The road from analytical CDSS invention to implementation in healthcare

BD4SB
BIG DATA FOR SMALL BABIES

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Preface

This is the master thesis of Rick Klein Koerkamp for the International Business Administration master at the University of Twente (UT). This six-month study focuses on the implementation of clinical decision support systems (CDSS) and has been carried out for SAS Netherlands. The CDSS aim to support the physicians' decision-making process to eventually improve the quality of care. CDSS incorporating advanced analytics have evolved within the research and development (R&D) environment, however, implementation of these kinds of CDSS is lacking. This study set out to discover the barriers within the transition from a R&D environment to implementation and propose solutions to implement an analytical CDSS.

During my first exploratory phase on the world of analytics in healthcare within a clinical context, by attending a data science meetup, an event at UMC Utrecht and the Mobile Health Congress, it became clear that there is a lot of invention with analytical CDSS, however, no implementation. The added value of these systems for the quality of care was often clear, however, further conversations with involved clinical experts and CDSS developers on the barriers for implementation resulted in divergent opinions relating to the complex implementation environment in healthcare. This complexity is apparent due to the involvement of several stakeholders such as methodologists, ethicists, management hospital, CDSS developers, information technology (IT) department hospital, physicians, patients and legal entities. Each stakeholder experiences different barriers for implementing an analytical CDSS.

SAS, a supplier of analytics software, aims to implement analytical CDSS which requires a profound understanding of the implementation environment and therefore supported this research. This research set out to determine the stakeholders, stakeholders' barriers and propose solutions for implementing a CDSS, more specifically, a predictive analytical CDSS called 'Big data for small babies' (BD4SB) that supports the physicians' decision-making process on ministering antibiotics to premature born babies. This study interviewed all the stakeholders to achieve this goal.

This study produced two artefacts that can bring analytical CDSS a step closer to implementation: (1) an analytical CDSS environment technology roadmap incorporating the current and to be implemented analytical CDSS, and (2) an implementation plan for BD4SB with the stakeholders' barriers, proposed solutions and determination of the key stakeholders. These two artefacts provide the stakeholders in analytical CDSS development with a profound understanding of each other's frame of reference which is required to move towards analytical CDSS implementation in healthcare.

I would like to thank Fons Wijnhoven and Erwin Hofman from the UT for their guidance within this research. Furthermore, I would like to thank Edwin Peters, Joost Huiskens and Jelle Brouwer from SAS for giving me the opportunity and support in my research period. Additionally, I would like to thank the UMC Utrecht for providing all the valuable knowledge from a clinical frame of reference.

Rick Klein Koerkamp

Executive Summary

Developments within analytics enhance the possibilities of predictions based on large datasets to optimize business processes, this is also applicable to healthcare. Clinical decision support systems (CDSS) powered by analytics can detect diseases and predict the development of the diseases. However, these CDSS remain within a research and development (R&D) environment and implementation is lacking. SAS, a supplier of analytics software, works together with UMC Utrecht to implement a CDSS called 'Big data for small babies' (BD4SB) which analyzes a vast amount of medical data to predict the probability on sepsis for premature born babies and supports the physicians' decision-making process on mistering antibiotics. This system shows promising results, however, the transition from the R&D environment to implementation is complex since numerous stakeholders are involved who each experience different implementation barriers. This research set out to support this transition for BD4SB.

To achieve this goal, this study explored the analytical CDSS environment with a technology roadmap to describe the problem context of implementing BD4SB. Furthermore, this study constructed the BD4SB implementation plan describing the (key)stakeholders, stakeholders' barriers and accompanying solutions. To construct this implementation plan, a literature review was executed on the involved stakeholders with implementing CDSS to select the respondents for the interviews which consists of a methodologist, ethicist, management hospital, CDSS developer, IT department hospital, physician and regulatory entities. Furthermore, a literature review on the stakeholders' barriers for implementing IT in healthcare provided input for the questionnaires of the interviews. Based on the literature reviews and the interviews, a thorough description of the stakeholders' barriers and proposed solutions for implementing an analytical CDSS as BD4SB was created and categorized per stakeholder.

This thorough description proves that the implementation environment of analytical CDSS is multidimensional and it emphasizes the magnitude of incorporating each stakeholders' frame of reference to move towards implementing analytical CDSS in healthcare. The key stakeholder groups consist of the regulator, physician and developer. Firstly, advancements in technology have surpassed regulation, regulatory entities need to construct legislation to enable implementation of analytical CDSS as a medical device. Secondly, physicians' lack of trust in analytical CDSS impairs implementation and should be mitigated by involving physicians in CDSS development. Thirdly, developers should execute technological solutions to improve data availability, integration, preparation and analysis of medical data to enable the analytical CDSS process within the required timespan to be clinically valuable.

The contribution of this research is threefold: (1) scientific – the BD4SB implementation plan provides specification of and solutions for the known technical and people related barriers and for the absent or undervalued legal, ethical, validation and impact related barriers from literature, (2) business- the analytical CDSS environment technology roadmap provides guidance for product development, (3) business- the BD4SB implementation plan contains reasoning on implementing analytical CDSS from every stakeholders' frame of reference and can be used by SAS in communication with the stakeholders.

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List of Abbreviations

ADAM	Applied Data Analytics in Medicine
AI	Artificial Intelligence
BD4SB	Big Data for Small Babies
CDSS	Clinical Decision Support Systems
CE	Conformité Européenne
CER	Clinical Evaluation Report
EHR	Electronic Health Record
FDA	Ferderal Drug Administration
HIS	Healthcare Information Systems
IA	Intelligence Amplification.
ICT	Information and Communications Technology
IGJ	Inspectie Gezondheidszorg en Jeugd
ISO	International Organization for Standardization
IT	Information Technology
MDR	Medical Device Regulation
METC	Medisch Ethische Toetsing Commissie
MSK	Memorial Sloan Kettering Hospital
NB	Notified Body
NLP	Natural Language Processing
PEOU	Perceived Ease Of Use
PU	Perceived Usefulness
QMS	Quality Management System
R&D	Research & Development
RCT	Randomized Control Trial
TAM	Technology Acceptance Model
UMCU	Universitair Medisch Ziekenhuis Utrecht
WFO	Watson For Oncology
WMH	Wet Medische Hulpmiddelen
WMO	Wet Medisch Onderzoek
ZiRA	Ziekenhuis Referentie Architectuur

