used to combine the judgments:
   a. Combined advice = Max(GP advice, physiotherapy advice, self-care advice);
   b. If all three advices are equal: Combined advice = physiotherapy advice;
   c. If 2 advices are equal and greater than the third advice, and physiotherapy advice is part of these 2 advices: Combined advice = physiotherapy advice;
   d. If 2 advices are equal and greater than the third advice, and physiotherapy advice is NOT part of these 2 advices: Combined advice = GP advice;

In this algorithm for combining the judgments, the Physiotherapy advice was set as preferred in case two, or three dimensions, were judged equally and most agreed and Physiotherapy advice was part of it. This is, because a GP often consults a physiotherapist in a multidisciplinary setting when treating a person with a musculoskeletal disorder\(^{108}\). Therefore, we safely could set Physiotherapy advice as preferred in the algorithm, also knowing that a physiotherapist still will refer a patient to a GP when new serious factors found during a consult will indicate for this\(^{84}\).
3. After combining the judgements to one advice, we performed a multinomial logistic regression\textsuperscript{109} to select those factors that allow classification of patients with (acute) low back pain for referral to a GP, a physiotherapist, or to self-care. Multinomial logistic regression enables the usage of logistic regression to predict the membership of an outcome in case there are more than two outcome categories\textsuperscript{109}. The likelihood-ratio was determined to gain the significance of a factor. Further, parameters estimates were used to determine the strength of these significances to an advice.

4. Returning to the goal of this study, we wanted to model the process of initial referral in primary care for patients with low back pain. When giving an advice it is also important that can be explained how this advice had been composed. As a decision tree can be converted to a set of simple rules that are easy to understand\textsuperscript{110}, and thus suitable to explain a decision, we wanted to model the process by means of a decision tree that leads to one of the following three outcomes: go to the GP, go to the physiotherapist, perform self-care (at first instance). The decision tree was generated on the results retrieved during the multinomial regression analysis. That is, we used the factors that have a significance of $p < .1$ to predict the advice in the referral process. The Classification and Regression Trees (CART) algorithm\textsuperscript{111} was used to construct the tree. The CART algorithm splits the data into child nodes that are as homogeneous as possible. The minimum number of cases was set to 50 for a parent node and 20 for a child node. For validation we used a training set (75\% of the samples) and a test set (25\% of the samples). Every time the learning tree algorithm is used, a new tree is generated, because the training set of sample is selected randomly. Therefore, we selected the classification tree with the best performance after several times of tree generation.

We used Microsoft Excel to generate the bubble plots, and we used IBM SPSS version 21 to perform the multinomial regression analysis, and to generate the decision tree.
Chapter 5 | Should I see a healthcare professional or can I perform self-care

5.3 Results
The study was conducted in the period from October 2015 to December 2015. In total, 1288 vignettes were judged by 63 participants (Figure 5.2). From the study participants, 52 (83%) were physiotherapists, 7 (11%) were general practitioners, and 4 (6%) were another kind of professional, as for example a doctor in training, and a researcher, who had been a physiotherapist previously. Forty persons (63%) also had a specialization, of which most were specialized in manual therapy. The gender ratio in this group was almost equally divided: 36 (57%) men and 27 (43%) women. Most of the participants saw patients with low back pain on a regular base: 43 (68%) of the participants saw patients with low back pain once a day, and 16 (25%) once a week. Next to this, 57 (90%) of the participants had more than 5 years of professional experience, of which 30 (48%) of the participants even had more than 20 years of professional experience.

Figure 5.2. The total number of judged vignettes and the distribution of judgements among these vignettes.
Should I see a healthcare professional or can I perform self-care? Chapter 5

Figure 5.3. Bubble plots used for an exploratory preview on the retrieved data during the vignette study to decide whether the collected data was appropriate to use or not. In this figure, the axes numbers correspond to: 1 = totally disagree, 2 = disagree, 3 = neutral, 4 = agree, and 5 = totally agree.
5.3.1 Exploratory preview

Figure 5.3 shows the bubble plots we used for an exploratory preview on the data. The first row of bubble plots in this figure shows the distribution of the given advice on self-care and physiotherapy on a fixed value for GP advice ranging from left to right from “total agree” to “total disagree”. The second row of bubble plots shows the distribution of the advice on self-care and GP on a fixed value for physiotherapy advice. The third row of bubble plots shows the distribution of the given advice on GP and physiotherapy on a fixed value for self-care advice. The ‘n’ value shown in a bubble plot is the number of vignettes judged for the concerning fixed advice. For example, the upper left bubble plot shows the distribution of the judgements on physiotherapy advice and self-care advice when GP advice was judged as “total agree”. This bubble plot shows that 656 (n=686) of the 1288 vignettes were judged “total agree” on GP by the study participants. Most of these vignettes were also judged “total disagree” on self-care and physiotherapy advice. This is a course that we expected beforehand. Other bubble plots show similar courses, and based on this view of joint distribution of the data we concluded that the data could be used for further statistical analysis.

5.3.2 Multinomial regression analysis

The judgements on the three 5-point Likert scales were combined to one advice per vignette. This was achieved by using the algorithm as described in the Methods-section. The distribution of GP advice, Physiotherapist advice, and Self-care advice among the vignettes was 843 (65%), 425 (33%), and 20 (2%) respectively.

Next, we performed a multinomial regression analysis. Table 5.2 shows the significance of the factors as predictors of the referral advice as determined by the likelihood ratio test of the multinomial regression analysis. Three of the 15 factors appear to be non-significant predictors (p > .1) in the multinomial regression model for predicting a referral advice, i.e. Course, Analgesics, and Radiation. In contrast, the other factors appear to be highly predictive, especially Weight Loss ($\chi^2(2) = 130.95$, $p < .001$).

Next to this, table 5.3 shows the parameter estimates with Self-referral as reference category. In this table, Weight Loss appears to be highly significant in predicting the GP referral advice. For example, when Weight Loss in the patient is less than 5 kg in the past month this significantly predicts that the patient will not be referred to the GP ($B = -2.06$, $p<.001$). The factor Trauma even has a bigger prediction weight: $B = -2.35$, $p<.001$. In the same way, the factors Well-being=“bad”, Corticosteroids, Serious Diseases, Continuous Pain, Nocturnal Pain, Loss of Muscle Strength, Failure Symptoms, and Preference=“GP” significantly predict a GP referral advice to the patient. In case of the significance of predictive factors are lower, compared to predictors for a GP advice. Table 5.3 shows Trauma, Corticosteroids, Serious Diseases, Continuous Pain, Failure Symptoms, Preference=“GP”, and Preference=“Physio” as significant predictors for physiotherapy advice.
Table 5.2. The significance of the factors as predictors to the model.

<table>
<thead>
<tr>
<th></th>
<th>Likelihood Ratio Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-2 Log Likelihood</td>
</tr>
<tr>
<td><strong>Intercept</strong></td>
<td>1461.280</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>1466.763</td>
</tr>
<tr>
<td><strong>Wellbeing</strong></td>
<td>1491.083</td>
</tr>
<tr>
<td><strong>Course</strong></td>
<td>1463.620</td>
</tr>
<tr>
<td><strong>Analgesics</strong></td>
<td>1465.351</td>
</tr>
<tr>
<td><strong>Trauma</strong></td>
<td>1508.787</td>
</tr>
<tr>
<td><strong>Corticosteroids</strong></td>
<td>1484.227</td>
</tr>
<tr>
<td><strong>Serious Diseases</strong></td>
<td>1474.053</td>
</tr>
<tr>
<td><strong>Weight Loss</strong></td>
<td>1592.226</td>
</tr>
<tr>
<td><strong>Continuous Pain</strong></td>
<td>1479.018</td>
</tr>
<tr>
<td><strong>Nocturnal Pain</strong></td>
<td>1509.003</td>
</tr>
<tr>
<td><strong>Neurogenic Signals</strong></td>
<td>1466.373</td>
</tr>
<tr>
<td><strong>Radiation</strong></td>
<td>1463.132</td>
</tr>
<tr>
<td><strong>Loss Of Muscle Strength</strong></td>
<td>1491.629</td>
</tr>
<tr>
<td><strong>Failure Symptoms</strong></td>
<td>1477.998</td>
</tr>
<tr>
<td><strong>Preference</strong></td>
<td>10476.324</td>
</tr>
</tbody>
</table>
**Chapter 5 | Should I see a healthcare professional or can I perform self-care**

**Table 5.3.** The estimated parameters for the multinomial regression model: $R^2=0.25$, (Cox & Snell). $32$ (Nagelkerke). Model $X^2(24)=362.43$, $P < .001$. * $P < .05$, ** $P < .01$, *** $P < .001.$

<table>
<thead>
<tr>
<th></th>
<th>B(SE)</th>
<th>95% CI for Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intercept</td>
<td>11.34 (1.75)**</td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td>0.12 (0.52)</td>
</tr>
<tr>
<td></td>
<td>Wellbeing=0 “bad”</td>
<td>1.71 (0.71)a</td>
</tr>
<tr>
<td></td>
<td>Wellbeing=1 “medium”</td>
<td>0.72 (0.59)</td>
</tr>
<tr>
<td></td>
<td>Course</td>
<td>-0.79 (0.54)</td>
</tr>
<tr>
<td></td>
<td>Analgesics</td>
<td>0.67 (0.52)</td>
</tr>
<tr>
<td></td>
<td>Trauma</td>
<td>-2.35 (0.68)***</td>
</tr>
<tr>
<td></td>
<td>Corticosteroids</td>
<td>-1.99 (0.67)**</td>
</tr>
<tr>
<td></td>
<td>Serious Diseases</td>
<td>-1.64 (0.57)***</td>
</tr>
<tr>
<td></td>
<td>Weight Loss</td>
<td>-2.06 (0.57)***</td>
</tr>
<tr>
<td></td>
<td>Continuous Pain</td>
<td>-1.66 (0.60)**</td>
</tr>
<tr>
<td></td>
<td>Nocturnal Pain</td>
<td>-1.25 (0.53)</td>
</tr>
<tr>
<td></td>
<td>Neurogenic Signals</td>
<td>-0.75 (0.53)</td>
</tr>
<tr>
<td></td>
<td>Radiation</td>
<td>-0.55 (0.51)</td>
</tr>
<tr>
<td></td>
<td>Loss Of MuscleStrength</td>
<td>-1.61 (0.61)***</td>
</tr>
<tr>
<td></td>
<td>Failure Symptoms</td>
<td>-1.79 (0.61)***</td>
</tr>
<tr>
<td></td>
<td>Preference=0 ”GP”</td>
<td>1.69 (0.84)**</td>
</tr>
<tr>
<td></td>
<td>Preference=1 ”Physio”</td>
<td>1.55 (0.84)</td>
</tr>
</tbody>
</table>

**Physiotherapy versus Self-care**

<table>
<thead>
<tr>
<th></th>
<th>B(SE)</th>
<th>95% CI for Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intercept</td>
<td>7.64 (1.74)***</td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td>0.42 (0.51)</td>
</tr>
<tr>
<td></td>
<td>Wellbeing=0 “bad”</td>
<td>0.88 (0.70)</td>
</tr>
<tr>
<td></td>
<td>Wellbeing=1 “medium”</td>
<td>0.16 (0.58)</td>
</tr>
<tr>
<td></td>
<td>Course</td>
<td>-0.80 (0.53)</td>
</tr>
<tr>
<td></td>
<td>Analgesics</td>
<td>0.43 (0.52)</td>
</tr>
<tr>
<td></td>
<td>Trauma</td>
<td>-1.51 (0.68)</td>
</tr>
<tr>
<td></td>
<td>Corticosteroids</td>
<td>-1.48 (0.67)</td>
</tr>
<tr>
<td></td>
<td>Serious Diseases</td>
<td>-1.33 (0.56)</td>
</tr>
<tr>
<td></td>
<td>Weight Loss</td>
<td>-0.54 (0.57)</td>
</tr>
<tr>
<td></td>
<td>Continuous Pain</td>
<td>-1.20 (0.60)</td>
</tr>
<tr>
<td></td>
<td>Nocturnal Pain</td>
<td>-0.33 (0.53)</td>
</tr>
<tr>
<td></td>
<td>Neurogenic Signals</td>
<td>-0.49 (0.53)</td>
</tr>
<tr>
<td></td>
<td>Radiation</td>
<td>-0.42 (0.51)</td>
</tr>
<tr>
<td></td>
<td>Loss Of MuscleStrength</td>
<td>-0.92 (0.61)</td>
</tr>
<tr>
<td></td>
<td>Failure Symptoms</td>
<td>-1.40 (0.60)</td>
</tr>
<tr>
<td></td>
<td>Preference=0 ”GP”</td>
<td>1.75 (0.84)</td>
</tr>
<tr>
<td></td>
<td>Preference=1 ”Physio”</td>
<td>2.05 (0.84)</td>
</tr>
</tbody>
</table>
Figure 5.4. The classification tree was retrieved by using the Classification and Regression Trees (CART) algorithm. The minimum number of cases was set to 50 for a parent node and 20 for a child node. The grey nodes are the leave nodes of the tree.

Should I see a healthcare professional or can I perform self-care | Chapter 5

...
Chapter 5 | Should I see a healthcare professional or can I perform self-care

Table 5.4. The risk and classification performance of the classification tree.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Overall Percentage</th>
<th>Overall Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Training</td>
<td>GP</td>
<td>Physiotherapist</td>
</tr>
<tr>
<td></td>
<td>31.3%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.0%</td>
<td></td>
</tr>
<tr>
<td>Correct Predicted</td>
<td>73.0%</td>
<td>73.2%</td>
</tr>
<tr>
<td>Risk Estimate</td>
<td>0.270</td>
<td>0.268</td>
</tr>
<tr>
<td>Std. Error</td>
<td>0.014</td>
<td>0.025</td>
</tr>
</tbody>
</table>

Figure 5.5. The normalized importance of the independent variables in the model of the classification tree.

After the multinomial regression analysis, a decision tree was generated by using the Classification and Regression Trees (CRT) algorithm\(^\text{111}\), the factors indicated in table 5.2 with a significance \(p < .1\) as independent variables, and Advice as dependent variable. Therefore, the included factors in tree generation were the factors Age, Wellbeing, Trauma, Corticosteroids, Serious Diseases, Weight Loss, Continuous Pain, Nocturnal Pain, Neurogenic Signals, Loss Of Muscle Strength, Failure Symptoms, and Preference. This resulted in the classification tree with 46 nodes is shown in Figure 5.4. The risk and classification performance of this tree is shown in Table 5.4.

The tree was trained and validated by a training set (75% of the vignettes) and a test set (25% of the vignettes). In the test set 73.2% of the cases were correctly predicted by this tree. Most of the cases were referred to the GP (71.9%), followed
by a referral to the Physiotherapist (28.1%). None of the cases, however, was referred to Self-referral. Figure 5.5 shows the normalized importance of the independent variables in the model. Again, the factor Weight Loss is shown as most important factor in determining the referral advice.

5.4 Discussion

The study described in this chapter has resulted in a decision tree as the next step in our research to design a CDSS for self-referral decision support for patients with low back pain to determine when it is best to go to the GP, the physiotherapist, or to perform self-care\textsuperscript{95,107}. This decision tree was based on judgements on low back pain cases by GPs and physiotherapists during a vignette study, as a vignette study can be used to investigate the effect of multiple factors in complex decisions\textsuperscript{92}.

Multinomial logistic regression analysis\textsuperscript{109} on the study data resulted in a good overview of the most significant classification factors in forming the self-referral advice. The factor Weight Loss, Trauma, and Nocturnal Pain appeared to be the strongest significant factor. The normalized importance of the independent variables in the model of the classification tree (Figure 5.5) essentially confirms the results of the multinomial logistic regression analysis, namely that the factors Weight Loss, Trauma, and Nocturnal Pain are the three most significant predictive variables in the decision process for initial triage of patients with low back pain.

Surprisingly, classification factors as Course, Neurogenic Signals, and Radiation appeared to be non-significant predictors. Although we expected the factor Course, the progress of the low back pain, would also be a significant predictor for a referral advice, the multinomial logistic regression analysis showed that this factor did not influence the outcome prediction for initial referral to GP, physiotherapist, or self-care. In literature, however, the course of low back pain is seen as a main predictor in the development of chronicity\textsuperscript{112}. Guidelines on the treatment of low back pain also use the course of the low back pain to classify patients in so called “patient profiles”\textsuperscript{84} for further treatment plans. As the factor Course was not indicated as significant during this vignette study, this factor was not included in the process to generate the decision tree. However, because the course of low back pain is seen in literature and guidelines as a main predictor in the development of chronicity\textsuperscript{84,113}, this factor still should be further examined during the consult with a GP or a physiotherapist.

5.4.1 Study limitations

In this study, in principal $3^2 \times 2^{13} = 73728$ different vignettes were possible. In total, only 1288 vignettes were judged. This is about 2% of the total of possible vignettes. However, the exploratory preview of the data, and the results of the multinomial regression analysis showed that the retrieved data already can be used to model the referral process.
Chapter 5 | Should I see a healthcare professional or can I perform self-care

Only a small number (13%) of the judged vignettes were judged as Total Agree or Agree for Self-care (Figure 5.2). Compared to GP (79%) and Physiotherapist (40%) this a low number and the main reason why Self-care advice does not appear as a leave node in the classification tree (Figure 5.4). The low number of Self-care advice is explained by the fact a large number of the investigated factors are related to serious problems, also called “red flags”, a patient should be screened on. Therefore, it is correct that self-care is only true if (almost) everything is in order, provided that other cases are well referred to GP or physiotherapy. Then a skewed decision tree is no issue. As self-care is encouraged by healthcare professionals in case of a normal course\textsuperscript{84,112,113}, the decision tree should be further adjusted on self-care in near future research so that it also contains a Self-care advice leaf node.

The number of physiotherapists in the group of study participants was much higher than the number of GPs: 83% and 11% respectively. The reason for this was the high response on a digital newsletter that was published by the Royal Dutch Society for Physical Therapy (KNGF) among physiotherapists. Although we cannot ascertain this presumption, this may have led to a higher score on the agreement of physiotherapy advise.

5.4.2 Study strengths
This study has led to a first version of the decision tree that will serve as the basis to build a tool that advices patients with low back pain from the very beginning and that was prepared by clinicians. Up to now, no comparable tools have been found elsewhere in literature.

5.4.3 Future work
Altogether, the study analysis described in this chapter has led to a classification tree that correctly predicted 73.2% of the vignettes in the test set. In near future research, the performance of the tree should be improved, and the tree should also be extended with Self-care advice leave nodes. An evaluation study of the current decision tree has been planned in the summer/autumn of 2016 on a real population of patients with (acute) low back pain, that contact primary health care for help. This evaluation study will provide a new set of low back pain cases. The expectation is that this set of real-life cases will contain a considerable amount of self-care cases. Based on this new data, the decision tree will be improved further, in which is also will be looked at the possibility of a lower threshold than $p < .1$. Next to this, this evaluation study will also contribute to a better understanding of the distribution of patients with a new episode of low back pain to different profiles. Subsequently, Self-care advice will be related to information on appropriate exercises to perform self-care by patients with (acute) low back pain. In the end, this all will lead to an important triage tool that is intended to achieve more efficient healthcare and, in case no risk factors are found in the patient, to more patients that work on self-management.

76
CHAPTER 6
Evaluation of Three Machine Learning Models for Self-Referral Decision Support on Low Back Pain in Primary Care

Abstract

Most people experience low back pain (LBP) at least once in their life and for some patients this evolves into a chronic condition. One way to prevent acute LBP from transiting into chronic LBP, is to ensure that patients receive the right interventions at the right moment. We started research in the design of a clinical decision support system (CDSS) to support patients with LBP in their self-referral to primary care. For this, we explored the possibilities of using supervised machine learning. We compared the performances of the three classification models - i.e. 1. Decision tree, 2. Random forest, and 3. Boosted tree - to get insight in which model performs best and whether it is already acceptable to use this model in real practice.

The three models were generated by means of supervised machine learning with 70% of a training dataset (1288 cases with 65% GP, 33% physio, and 2% self-care cases). The cases in the training dataset were fictive cases on low back pain collected during a vignette study with primary healthcare professionals. We also wanted to know the performance of the models on real-life low back pain cases that were not used to train the models. Therefore we also collected real-life cases on low back pain as test dataset. These cases were collected with the help of patients and healthcare professionals in primary care. For each model, the performance was measured during model validation - with 30% of the training dataset - as well as during model testing - with the test dataset containing real-life cases. The total observed accuracy as well as the kappa, and the sensitivity, specificity, and precision were used as performance measures to compare the models.

For the training dataset, the total observed accuracies of the decision tree, the random forest and boosted tree model were 70%, 69%, and 72% respectively. For the test dataset, the total observed accuracies were 71%, 53%, and 71% respectively. The boosted tree appeared to be the best for predicting a referral advice with a fair accuracy (Kappa between 0.2 and 0.4). Next to this, the measured evaluation measures show that all models provided a referral advice better than just a random guess. This means that all models learned some implicit knowledge of the provided referral advices in the training dataset.

The study showed promising results on the possibility of using machine learning in the design of our CDSS. The boosted tree model performed best on the classification of low back pain cases, but still has to be improved. Therefore, new cases have to be collected, especially cases that are classified as self-care cases. This to be sure that also the self-care advice can be predicted well by the model.
6.1 Introduction
Most people experience low back pain (LBP) at least once in their life. As such, it is one of the most common health problems in the world\(^{78,114,115}\). A formal definition of LBP is “pain, muscle tension, or stiffness localized below the costal margin and above the inferior gluteal folds, with or without leg pain\(^{116}\). This means that LBP is in fact a symptom referring to the location of the problem, rather than a specific pathology that causes the problem\(^{117}\).

Some patients with LBP develop a chronic condition. The risk of chronic LBP continues to increase with age\(^{115,118}\). Because LBP causes considerable disability and financial burden globally\(^{119}\), it is of importance to prevent the development of chronic LBP wherever possible. One way to prevent acute LBP from transiting into chronic LBP, is to ensure that patients receive the right interventions at the right moment\(^{99}\). However, this group of patients is heterogeneous, and individual patients respond differently to interventions. Therefore, relevant studies have been conducted in an attempt to classify patients with LBP to the most optimal interventions\(^{59,75,97,120,121}\).

Normally, a patient with a new episode of LBP starts in primary care\(^{59}\) by visiting a general practitioner (GP) or physiotherapist. In an increasing number of countries, patients with musculoskeletal disorders can make use of patient self-referral to a physiotherapist\(^{82,100}\). Characteristics of patients that utilize self-referral are higher education level, a shorter duration of symptoms and recurrent symptoms\(^{122,123}\). However, for a group of patients it is still unclear what to do first: consult a GP or consult a physiotherapist. There is also a third option, namely performing self-care at first\(^{101}\). During self-care, the patient is not treated by a professional and continues ordinary activities within the limits permitted by the pain. This usually leads to faster recovery than either bed rest or back-mobilizing exercises\(^{100}\). When a patient visits a GP or physiotherapist, (s)he can refer the patient further to other options when needed. In the Netherlands, for example, the GP can refer the patient to the emergency room, but also to other secondary and tertiary care specialists as neurology, orthopedics, spine centers, pain centers, or psychologically augmented physiotherapy in the case of psychological and social factors causing the LBP\(^{75}\). In this paper, we focused on self-referral to GP, physiotherapist, or self-care as these are the first steps in a new episode of LBP in the Dutch care system, and further referral to other options sought by patients experiencing LBP can only be taken if one or more of these three steps have been performed.

In 2015, we started research to design a clinical decision support system (CDSS) to support patients with LBP in their self-referral process\(^{107}\). This is a classification process that leads to one of the three following referral advices: 1. consult a GP, 2. consult a physiotherapist, or 3. perform self-care. As self-referral can be seen as a classification process, we opted for supervised machine learning to design a classification model representing this process. Machine learning offers algorithms that can be used to learn computers based on data\(^{31}\). In supervised machine learning, a classification model learns from labelled examples.
Machine learning is increasingly used in healthcare informatics, also in the case of patient referral. Recent examples are systems in emergency departments to identify patients with suspected infection and to identify low-complexity patients that can be included in a separate fast track patient stream to save waiting time and capacity. In case of musculoskeletal problems, the Work Assessment Triage Tool (WATT) is an example of a machine learned CDSS that refers workers with musculoskeletal injuries to optimal rehabilitation interventions. For LBP in particular, there is the Nijmegen Decision Tool for referral of chronic LBP to be used by secondary or tertiary spine care specialists. However, the design of this tool was not based on a machine learning approach and is not intended for patient self-referral in primary care.

In this chapter, we explore the possibilities of using supervised machine learning in the design of our CDSS to support patients with LBP in their self-referral to primary care, as machine learning can often be successfully applied for classification problems. Our exploration is the follow-up of two steps we already have undertaken so far: 1. an inventory of important features to classify LBP, and 2. a vignette study in which fictive cases of LBP were judged on referral advice by healthcare professionals. The vignette study has resulted in a dataset containing labelled examples that can be used for supervised machine learning. In this chapter, this dataset is used as training dataset to train three machine learning models, i.e. 1. Decision tree, 2. Random forest, and 3. Boosted tree. Next to this, we also describe the process used to construct a test dataset with real-life cases of LBP. With this test dataset, we compare the performances of the three classification models on real-life cases. In this way, we get insight in which model performs best and whether it is already acceptable to use this model in real practice.

6.2 Methods

6.2.1 Machine learning

At first, the intension was to build a decision tree only, as decision trees are self-explanatory and easy to follow. However, a decision tree is a single classifier and ensembles of classifiers often perform better than a single classifier. Therefore, we also focused on tree ensembles. The following three classification models were generated: 1. Decision tree, 2. Random forest, and 3. Boosted tree. The first model is a single tree, the second and third models are ensembles of trees. In a random forest, different decision trees are generated on subsets that are sampled with replacement from the original training dataset. Classification of a new case takes place by majority vote of the trees in the random forest. The difference with boosted tree is that for boosted tree the distribution of the training set for generating the next tree is adaptively changed, based on the performance of previous classifiers. R in RStudio was used to train these classification models with our training dataset.
### Table 6.1. Overview of the input variables (features) and response variable (output) that describe the cases in the dataset that was used to train the three classification models.

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
<th>Type</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>The age of the patient</td>
<td>Input variable -</td>
<td>“&lt;50”, “&gt;=50”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Factor w/2 levels</td>
<td></td>
</tr>
<tr>
<td>Wellbeing</td>
<td>The state of being healthy as perceived by the patient by using the questions of the WHO-5 Well-Being Index135</td>
<td>Input variable -</td>
<td>“bad”, “good”, “medium”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Factor w/3 levels</td>
<td></td>
</tr>
<tr>
<td>Course</td>
<td>The duration of the current low back pain episode</td>
<td>Input variable -</td>
<td>“&lt;2weeks”, “&gt;=2weeks”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Factor w/2 levels</td>
<td></td>
</tr>
<tr>
<td>Analgesics</td>
<td>Does the patient use analgesics - e.g. paracetamol, ibuprofen or diclofenac - on a daily basis?</td>
<td>Input variable -</td>
<td>“no”, “yes”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Factor w/2 levels</td>
<td></td>
</tr>
<tr>
<td>Trauma</td>
<td>Was the low back pain caused by a trauma?</td>
<td>Input variable -</td>
<td>“no”, “yes”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Factor w/2 levels</td>
<td></td>
</tr>
<tr>
<td>Corticosteroid</td>
<td>Does the patient use corticosteroids - e.g. prednisone - on a daily basis?</td>
<td>Input variable -</td>
<td>“no”, “yes”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Factor w/2 levels</td>
<td></td>
</tr>
<tr>
<td>Serious diseases</td>
<td>Does the patient has serious diseases, namely one of the following: osteoporosis, vertebral fracture, cancer, rheumatic disorder (e.g., Bechterew disease, osteoarthri-tis), narrowing of the spinal canal (Canal Stenosis), shifted vertebra(s) or damaged vertebrae demonstrated on X-rays?</td>
<td>Input variable -</td>
<td>“no”, “yes”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Factor w/2 levels</td>
<td></td>
</tr>
<tr>
<td>Weightloss&gt;5kg</td>
<td>Has the patient lost more than 5 kilograms in the past month without a reason e.g. a diet?</td>
<td>Input variable -</td>
<td>“no”, “yes”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Factor w/2 levels</td>
<td></td>
</tr>
<tr>
<td>Continouspain</td>
<td>Does the patient currently has constant pain, which does not decrease with rest or when changing posture?</td>
<td>Input variable -</td>
<td>“no”, “yes”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Factor w/2 levels</td>
<td></td>
</tr>
<tr>
<td>Nocturnalpain</td>
<td>Does the patient also has low back pain at night that wakes the patient up?</td>
<td>Input variable -</td>
<td>“no”, “yes”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Factor w/2 levels</td>
<td></td>
</tr>
<tr>
<td>Neurogenicsignals</td>
<td>Does the patient has more pain if the patient has to cough or sneeze, or when the patient is lifting something?</td>
<td>Input variable -</td>
<td>“no”, “yes”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Factor w/2 levels</td>
<td></td>
</tr>
<tr>
<td>Radiation</td>
<td>Does the patient suffer from tingling or pangs in one or both legs?</td>
<td>Input variable -</td>
<td>“no”, “yes”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Factor w/2 levels</td>
<td></td>
</tr>
<tr>
<td>Lossmusclestrength</td>
<td>Does the patient has reduced strength in one or both legs?</td>
<td>Input variable -</td>
<td>“no”, “yes”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Factor w/2 levels</td>
<td></td>
</tr>
<tr>
<td>Failuresymptoms</td>
<td>Does the patient suffer from failure symptoms in one or both legs, which makes it impossible to move a leg, or legs, or leads to urinary loss?</td>
<td>Input variable -</td>
<td>“no”, “yes”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Factor w/2 levels</td>
<td></td>
</tr>
<tr>
<td>Preference</td>
<td>Referral preference of the patient</td>
<td>Input variable -</td>
<td>“GP”, “Physio”, “Selfcare”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Factor w/3 levels</td>
<td></td>
</tr>
<tr>
<td>Advice</td>
<td>Referral advice for this patient case</td>
<td>Response variable -</td>
<td>“GP”, “Physio”, “Selfcare”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Factor w/3 levels</td>
<td></td>
</tr>
</tbody>
</table>
Chapter 6 | Three machine learning models for self-referral decision support on low back pain

6.2.2 Datasets
6.2.2.1 Training dataset
The training dataset consisted of 1288 fictive cases of LBP. These cases were judged by 63 physiotherapists and GPs on referral advice during a vignette study\textsuperscript{128}. Table 6.1 provides a detailed overview of the variables - 15 input variables, 1 response variable - that describe the cases in this training dataset. During the vignette study, cases of LBP were presented that were generated by using a fixed text in which the values of the 15 input variables varied randomly. No combination of variable values was used twice, therefore the training dataset exists of unique cases. The referral advices among the cases in the training dataset were classified as follows: 843 (65 \%) GP advice, 425 (33 \%) physiotherapy advice, and 20 (2 \%) self-care advice.

Figure 6.1. Study design that was used to collect real-life cases on low back pain. These cases were used as test dataset in the evaluation of the three classification models.
6.2.2.2 Test dataset
From September 2016 to April 2017, we collected a set of real-life cases of LBP to construct a test dataset. The intention was to collect as much as possible patient cases during the time the study was conducted. This was done in collaboration with 5 centres for physical therapy and 6 GP centres. We presented our study to the medical ethical committee. We received a statement that ethics approval was not required for our study, as the normal healthcare path was not influenced and the patients remained anonymous to the researchers.

The study design that was used to collect real-life cases of LBP is shown in Figure 6.1. This process started when a patient with a new episode of LBP called a centre to make an appointment (1). Subsequently, the patient was asked to participate the study (2). If agreed, the patient was informed about the study and received a web-address to an online questionnaire with questions related to the input variables of Table 6.1. After the patient had given informed consent, the patient answered the questions (3). Next, the patient visited the healthcare professional of his/her preference. After the consult, the healthcare professional filled in a form indicating what the advice to the patient should have been: visit a GP, a physiotherapist, or perform self-care (4). The answers of the patients on the questions were entered compared to the referral advice provided by the healthcare professional (5). Finally, per model the predicted advice was compared to the referral advice provided by the healthcare professional (6).

6.2.3 Model performance assessment
The models were explored by comparing their performances. A performance measure often used to evaluate a model is accuracy, also known as the recognition rate. However, using accuracy is only a good indicator in the evaluation of a model when the class distribution in the training dataset is well-balanced. In our study, we had an unbalanced multiclass training dataset: 65 % GP advice, 33 % physiotherapy advice, and 2 % self-care advice. Therefore, also other evaluation measures were taken into account (Figure 6.2). Per model, we used a confusion matrix to calculate the sensitivity (true positive rate), the specificity (true negative rate), and the precision (positive predictive value) to gain more insight into the performances of the models. The kappa of the models were compared too. The kappa is a metrics for the strength of agreement of a model that compares the observed accuracy with the expected accuracy with a Kappa of 0-0.20 as slight, 0.21-0.40 as fair, 0.41-0.60 as moderate, 0.61-0.80 as substantial, and 0.81-1 as almost perfect.

Each model was trained with 70% of the training dataset (model training), validated with 30% of the training dataset (model validation), and tested with the test dataset (model testing) (Figure 6.3). The cases in the test dataset were not used to train the model to be able to measure the performances of the models more accurately. For each model, all evaluation measures were calculated during model validation as well as during the model testing.
Chapter 6 | Three machine learning models for self-referral decision support on low back pain

Figure 6.2. Confusion matrix and evaluation measures that were used to explore the performances of the three classification models, where G represents the class GP, P the class physiotherapy, and S the class self-care.

Figure 6.3. Overview of the different phases in exploring the performance of each model as performed in this study.
6.3 Results
6.3.1 Test dataset
In total, 45 patients completed the online questionnaire before visiting the healthcare professional. Next to this, 44 healthcare professionals provided a referral advice after seeing patients. However, not all 44 referral advices could be connected to a completed questionnaire, as some patients intended to participate into the study, but for some reason did not fill in the online questionnaire. Next to this, some patients filled in the questionnaire, but no referral advice was provided by the healthcare professional. In the end, 38 of the 45 completed questionnaires could be connected to a provided referral advice. This resulted into a set of 38 real-life cases of LBP.

The average age of the patients was 40.00 years (SD 14.53; range 17.00-79.00 years). Table 6.2 shows that 33 patients visited a physiotherapist and 5 visited a GP. The 38 cases were classified as follows: 4 (11 %) GP advice, 30 (78 %) physiotherapy advice, and 4 (11 %) self-care advice. Thus the test dataset also became an unbalanced dataset. However, in contrast to the training dataset, in the test dataset physiotherapy advice was the overrepresented class. Table 6.2 shows that in the test dataset, just as in the training dataset, “self-care” was the underestimated class.