Introduction

Our society is exponentially producing data and we are developing new sophisticated systems to utilize it, this is also the case in healthcare. These systems refer to clinical decision support systems (CDSS) that minimize practicing variation for physicians and improve patient care via diagnostic standardization (Marakas, 2003). These inventive systems are developing rapidly and incorporate artificial intelligence (AI) nowadays. Ongsulee (2017) defines AI as "a machine that mimics cognitive functions that humans associate with other human minds, such as learning and problem solving" (p.1). AI CDSS range from complex systems such as IBM Watson for oncology (WFO) to less complex CDSS with algorithms that support clinicians in everyday proceedings (Vijlbrief & Huiskens, 2018; Nijhof, 2017). However, healthcare has the lowest adoption rate and maturity of AI (Batra, Queirolo & Santhanam, 2018) (Appendix B, figure 16 and 17). It is complicated to implement CDSS in healthcare due to its effect on the patients' health and the involvement of numerous stakeholders. (Sligo, Gauld, Roberts, & Villa, 2017; Jha, Doolan, Grandt, Scott & Bates, 2008). The transition of a CDSS invention, from a research & development to an implementation environment is the focus area of this study. This transition should be easier with less risky, less complex, more transparent and supportive forms of AI CDSS which relates to the concept of intelligence amplification (IA) that describes the symbiotic interaction between human and machine (Licklider, 1960; Dobrkovic, Liu, Iacob & Hilegersberg, 2016). This study its scope focuses on the implementation process of an IA CDSS as will be further described in chapter 1.1 alongside the focus on analytics since SAS institute BV, an organization that primarily supplies data analytics software (more information in Appendix A), has an interest in expanding in healthcare.

This explorative research aims to identify stakeholders' barriers and solutions for implementing an analytical CDSS. Firstly, this study explores the analytical CDSS implementation environment by means of constructing an analytical CDSS environment technology roadmap based on available knowledge from literature supported by knowledge obtained via interviews with involved stakeholders. This roadmap describes the problem context for the successive implementation plan, containing the relevant stakeholders, stakeholders' barriers and accompanying solutions based on empirical data for a case study on 'Big data from small babies' (BD4SB) which is an analytical CDSS that supports the physicians' decision process for ministering antibiotics for sepsis to premature babies. This research aims to achieve this goal by answering the following research question:

"What are the stakeholders' barriers and possible solutions for implementing the 'Big data for small babies' clinical decision support system within the analytical clinical decision support system environment in the Netherlands?"

This research question will be answered via the following sub-questions:

(1) **The analytical CDSS environment technology roadmap: (**SQ1) 'what analytical CDSS are currently implemented in the Netherlands?' and (SQ2) 'what analytical CDSS will be implemented within 10 years in the Netherlands?'
(2) **BD4SB CDSS implementation plan: (**SQ3) 'what are the stakeholders' barriers for implementing the BD4SB CDSS?', and (SQ4) 'what are the proposed solutions for these stakeholders' barriers for implementing the BD4SB CDSS?'.

To answer these questions, this research constructed a model based upon the laddering technique of Jensen (2005) to extract empirical data to subsequently categorize the stakeholders' barriers and proposed solutions. This categorization is realized by a literature review on the barriers from the IT innovation adoption, technology acceptance model (TAM), health information systems (HIS) implementation and big data analytics in healthcare literature (Jensen, 2005; Hameed, Counsell & Swift, 2012; Holden & Karsh, 2010; Sligo et al., 2017). Additionally, this study determines which stakeholders must execute which solutions by executing a stakeholder path analysis. More specifically, this determines who the key stakeholders are for implementing an analytical CDSS as BDFSB.

The two artefacts of this study contribute to the literature. Firstly, there is literature available on the development of analytical CDSS, however, not specifically on what is currently and will be implemented in the future as this study does. Secondly, current literature discusses the barriers for implementing healthcare information systems, however, these are often quite abstract and not tailored for analytical CDSS. This study its discovered barriers for implementing analytical CDSS within the Netherlands show to what extent the related barriers extracted from literature fall short, can be specified or are sufficient. Furthermore, this study also proposes possible solutions for these barriers. All in all, this study contributes to literature by specifying the analytical CDSS implementation environment and providing a greater understanding of the abstract barriers in the literature and how to overcome these.

The practical relevance of this study is also twofold. Firstly, the analytical CDSS environment technology roadmap provides CDSS developers with a description of the current and possible future position of analytical CDSS which provides guidance for product development. Secondly, the BD4SB CDSS implementation plan highlights who the stakeholders are, what the stakeholders' barriers are, which stakeholders must execute which solutions to overcome certain barriers. This pinpoints how and what stakeholders can kickstart implementation of analytical CDSS such as BDFSB.

The first chapter of this research entails the theoretical framework with the description of scope of this research, the theories used for the technology roadmap and the BD4SB implementation plan, and the literature review on stakeholders' barriers for implementing IT in healthcare. The second chapter explains the used methodology. Subsequently, the third chapter discusses the results of the research. Lastly, the fourth chapter entails the conclusion, discussion and gives the recommendations.

1. Theoretical Framework

The theoretical framework describes the scope of this research, theories used for the analytical CDSS environment roadmap and the BD4SB implementation plan. Furthermore, this section executes a literature review on stakeholders' barriers for implementing IT in healthcare.

1.1 Scope

This section describes the scope of this study by assessing the main topics: CDSS, AI versus IA and analytics (within implemented CDSS in healthcare).

1.1.1 Clinical context

This study focuses on CDSS which are systems that improve patient safety, quality of care or efficiency in healthcare delivery (Maracas, 2003). These systems function within the clinical process wherein the care is delivered to the patient as shown in figure one (Zira, z.d.).

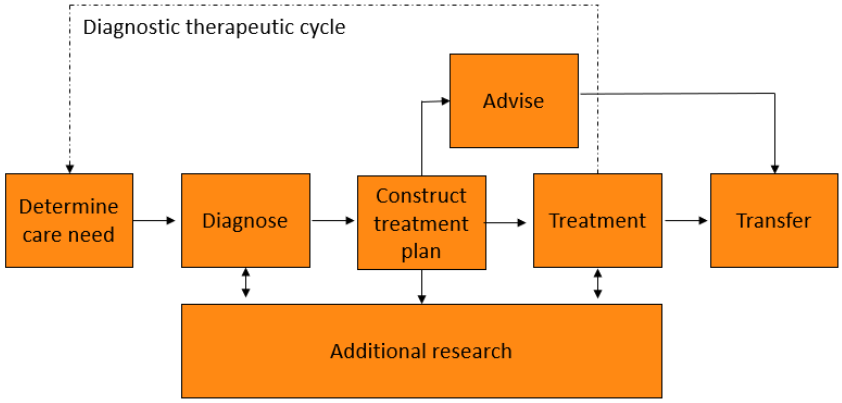

Figure 1: Clinical process in healthcare (Zira, n.d.)

Furthermore, this study focuses on CDSS legalized as medical devices. A medical device is any instrument, apparatus, appliance, software, material or other article, including software to be used specifically for diagnostic and/or therapeutic purposes as shown in figure one (EU, 2016).

1.1.2 Artificial intelligence versus intelligence amplification

This study excludes AI CDSS and includes IA CDSS within the research scope. AI CDSS remain a highly debatable form of technology and are not likely to be implemented in the near future. AI CDSS collect and analyze knowledge in such a way that simulates human reasoning to generate advice, however, sometimes in such a way that is not transparent enough for the user. Once the knowledge is acquired and stored from structured and unstructured datasets, computational reasoning provides diagnostic or treatment assessments for physicians. Such a cognitive-support system was firstly introduced by IBM with WFO (Somashekhar et al., 2018). WFO was trained with data of 15.000 patients, protocols, patients' cases and experts from Memorial Sloan Kettering (MSK) Cancer Center. The physician enters specific patient data in WFO and the system compares it with the historical patient

data, 600 journals, 400k other data sources and statistical evidence from literature. Based on this data, WFO advises the physician on the diagnosis and rank orders treatments (IBM, 2017). Somaskehar et al. (2018) analyzed 638 breast cancer cases in which WFO and the multidisciplinary tumor board reached a concordance for 93% of the cases. This shows that WFO might be helpful within breast cancer treatment. Contradictory, WFO got cancelled at MSK and according to Fuchs, computational pathologists at MSK, this was a result of WFO its inability to properly function in a specialized domain in medicine with uncommon cases. To achieve this specialized knowledge, it needs experts to train it with labelled information which takes a substantial amount of time (Freedman, 2017; Gorski, 2017). Moreover, medical journalists claim that MSK physicians trained WFO with data from hypothetical patients which results in a biased analysis based on the MSK physicians' preferences (Petitjean, 2018; Ross, 2018). Due to these all conflicting views, it is reasonable to assume that AI CDSS such as WFO remain highly debatable CDSS.

Other technological companies such as Google and Microsoft also develop products for healthcare that can be categorized as AI CDSS. Microsoft aims to order large amount of oncology research with machine learning and Google explores how machines can support physicians in curing head and neck cancer with deepmind (Nijhof, 2017). These systems remain within the R&D environment and have not been implemented within healthcare (Batra et al., 2018; Dr. J. Huiskens, personal communication, July 6, 2018). Due to the embryonic stage of implementing AI CDSS, this study excludes these systems from the scope and will focus on IA CDSS since this form of technology can be seen as less complex, more transparent and supportive than AI. IA centralizes the role of the human by augmenting human brain activities with improved information input (Dobrkovic et al., 2016). This implicates a more intuitive and transparant CDSS which is more likely to be implemented. This IA CDSS description will be specified within this research by means of the analytical CDSS environment roadmap and BD4SB CDSS implementation plan.

1.1.3 Analytics

The IA CDSS scope within this research is specified by the incorporation of analytics. This will be discussed within this section to provide the contextual knowledge of analytics required for execution of this study.

Nowadays, the term 'big data' is commonly used to refer to the new possibilities within analytics. Big data refers to the collection, processing, analysis and visualization of large datasets, however, several scholars agree that this definition of big data is insufficient (Gupta & Tyagi, 2015; Suresh, 2014; Uddin & Gupta, 2014). To understand big data, scholars have decided to dissect the term or look at it from another perspective to apply their own theories. These will be briefly discussed in this section to determine the applicability of the definitions to this study.

Firstly, Emmanuel and Stanier (2016) claim that big data is implementation driven and therefore is not based around a single theory of paradigm. They suggest that the definition of big data differs, it is

dependent on the specific application and process of big data in a certain situation. Hence these authors do not provide a uniform definition of big data.

Secondly, De Mauro, Greco & Grimaldi (2015) concluded that big data can be defined by its features concerning information, technology, method and impact. Information, or data, is seen as the fuel for big data which is produced in unknown quantities by digitalization of society. Technology entails the computational power required to process the large amount of fuel. Method concerns the transition from data into valuable insights, such as with text and sentiment mining or cluster analysis (Žunić, Djedović & Đonko, 2016). Impact refers to the way big data is influencing society and companies. This entails the beneficial cases, however, also the privacy concerns related to big data. All in all, these authors describe big data in terms of its features instead of providing a uniform definition.

Thirdly, big data can be defined based upon its attributes concerning three concepts: volume, velocity, and variety. Volume refers to size and scale of data, this can also be the magnitude of the data according to Gandomi & Haider (2015). Velocity entails the speed at which the data is obtained, stored, processed and analyzed (Bedi et al., 2014). Lastly, variety focuses on the role of semi-unstructured and unstructured data (Sagiroglu & Sinanc, 2013; Gadoni & Haider, 2015; Demchenko, Grosso, Laat, Membrey, 2013). Additionally, other scholars determined that big data can be further specified by adding the following concepts: variability, veracity, visualization and value. Variability refers to the continuous change in meaning of data (Sivarajah, Kamal, Irani, Weerakkody, 2017). Veracity entails the imprecision or inconsistency in large datasets. Visualization includes the way which key information is visualized instinctively and effectively through using different visual formats (Taheri, Zomaya, Siegel, & Tari, 2014). Lastly, value entails to what extent knowledge/value can be extracted from vast amounts of unstructured and structured data (Sivarajah et al., 2017).