We asked the GPs in our study if they could explain why they did not see as many patients with LBP as the physiotherapists. It appeared that most patients with acute low back get advice from the doctors’ assistant first on how to cope with the LBP and to wait a couple of days to see what happens in first instance. Then the GP did not see these patients. Next to this, the GPs also indicated that patients more often find the direct way to the physiotherapist for musculoskeletal problems.

By handling Table 6.2 as confusion matrix, we could determine the accuracy of the choice of a patient for a healthcare professional. We found a total accuracy rate of 0.868 (95% C.I. 0.719, 0.956). This means that in about 87% of the cases the patient consulted the same type of healthcare professional – GP or physiotherapist - as also was indicated in the referral advice.

Table 6.2. Overview of the numbers of healthcare professionals that were visited by the patients in the test dataset and the referral-advices as provided by these healthcare professionals. G represents the class GP, P the class physiotherapy, and S the class self-care.
6.3.2 Results of model training, model validation and model testing

6.3.2.1 Decision tree

The decision tree is shown in Figure 6.4. This figure shows that from the original 15 features (Table 6.1) only 4 features were used in the decision nodes i.e. Weight loss, Wellbeing, Usage of corticosteroids, and Loss of muscle strength. Furthermore, this decision tree never provides a self-care advice, probably because only 2% of the cases in the training dataset was classified as self-care advice class and therefore never could reach the highest fraction of a class in a node of leaf.

Table 6.3 shows the confusion matrix, accuracy, sensitivity, specificity, and precision measures of the decision tree.

![Decision tree](image)

**Figure 6.4.** Decision tree as generated in R on the training dataset. The class of a node/leaf in this tree is based on the highest fraction of a class in this node/leaf, which have been marked with a red circle in this figure.
Table 6.3. Performance of the decision tree during model validation and during model testing (Figure 6.3), where G represents the class GP, P the class physiotherapy, S the class self-care, and C.I. is Confidence Interval.

<table>
<thead>
<tr>
<th>Decision tree</th>
<th>Calculated evaluation measures on the Validation dataset</th>
<th>Calculated evaluation measures on the Test dataset</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Reference</td>
<td>G</td>
</tr>
<tr>
<td>Prediction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G</td>
<td>212</td>
<td>38</td>
</tr>
<tr>
<td>P</td>
<td>74</td>
<td>62</td>
</tr>
<tr>
<td>S</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.7361</td>
<td>0.6078</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.6275</td>
<td>0.7431</td>
</tr>
<tr>
<td>Precision</td>
<td>0.8480</td>
<td>0.4559</td>
</tr>
<tr>
<td>Accuracy / 95% C.I.</td>
<td>0.7026</td>
<td>(0.6545, 0.7475)</td>
</tr>
</tbody>
</table>

6.3.2.2 Random forest
A random forest cannot be presented like a decision tree, but Figure 6.5 shows multiclass ROC curve of this random forest. For all three advice classes, the prediction performance of the random forest is better than just a random choice. Figure 6.6 shows the determined variable importance in the random forest for each class. Weight Loss more than 5 kg is the most important feature in the process of classifying a referral advice.

Table 6.4 shows the confusion matrix, accuracy, sensitivity, specificity, and precision measures of the random forest.
Figure 6.5. The multiclass ROC Curve of the random forest.

Figure 6.6. Determined variable importance in the random forest for each class. The variable importance values are scaled to have a maximum value of 100.
Three machine learning models for self-referral decision support on low back pain | Chapter 6

Table 6.4. Performance of the random forest as estimated during model validation and during model testing (Figure 6.3), where G represents the class GP, P the class physiotherapy, S the class self-care, and C.I. is Confidence Interval.

<table>
<thead>
<tr>
<th>Random Forest</th>
<th>Calculated evaluation measures on the Validation dataset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prediction</td>
<td>Reference</td>
</tr>
<tr>
<td>G</td>
<td>G</td>
</tr>
<tr>
<td>Prediction</td>
<td>G</td>
</tr>
<tr>
<td>P</td>
<td>105</td>
</tr>
<tr>
<td>S</td>
<td>2</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.6916</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.7674</td>
</tr>
<tr>
<td>Precision</td>
<td>0.9600</td>
</tr>
<tr>
<td>Accuracy / 95% C.I.</td>
<td>0.6949 / (0.6465, 0.7402)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Calculated evaluation measures on the Test dataset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prediction</td>
</tr>
<tr>
<td>G</td>
</tr>
<tr>
<td>Prediction</td>
</tr>
<tr>
<td>P</td>
</tr>
<tr>
<td>S</td>
</tr>
<tr>
<td>Sensitivity</td>
</tr>
<tr>
<td>Specificity</td>
</tr>
<tr>
<td>Precision</td>
</tr>
<tr>
<td>Accuracy / 95% C.I.</td>
</tr>
</tbody>
</table>

6.3.2.3 Boosted tree
Figure 6.7 shows the multiclass ROC curve of the boosted tree, which shows that for the boosted tree model the prediction performance is better than a random choice. Figure 6.8 shows the determined total variable importance in the boosted tree. Again, Weight Loss more than 5kg is the most important feature in the process of classifying a referral advice.

Table 6.5 shows the confusion matrix, accuracy, sensitivity, specificity, and precision measures of the boosted tree.
Figure 6.7. The multiclass ROC Curve of the boosted tree.

Figure 6.8. Determined total variable importance in the boosted tree. The variable importance values are scaled to have a maximum value of 100.
Three machine learning models for self-referral decision support on low back pain | Chapter 6

6.3.3 Model comparison

The measured performances show that all models provided a referral advice better than just a random guess. When taking the majority referral class (GP advice) of the training dataset as default class, the baseline values of sensitivity during model validation and model testing are 0.65 and 0.11 respectively. This is because 65% of the cases advice in the training dataset, and 11% of the cases in the test dataset, were classified as GP advice. All measured sensitivities were higher than these baseline values. This means that all models learned some implicit knowledge of the provided referral advices in the training dataset.

Table 6.5. Performance of the boosted tree as estimated during model validation and during model testing (Figure 6.3), where G represents the class GP, P the class physiotherapy, S the class self-care, and C.I. is Confidence Interval.

<table>
<thead>
<tr>
<th>Boosted tree</th>
<th>Calculated evaluation measures on the Validation dataset</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Reference</td>
</tr>
<tr>
<td>Prediction</td>
<td>G</td>
</tr>
<tr>
<td></td>
<td>P</td>
</tr>
<tr>
<td></td>
<td>S</td>
</tr>
<tr>
<td>Sensitivity</td>
<td></td>
</tr>
<tr>
<td>Specificity</td>
<td></td>
</tr>
<tr>
<td>Precision</td>
<td></td>
</tr>
<tr>
<td>Accuracy / 95% C.I.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Boosted tree</th>
<th>Calculated evaluation measures on the Test dataset</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Reference</td>
</tr>
<tr>
<td>Prediction</td>
<td>G</td>
</tr>
<tr>
<td></td>
<td>P</td>
</tr>
<tr>
<td></td>
<td>S</td>
</tr>
<tr>
<td>Sensitivity</td>
<td></td>
</tr>
<tr>
<td>Specificity</td>
<td></td>
</tr>
<tr>
<td>Precision</td>
<td></td>
</tr>
<tr>
<td>Accuracy / 95% C.I.</td>
<td></td>
</tr>
</tbody>
</table>

Figure 6.9 shows the estimated spread and mean of the accuracy, as well as of the kappa, for each model. The boosted tree appeared to be the best for predicting a referral advice with a fair accuracy (Kappa between 0.2 and 0.4). Next to this, Figure 6.10 shows that the boosted tree performed best on accuracy both during model...
validation as well as during model testing (72% and 71% respectively). Furthermore, the averaged sensitivity and specificity of the boosted tree model were the highest during model testing, meaning that the boosted tree model performs best on a dataset with real-life cases.

![Graphical presentation of the evaluation measures of the models as estimated during model validation as well as during model testing. The Accuracy is the total observed accuracy, and Sensitivity, Specificity, and Precision are the averaged Sensitivity, Specificity, and Precision of the three self-referral classes GP, Physio and Self-care.](image)

**Figure 6.9.** Overview of the spread and the mean of the accuracy, as well as of the kappa, for each model.

**Figure 6.10.** Graphical presentation of the evaluation measures of the models as estimated during model validation as well as during model testing. The Accuracy is the total observed accuracy, and Sensitivity, Specificity, and Precision are the averaged Sensitivity, Specificity, and Precision of the three self-referral classes GP, Physio and Self-care.
6.4 Discussion

In this study, we explored the possibility of using machine learning in the design of a CDSS to support patients with a novel episode of LBP in their self-referral to primary care. At this moment, mainly patients with a higher education level, a shorter duration of symptoms and recurrent symptoms use the option of self-referral\(^{122,123}\). For a group of patients it is still unclear what to do first: consult a GP, consult a physiotherapist, or perform self-care first. It is important is to ensure that all patients receive the right interventions at the right moment to prevent that acute LBP becoming chronic\(^9\) with considerable more impact for the patient and costs for the society\(^{119}\).

A CDSS relays on computational models that can also be constructed and maintained based on machine learning\(^{52}\). This instead of a knowledge-based approach, in which a knowledge base and an inference engine are constructed and maintained based on knowledge elicited from literature and experts. This process of knowledge acquisition and maintenance can be very time consuming, and too expensive, and is also known as the “knowledge-acquisition bottleneck”\(^{137}\). When machine learning can be used in the design of our CDSS, we expect to avoid this kind of problems. Especially because digital data sources, as for example electronic health records, are becoming increasingly available. These sources contain data that can subsequently be used to train and maintain/improve the models.

During this study, we focused on the classification models decision tree, random forest and boosted tree. One should be aware that more types of classification models can be generated by machine learning algorithms. Other common machine learning algorithms are for example linear regression, neural networks, and support vector machines. Each machine learning algorithm has its own pros and cons\(^{127,196}\) that may differ on the type of features used, (e.g., continuous, categorical). Decision tree is the machine learning algorithm that can handle both categorical and continuous features, and is used most for classification problems as decision trees are self-explanatory and easy to follow\(^{129}\). Therefore, we have chosen for decision tree, random forest and boosted tree - i.e. tree based models – for this study.

In our study, the performance measures of three models - i.e. decision tree, random forest and boosted tree - were estimated twice: 1. during model validation with 30% of the training dataset, and 2. during model testing with a test dataset with real-life cases of LBP. The exploration with the models shows that the boosted tree performed best. The measured performances also show that all models provided a referral advice better than just a random guess, meaning that all models learned some implicit knowledge from the examples in the training dataset.
6.4.1 Study limitations
The distribution of the referral advice classes in the training dataset as well as in
the test dataset was imbalanced. For the training dataset, the cases in the vignette
study mainly contained serious factors indicating that the patient should see a
GP. Therefore, most cases in the training dataset were classified as “GP advice”. Subsequently, the models in this study were trained with an overrepresentation of GP advices. In the test dataset most cases were classified as “physiotherapist advice”. Despite the overrepresentation of the GP class in the training dataset, for the test dataset the sensitivities of the models still scored well on physiotherapy advice. Nevertheless, this wide variation in referrals (GP referral, physiotherapist referral and the very small number of self-care referral) will be an area to be improved in future work.

6.4.2 Future research
The study showed promising results on using machine learning in the design of our
CDSS. However, before machine learning can really be used, we have to collect more
cases classified as self-care to be sure that also the self-care advice can be predicted
well. This is also the most interesting referral class, because there is an increasing
interest in using digital interventions to support patient self-management in
LBP. When self-care can be predicted well, a next step is to provide patients with
personalized information on how to cope with the LBP and what exercises may be
helpful. In this, a web-based program for self-management of LBP can be deployed,
just as for example the system that is used for patients with COPD.

6.4.3 Concluding remarks
Our study showed promising possibilities of using machine learning in the design
of a CDSS to support patients with LBP in their self-referral process to primary care.
CDSSs that support self-referral as well as further referral by healthcare professionals
have the potential to decrease the current long waiting lines in healthcare in many
countries. However, getting there is a long process and further study is needed on
machine learning with larger data sets containing new cases, especially cases that
are classified as self-care cases, to improve the model performances.
CHAPTER 7
Using machine learning and patient-reported data to model decision support for physicians on the selection of appropriate treatments for low back pain

Submitted 2017
Chapter 7 | Decision support for physicians on the selection of treatments for low back pain

Abstract
Patients with low back pain (LBP) can be referred to secondary/tertiary care by their general practitioner or medical specialist when needed. Contradictory advice and treatments may have negative consequences for optimal recovery. A clinical decision support system (CDSS) may support physicians in selecting appropriate treatments for patients with LBP according to the expertise of healthcare specialists on LBP. The objective of this study was to determine if it is possible to use machine learning and patient-reported data to model decision-making on treatments for LBP.

We used a database of a university spine center containing patient-reported baseline and treatment data from 1546 patients with LBP. From this dataset, a training dataset was labeled on the treatments Rehabilitation and Surgery. Classification algorithms in WEKA were trained, and validated during 10-fold cross validation. A test dataset was constructed with 50 cases judged by 4 experts on LBP. This dataset was used for interrater agreement analysis and to test the models with data not used to train the models. Prediction accuracy and average area under curve (AUC) were used as performance measures.

The interrater agreement among the 4 experts was substantial (Fleiss Kappa 0.67). The best performing models for decision-making on LBP treatments differed per treatment. The AUC values indicated small to medium (machine) learning effects. Machine learning to model decision-making processes on treatments for LBP is possible. However, model performances have to be improved before these models can be actually used in a CDSS.
7. 1 Introduction

Low back pain (LBP) is experienced by about 80% people once in their lifetime\textsuperscript{71} and causes considerable disability in patients and financial burden for society\textsuperscript{119,140}. Although most episodes of acute LBP fade after a period of time\textsuperscript{141}, about 20\% of the people with LBP develop a chronic condition, of which around 11\% become disabled\textsuperscript{71}. The prevention of chronic LBP and disability are therefore major societal challenges\textsuperscript{99,142}.

Most patients with (chronic) LBP have non-specific LBP\textsuperscript{71}. Because the LBP in this group of patients is very heterogeneous, it is difficult to determine what treatment(s) suit which patients best in a specific situation. This has led to a substantial variation of diagnostic and therapeutic management of patients with LBP among healthcare providers\textsuperscript{59,142,143}. This plethora of treatments and contradictory advises may have negative consequences for an optimal recovery and may lead to passive coping style, somatization in patients and consequently to chronic pain\textsuperscript{144}. To standardize treatments and advises to patients with LBP, research has been focused on developing methods for classifying patients with LBP into more homogeneous subgroups based on patho-anatomical, mechanical, and bio-psychosocial characteristics\textsuperscript{59,75,97,120,121}.

In the Netherlands, patients with chronic LBP (with pain lasting for more than 3 months) can be referred to secondary or tertiary care by their general practitioner (GP) or medical specialist, although with mixed effects. Frequently, LBP recurs after discharge within 1 year in about 24\% to 80\%\textsuperscript{145}. When LBP recurs, the patient may start again in primary care. Therefore, communication among both secondary and primary care practitioners is of great importance to avoid passivity and somatization in patients. For this, a clinical decision support system (CDSS) that supports physician providers in primary care in the selection of appropriate treatments and advises for patients with LBP may be helpful.

CDSSs assist healthcare providers in making clinical decisions for the benefit of their patients\textsuperscript{19,30,137}. Most of these clinical decisions are used for diagnostic purposes, selection of treatments, or improving the uptake of guideline recommendations\textsuperscript{19,126,137,146}. The most common type of a CDSS in routine clinical care are knowledge-based systems\textsuperscript{30}. The development of knowledge-based systems focuses on the construction and maintenance of a knowledge base and inference engine. For this, knowledge is elicited from literature and domain experts, for example by conducting interviews. An example of a knowledge-based approach is the Nijmegen Decision Tool for referral of chronic LBP to be used by secondary or tertiary spine care specialists to decide which patients with chronic LBP should be seen by a spine surgeon or by other non-surgical medical specialists\textsuperscript{117}. Knowledge for this system was elicited during a three-round Delphi study with experts on LBP treatment.
The construction and maintenance of a knowledge base and inference engine can be very time consuming, and therefore too expensive\textsuperscript{137}. Instead of using a knowledge-based approach, a data-driven approach with the help of machine learning technologies is increasingly more often used in healthcare informatics\textsuperscript{32}. The application of machine learning in healthcare highly benefits from the increasing amount of available digital health data sources, especially by the application of electronic health records (EHR) in healthcare processes. Because of this growing amount of available data, the use of a data-driven approach in the design of CDSSs may facilitate the process of building and maintaining the CDSS, compared to a knowledge-based approach.

In this chapter, we describe a study that aims to determine whether a data-driven approach can model the decision-making process of a CDSS that can support physicians in the selection of appropriate treatments for patients with LBP. The objective of this study was to determine if it is possible to use machine learning and patient-reported data to model decision-making on treatments for LBP.

### 7.2 Materials and methods

In this study, we followed steps that are generally used in data mining processes\textsuperscript{147}, namely:

1. Data understanding
2. Data preparation
3. Modelling and evaluation

#### 7.2.1 Data understanding

Knowledge on the referral to LBP treatments was stored in a database provided by the Groningen Spine Center (GSC) containing patient reported data from 1546 patients with LBP that were collected in the period 2008-2015. The GSC is a tertiary care center for comprehensive care for patients with spine related disorders and pathology\textsuperscript{148}. By using this data, knowledge of healthcare specialists on LBP on the referral of patients to treatments was used as gold standard.