This study concludes that the seven V's (volume, velocity, variety, variability, veracity, visualization and value) provide the most thorough definition of the aspects of big data. These seven concepts will be considered in describing the stakeholders' barriers and possible solutions within the result and conclusion sections.

These seven V's relate to the workflow of big data analytics as shown in figure two. This figure dissects the analytics workflow starting with integrating several data sources which can subsequently be pre-processed, filtered, aggregated, transformed or exposed to other related proceedings within the data management section. The resulting dataset is utilized to train a model and estimate its parameters. Usually this is realized by means of original or external input data and tailored methods to validate the created model. Finally, the model is operationalized and can be applied to the data it was designed for. This stage is referred to as model scoring and used to generate predictions, prescriptions, and recommendations. These results can be interpreted and evaluated to subsequently create new models, calibrate existing ones or integrate new pre-processed data (Assunção, Calheiros, Bianchi, Netto, & Buyya, 2015).

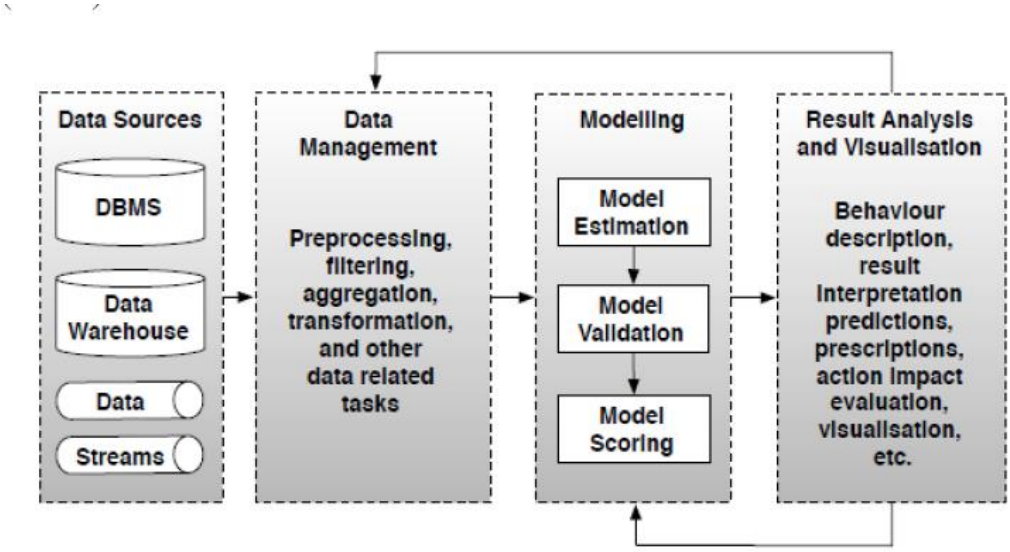

Figure 2: Workflow for Big Data (Assunção et al., 2015)

The specification of big data analytics by means of the seven V's and the analytics workflow can be further specified by the descriptive, predictive and prescriptive segments of analytics (Sivarajah et al., 2017). Firstly, descriptive analytics uses historical data to identify patterns that occurred in the past to construct management reports which entails reporting, scorecards and data visualization (Sivarajah et al., 2017; Assunção et al., 2015). Secondly, predictive analytics predicts values by analyzing current and historical data. This concerns forecasting, statistical modelling with the use of supervised, unsupervised, and semi-unsupervised learning models (Joseph & Johnson, 2013; Rehman, Chang, Batool & Wah, 2016; Waller & Fawcett, 2013). Lastly, prescriptive analytics enables responding to the predicted values, it enables organizations to optimize their business process models by using the feedback of predictive analytical models (Banerjee, Bandyopadhyay & Achary, 2013). WFO incorporates a form of prescriptive analytics by prescribing a treatment to the patient as a physician normally does.

Within this categorization, descriptive and predictive analytics solely provide insight to the decision maker which refers to IA whereas prescriptive analytics makes a decision which relates to AI. The scope of this research excluded AI which implicates that only descriptive and predictive analytics will be incorporated within the analytical CDSS environment roadmap.

In summation, this study utilizes the seven V's (volume, velocity, variety, variability, veracity, visualization and value), descriptive and predictive segments of analytics and the workflow as shown in figure two for studying the analytical CDSS environment. Furthermore, it will be referring to big data as analytics since there is no consensus about the definition of big data. Analytics within this study is used as an umbrella term for retrieving, saving, managing, analyzing and visualizing data which leads to new insights and a new way of reasoning (Davenport, 2014; Nationale DenkTank, 2014).

1.2 Analytical CDSS environment technology roadmap

This section discusses the theory applied for the analytical CDSS environment roadmap and executes a literature review for construction of the preliminary roadmap.

1.2.1 Technology roadmap

Roadmaps provide a structure that describes the journey from the current state business to a future state of business (Phaal, Farrukh, & Probert, 2004). According to Phaal et al. (2004) a technology roadmap has two functions: (1) allow technology developments to be implemented in business planning to assess impact of new technologies and market developments and (2) capture the environment landscape, opportunities, threats related to a specific group of stakeholders within a technology or application field. Technology roadmaps provide the basis for technology management and planning, discovering relations between technological resources, organizational objective and changing environment (Phaal et al., 2004). The several layers of the roadmap reflect the fundamental aspects of the business and issues at hand which are based on the knowledge dimensions of the business such as why, what, when, who, where and how (Phaal et al., 2004).

This study uses the roadmap theory as a foundation, however, tailors it to the purposes of this research. Phaal et al. (2004) designed a multi layered roadmap based on several roadmaps as shown in figure three. The bottom layer ‘resources’ refers to the resources such as budget or infrastructure needed for development and meeting the demand within the top the top layers, products and markets (Phaal et al., 2004). This resource layer is not utilized within the roadmap of this study. The second bottom layer ‘technology’ refers to the technological knowledge that will be deployed to meet the demand from the top layers, products and markets (Phaal et al., 2004). More specifically, according to Tushman et al. (1997), a product consists of a set of subsystems, each of which has its own innovation streams. In this study, the product is the CDSS and the set of subsystems refers to the analytics underlying the CDSS which will be shown in technology layer. The third layer involves the ‘products or services’ which are currently and to be implemented analytical CDSS in the Netherlands within this study. The top layer entails the ‘external environment’ which will not be applied within the roadmap of this study. The BD4SB implementation plan already describes the external environment by the stakeholders’ barriers and proposed solutions which will be additional layers within the roadmap as shown in figure four.

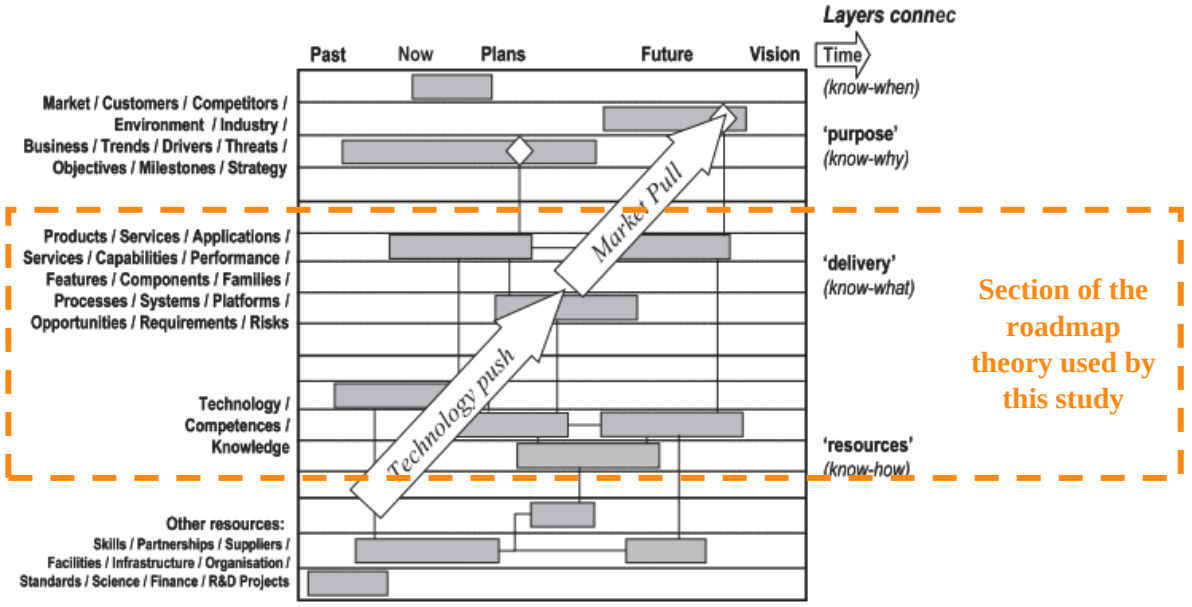

Figure 3: Generalized technology roadmap architecture (Phaal et al., 2004)

1.2.2 Analytics in healthcare

This section discusses implemented analytical CDSS via a literature review utilizing the descriptive and predictive categorization and the analytical workflow shown in figure two to describe the technology and product layer of the preliminary roadmap. Firstly, the categorization, according to literature, healthcare has seen improvement of quality of care by means of incorporating descriptive analytics (Mehta & Bandit, 2018; Assante & Jacobs, 2016; Groves, Basel, Knott & Van Kuiken, 2013). Literature shows no indication of implemented predictive analytical CDSS. Secondly, the analytical workflow. Data is the foundation for analytics and must be available in the required quantity and quality. Within healthcare, the electronic healthcare record (EHR) is a CDSS that contains qualitative/ unstructured data (text), quantitative/structured data (statistical values) data and transactional data (registration of ministered medicine). The EHR is a system that has not been fully developed. More specifically, Meyenhoefer et al. (2018) state that physicians are not that satisfied with the EHR since it negatively affects their work processes. Moreover, healthcare ICT has developed independently from the EHR which results in integration issues (Michel-verkerke, Stegwee & Spil, 2015). It can be concluded that the EHR has some obstacles to overcome. This conclusion will be challenged by means of the qualitative section of this study since the EHR can play a role in the implementation of analytical CDSS.

The following data management stage in the analytics workflow describes integration of several data sources which is complex within healthcare. For example, health data contains the structured and unstructured data from the EHR as explained in the previous section. Furthermore, there are other data sources with different formats as images, signals, audio transcripts, and handwritten text which makes the total dataset of healthcare multidimensional, this results in integration hurdles (Dimitrov, 2016). Integration of these different sources requires techniques that convert these different sources into a

homogenous outcome before entering the modelling stage as shown in figure two. There are several techniques which can do this among which natural language processing (NLP). NLP is a form of text analysis that can automatically extract the meaning from natural language text which is beneficial for clinicians since laboratory and medication records can be natural language notes which are time consuming to read (Holzinger, Geierhofer, Modrischer & Tatzel, 2008). However, NLP can be complex due to differentiating terminology in natural language and the negation of certain symptoms to exclude diseases for example which makes the text harder to interpret for NLP (Menasalvas & Gonzalo-Martin, 2016). Still, literature shows that NLP is most the frequently implemented analytical technology within clinical context (Mehta & Pandit, 2018). This NLP implementation claim will be challenged by the qualitative section of this study.

Furthermore, current literature on analytics in healthcare within a clinical context shows the appliance of cluster analysis, data mining, graph analysis, machine learning, neural networks, pattern recognition and spatial analysis next to NLP as shown in table one (Mehta & Pandit, 2018).