##### 7.2.1.1 Ethical considerations

All patients included in this study signed informed consent. The Medical Ethical Committee of the University Medical Center Groningen in the Netherlands approved the usage of data from the database of the GSC for this study at February 11, 2016.

#### 7.2.2.2 Database content

The database contained self-reported baseline and treatment data from 1546 patients of which 894 (58\%) were female and 652 (42\%) were male. The mean age of these patients was 52.3 years (SD 15.1; range 37.0-91.0 years).
The baseline data was used for patient referral to treatments in the GSC. This referral was performed by one of the four master physician assistants (MPAs) of the GSC. These MPAs had a background in physical therapy or nursing and were specifically trained in triaging by all specialists at the spine center. The mean clinical experience of these MPAs was 10 years. After discharge, the patient reported, via a follow-up form, one or more of the following treatments he/she had received: 1. Explanation and reassurance, 2. Rehabilitation, 3. Injections, 4. Medication, 5. Surgery, 6. Psychological counselling, 7. Physiotherapy, and 8. Other.

During the referral process patients had to fill in an online biopsychosocial questionnaire. This questionnaire consisted of descriptive questions and questions from the following survey-instruments:

1. The Pain disability Index (PDI)$^{149}$ to assess the degree to which the chronic pain interfered with various daily activities.
2. The Örebro Musculoskeletal Pain Questionnaire (OMPQ) as screening questionnaire to identify patients at risk for developing persistent back pain problems and related disability$^{88}$.
3. The Roland-Morris Disability Questionnaire (RMDQ)$^{150,151}$ was used to assess physical disability due to LBP.
4. The EQ-5D-3L to measure health-related quality of life on five dimensions: mobility, explanation and reassurance, usual activities, pain/discomfort and anxiety/depression$^{152}$.

Each question led to one or more data items that were stored in the database. For example, the OMPQ contained the question “Where do you have pain? Place a tick for all appropriate sites.” where Neck, Shoulder, Upper Back, Lower Back, and Leg could be checked. This led to 5 data items in the database. Table 7.1 shows the number of data items retrieved from the questionnaire.

<table>
<thead>
<tr>
<th>Used survey-instruments</th>
<th>Number of data items</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain disability Index$^{149}$</td>
<td>14</td>
</tr>
<tr>
<td>Örebro Musculoskeletal Pain Questionnaire$^{88}$</td>
<td>25</td>
</tr>
<tr>
<td>Roland Morris Disability Questionnaire$^{150,151}$</td>
<td>24</td>
</tr>
<tr>
<td>EQ-5D-3L Questionnaire$^{152}$</td>
<td>6</td>
</tr>
</tbody>
</table>

Additional information:

- Date of answering the questions, anonymized ID, Gender, Date of birth 4
- Questions on social life and work 30
- Questions on reasons for referral, medical history and lifestyle 251

**Total number of data items at baseline** 354
7.2.2.3 Training dataset
The data in the database were used to construct a training dataset for machine learning. The self-reported data collected at baseline were used as input variables (features). The reported treatments were used as response variables which can either be received (positive class “yes”) or not received (negative class “no”). Table 7.2 shows the distribution of received treatments among the 1546 cases. Because the dataset consisted of cases that could be labeled with “yes” or “no” for a treatment, the dataset could be used for a supervised machine learning approach.31,127

Table 7.2. Distribution of received treatments among the 1546 cases.

<table>
<thead>
<tr>
<th>Treatment received</th>
<th>no</th>
<th>yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Explanation and reassurance</td>
<td>669 (43%)</td>
<td>877 (57%)</td>
</tr>
<tr>
<td>Rehabilitation</td>
<td>1143 (74%)</td>
<td>403 (26%)</td>
</tr>
<tr>
<td>Injection</td>
<td>1242 (80%)</td>
<td>34 (20%)</td>
</tr>
<tr>
<td>Medication</td>
<td>1405 (91%)</td>
<td>141 (9%)</td>
</tr>
<tr>
<td>Surgery</td>
<td>1407 (91%)</td>
<td>139 (9%)</td>
</tr>
<tr>
<td>Psychology</td>
<td>1337 (86%)</td>
<td>209 (14%)</td>
</tr>
<tr>
<td>Physiotherapy</td>
<td>1245 (81 %)</td>
<td>301 (19%)</td>
</tr>
<tr>
<td>Other</td>
<td>1178 (76 %)</td>
<td>368 (24%)</td>
</tr>
</tbody>
</table>

7.2.2.4 Interrater agreement analysis
We wanted to be sure about the consistency of decision making on treatment referral by the MPAs of the GSC, because this relates to the quality of the treatment labels in the training dataset. Therefore, an interrater analysis was performed among the MPAs. For 50 cases, the MPAs selected those treatment(s) which they found most suitable, based on the baseline data. To keep the burden for the MPAs acceptable, each PA was asked to judge 25 out of the 50 cases. Next to this, 25 of the 50 cases were judged 3 times by three different MPAs.

As there were more than two raters per case, we calculated Fleiss’ Kappa, which is an extension of Cohen’s kappa for three raters or more.153 We calculated this score per treatment and then assessed the mean Fleiss Kappa. For interpretation, we used the values according to Landis and Koch: agreement with a value smaller than 0 is indicated as ‘poor’, between 0-0.20 as ‘slight’, between 0.21-0.40 as ‘Fair’, between 0.41-0.60 as ‘Moderate’, between 0.61-0.80 as ‘substantial’, and a value higher than 0.81 as ‘almost perfect’. 
7.2.3 Data preparation

7.2.3.1 Handling missing values
The values in the training dataset were not complete, because 32% of the values were missing. First, we removed the features that contained no values in the dataset. In some cases, we could impute the empty fields with zero. For example, when the patient only indicated which healthcare professionals he/she had seen before visiting the GSC, leading to empty values for the non-visited professionals. We did not remove all cases with missing values as this may lead to a bias in study results because of the possible exclusion of a substantial proportion of the original sample154.

7.2.3.2 Feature engineering
Most features in the dataset were categorical. Many classification algorithms require a discrete feature space155 meaning all data should be categorical. Therefore, all non-categorical features in the training dataset were transformed into categorical data. For example, ages in years were binned in a feature called “Age” representing age groups i.e. 0-19, 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, >=80.

After data preparation, 287 features remained, 67 features less than the original amount of 354 features (Table 7.1).

7.2.4 Modelling and evaluation
Finally, machine learning was applied to model the decision-making process on the selection of treatments for a patient with LBP. As this was a study to determine whether it is possible to use machine learning or not, we focused on two of the 8 treatments: 1. Rehabilitation, and 2. Surgery. These two treatments - non-invasive and invasive - were chosen to be compared. Two separate decision making processes were modeled. For each process, the outcome was whether or not a patient with LBP should receive the treatment based on the known baseline data.

Waikato Environment for Knowledge Analysis (WEKA) version 3.8.1 was used for analysis156. WEKA classification algorithms were used that can be grouped into base classifiers and meta classifiers. A meta algorithm can be wrapped around base learning algorithms to widen applicability or enhance performance156. The machine learning was performed in two steps: 1. all WEKA base classification algorithms were trained with the training dataset, 2. machine learning was applied again, but with cost-sensitive learning of the WEKA meta classification algorithm CostSensitiveClassifier. The base classification algorithms that performed best in the first step were used as input for this meta classification algorithm.
Chapter 7 | Decision support for physicians on the selection of treatments for low back pain

The cost-sensitive learning step was added, because the training dataset was imbalanced. The patients that did not receive the treatment were the over-represented group of patients for both rehabilitation and surgery. The distribution of the “no”/“yes” classes were 74%/26% and 91%/9% for rehabilitation and surgery respectively (Table 7.2). Cost-sensitive learning can be applied when data is highly imbalanced in an attempt to reduce the number of false-negative or false-positive errors to get better performing models\textsuperscript{157,158}.

The resulting models were validated with 10-fold cross validation in order to assess and compare the performances of the different classification algorithms.

7.2.4.1 Model testing on test dataset with PA judgements
The models were tested on a test dataset consisted of the 50 cases that were judged by the MPAs. Some of the 50 cases were judged by three MPs. In the preparation of this test dataset, for these cases the most voted judgements were taken.

7.2.4.2 Performance measures
Prediction accuracy and the average area under the curve (AUC) were calculated as performance measures. The prediction accuracies of the models should at least be equal to the percentage of the majority class in the dataset. The performance measure AUC was used as it is a common performance measure in the evaluation of machine learning algorithms\textsuperscript{159}. We used an AUC greater than 0.55 as threshold to select the best predicting models. An AUC between 0.55 and 0.64 indicates a small effect, an AUC between 0.64 and 0.71 a medium effect, and an AUC equal of greater than 0.71 a large effect\textsuperscript{160}.

7.3 Results
7.3.1 Test dataset
The MPAs judged 50 cases on treatments and Table 7.3 shows the distribution of these judgments among these 50 cases in the test dataset.

<table>
<thead>
<tr>
<th>Judged treatments</th>
<th>no</th>
<th>yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Explanation and reassurance</td>
<td>5 (10%)</td>
<td>45 (90%)</td>
</tr>
<tr>
<td>Rehabilitation</td>
<td>27 (54%)</td>
<td>23 (46%)</td>
</tr>
<tr>
<td>Injection</td>
<td>43 (86%)</td>
<td>7 (14%)</td>
</tr>
<tr>
<td>Medication</td>
<td>50 (100%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Surgery</td>
<td>48 (96%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Psychology</td>
<td>50 (100%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Physiotherapy</td>
<td>44 (88 %)</td>
<td>6 (12%)</td>
</tr>
<tr>
<td>Other</td>
<td>40 (80 %)</td>
<td>10 (20%)</td>
</tr>
</tbody>
</table>

Table 7.3. Distribution of treatment among the judged 50 cases.
7.3.2 Interrater agreement analysis
The interrater agreement analysis on the 25 cases that were judged 3 times showed that the agreement among MPAs of the GSC was substantial, with an average Fleiss Kappa of 0.67 (Figure 7.1). The highest consensus was observed for Rehabilitation, namely 0.77. The consensus on Surgery was 0.65.

![Fleiss Kappa estimations per treatment on the interrater agreement among the MPAs in the selection of treatments for patients with LBP.](image)

**Figure 7.1.** Fleiss Kappa estimations per treatment on the interrater agreement among the MPAs in the selection of treatments for patients with LBP.

7.3.3 Machine learning
In WEKA, 25 different base classification algorithms were trained to model decision making on Rehabilitation and Surgery. The performances of the models with an AUC > 0.55 in both, 10-fold cross validation and testing, in step 1 are shown in Table 7.4. The second part of Table 7.4 shows the model performances when these algorithms where used as input for the WEKA meta classification algorithm CostSensitiveClassifier.

Table 7.4 shows that the best performing models on decision making for treatments may differ per treatment. The AUC values indicate small to medium learning effects\(^1\). The model accuracies approached, or were equal, to the percentages of the majority classes in the datasets. For the 10-fold cross validation on the training dataset these percentages were 74%/91% for Rehabilitation/Surgery (Table 7.2). For test dataset, these percentages were 54%/96% for Rehabilitation/Surgery (Table 7.3). Table 7.4 shows that cost-sensitive learning has effect on model accuracies. For example, the 10-fold cross validation accuracy of the BayesNet model for Rehabilitation improves from 65% to 67%. On the other hand, the testing accuracy of the PART model for Rehabilitation drops from 56% to 54%.
Table 7.4. Model performances on 10 folds-cross validations and testing with the test dataset of the
models with an AUC > 0.55 after step 1. C.I. = confidence interval.

<table>
<thead>
<tr>
<th>Step 1: Base classification algorithms AUC &gt; 0.55</th>
<th>Treatment Rehabilitation</th>
<th>Treatment Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-folds cross-validation</td>
<td>Accuracy % (95%-CI)</td>
<td>AUC</td>
</tr>
<tr>
<td>RandomForest</td>
<td>0.74 (0.72 – 0.76)</td>
<td>0.63</td>
</tr>
<tr>
<td>PART</td>
<td>0.74 (0.72 – 0.76)</td>
<td>0.63</td>
</tr>
<tr>
<td>DecisionStump</td>
<td>0.74 (0.72 – 0.76)</td>
<td>0.56</td>
</tr>
<tr>
<td>REPTree</td>
<td>0.72 (0.69 – 0.74)</td>
<td>0.62</td>
</tr>
<tr>
<td>VotedPerceptron</td>
<td>0.72 (0.69 – 0.74)</td>
<td>0.57</td>
</tr>
<tr>
<td>NaiveBayes</td>
<td>0.66 (0.63 – 0.68)</td>
<td>0.66</td>
</tr>
<tr>
<td>BayesNet</td>
<td>0.65 (0.63 – 0.67)</td>
<td>0.67</td>
</tr>
</tbody>
</table>

| Treatment Rehabilitation |
|-----------------------------------------------|--------------------------|
| 10-folds cross-validation | Accuracy % (95%-CI) | AUC | Accuracy % (95%-CI) | AUC |
| PART | 0.74 (0.72 – 0.76) | 0.63 | 0.54 (0.40 – 0.67) | 0.56 |
| RandomForest | 0.74 (0.72 – 0.76) | 0.62 | 0.56 (0.42 – 0.69) | 0.64 |
| DecisionStump | 0.74 (0.72 – 0.76) | 0.56 | 0.54 (0.40 – 0.67) | 0.59 |
| VotedPerceptron | 0.74 (0.72 – 0.76) | 0.53 | 0.56 (0.42 – 0.69) | 0.51 |
| REPTree | 0.73 (0.71 – 0.76) | 0.62 | 0.54 (0.40 – 0.67) | 0.57 |
| NaiveBayes | 0.68 (0.66 – 0.70) | 0.66 | 0.62 (0.48 – 0.74) | 0.68 |
| BayesNet | 0.67 (0.65 – 0.70) | 0.67 | 0.62 (0.48 – 0.74) | 0.62 |

| Treatment Surgery |
|-----------------------------------------------|--------------------------|
| 10-folds cross-validation | Accuracy % (95%-CI) | AUC | Accuracy % (95%-CI) | AUC |
| DecisionStump | 0.91 (0.89 – 0.92) | 0.66 | 0.96 (0.87 – 0.99) | 0.56 |
| RandomForest | 0.91 (0.89 – 0.92) | 0.59 | 0.94 (0.84 – 0.98) | 0.71 |
| RandomTree | 0.86 (0.85 – 0.88) | 0.58 | 0.92 (0.81 – 0.97) | 0.84 |
| NaiveBayes | 0.77 (0.75 – 0.79) | 0.67 | 0.80 (0.67 – 0.89) | 0.72 |
| BayesNet | 0.76 (0.74 – 0.79) | 0.67 | 0.78 (0.68 – 0.87) | 0.70 |

<table>
<thead>
<tr>
<th>Step 2: Meta classification algorithm CostSensitiveClassifier</th>
<th>Treatment Rehabilitation</th>
<th>Treatment Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-folds cross-validation</td>
<td>Accuracy % (95%-CI)</td>
<td>AUC</td>
</tr>
<tr>
<td>PART</td>
<td>0.74 (0.72 – 0.76)</td>
<td>0.63</td>
</tr>
<tr>
<td>RandomForest</td>
<td>0.74 (0.72 – 0.76)</td>
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<td>DecisionStump</td>
<td>0.74 (0.72 – 0.76)</td>
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<tr>
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<td>0.74 (0.72 – 0.76)</td>
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<tr>
<td>REPTree</td>
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<td>NaiveBayes</td>
<td>0.68 (0.66 – 0.70)</td>
<td>0.66</td>
</tr>
<tr>
<td>BayesNet</td>
<td>0.67 (0.65 – 0.70)</td>
<td>0.67</td>
</tr>
</tbody>
</table>

| Treatment Surgery |
|-----------------------------------------------|--------------------------|
| 10-folds cross-validation | Accuracy % (95%-CI) | AUC | Accuracy % (95%-CI) | AUC |
| DecisionStump | 0.91 (0.89 – 0.92) | 0.66 | 0.96 (0.87 – 0.99) | 0.56 |
| RandomForest | 0.91 (0.89 – 0.92) | 0.59 | 0.96 (0.87 – 0.99) | 0.75 |
| RandomTree | 0.87 (0.85 – 0.88) | 0.53 | 0.90 (0.79 – 0.96) | 0.77 |
| NaiveBayes | 0.79 (0.77 – 0.81) | 0.66 | 0.84 (0.71 – 0.92) | 0.73 |
| BayesNet | 0.78 (0.76 – 0.80) | 0.67 | 0.80 (0.67 – 0.89) | 0.69 |
7.4 Discussion
In this study, we investigated the possibility of using machine learning and patient-reported data to model the decision-making of a CDSS that can support physicians in the selection of appropriate treatments for patients with LBP. As this was a pilot study, we focused on two treatments: Rehabilitation and Surgery. With the idea to expand to other treatments in future studies when machine learning proves to be rewarding.

The interrater agreement among the 4 MPAs of the GCS was proven substantial, and therefore it could be concluded that all patients were referred to treatments in the same way. This also meant that the patient-reported treatments could be used for reliable labeling of the training dataset used for the machine learning. It may be questioned whether patient reported data is reliable or not, but other studies show that accuracy of self-reported data is high\textsuperscript{161,162}.