Table 1: Analytics in healthcare within clinical context (Mehta & Pandit, 2018)

Technique	Healthcare application	References
Cluster analysis	Detecting obesity clusters for high-risk groups	Clark, Morlet & Semmens (2016)
	Detecting clusters with specific health determinants in need of treatment	Swain (2016)
Data mining	Bio-signal monitoring for health epidemics	Forkan, Khalil & Atiquzzaman (2017)
	Detecting epidemics	Ghani, Zhen, Wei & Friedman (2014)
	Exploratory analysis and inductive reasoning	Roski, Bo-Linn & Andrews (2014)
Machine learning	Predicting disease risk	Chen, Hao, Hwan, Wang & Wang (2017)
	Detecting epidemics	Ghani et al. (2014)
NLP	Detecting high risk factors	Martin-Sanchez, Pulido, Lopez, Peek & Sacchi (2017)
	Extracting information from clinical notes	Roski, et al. (2014)
	Reduction probability of morbidity & mortality	Roski, et al. (2014)
Neural networks	Diagnosing chronic diseases	Al-Jumeily, Hussain, Malluci & oliver (2015)
	Prediction patients' future diseases	Martin-Sanchez et al. (2017)
Pattern recognition	Improving public health surveillance	Martin-Sanchez et al. (2017)

Further analysis of these studies shows than not one of these analytical CDSS is implemented and used by clinicians in a non-R&D environment within clinical context. All these studies describe, develop and test a model or algorithm to show its added value, however, do not mention anything about implementation and only give suggestions for future research. This literature review indicates a paucity of information on implementation of analytical CDSS in healthcare. According to Mehta & Pandit (2018) the current body of literature does not provide the adequate quantitative validation foundation healthcare needs for implementing analytical CDSS. This study will challenge this statement in the qualitative section of this study by assessing the implementation of analytical CDSS.

1.2.3 Preliminary roadmap

The results of the literature review on the technology (analytics) and product (CDSS) layers are incorporated in the preliminary roadmap shown in figure four. It shows that current implemented analytical CDSS are in the descriptive realm whereas literature indicates implementation of an NLP CDSS. This study aims to specify these layers by means of the qualitative section of this study. Furthermore, this study will place the BD4SB CDSS within the CDSS layer, just as NLP, and connects it to results of the BD4SB implementation plan analysis containing the stakeholders' barriers and proposed solutions within the grey layer as will be discussed in the next section.

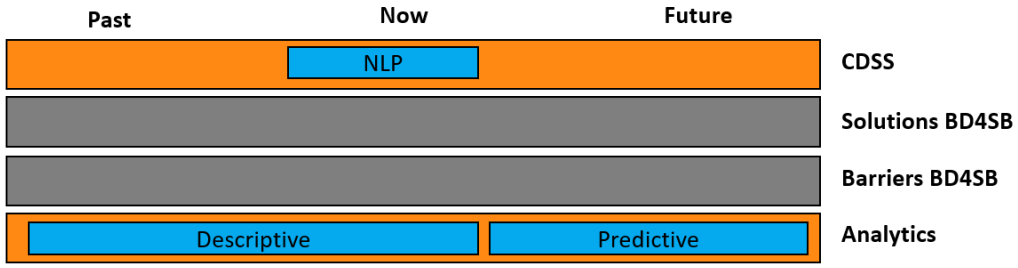

Figure 4: Preliminary roadmap based on literature review

1.3 BD4SB Implementation plan

This section specifies the BD4SB CDSS, the stakeholders involved in implementation and the connection of the analytical CDSS environment roadmap with the BD4SB implementation plan.

1.3.1 BD4SB CDSS specification

The UMCU initiated ADAM 'Applied Data Analytics in Medicine' project in spring of 2017 to make healthcare more personalized with analytics in collaboration with external partners such as Siemens, Philips, SAS and Accenture. This is a hospital wide project with a special team of clinicians and data scientists and is supported by the board of directors. ADAM enabled pilots on four departments within the UMCU among which the BD4SB pilot within the 'neonatology' department that focuses on care of premature babies. Babies that are born too early are sensitive to bacterium and possibly treated by means of infusion, blood samples or ventilation which are also all entries for bacterium which gets certain patients ill. The BD4SB project focuses on a specific case in relation to sepsis also known as blood poisoning. The neonatology department focuses on the questions: when will which patient get ill? When blood poisoning is suspected, what is the best treatment? Within these questions, the prediction on the kind of bacterium is considered. The current healthcare process in relation to blood poisoning within neonatology goes as follows: (1) the physician detects suspicious values (e.g. skin color, blood pressure or temperature) which can indicate an infection, (2) the physician takes a blood sample, (3) the blood culture is examined on bacterium in the laboratory and (4) the blood is examined on gram coloring (bacterium are colored to make them visible under the microscope to detect the species). This whole process takes up 24 to 48 hours which can be crucial in the development of the infections and ministering antibiotics or not. Ministering antibiotics must be thought-out carefully since sepsis has negative

consequences for the patient, however, ministering antibiotics can also have negative consequences such as an increased chance on other diseases as asthma, cancer, intestinal diseases or obesity according to doctor Vijlbrief, clinical owner of the BD4SB project. (Dr. D. Vijlbrief, personal communication, February 7, 2019).

The BD4SB CDSS aims to support the physicians when they doubt if they should minister antibiotics or not. The CDSS focuses on predicting as least as possible false negatives (Ragan, 2018). This implies a prediction of at least as possible patients that are ill which the BD4SB CDSS shows as not ill. This is considered the most dangerous situation possible where the physicians are advised to not give antibiotics whereas they should. Furthermore, the BD4SB CDSS supports the physician in the decision-making process and is considered as additional research as shown by the placement within the healthcare process shown in figure five.

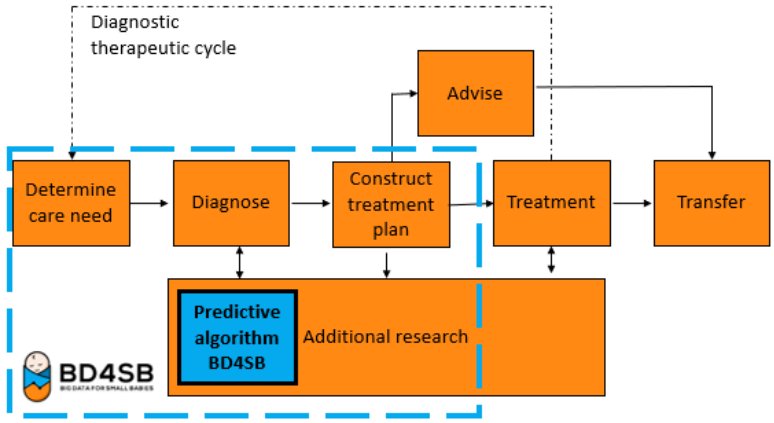

Figure 5: BD4SB CDSS within the healthcare process

The BD4SB CDSS uses different data sources from the database of neonatology which consists of 6000 children born between 24 and 32 weeks. This data originates from several systems as shown in figure six and table two and must be integrated and prepared within data management before analysis.

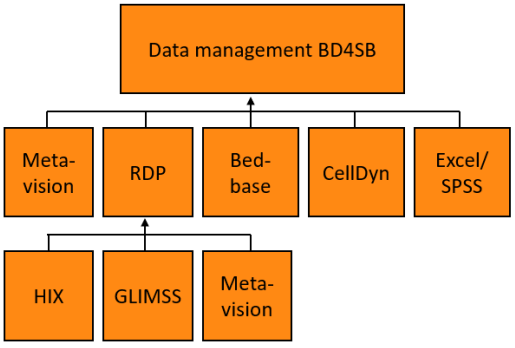

Figure 6: Data input from systems BD4SB CDSS

Table 2: Data input systems BD4SB CDSS

System	Specification
Hix	Electronic health record
GLIMSS	Lab information system
Metavision	Patient data management
RDP	Remote desktop protocol
Bedbase	Software designed for data compilation
CellDyn	Software designed for in vitro diagnostic use
Excel/SPSS	Data from UMCU research database

The resulting data input for the BD4SB CDSS consists of the parameters as shown in figure seven. The model applied for analysis is a 'gradient boosting' technique which is a form of machine learning and can be categorized under predictive analytics. Gradient boosting converts a sequence of weak learners into a complex predictor. In this case, the technique converts the individual parameters into a prediction on the result of the 'X% negative culture' (probability blood infection) and the 'X% gram-positive and X% gram-negative' (probability on a specific bacterium) which indicate the probability on sepsis.

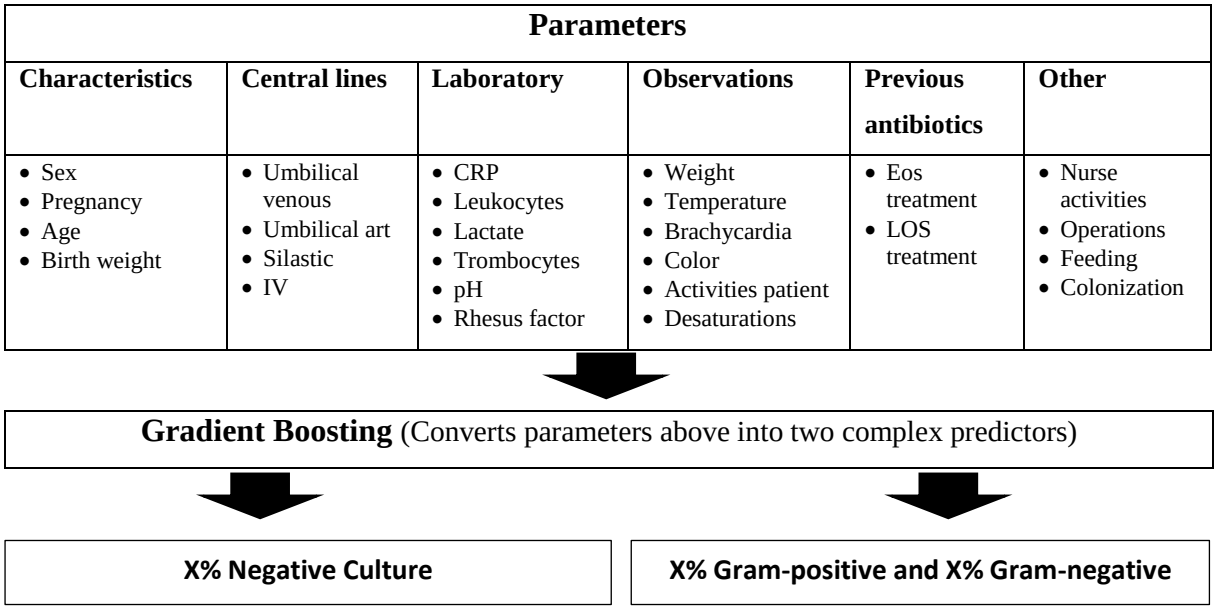

Figure 7: Analytical process BD4SB CDSS

1.3.2 Stakeholders for implementing BD4SB

According to Freeman (1984) a stakeholder is "any group or individual who can affect or is affected by the achievement of the organization's objectives" (p.3). Within this study the stakeholders concern the individuals or groups that affect the implementation process of the BD4SB CDSS. To determine who the stakeholders are, this study firstly applies the IT innovation adoption theory that considers stakeholders at an organizational and individual level for the adoption of an new IT system by an organization (Hameed et al., 2012). Within this study, the organization relates to the hospital 'Universitair Medisch Centrum Utrecht' (UMCU) and the neonatalogy department within the UMCU. The individual concerns the physicians from the UMCU that will be using the BD4SB CDSS in his/her proceedings. However, this organizational and individual distinction is considered insufficient for the stakeholder specification in this study, hence it applies additional theories and emperical data to determine the stakeholders. Firstly, the theory of Alexander (2005) on the stakeholders for IT innovation which segments groups around the central product via surrounding circles in the 'onion model' (Appendix B figure 19, table 28 and 29). Secondly, the stakeholders checklist from the theory on 'stakeholders creep' is incorporated which relates to not clearly defining all the stakeholders within a health IT project (Appendix B table 30) (Panyard, Ramly, Dean, & Bartels, 2018). Thirldly, the input of

Dr. J. Huiskens shows the relevance of three additional stakeholders (Dr. J. Huiskens, personal communication, July 6, 2018). This reseach aligns the three stakeholder descriptions and provides a summarized definition tailored for this study as shown in table three in order to select respondents for the qualitive section of this study.