The results showed small to medium machine learning effects based on the AUC values of the models. This indicated that the classification algorithms indeed learned from the training dataset. The model performances should be improved further before the models can be actually used in a CDSS that can support physicians in the selection of appropriate treatments for patients with LBP. The AUC of the model should at least be 0.72 as this will indicate a large effect\textsuperscript{160}. Next to this, the prediction accuracy of a model should preferably also be higher than the percentage of the majority class in the dataset to be sure that the model does not classify all cases as majority class\textsuperscript{158}.

7.4.1 Future research
In this study, we used patient-reported data. It would be of great benefit when in future research also data from EHRs can be involved. This way, data imbalance can be limited and more cases can be retrieved to increase the size of the training dataset with data. At this moment, it is a very time consuming process to gain data out of EHRs\textsuperscript{162}, but health data integration and interoperability between healthcare systems is a main topic in current research\textsuperscript{163}. When EHR data, and other data sources on (chronic) LBP, can be integrated in the application of machine learning, this also will improve model performances and facilitate model maintenance.

The dataset in this study contained 287 features as input variables for the classification algorithms. These features were related to all data variables a patient could enter into the baseline questionnaire. Future research should focus on which features are most predictive on the selection of a treatment and to see if the number of features can be reduced without dropping model performances. Or to put it even more strongly, to see if model performances can increase by using the most predictive features only. For Surgery, a study already showed some features – e.g. gender, previous surgery, treatment expectations, body weight/body mass index – that could partly predict whether a patient should be referred to surgery or not\textsuperscript{164}.
We expect that predictive features will differ per treatment, because this study also showed different best performing decision making models per treatment. This means that the future CDSS on the selection of appropriate treatments for patients with LBP will exist of different decision support models.

7.4.2 Study limitations
The database we used contained imbalanced data. The patients that did not receive the treatment were the over-represented group of patients for both Rehabilitation and Surgery. This makes it difficult to create classification models that can predict that a patient should receive treatment. This also influenced the currently retrieved model performances. We applied cost-sensitive learning on the classification algorithms that performed best on the data, because cost-sensitive learning may help to reduce the number of false-negative or false-positive errors to get better performing models\textsuperscript{157}. This helped to increase the performances of most models a little as estimated during 10-fold cross validation.

7.5 Conclusion
It seems possible to apply machine learning to model decision making on the selection of treatments for LBP, where decision making models differ per treatment. However, model performances have to be improved further before machine learned decision support tools can actually be used in real practice.
CHAPTER 8
Design and Evaluation of an Interoperable eHealth Reference Architecture for Primary Care

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### Abstract

eHealth is still not widely used in primary care, because barriers still exist around integrated and interoperable technological infrastructures for eHealth. This chapter describes the design of an interoperable eHealth reference architecture for primary care that can be used by IT specialists as a basis during the technical design of interoperable eHealth infrastructures within primary healthcare organizations.

The design of the reference architecture was based on the Refined eHealth European Interoperability Framework (ReEIF) and on results of 14 working sessions with 10 eHealth Small and Medium sized Enterprises (SMEs). The application of the reference architecture was demonstrated in a practical case, focused on the primary healthcare process of patients with acute low back pain. Subsequently, the reference architecture and the practical case were evaluated with eight IT health information experts to investigate whether the reference architecture can be used in real practice to accelerate the development of interoperable eHealth infrastructures in primary care.

The evaluation study showed that there are additional conditions needed before interoperable eHealth in primary care actually can be achieved i.e. 1. Consensus between different stakeholders is essential in setting up an interoperable eHealth infrastructure, 2. Communication and terminology standards to be used should be available, complete, usable and up-to-date, 3. The profits for business should be clear when involving SMEs in setting up interoperable eHealth infrastructures, 4. Most primary healthcare organizations have limited financial options and therefore, the possibility to access to an own customized environment within an (inter)national interoperable eHealth infrastructure would be beneficial to achieve interoperable eHealth within these organizations, and 5. A potential (inter)national interoperable eHealth infrastructure should be managed by a neutral party.

The study has resulted in an interoperable eHealth reference architecture for primary care. This reference architecture can be used to translate primary healthcare processes into interoperable eHealth infrastructures that can technically support the HIE within these healthcare processes. However, additional conditions are still needed before interoperable eHealth in primary care can actually be achieved.
8.1 Introduction

eHealth technologies are health services delivered or enhanced through the Internet and related technologies\(^4\). But although eHealth is seen as a promising means to improve the quality of care, it is still not widely used in primary care\(^{165}\). One significant reason is that barriers exist around integrated and interoperable technological infrastructures for eHealth\(^{166}\). Interoperability is defined as the ability for two (or more) systems or components to exchange information and to use the information that has been exchanged\(^{167}\). Medical interoperability is termed health information exchange (HIE). HIE is focused on reliable and interoperable electronic sharing of clinical information among physicians, nurses, pharmacists, other health care providers, and patients across the boundaries of health care institutions, health data repositories, laboratories, public health agencies, and other entities that are not within a distinct organization or among affiliated providers\(^{26}\). Unfortunately, current available health information systems and digital devices in primary care do not facilitate smooth HIE. One important cause is the usage of standalone systems that store data in different formats and without means for data exchange. To enhance interoperability among IT applications in primary care, primary organizations should be able to set up interoperable infrastructures that allow for easy integration of existing IT systems and new eHealth technologies.

![Diagram](image.png)

**Figure 8.1.** The refined eHealth European Interoperability Framework (ReEIF) and the alignment activities between organizations. *Image source: eHealth Network - Refined eHealth European Interoperability Framework\(^{27}\) used with permission of Nictiz.*
Chapter 8 | An interoperable eHealth reference architecture for primary care

Issues that have been found to hinder the development of interoperable infrastructures in healthcare include the complexity of the healthcare domain due to its many stakeholders, the large amount of possible IT health standards that can be chosen from, and problems affecting privacy and security.\textsuperscript{168,169,170,171} One research project on interoperable eHealth resulted in the Refined eHealth European Interoperability Framework (ReEIF)\textsuperscript{27,171}. The idea behind the ReEIF is: “Interoperability between two independently operating organizations (e.g. hospital, GP, patient) can only be established when the internal architecture is well appointed by making agreements with all stakeholders at all levels in the organization”\textsuperscript{27}. The ReEIF identifies 6 different interoperability levels at which different stakeholders have to collaborate to make the corresponding level operational. These six levels involve the following topics: 1. Legal and regulatory, 2. Policy, 3. Care process, 4. Information, 5. Applications, and 6. IT infrastructure (Figures 8.1 and 8.2). Interoperability issues can be addressed efficiently and in the right sequence by successively go top down through these different interoperability levels with the right stakeholders.

This chapter presents the design and evaluation of an interoperable eHealth reference architecture based on the ReEIF and on results of working sessions with eHealth providers. This reference architecture is intended to support the technical design of interoperable eHealth infrastructures in primary care and illustrates how to translate a primary healthcare process into an interoperable eHealth infrastructure that can technically support the HIE within this healthcare process. Besides the architecture, the chapter also shows the application of the reference architecture.
within a practical case: a web-based decision support system for patients with acute low back pain \(^{107,128}\) with other relevant IT systems within a primary care practice. Finally, the reference architecture, and the case study, were evaluated on technical and financial feasibility by IT health information experts. This evaluation has resulted into relevant insights that need to be known before interoperable eHealth in primary care actually can be achieved.

## 8.2 Methods

![Step 1 diagram](image)

**Figure 8.3.** Quick overview of the applied methods and how these are related to each other. “SME” in this figure stands for “Small and Medium sized Enterprises”.

Figure 8.3 shows a quick overview of the applied methods, with the following three main steps:

1. **Design of an interoperable eHealth reference architecture for primary care:**

   In the autumn of 2014 and the spring of 2015, 14 working sessions were held with 10 Small and Medium sized Enterprises (SMEs). These SMEs offered eHealth functionalities, like video consultations, activity monitoring via on-body sensors, training programs for rehabilitation of musculoskeletal problems, and coaching programs for patients with COPD and Asthma. The sessions were focused on the implementation of eHealth technologies in primary care. The SMEs discussed how their existing eHealth applications could be integrated into...
one common interoperable infrastructure. All working sessions were recorded into minutes. The outcomes of the sessions as well as the interoperability levels “care process”, “information” and “applications” of the refined eHealth European Interoperability Framework (ReEIF) were used as input in the design of an interoperable eHealth reference architecture for primary care;

2. Example application of the reference architecture in a case study:

The application of the reference architecture was demonstrated in a case study that was focused on the primary healthcare process of patients with acute low back pain. An interoperable eHealth infrastructure was designed on paper that integrated a web-based decision support system and a web-based training system with other, relevant IT systems.

3. Evaluation study:

The reference architecture and the case study were evaluated by eight IT health information experts. These experts had at least 5 years of experience in the health informatics domain and possessed theoretical knowledge of and experience with interoperability and e-standards in healthcare. The main research question of this evaluation study was:

*Can the reference architecture be used in practice to accelerate the development of interoperable eHealth infrastructures in primary care?*

Each participant was questioned during a semi-structured phone interview about:

- Participant characteristics – educational background, knowledge of and experience in health information exchange and standardization;
- SME characteristics (when applicable) – eHealth solutions provided by the SME the participant is working for, and applied interoperability approaches (network communication standards, coding systems, et cetera);
- Evaluation of the reference architecture and its usage – readability, completeness, and financial and technical feasibility of this reference architecture for their work context.

The references architecture and the practical case were described in a document that was sent to each participant prior to the phone interview. All interviews were recorded and summarized in a report. Each report was sent to the corresponding participant for feedback on completeness and interpretation of what was said. Then, these reports were analyzed based on the approach of Framework analysis. This means that the analysis was guided by data retrieved from the reports, starting the analysis with the global topics from the interview scheme, and theme concepts emerged during the analysis.
8.3 Results

8.3.1 Design interoperable eHealth reference architecture

8.3.1.1 SME working sessions on integrating eHealth applications

The infrastructure that resulted from the working sessions consisted of three layers: 1. Frontend layer, 2. Middleware layer, and 3. Data layer. The different eHealth functionalities in this infrastructure were supplied by the eHealth applications in the middleware. During these sessions, the following technical issues appeared to be the most important, and were solved in the following way:

1. Service oriented architecture (SOA): Functionalities of an eHealth application represent the services that are delivered by this eHealth application. The infrastructure should focus on the core functionalities of each eHealth application strengthened by adding the core functionalities of other eHealth applications. In this way, the infrastructure is oriented on bringing together and integrating the best services.

2. Single sign-on: All different eHealth functionalities a user has rights to, should be accessible at once by means of single sign-on. Single sign-on will save the user time, because extra login actions are no longer needed.

3. Shared core dataset: Data exchanged among different eHealth applications should be part of a shared core data set with data items agreed upon by all involved SMEs. Using a shared core data set has the advantage that shared data is not redundantly stored and when changed by functionality ‘a’ also immediately available for functionality ‘b’. Other data, used by a single eHealth application, should be stored locally for the benefit of speed of data accessibility.

4. Communication bus: A communication bus should be used to keep the integration of the eHealth services manageable. In the bus, general services are located that are needed by multiple applications, like single sign-on, authorization, logging, data import, data export, et cetera. An application should connect to the bus through an application programming interface (API) to be able to use these general services, to deliver its functionalities to the infrastructure, and to exchange data with other applications. When a new eHealth application has to be connected, this connection should meet the specifications of the API.

These decisions on technical issues were also used in the design of the interoperable eHealth reference architecture.
8.3.1.2 Usage of ReEIF levels in the design of the reference architecture

Next to the conclusions of the working sessions, three levels of ReEIF were used in the design of the interoperable eHealth reference architecture, i.e. 1. Care process level, 2. Information level, and 3. Applications level (Figure 8.2). Only these 3 levels were involved, as the design of the reference architecture was zoomed in on the translation of a primary healthcare process into an interoperable eHealth infrastructure that can technically support this healthcare process. An important part of this translation is choosing the right IT health standards. To keep the reference architecture readable, the interoperability level “IT infrastructure” was not involved as for the IT infrastructure it is often enough to align already existing general web-based standards and protocols.

In general, healthcare processes in primary care can be presented as shown in Figure 8.4. In the case of primary care, this process starts with a healthcare problem that can be treated in primary care. During the consult with the healthcare professional, a decision is made on the care plan, based on anamnesis and physical examination. The care plan can be actual treatment, or a self-care advice to the patient, or further referral to another healthcare professional with a specialization that better suits the healthcare problem. When the patient stays in this healthcare process, the effects of the care plan will be monitored to determine whether the healthcare problem has been solved or not.

When the general process shown by Figure 8.4 is worked out into further detail for a specific healthcare problem, this will result into a specific care path. For example, the care path for a patient with acute low back pain differs from the care path for a patient with COPD. In primary care, stakeholders that should analyze and agree on the details of care paths are primary healthcare professionals, and preferably also patients (Figure 8.2). In case a care path should also be supported technically by an interoperable eHealth infrastructure, information analysts should be involved for the technical analysis of information that should be exchanged.
8.3.1.2.1 Information level
Throughout a healthcare process, (health) information is gained and used during different actions at different moments. eHealth functionalities can support the retrieval and usage of this information. Figure 8.5 shows examples of possible eHealth functionalities at different moments in a healthcare process. In order to exchange data between parties – i.e. patients, healthcare professionals, IT systems – data should be standardized and represented in a data model (Figure 8.6). The data model should be agreed upon by healthcare professionals, information analysts, and terminologists (Figure 8.2). Health terminology and code systems are used to enable interoperability of data elements. International terminology and code systems relevant for primary care are the International Classification of Primary Care (ICPC)\(^{173}\), the International Classification of Diseases (ICD)\(^{174}\) and SNOMED CT\(^{45}\).
8.3.1.2.2 Applications level
The eHealth functionalities as shown in Figure 8.5 represent services delivered by eHealth applications (Figure 8.6). One application can deliver one or more eHealth functionalities. Agreements have to be made about which applications have to be involved in the infrastructure, how these applications will handle import and export of health information, and how information is integrated and processed in a user-friendly way\textsuperscript{27}. Here, software engineers should be involved (Figure 8.2). For the import and export of health information, health communications standards can be deployed. International health communication standards used in primary care are versions of HL7\textsuperscript{42} and EDIFACT\textsuperscript{175}.

8.3.1.3 Interoperable eHealth reference architecture
The resulting interoperable eHealth reference architecture for primary care is shown in Figure 8.7. It has been set up as a service-oriented architecture (SOA) and uses a communication bus that connects distributed applications. The reference architecture contains four layers: 1. Presentation services, 2. Functional services, 3. Middleware services, and 4. Data services. The Middleware services and Data services are part of the communication bus. These two layers contain generic services that are needed to manage smooth communication and data management among the distributed applications and data sources taking into account standardization, privacy, and security issues. Figure 8.7 shows some examples of generic services, as single sign-on, authentication and authorization, and structured data storage. For each single primary healthcare organization, it should be possible to customize services in the bus to the specific situation and wishes of the organization. Figure 8.7 also shows data adapters. These data adapters take care of the necessary data transformations to enable data exchange among applications connected to the communication bus.

The functional services layer contains services that support a healthcare path. This can be a specific eHealth functionality, like eCoaching or eTraining, but can also entail communication functionalities, such as eConsult or online repeat medication prescriptions (Figure 8.5). The functionalities of electrornical medical record systems (EMR) are located in this layer as well, as these systems support health information management during the healthcare process and healthcare professionals prefer working from these systems\textsuperscript{36}.

The interoperable eHealth reference architecture shows three different kinds of health records: 1. Patient Health Record (PHR), 2. Electronical Medical Record (EMR), and 3. Electronical Health Record (EHR). In a PHR, a patient can access, manage and share health information in a private, secure, and confidential environment\textsuperscript{176}. An EMR is a longitudinal electronic record of patient health information generated by one or more encounters in a care delivery setting\textsuperscript{177}. An EHR, finally, is a repository of patient data in digital form, stored and exchanged securely, and accessible by multiple authorized users. It contains retrospective, concurrent, and prospective
Figure 8.7. Interoperable eHealth reference architecture for primary care. PHR stands for Patient Health Record, EMR for Electronical Medical Record, and EHR for Electronical Health Record.
information and its primary purpose is to support continuing, efficient and quality integrated health care. As the goal of the shared dataset in Figure 8.7 is to support data exchange among different parties, the shared dataset can be seen as an EHR.

The Presentation services level contains user interfaces as services. These interfaces allow end-users to interact with the connected eHealth functionalities. User interfaces in the Presentation services level can be user interface services delivered by applications, for example a GP who uses the user interface of his EMR system to interact with connected eHealth functionalities.

Connections with systems outside the environment of the primary care organization take place through external connections. In case of other healthcare organizations, secured national, regional or local networks are available. If possible, these networks should be used to connect with the primary healthcare organization for privacy and security reasons. Here, it is preferable to apply HL7 as communication standard for health data exchange, as this is the most commonly used international communication standard in healthcare. Several HL7 versions exist, and the most applicable HL7 version for a given situation will depend on existing agreements between the primary care center and the external organization. Furthermore, it should also be possible to connect with external web-based eHealth applications, like quantified-self applications the patient uses e.g. a Fitbit activity tracker. In case of external web-based eHealth applications, HL7 FHIR is the preferred standard for data exchange as this HL7 Standard uses a RESTful approach which is a standard communication approach for web applications. Privacy and security should also be taken into account when connecting with mobile health apps. In all cases of external connections, it is preferable to use SNOMED CT and ICD in the mapping of a legacy terminology into a standard terminology and as health terminologies to ensure meaningful data exchange.

8.3.2 Example usage of the reference architecture in case study

The following case study shows in three steps how the reference architecture can be used to translate a care path into an interoperable eHealth infrastructure that can technically support the HIE during this process. To this end, we focus on patients with low back pain (LBP) as an example.

8.3.2.1 Case description

Based on a patient’s answers to 15 questions, an online clinical decision support system (CDSS) on triage of LBP provides one of the following advices:

1. Go see your general practitioner;
2. Go see your physiotherapist;
3. Perform self-care in first instance, for example by doing exercises.
In case of a self-care advice with exercises, an online training program is provided to the patient with information on how to cope with the LBP and how to perform exercises in the right way according to a personalize trainings program. After two weeks, the low back pain should be gone. If not, the patient should see a healthcare professional.

**Figure 8.8.** Model of the (self-)referral and care path of patients with low back pain, supported by eHealth.
8.3.2.2 Step 1
At first, we describe the total process of this (self-)referral and healthcare process of patients with low back pain as seen by its stakeholders. In our case, relevant stakeholders are general practitioners (GPs), physiotherapists, medical assistants, and patients. An overview of the process is shown in Figure 8.8. Different points in this process can be supported by eHealth functionalities (blue circles and blue blocks).

8.3.2.3 Step 2
In the process presented by Figure 8.8, the following functionalities are distinguished that have to be delivered by (web-based) eHealth applications:

1. CDSS Triage:
To select relevant healthcare at a specific moment, which will be GP, physiotherapist, or self-care when the LBP exists less than 2 weeks.

2. eTraining:
To provide information on how to cope with low back pain and training exercises that can be performed to reduce the low back pain.

3. Informing:
To provide the next healthcare professional with relevant information about the patient with low back pain in case of further referral within primary care (GP->Physio or Physio ->GP) or outside primary care (GP -> 2nd or 3th care).

Per eHealth functionality, Table 8.1 shows who provided information (S=sender), and who will use this information (R=receiver). In case of further referral, the forwarding healthcare professional provides the next healthcare professional with relevant health information about the patient. This information exchange is supported by an HL7 communication standard, namely HL7 CDA in case of further referral within primary care, and HL7 V2 in case of further referral outside primary care.

The information in the *cursive rows* is shared among more than two different stakeholders. This information contains the answers given on questions about the LBP, and the referral advice. Answers on the questions can be used by the healthcare professional during the consult with the patient to ask more focused questions. The shared information is presented by data items as shown in table 8.2. Next to these data items, corresponding SNOMED CT codes are shown in table 8.2. These codes provide the exact clinical meaning for an item to enable meaning-based retrieval of the data45. These codes can be used to set up the data model for data storage in the shared data set. In addition, the codes can also be used as a basis for writing data adapters for exchanging data from a local data storage through the communication bus to another location in the infrastructure.
Table 8.1. Overview of information that is sent (S) and received (R) during the self-referral process. The italic rows are related to information that is shared among more than 2 different stakeholders.

<table>
<thead>
<tr>
<th>Functionality</th>
<th>Type of information</th>
<th>eHealth service</th>
<th>Patient</th>
<th>GP</th>
<th>Physiotherapist</th>
<th>2nd or 3rd care</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDSS Triage</td>
<td>Triage questions on LBP</td>
<td>S</td>
<td>R</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDSS Triage</td>
<td>Answers on questions about the LBP</td>
<td>R (in case of further referral to self-care)</td>
<td>S (in case of further referral to self-care)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDSS Triage</td>
<td>Referral advice based on given answers</td>
<td>S</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td></td>
</tr>
<tr>
<td>eTraining</td>
<td>Information how to cope with LBP</td>
<td>S</td>
<td>R</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>eTraining</td>
<td>Information on exercises that can be performed to reduce the LBP.</td>
<td>S</td>
<td>R</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Informing GP-&gt;Physio</td>
<td>Relevant information about the patient with low back pain</td>
<td>S</td>
<td>R</td>
<td>HL7 CDA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Informing Physio-&gt;GP</td>
<td>Relevant information about the patient with low back pain</td>
<td>R</td>
<td>S</td>
<td>HL7 CDA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Informing GP -&gt; 2nd or 3rd care</td>
<td>Relevant information about the patient with low back pain</td>
<td>S</td>
<td>R</td>
<td>HL7 V2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

8.3.2.4 Step 3
In the last step, the applications have to be identified that should be part of the interoperable eHealth infrastructure. In this case, applications to be involved are:

- Online clinical decision support system for self-referral of patients with low back pain (Online CDSS triage);
- Online system for providing information on how to cope with the low back pain and to provide personalized exercises for training (Online training system);
- The EMR system of the general practitioner (EMR system);
- The EMR system of the physiotherapist (EMR system);
- The EMR system of the 2nd or 3rd care specialist, in case of further referral outside primary care (EMR system);

Data to be shared will be stored in the shared dataset, which can be accessed by all systems connected to the communication bus.

Based on these three steps, Figure 8.9 shows the resulting interoperable eHealth infrastructure that technically supports the (self-)referral and healthcare process of patients with low back pain as shown in Figure 8.8.
## Table 8.2. Data items and corresponding SNOMED CT codes.

<table>
<thead>
<tr>
<th>Triage Item</th>
<th>Description</th>
<th>SNOMED CT Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well-being</td>
<td>Well-being as experienced by patient?</td>
<td>273726005</td>
</tr>
<tr>
<td>Course</td>
<td>Course of the low back pain?</td>
<td>279039007</td>
</tr>
<tr>
<td>Age</td>
<td>Start of the low back pain after age of 50?</td>
<td>445518008</td>
</tr>
<tr>
<td>Analgesics</td>
<td>Response on analgesics?</td>
<td>53009005</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Prolonged use of corticosteroids?</td>
<td>9440004</td>
</tr>
<tr>
<td>Serious diseases</td>
<td>Serious diseases, such as cancer, in patient history?</td>
<td>417662000</td>
</tr>
<tr>
<td>Neurogenic signals</td>
<td>Neurogenic signals?</td>
<td>279058003</td>
</tr>
<tr>
<td>Continuous pain</td>
<td>Continuous pain, regardless of posture and movement?</td>
<td>222530000</td>
</tr>
<tr>
<td>Radiation</td>
<td>Radiation in the leg below the knee?</td>
<td>23056005</td>
</tr>
<tr>
<td>Nocturnal pain</td>
<td>Nocturnal pain?</td>
<td>22253000</td>
</tr>
<tr>
<td>Weight</td>
<td>Rapid weight loss, more than 5 kg per month?</td>
<td>89362005</td>
</tr>
<tr>
<td>Muscle strength</td>
<td>Loss of muscle strength?</td>
<td>26544005</td>
</tr>
<tr>
<td>Trauma</td>
<td>Presence of a trauma?</td>
<td>417746004</td>
</tr>
<tr>
<td>Failure symptoms</td>
<td>Failure symptoms during increased pressure?</td>
<td>105719004</td>
</tr>
</tbody>
</table>
An interoperable eHealth reference architecture for primary care | Chapter 8

Figure 8.9. Interoperable eHealth infrastructure to enable self-referral and self-care for patients with low back pain.
Table 8.3. Overview of the participant characteristics (n=8).

<table>
<thead>
<tr>
<th>Theme concepts</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Employee of</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SME IT &amp; Health</td>
<td>7</td>
<td>88%</td>
</tr>
<tr>
<td>Expertise center IT &amp; Health</td>
<td>1</td>
<td>13%</td>
</tr>
<tr>
<td><strong>Education background</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical technician</td>
<td>1</td>
<td>13%</td>
</tr>
<tr>
<td>Software developer/programmer</td>
<td>2</td>
<td>25%</td>
</tr>
<tr>
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<td>EDIFACT</td>
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<td>JSON REST API</td>
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8.3.3 Evaluation study
The interoperable eHealth reference architecture and its application were evaluated by IT health information experts to determine whether it can be used in practice to accelerate the development of interoperable infrastructures in primary care. All study participants received a description in a document prior to a semi-structured phone interview. After the interview, they gave written feedback on a written summary.

8.3.3.1 Participant characteristics
Eight IT health information experts were interviewed. Table 8.3 shows the demographics of this group. Most of them work in an SME (88%), are information analyst (75%), and have general knowledge on HL7 (63%) and SNOMED CT (50%).

8.3.3.2 SME characteristics
Seven interviewees (n=7) were employed by SMEs. In these SMEs, if their technology was interoperable with other systems, custom-made solutions were used mostly (57%). In this, communication and terminology standards were only used when wished and agreed upon by the customer. During the interviews, interesting quotes on interoperability were:

“We only have custom-made data exchange solutions with other systems, e.g. the GP information system, and these solutions were only made when desired for by the healthcare professional”.

“Interoperability with other systems is limited and not structured according to a standard yet. This is also because the other parties to connect to are not ready. For example, we looked at HL7 v3 to receive patient data. But other parties could not send HL7 v3 messages. So it is a chicken-egg problem. Nevertheless, we do offer a local solution through an API according to a REST methodology.”

and

“In the projects we are working on there is no demand for interoperability of data, except for sensor data.”

It was also interesting to see that only one SME used SNOMED as terminology coding system. This participant mentioned the following:

“If the code is found in SNOMED, it will be the code used internally, but there is not always a SNOMED code possible because SNOMED is not complete. LOINC is used as code system in the data exchange with laboratories, because this was mutually agreed. NHG (=Dutch College of General Practitioners) codes are also used, especially when connecting with GP information systems, but also because these codes are also received from the laboratories. In that respect SNOMED is still not very much in use in the exchange of health data.”
Another participant mentioned the following about SNOMED and the NHG codes:

“In the reference architecture SNOMED is mentioned, but the NHG has its own rules. The NHG prefers the usage of things they already have. They do not see why new things are needed.”

This may also be the reason that the interviewees (43%) mentioned Dutch coding systems are often used to achieve interoperability.

**8.3.3.3 Evaluation of the reference architecture and its application**

The following main theme concepts emerged from the analysis:

- Readability
- Completeness
- Financial feasibility
- Barriers to use the reference architecture
- Positive points of the reference architecture

**8.3.3.3.1 Readability**

For most participants (63%), the interoperable eHealth reference architecture became clear after additional explanation. They mentioned that it was difficult to see that the reference architecture was meant as reference in the design of local interoperable eHealth infrastructures. Next to this, it was unclear to some participants to view the reference architecture from a technical point of view instead of the viewpoint of the end-users.

**8.3.3.3.2 Completeness**

Half of the participants missed some elements and standards. One missing element was a service for user management. The other missing element was a service for customizing the communication bus settings. These services should be added in the Middleware layer of the reference architecture. Standards that were missed were EDIFACT and XDS for document sharing, and NHG (lab) codes.

**8.3.3.3.3 Financial feasibility**

Half of the participants mentioned that using the reference architecture is not financially feasible, because distinct primary healthcare organizations have limited financial options. Therefore, building a local interoperable eHealth infrastructure within a distinct primary care center is not interesting for business from the viewpoint of SMEs. Next to this, SMEs also want to know the profits for business beforehand and this is not clear yet.

**8.3.3.3.4 Barriers to use the reference architecture**

The lack of financial feasibility is one barrier to use the reference architecture. Another barrier seen by the participants is the gap between theory and practice, caused by reasons related to cost aspects, time pressure, and unwillingness of different parties to cooperate. Next to this, no consensus between stakeholders and
a lack of vision of stakeholders were mentioned as obstacles in the achievement interoperable eHealth in primary care. One participant formulated this lack of vision in the following way:

“As an engineer you see the advantages of new developments. However, doctors determine what should be new within the GP information system. Unfortunately, they are lacking IT knowledge to enable to look deeper than what is needed. This makes it difficult to make fast steps towards new developments.”

8.3.3.5 Positive points of the reference architecture
The participants indicated as positive that the reference architecture forces structural thinking about the topic and it forces the usage of health communication and terminology standards. Another aspect seen as positive was the focus on specific roles of the applications, and the way data is shared across applications via the communication bus and the shared data set. Furthermore, participants see the reference architecture as a good base for further discussion on achieving interoperable eHealth in primary care.

8.4 Discussion
This chapter describes a study that has resulted in an interoperable eHealth reference architecture for primary care (Figure 8.7). This reference architecture uses a service-oriented approach and contains a communication bus that connects distributed applications. It is intended for IT specialists who want to set up an interoperable eHealth infrastructure within a distinct primary care organization in close co-operation with the stakeholders. The results of an evaluation study on this reference architecture show that there are additional conditions needed before interoperable eHealth in primary care actually can be achieved. These conditions are:

1. Consensus between different stakeholders is essential in setting up an interoperable eHealth infrastructure,
2. Communication and terminology standards to be used should be available, complete, usable and up-to-date,
3. The profits for business should be clear when involving SMEs in setting up interoperable eHealth infrastructures,
4. Most primary healthcare organizations have limited financial options and therefore, the possibility to access to an own customized environment within an (inter)national interoperable eHealth infrastructure would be beneficial to achieve interoperable eHealth within these organizations, and
5. A potential (inter)national interoperable eHealth infrastructure should be managed by a neutral party.

The reference architecture makes use of a shared data set for health information exchange (HIE). Next to this, the connected distributed eHealth applications can also have their own local data storage. One could say that it would be more efficient to store all data centralized in the shared dataset, because than all data is available
Chapter 8 | An interoperable eHealth reference architecture for primary care

for all services in the infrastructure and data does not have redundantly be stored. However, applications provide quick access to data and are available independently of a working internet connection when using local storages\textsuperscript{183}. For example, when a patient wants to monitor blood values at home that should be stored in the shared dataset, this will fail when internet access is not available. Next to this, central data storage also has security issues\textsuperscript{183} which will become much more complex when storing all collected data into the shared dataset. And when storing all data at a central place, the data model of the central dataset becomes much more complex and much more difficult to be agreed upon on by all stakeholders. Therefore, the interoperable eHealth reference architecture described in this chapter contains centralized as well as local data storages. In all cases, data has to be managed on accuracy, completeness, granularity, timeliness, and interoperability\textsuperscript{184}.

The interoperable eHealth reference architecture advises the usage of terminology standards in data storage. This is, because a standardized health record serves as a bridge between different systems: “eHealth capability is supported by sound information management and health informatics standards – such as the SNOMED nomenclature and ICD10 classification”\textsuperscript{166}. Although the evaluation study brought forward that the usage of national standards instead of international standards can be forced by national organizations – in the interviews the Dutch College of General Practitioners (NHG) – the recommendation of the reference architecture is to prefer international standards. In this way, designed infrastructures will become open to national as well as international parties when needed. This also applies for existence of international health communication standards, as HL7 FHIR, HL7 CDA, and HL7 v2 in the reference architecture\textsuperscript{28,42,185}.

The design of the reference architecture was based on experiences on building interoperable eHealth infrastructures in real practice. In this way, issues that hinder the development of interoperable infrastructures in healthcare could be taken into account. Next to this, the reference architecture forces structured thinking on eHealth interoperability by its stakeholders and is identified as a good starting point for further discussion on the achievement of interoperable eHealth in primary care.

8.4.1 Study limitations

Consensus had to be made in the level of detail of the interoperable eHealth reference architecture. The reference architecture could be supplemented with more detail by also using the legal and regulatory, policy, and IT infrastructure levels of the refined eHealth European Interoperability Framework (ReEIF)\textsuperscript{27} in the design of the reference architecture. However, this study was focused on how to translate a primary healthcare process into an interoperable eHealth infrastructure that can technically support the HIE within this healthcare process. Next to this, a balance was needed between the level of detail and complexity, as increased complexity would make the reference architecture unreadable. However, this does not mean that legal and regulatory and policy issues should not be taken into account when realizing an interoperable eHealth infrastructure.
8.5 Conclusions
The study has resulted in an interoperable eHealth reference architecture for primary care. This reference architecture can be used to translate primary healthcare processes into interoperable eHealth infrastructures that can technically support the HIE within these healthcare processes. This in close co-operation with the stakeholders. However, additional conditions are still needed before interoperable eHealth in primary care can actually be achieved.
CHAPTER 9
General Discussion
The aim of this thesis is to contribute to achieving interoperable eHealth technology for primary care, and subsequently, to utilize this interoperability for decision support, using a data-driven approach with the help of machine learning. Research on this topic was performed in the application area of an interoperable clinical decision support system (CDSS) for low back pain (LBP). The aim of this CDSS was to optimize referral of patients in primary care that suffer from LBP to treatment paths and/or other (secondary) healthcare professionals.

9.1 Research contributions

In the first study, 33 healthcare professionals were interviewed (see Chapters 2 and 3) to uncover the awareness of healthcare professionals on the usage of eHealth technology in primary care. From these interviews, two main conclusions were drawn that are fundamental for developing CDSSs for primary care:

1. New eHealth applications should only be developed and introduced when they are really needed by primary care and should not be forced upon them from outside. Otherwise, acceptance will be low.
2. Interoperability issues should be solved before new eHealth technologies can be efficiently used in practice. Otherwise, professionals have to work with too many different systems, leading to an unmanageable workload.

The interviewed healthcare professionals expressed a desire for a CDSS that could help them to decrease their workload by optimizing the referral of patients. This starts with the proper self-referral of patients to primary care, for example in the case of a new episode of low back pain (LBP). A CDSS should guide a patient through the triage process, posing questions based on relevant pre-consult questionnaires. Self-referral will save time in telephone triage and during the first consult, as relevant information is already available. Subsequently, the CDSS should support healthcare professionals on how to refer and/or intervene next, based on all available data. Figure 9.1 shows the different moments such a CDSS can support optimized referral of patients in the primary care. The first moment is the triage towards primary care. The second moment is referral to another healthcare professional, for example secondary care, or to an intervention.

The two different moments shown in Figure 9.1 have been worked out into detail for the application area of LBP (chapters 4 to 7). For this, it was necessary to identify classification factors on LBP that are indicative of the referral of LBP. In total, 43 classification factors were identified, of which 15 - only general and serious factors (“Red Flags”) – appeared to be important during the triage towards primary care.

Figure 9.2 shows how the CDSS on LBP referral can be embedded within the IT infrastructure of a primary care practice, based on the reference architecture as described in chapter 8. The grey square in Figure 9.2 contains the elements that are added to the original situation. In this infrastructure, healthcare professionals (the GP, physiotherapist or nurse practitioner) work from their original EHR system.
that discloses the CDSS, for patients, this will be a web portal. Figure 9.1 shows a loop between the EHR database and the CDSS. This loop enables the CDSSs to gather new knowledge from new cases. Additionally, a web-based training system was added to the infrastructure. With the help of this training system, patients can perform prescribed exercises themselves and at home (chapter 4).

To achieve a proper functioning of the infrastructure shown in Figure 9.1, at least the following conditions should be met first (chapters 2 and 8):

1. Consensus among different stakeholders at different interoperability levels in the interoperable eHealth infrastructure. These different levels include the organization of the care process, what information should be exchanged within this process, and how this information should be presented;
2. Completeness, usability and timeliness of communication and terminology standards. For example, the terminology standard to be used should contain all relevant elements to be able to present the information to be exchanged conform the actual state of knowledge on this specific element.

Next to this, my research showed that, in general, primary healthcare organizations have limited financial options to achieve an interoperable eHealth infrastructure within their organization (chapter 8). Therefore, it is recommended for governments to set-up an (inter)national interoperable eHealth infrastructure to which primary healthcare centers can connect, and have access to their own, secure and customizable environments. This infrastructure should be managed by a neutral party (chapter 8). Other studies also indicated that the involvement of governments
Figure 9.2. Complete overview of the CDSS embedded within the IT infrastructure of a primary care practice.
through policy interventions and financial investments is necessary to achieve interoperability in healthcare, and thus, to develop such (inter)national interoperable eHealth infrastructure.

9.1.1 Methodological considerations
In chapter 6, I described a vignette study that was used to collect cases of low back pain with a self-referral advice. In this study, 73,728 different vignettes could possibly be generated from the 15 factors the cases were based on. In the end, 1,288 vignettes were judged. Knowledge on the inter-relationships among the different features may be beneficial to the model, as this knowledge can be used for feature engineering to reduce the number of features without decreasing model performances. This also means that, in the case of a CDSS for patients with LBP to support self-referral, the number of necessary questions to perform a triage can be reduced when the number of features can be decreased. However, if I also want to know the inter-relationships between the different features on the self-referral outcome, all 73,728 cases should have been judged. To do so, I would have needed 2,000 participants and each one of them should have been willing to judge 32 cases. Because of cost-benefit reasons, it is more efficient to gain knowledge on the inter-relationships among the different features through EHR data (Figure 9.1) than to perform an additional vignette study. Next to this, machine learning algorithms often require millions of observations to reach acceptable performance levels. Interoperability among CDSSs and EHRs will help to gain knowledge on the inter-relationships among the different features, and to increase the number of observations needed to improve model performances. Other studies have shown that machine learning algorithm performances improve with data retrieved from EHRs, like a study on cardiovascular risk prediction.

In my research, all data that were used to train machine learning algorithms were categorical data, including the predicted outcomes. During feature engineering, all continuous data were transformed into discrete data to be treated as categorical data because discretization is a requirement for some classification algorithms. The transformation to discrete data is adequate for exploring whether the available data could be used to train machine learning algorithms to model the referral processes for the CDSS. When involving data from EHR records, the usage of continuous and text data should also be considered. Continuous data, for example, represent measurements. Text data are often entered in open text boxes to provide additional information. Natural language processing can be used on text data to gain information for clinical decision support. Continuous data as well as text data are stored of EHR records and can be of interest to increase the performances of the models.

Another key issue in machine learning is the quantity and quality of input data. Data quality should be ensured to enable models to predict good outcomes. In addition, biases in training datasets as outliers, missing data, and imbalanced data can substantially affect both performance and generalizability of models retrieved...
by machine learning\textsuperscript{188}. Therefore, outliers, missing data, and imbalanced data should be handled with care when preparing data for machine learning purposes. The handling of missing data and imbalanced data can benefit from the aggregation of high-quality, unbiased data through smooth IHE to feed machine learning algorithms. For this, existing data in, for example, electronic health records (EHRs) need careful curation and processing before they are usable\textsuperscript{188}.

In my research I wanted to know which healthcare professional and/or what intervention is best for a patient with LBP in a specific situation. It was obvious to approach this as a classification problem. In particular because labelled data for supervised learning were available from the vignette study and from the Groningen Spine Centre (GSC). However, when bigger sources with complete, high quality and well-balanced data are available, the usage of clustering algorithms can also be considered. With clustering algorithms, unsupervised learning is applied to discover groupings based on a large amount of data. Then, a set of data objects that have high similarity are grouped within a cluster\textsuperscript{21}. With clustering, it is expected that new knowledge on how to approach LBP can also be discovered.

### 9.2 Generalization to other domains

In my research, the focus of the application area was on low back pain. But the same methods can also be applied to develop (self)-referral CDSSs for other musculoskeletal problems, provided that appropriate data are available that can be used as training dataset. Moreover, extension to other domains will certainly be beneficial for other patient groups. Research on the effects of self-referral of patients with knee and ankle problems\textsuperscript{123} has shown that self-referred patients with knee and ankle problems needed fewer treatment sessions than GP-referred patients. I assume that this advantage of appropriate self-referral will apply to all patients with musculoskeletal problems. Finally, one can even think of using machine learning in the development of CDSSs to achieve more appropriate referrals for all health problems that are seen in generally by primary care when full interoperability among all systems with relevant health data can be achieved.

### 9.3 Directions for future research

At this moment, different research groups are busy studying how to classify LBP for decision support for further referral and treatment. These are mainly research projects performed from a clinical point of view. Important ones are the StartBack Tool\textsuperscript{75} and the Nijmegen Decision Tool\textsuperscript{117}. The research described in this thesis was performed mainly from a technical point of view. Certainly, clinical aspects have been taken into account during my research, among others by involving clinical guidelines on LBP and conducting interviews with healthcare professionals. For future research, I also encourage to collaborate with other related clinical research projects, because combining technical and clinical knowledge will benefit the development and performances of CDSSs for appropriate referral of LBP.
Another topic for future research is the self-management of patients. There is a growing interest in using digital interventions to support patient self-management in LBP. This can be supported by a web-based training system within the infrastructure, as is shown in Figure 9.2. Future research should further develop two situations in which the training system in Figure 9.2 can be used. The first situation is when the CDSS proposes a self-care advice to the patient. Then, the next step is to provide the patient with personalized information on how to cope with the low back pain and what exercises may be helpful. This is comparable to a system that was intended for patients with COPD. In the second situation, the CDSS supports the healthcare professional in selecting the best exercise path for the patient when the appropriate treatment for this patient is exercising at home.

As referrals and interventions are parts of healthcare processes, it will also be of interest to involve process mining in future research. Process mining is a relatively young research discipline. With the help of process mining, process models can automatically be discovered, the conformance of process models described in clinical guidelines can be checked to reality, and existing healthcare processes can be extended or improved by using data of actual process executions based on event logs. Event log data from EHRs can be used for process mining to answer, for example, questions as “Are there differences in care paths followed by different patient groups?” and “Where are the bottlenecks in the process?” can be answered. Knowledge on the current processes combined with knowledge on appropriate referrals - one of the topics of this thesis - will help to improve healthcare paths to ensure that patients become the right intervention at the right moment.

9.4 Closing remarks
Interoperable eHealth technology in primary care is possible. However, there is still a long way to go, as consensus among different stakeholders is needed on different interoperability issues, such as finances, process organization, standards to be used, data ownership, privacy and security. When interoperability can be achieved, this will also benefit smooth HIE that can be used for machine learning and utilizing big data in healthcare. This thesis contributed to achieving fully interoperable eHealth technology and to apply machine learning in primary care.


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Summary

The term eHealth is commonly defined as "Health services and information delivered or enhanced through the Internet and related technologies". General examples of eHealth applications are websites that make health information accessible to patients, or eConsult environments for secure digital communication between a patient and his/her general practitioner (GP). More specific eHealth applications are web based environments that support patients to work on their own health (self-management), systems that support remote diagnosis and treatment of patients (telemedicine), and clinical decision support systems (CDSSs).

A CDSS can be defined as “Any computer program designed to help healthcare professionals to make clinical decisions”. Over time, CDSSs have been shown to improve both patient outcomes and costs of care by prompting, reminding and cautioning clinicians whether or not to intervene under specific clinical circumstances. Nowadays, some CDSSs are already used in daily primary care, because they are implemented as functionalities of the healthcare information systems of the healthcare professionals. These functionalities are mainly used for prevention and screening, drug dosing, medical management of acute diagnoses and chronic disease management through the usage of alerts and computerized protocols.

eHealth technology can benefit the healthcare system in a variety of ways. It can help to achieve efficient management of health data and the possibility to share these data among healthcare professionals, informal caregivers, and patients within patient care processes. The quality and sustainability of healthcare can be improved as well, by supporting the self-management of patients. Next to this, big data solutions, based on connected digital health data from different sources, can support the development of CDSSs.

Despite of its benefits, eHealth is still not widely used in primary care. One reason is that both healthcare providers and patients are not aware of the possibilities of eHealth in primary care. Awareness is important, which is also expressed by the remainder of the eHealth definition: "eHealth characterizes not only a technical development, but also a state-of-mind, a way of thinking, an attitude, and a commitment for networked, global thinking, to improve healthcare locally, regionally, and worldwide by using information and communication technology". Another reason that hinders the implementation of eHealth in primary care is that barriers still exist around integrated and interoperable technological infrastructures for eHealth.

Interoperability is defined as the ability of two or more systems or components to exchange information and to use the information that has been exchanged. Interoperability between health systems facilitates health information exchange (HIE). Interoperability barriers that hinder smooth HIE are related to technical, organizational, safety, privacy, and security issues. For example, standalone systems
are used that store data in different formats and without means for data exchange, despite the existence of available HIE communication standards, like HL7 and terminology standards as SNOMED CT.

The objective of this thesis is achieving interoperable eHealth technology for primary care and to utilizing this interoperability for decision support via a data-driven approach with the help of machine learning. Different studies were performed to achieve this objective.

In the first study, thirty-three healthcare professionals from seven Dutch primary care centers were questioned about their view on the usage of eHealth technology within their daily practice, and areas in which decision support can play a role. This study was performed by means of interviews and an online survey. Qualitative analysis resulted in the identification of context-driven requirements for, and barriers towards, interoperable eHealth technology from the perspective of healthcare professionals (chapter 2). These requirements and barriers were subdivided according to Refined eHealth European Interoperability Framework (ReEIF) into levels of interoperability, as workflow process, information, applications, and IT infrastructure. Only when all these identified levels of interoperability are taken into account, implementation of interoperable eHealth technology in primary care can succeed.

Next to this, the qualitative analysis also resulted in an overview of desired eHealth functionalities and promising areas for decision support technology within primary care (chapter 3). Based on these results, the second part of the thesis focused on the development of a clinical decision support system (CDSS) for optimized patient referral. Patients with low back pain (LBP) were chosen as first application area, as LBP is the most common cause for activity limitation and has a tremendous socioeconomic impact in Western society.

In primary care, LBP is commonly treated by general practitioners (GPs) and physiotherapists. In the Netherlands, patients can opt to see a physiotherapist without referral from their GP (so called ‘self-referral’). Although self-referral has improved the choice of care for patients, this also requires that a patient knows exactly how to select the best next step in care for his or her situation; something which is not always evident.

The second study was focused on the identification of significant factors in the referral of patients with LBP, because a direct correct referral is essential for effective treatment and to prevent the development of chronic LBP. First, literature and guidelines on LBP were studied. Subsequently, three general practitioners and five physiotherapists were questioned during semi-structured interviews on the classification of LBP with respect to the best first step in care (triage) for a patient with a new episode of LBP: visit the GP, visit the physiotherapist, or perform self-care. The interview results were validated by means of an online survey. This resulted in the identification of a select group of 15 key classification factors for triage, mainly so-called “red flags” (chapter 4).
The third study was an online vignette study in which these 15 key classification factors for triage were used to construct fictive patients cases (vignettes) (chapter 5). Sixty-three healthcare professionals (GPs and physiotherapists) participated in this vignette study. They had to judge 32 LBP cases and to indicate whether they thought the following options were applicable: 1. see a general practitioner, 2. see a physiotherapist, and 3. perform self-care. In total, 1288 vignettes were judged. Multinomial regression analysis indicated Weight Loss, Trauma, and Nocturnal Pain as the three most significant predictive variables.

The vignette study led to a large dataset. In the fourth study, this dataset was used for supervised machine learning in RStudio to model the triage process as part of a web based CDSS for patients. Three models - 1. decision tree, 2. random forest, and 3. boosted tree – were compared on their performances (chapter 6). As the cases in the training dataset were fictive, it was important to determine whether the performance of the models on real-life LBP cases as well. Therefore, real-life cases on LBP were collected in collaboration with 5 centers for physical therapy and 6 GP centers. This resulted into 38 usable real-life patient cases to construct a test dataset. The boosted tree approach appeared to be the best model for predicting a referral advice for a patient with a new episode of LBP. However, this model still has to be improved before it can be used in a CDSS for patients. Therefore, new cases on LBP have to be collected to increase the training dataset.

When a patient with LBP consults a primary care professional, he/she can be referred to secondary/tertiary care. Unfortunately, LBP may recur after treatment and discharge. Contradictory advises and treatments may have negative consequences for optimal recovery leading to passive coping style, somatization in patients and consequently in chronic pain. Therefore, communication between both secondary/tertiary care and primary care practitioners is of great importance. A CDSS that supports physicians to select appropriate treatments for patients with LBP according to the expertise of healthcare specialists on LBP will therefore be helpful.

In the fifth study, a dataset with 1546 cases on LBP from patients of the Groningen Spine Center (GSC) was used for machine learning (chapter 7). This dataset contained patient-reported baseline and treatment data, used to train classification algorithms in WEKA. The resulting models were validated during 10 folds cross-validations. Next to this, a test dataset was constructed with 50 cases judged by four experts on LBP to perform an interrater agreement analysis and to re-evaluate the models with data that were not used to train the models. For this study, the prediction accuracy and the average area under curve (AUC) of the models were used as performance measures. The interrater agreement among the four experts was substantial. The best performing models on decision making for LBP treatments differed per treatment. The AUC values of the models indicated small to medium machine learning effects. This means that machine learning to model decision making on the selection of treatments for LBP seems possible, where decision making models differ per treatment.
Summary

In the last study (chapter 8) the issue of interoperability was revisited to design of an interoperable eHealth reference architecture for primary care that can be used by IT specialists as a basis during the technical design of interoperable eHealth infrastructures within primary healthcare organizations. The design of this reference architecture was based on the Refined eHealth European Interoperability Framework (ReEIF) and on results of 14 working sessions with 10 eHealth Small and Medium sized Enterprises (SMEs). The application of the reference architecture was demonstrated in a practical case, focused on the CDSS that will support patients with LBP in their first referral to primary care. Subsequently, the reference architecture and the practical case were evaluated with eight IT health information experts on their opinion whether the reference architecture can be used in real practice to accelerate the development of interoperable eHealth infrastructures in primary care. Interoperable eHealth technology in primary care is possible, but there is still a long way to go. Consensus among different stakeholders is needed on different interoperability issues, such as finances, process organization, standards to be used, data ownership, privacy and security.

Finally, chapter 9 gives a complete picture when all studies are integrated. It reflects on barriers and requirements for CDSS development, and machine learning and interoperability. With this research, an interoperable eHealth reference architecture for primary care is available now. Future challenges are the actual achievement of interoperability in primary care. When interoperability can be achieved, this will also benefit smooth HIE that can be used for machine learning and utilizing big data in healthcare. This thesis contributed to achieving fully interoperable eHealth technology and to apply machine learning in primary care.
Summary

Samenvatting

eHealth wordt vaak gedefinieerd als “Gezondheidsdiensten en informatie geleverd of verbeterd via het internet en aanverwante technologieën”. Deze definitie laat zien dat veel toepassingen binnen de zorg onder het begrip eHealth vallen. Algemene voorbeelden zijn websites die gezondheidsinformatie voor patiënten toegankelijk maken, of eConsult-omgevingen, waarbij een patiënt binnen een beveiligde omgeving vragen kan stellen aan de huisarts. Daarnaast zijn er ook eHealth toepassingen die gericht zijn op het ondersteunen van patiënten om het zelf aan de slag gaan met de eigen gezondheid (zelfmanagement), het behandelen van patiënten op afstand (telemedicine), en het ondersteunen van beslissingen rondom het stellen van diagnoses en behandelingen (clinical decision support).

Een clinical decision support systeem (CDSS) kan worden gedefinieerd als “een computerprogramma dat is ontwikkeld om zorgprofessionals te helpen bij het nemen van klinische beslissingen”. Het is aangetoond dat het inzetten van CDSSs zowel de patiëntenzorg als de kosten van de zorg kunnen verbeteren. Tegenwoordig wordt clinical decision support voornamelijk toegepast in de dagelijkse eerstelijnszorg als functionaliteiten van zorginformatiesystemen, zoals bijvoorbeeld binnen het huisartsen informatie systeem (HIS). Deze decision support functionaliteiten worden voornamelijk gebruikt voor preventie en screening, medicatiedosering, medisch management van acute diagnoses en chronisch ziektebeheer door middel van waarschuwingen en geautomatiseerde protocollen.

De inzet van eHealth kan het zorgsysteem ook op andere manieren ten goede komen. Zo kunnen gezondheidsgegevens van patiënten efficiënter beheerd worden. Daarnaast wordt het mogelijk om deze gegevens te delen met zorgverleners en mantelzorgers, de betrokken zijn bij het zorgproces van de patiënt. Tevens helpt het ondersteunen van zelfmanagement van de patiënt door middel van eHealth ook om de kwaliteit en duurzaamheid van de gezondheidszorg te verbeteren. Wanneer gegevens vanuit verschillende eHealth bronnen beschikbaar komen, en gekoppeld kunnen worden, dan kunnen ook big data-oplossingen gebruikt worden om de ontwikkeling van CDSSs te ondersteunen.

Ondanks de voordelen wordt eHealth nog steeds niet veel gebruikt binnen de eerstelijnszorg. Een van de redenen is dat zowel zorgaanbieders als patiënten zich niet bewust zijn van de mogelijkheden van het gebruik van eHealth in de eerste lijn. Bewustzijn is belangrijk, wat ook tot uiting komt in de rest van de definitie van eHealth: “eHealth is niet alleen een technische ontwikkeling, maar ook een gemoedstoestand, een manier van denken, een houding en het belang zien van een verbonden, wereldwijd denken, om de gezondheidszorg lokaal, regionaal en wereldwijd te verbeteren door informatie- en communicatietechnologie te gebruiken”. Een andere reden die de implementatie van eHealth binnen de eerstelijnszorg belemmert, is dat er nog steeds barrières bestaan rondom geïntegreerde en interoperabele technologische infrastructuren voor eHealth.
Samenvatting

Interoperabiliteit wordt gedefinieerd als “de mogelijkheid van twee of meer systemen of componenten om informatie met elkaar uit te wisselen en om deze uitgewisselde informatie te gebruiken”. Interoperabiliteit tussen gezondheidsystemen vergemakkelijkt dus de uitwisseling van gezondheidsinformatie. Helaas wordt een soepele informatie-uitwisseling tussen systemen nog vaak verhinderd door technische, organisatorische, veiligheids-, privacy- en beveiligingsproblemen. Zo worden er op dit moment nog steeds veel standalone systemen gebruikt die gegevens opslaan in verschillende formaten en zonder middelen voor gegevensuitwisseling, ondanks het bestaan van beschikbare communicatie- en terminologie standaarden voor de zorg, zoals HL7 en SNOMED CT.

Dit proefschrift gaat in op het realiseren van interoperabele eHealth voor de eerstelijnszorg, en het gebruik van deze interoperabiliteit voor het realiseren van clinical decision support systemen op basis van een data gedreven aanpak met behulp van machine learning. In het kader hiervan zijn verschillende studies uitgevoerd, die binnen dit proefschrift worden beschreven.

In de eerste studie werden 33 zorgprofessionals van zeven Nederlandse eerstelijnscentra ondervraagd over hun visie op het gebruik van eHealth-technologie in hun dagelijkse praktijk en op gebieden waar decision support een rol kan spelen. Deze studie werd uitgevoerd door middel van interviews en een online enquête. Kwalitatieve analyse van deze interviews en online enquête resulteerde in de identificatie van context afhankelijke eisen en belemmeringen ten aanzien van interoperabele eHealth vanuit het perspectief van deze zorgprofessionals (hoofdstuk 2). Deze eisen en belemmeringen werden onderverdeeld op verschillende interoperabiliteitsniveaus zoals gedefinieerd binnen het Refined eHealth European Interoperability Framework (ReElF), zoals workflow process, information, applications, and IT infrastructure. Al deze geïdentificeerde interoperabiliteitsniveaus moeten meegenomen worden om implementatie van interoperabele eHealth in de eerste lijn te kunnen laten slagen.

Naast de identificatie van eisen en belemmeringen ten aanzien van interoperabele eHealth resulteerde de kwalitatieve analyse ook in een overzicht van gewenste eHealth-functionaliteiten en veelbelovende gebieden voor clinical decision support technologie binnen de eerste lijn (hoofdstuk 3). Naar aanleiding hiervan richtte het onderzoek naar clinical decision support zich op de ontwikkeling van een CDSS voor de optimale (door)verwijzing en behandeling van patiënten. Als eerste toepassingsgebied werd gekozen voor patiënten met lage rugpijn, omdat lage rugpijn de meest voorkomende oorzaak is voor beperking van activiteiten en tevens een enorme sociaaleconomische impact heeft binnen de westerse samenleving.

Binnen de eerstelijnszorg wordt lage rugpijn voornamelijk behandeld door huisartsen en fysiotherapeuten. In Nederland kunnen patiënten ervoor kiezen om een fysiotherapeut te bezoeken zonder verwijzing van hun huisarts (direct
Samenvatting

toegekend fysiotherapie (DTF)). Hoewel DFT de keuze voor de zorg voor patiënten heeft verbeterd, vereist dit ook dat een patiënt precies weet waar hij of zij het best naartoe kan in zijn of haar situatie; iets dat niet altijd evident is.

De tweede studie richtte zich op de identificatie van significante factoren voor een goede verwijzing van patiënten met lage rugpijn, omdat een direct correcte verwijzing essentieel is voor een effectieve behandeling om zo ook de kans op de ontwikkeling van chronische lage rugpijn zoveel mogelijk te voorkomen. Hiervoor werden eerst de literatuur en lage rugpijn richtlijnen bestudeerd. Vervolgens werden drie huisartsen en vijf fysiotherapeuten geïnterviewd over de classificatie van lage rugpijn met betrekking tot de beste eerste stap in de zorg (triage) voor een patiënt met een nieuwe lage rugpijn episode: 1. Bezoek de huisarts, 2. Bezoek de fysiotherapeut, of 3. Ga eerst zelf aan de slag met de lage rugpijn door oefeningen en/of medicatie (zelfzorg). De resultaten die uit deze interviews voortkamen werden gevalideerd door middel van een online enquête. Dit resulteerde in de identificatie van een selecte groep van 15 belangrijke classificatiefactoren voor de triage van lage rugpijn, voornamelijk factoren, die door fysiotherapeuten "rode vlaggen" worden genoemd (hoofdstuk 4).

De derde studie was een online vignetten studie waarin deze 15 belangrijkste classificatiefactoren voor de triage van lage rugpijn werden gebruikt om fictieve patiëntcasussen (vignetten) te construeren (hoofdstuk 5). Drieënzestig zorgprofessionals (huisartsen en fysiotherapeuten) hebben deelgenomen aan deze online vignetten studie. Iedere deelnemer moest 32 lage rugpijn casussen beoordelen en aangeven wat voor deze casus het beste was: 1. Een huisarts bezoeken, 2. Een fysiotherapeut raadplegen of 3. Eerst zelfzorg uitvoeren. In totaal werden 1288 vignetten beoordeeld. Multinomiale regressie analyse gaf gewichtsverlies, trauma en nachtelijke pijn aan als de drie belangrijkste voorspellende variabelen.

De vignetten studie leidde tot een grote dataset. In de vierde studie werd deze dataset gebruikt voor machine learning binnen RStudio om het triageproces te modelleren als basis voor een CDSS voor patiënten. Drie modellen - 1. Decision tree, 2. Random forest en 3. Boosted tree - werden met elkaar vergeleken op hun prestaties (hoofdstuk 6). Omdat de casussen in de training dataset fictieve casussen waren, was het ook belangrijk om te bepalen of de prestaties van de gegenereerde modellen ook toegepast kunnen worden op lage rugpijn casussen uit de praktijk. Daarom werden in samenwerking met 5 fysiotherapiepraktijken en 6 huisartsenpraktijken ook lage rugpijn casussen uit de praktijk verzameld. Dit resulteerde in 38 bruikbare casussen om een test dataset samen te stellen. De 'boosted tree'-benadering bleek het beste model voor het voorspellen van een verwijzingsadvies voor een patiënt met een nieuwe lage rugpijn episode. Dit model moet echter nog verder worden verbeterd voordat het daadwerkelijk kan worden gebruikt binnen een CDSS voor patiënten. Hiervoor zullen in een vervolgonderzoek nog meer lage rugpijn casussen uit de praktijk worden verzameld om de training dataset te vergroten.
Samenvatting

Wanneer een patiënt met lage rugpijn een huisarts raadpleegt, dan kan hij of zij worden behandeld, maar ook doorverwezen worden naar tweede of derdelijnszorg. Helaas kan lage rugpijn ook na behandeling weer terugkeren. Tegenstrijdige adviezen en behandelingen kunnen negatieve gevolgen hebben voor een optimaal herstel en leiden tot een passieve coping stijl en somatisatie bij patiënten en bijgevolg leiden tot chronische pijn. Daarom is communicatie tussen eerste- tweede- en derdelijns zorgprofessionals van groot belang. Hierbij kan een CDSS voor zorgprofessionals nuttig zijn dat ondersteuning kan bieden bij het selecteren van een geschikte behandeling voor, of doorverwijzing van, een lage rugpijn patiënt op basis van de expertise van medische specialisten op het gebied van lage rugpijn.

In het vijfde onderzoek werd een geanonimiseerde dataset met 1546 lage rugpijn casussen van patiënten van het UMCG Wervelkolom Centrum gebruikt voor het modelleren van behandeladviezen met behulp van machine learning (hoofdstuk 7). Deze dataset bevatte door de patiënt gerapporteerde baseline- en behandelingsgegevens. Deze gegevens werden gebruikt om classificatie-algoritmen binnen de datamining tool WEKA te trainen. De resulterende modellen werden gevalideerd gedurende 10 folds cross-validations. Daarnaast werd een test dataset samengesteld met 50 cases beoordeeld door vier lage rugpijn experts voor het uitvoeren van een interrater agreement analyse en om de op basis van de training dataset gegenereerde modellen opnieuw te evalueren met gegevens die niet zijn gebruikt om de modellen te trainen. Voor deze studie werden de voorspellingsnauwkeurigheid en de gemiddelde area under curve (AUC) van de modellen gebruikt als prestatiematen. De interrater agreement tussen de vier experts bleek aanzienlijk. De best presterende modellen voor besluitvorming voor lage rugpijn behandelingen verschilten per behandeling. De AUC-waarden van de modellen duidden op kleine tot middelgrote machine learning effecten. Dit betekent dat machine learning om besluitvorming voor lage rugpijn behandeling te modelleren mogelijk lijkt, en dat deze beslissingsmodellen per behandeling kunnen verschillen. De prestaties van de modellen moeten echter nog wel verder worden verbeterd voordat deze daadwerkelijk binnen een CDSS kunnen worden gebruikt.

Binnen de laatste studie (hoofdstuk 8) werd de kwestie van interoperabiliteit opnieuw bekeken. Daarbij werd een interoperabele eHealth referentiearchitectuur voor eerstelijnszorg ontworpen, die door IT-specialisten kan worden gebruikt als basis bij het technisch ontwerp van interoperabele eHealth infrastructuren binnen eerstelijnszorg organisaties. Het ontwerp van deze referentiearchitectuur was gebaseerd op het Refined eHealth European Interoperability Framework (ReEIF) en resultaten uit 14 werksessies met 10 eHealth Small en Medium Enterprises (MKB).

De toepassing van de referentiearchitectuur werd gedemonstreerd binnen een casus waarin een CDSS lage rugpijn patiënten ondersteunt bij hun eerste verwijzing naar eerstelijnszorg. Vervolgens werden de referentiearchitectuur en de casus geëvalueerd met acht IT en zorg experts. Deze experts gaven hun mening of de referentiearchitectuur ook daadwerkelijk kan worden gebruikt om de ontwikkeling
Samenvatting

van interoperabele eHealth infrastructuren binnen de eerstelijnszorg te versnellen. Interoperabele eHealth technologie in de eerste lijn is mogelijk, maar er is nog een lange weg te gaan. Er is consensus tussen verschillende belanghebbenden nodig over verschillende interoperabiliteitskwesties, zoals financiën, de organisatie van zorgprocessen, over te gebruiken standaarden, eigendom van gegevens, privacy en beveiliging.

Tot slot geeft hoofdstuk 9 een volledig beeld van hoe de verschillende beschreven studies met elkaar samenhangen. Het reflecteert op eisen en belemmeringen voor de ontwikkeling van CDSSs op basis van machine learning en interoperabiliteit. Met dit onderzoek is nu een interoperabele eHealth referentiearchitectuur voor de eerstelijnszorg beschikbaar. Toekomstige uitdagingen zijn de daadwerkelijke realisatie van interoperabiliteit binnen de eerstelijnszorg. Wanneer dit kan worden bereikt, dan zal dit ook ten goede komen aan een soepel informatieverwisseling tussen systemen die kan worden gebruikt voor machine learning en voor de toepassing van big data binnen de gezondheidszorg. Dit proefschrift heeft bijgedragen aan meer kennis op het gebied van de realisatie van volledig interoperabele eHealth en de mogelijkheid van het toepassen van machine learning voor de ontwikkeling van CDSSs binnen de eerstelijnszorg.
Wel een beetje gek, want nu ik dit schrijf voelt het nog steeds alsof ik net begonnen ben aan mijn promotieonderzoek. Toch ligt hier nu een proefschrift. De vier jaar zijn voorbij gevlogen. Ik heb ervan genoten en dat doe ik nog steeds. Tijdens deze vier jaar zijn allerlei puzzelstukjes op hun plaats gevallen. Daarnaast, ook niet onbelangrijk, heeft het mij de mogelijkheid gegeven om vanuit Dalfsen mijn familie meer te zien die allemaal in Twente wonen. Ik koester alle momenten die de afgelopen vier jaar mij hebben opgeleverd, zowel privé als in mijn werk. En dit alles was niet mogelijk geweest zonder de hulp van heel veel mensen, niet in de laatste plaats mijn promotor, Hermie Hermens, en mijn dagelijks begeleider, Lex van Velsen. Zij hebben mij de kans gegeven om in januari 2014 te starten met het promotieonderzoek dat nu beschreven staat in dit proefschrift.

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Dankwoord

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Dankwoord


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mee heb kunnen krijgen van de laatste jaren van oma, en dat ik je begin dit jaar heb kunnen ondersteunen in een heel moeilijke tijd met gelukkig een heel goede afloop. Jan, jammer dat jij het onderzoek niet tot het eind hebt kunnen blijven volgen. We missen je, maar ook van jou weet ik dat je hebt meegekeken en waarschijnlijk ook nog eens wat extra kaarsjes hebt opgestoken.

Curriculum Vitae

Wendy Oude Nijeweme – d’Hollosy was born on November 27th, 1966 in 's-Gravenhage, the Netherlands. After graduating secondary school (VWO, Twents Carmelcollege, Oldenzaal) she wanted to become a general practitioner. However, the study medicine had a numerus fixes and she could not start a study medicine directly after secondary school. To wait for another year, she started a study nursery at the former Sint Gerardus Majella hospital (currently Ziekenhuis Groep Twente (ZGT)) in Hengelo and worked a couple of months in the internal medicine department. During this year, she changed her mind about the study medicine and decided to study computer science at the University of Twente.

In 1990, she did an internship at the Shriners Hospital for Crippled Children in Philadelphia and in 1991 she earned her MSc degree in computer science with a biomedical note. From 1991 to 1996 she worked as a computer scientist and researcher in the department Urologic Information Center Biomedical Engineering (UIC/BME) at the Radboud UMC, Nijmegen. Subsequently till 2000, she worked as lecturer in knowledge systems, artificial intelligence, computer graphics and internet applications in the department Technical Computer Science of the HAN University of Applied Sciences in Arnhem. From 1999 she had her own company Ilca Media in web development and IT advice. From 2003 till 2005, she also worked at Roessingh Research and Development (RRD) on different eHealth projects as Exozorg, ALS telecare and CP Zorgketen.

From 2007 to 2012 she worked from Ilca Media as external project leader in the Historisch Centrum Overijssel (HCO) on the development and implementation of the digital cultural heritage platform www.MijnStadMijnDorp.nl that shares all kinds of digital heritage sources about the Dutch province Overijssel. She enjoyed this project very much, but after this project she decided to go back to health informatics. In her opinion the fastest way to become really updated about health informatics was to perform PhD research. The Telemedicine group of the Biomedical Signals and Systems group (BSS) of the University of Twente gave her this opportunity.

On January 1st, 2014 she started her PhD research on interoperable eHealth and telemedicine technologies, clinical decision support and machine learning as part of the eLabEL project of the Center for Care in Technology Research (CCTR). Currently, she is also working for the Centre of Monitoring and Coaching (CMC) of the CTIT institute of the University of Twente. The CMC aims to develop smart, innovative technological solutions for applied questions on health and well-being in a multidisciplinary way.
List of publications

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List of publications


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A clinical decision support system for low back pain