Table 3: Alignment stakeholder descriptions (Alexander, 2005; Panyard et al., 2018)

Onion model	**Stakeholders checklist**	**Input Dr. Huiskens**	**Summerized definition:**
Normal operator: *Gives the routine commands and monitors output from the product*	Radiology,cardiology and health info team	Clinician	Physician Neonatology UMCU
Maintenance operator(s): *Responsible for maintaining the IT product (e.g. solving bugs)*	Environment manager and decision support team	Technical	Developer CDSS and IT department UMCU
Operational support: *Responsible for support rather than productively use the software*	System education/ training team	Technical	Developer CDSS and IT department UMCU
Functional benificiary: *Responsible for the interfacing system of the product*	Interfacing team	Management	Developer CDSS
Political benificiary: *Anybody who benefits from the systems' sucess in terms of power, influence and prestige*	Medical board	Management	Management UMCU, SAS and developer CDSS
Financial beneficiary: *Any role that financially benefits from the product success*	Purchasing director and medical board	Management	Management UMCU, SAS and developer CDSS
Regulator: *Responsible for regulation of the safety, quality, costs or other relations to the product*	Health info team, security team and health system legal team	Legal	Government and quality assurance related organizations in healthcare
Developer: *All the roles involved directly in product development (from programmer to projectmanager)*	Coding team and server team	Technical	SAS, developer CDSS and IT department UMCU
No relevant stakeholder stated in theories for 'patient' group		Patient: *The person who receives the care*	Parents patient (pre-mature born baby)
No relevant stakeholder stated in theories for 'ethicist' group		Ethicist: *Expert who focuses on the critical reflection of right action*	Ethicist UMCU
No relevant stakeholder stated in theories for 'methodologist' group		Methodologist: *Expert who focuses on the system of methods applied in healthcare*	Methodologist UMCU

1.3.3 Framework roadmap & implementation plan BD4SB

The UMCU, initiator of the BD4SB project, utilizes an innovation funnel for project planning as shown in figure twenty in Appendix B. This figure shows that the BD4SB CDSS is currently within the pilot stage of the funnel, this stage aims to prove the clinical relevance of the BD4SB CDSS to pass through the relevance & validation gate. This study aims to determine the stakeholders' barriers and possible solutions to pass through this gate and enter the following stages, firstly the pre-production (implementation preparation) and secondly the production stage in which the BD4SB CDSS will be implemented and monitored.

The analytical CDSS environment roadmap of this study describes the problem context for the implementation plan of BD4SB as shown in figure eight. The BD4SB CDSS applies gradient boosting with a predictive algorithm which approximates the placement within the roadmap as shown in figure eight. Furthermore, this figure incorporates the two pillars from the BD4SB implementation plan constituting the stakeholders' barriers and proposed solutions. These layers show which solutions belong to which barriers by color and the approximated timespan for executing the solution by the length of the colored figure. The framework randomly visualizes four barriers and solutions to exemplify the final visualization of the implementation plan incorporated within the roadmap.

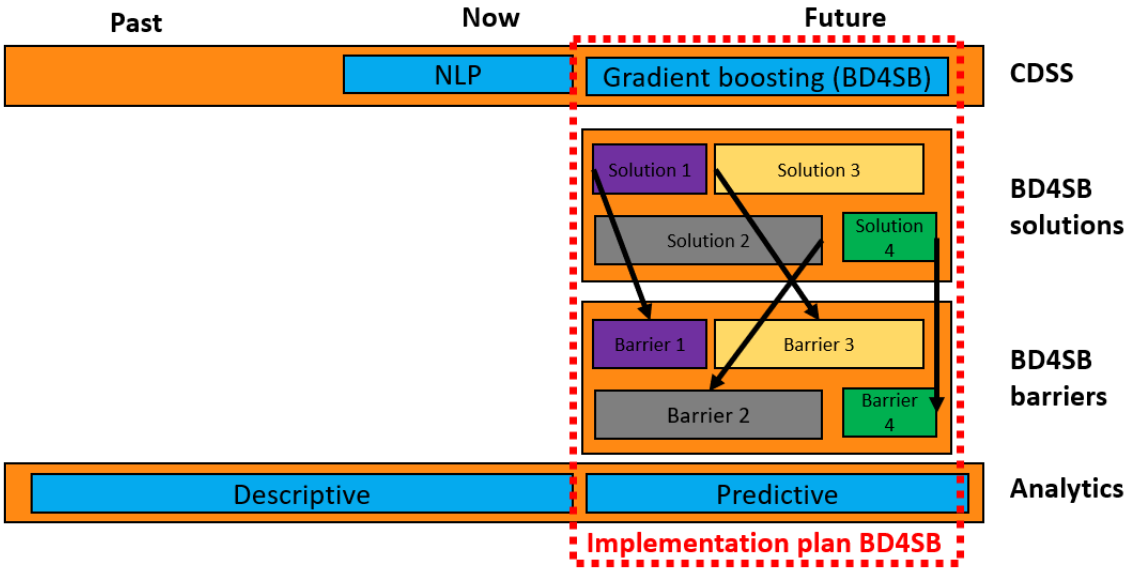

Figure 8: Proposed framework roadmap & BD4SB implementation plan

Additionally, the BD4SB implementation plan incorporates a stakeholder path analysis that shows how many proposed solutions each stakeholder has to execute to overcome the determined barriers. The number of solution combined with the approximated time to execute each solution will provide the basis for determining the key stakeholders for implementing an analytical CDSS such as BD4SB.

1.4 Literature review: Stakeholders' barriers for implementing IT in healthcare

The following literature review determines the most robust barriers for implementing IT in healthcare as shown in table four based on the technology acceptance model (TAM), healthcare information system (HIS) and occurrence of big data analytics in healthcare literature. This study compares these barriers with the BD4SB stakeholders' implementation barriers obtained from the qualitative section of this study to determine if the barriers extracted from literature fall short, can be specified or are sufficient. Subsequently, this study proposes solutions for these categorized barriers, hence for the barriers extracted from literature and the BDFSB case.

The TAM literature is the most dominant theory within information technology implementation literature. Current TAM literature shows 'perceived usefulness' (PU) as the most significant factor in technology acceptance in healthcare (Holden & Karsh, 2010; Althuizen, Reichel & Wierenga, 2012; Sligo et., al 2017). Davis (1989) defines PU as "the degree to which a person believes that using a particular system would enhance his or her job performance" (p.320). Moreover, 'perceived ease of use' (PEOU) is the second most significant variable, defined by Venkatesh & Davis (2000) as "the extent to which a person believes that using the system will be free of effort" (p.187) (Appendix B table 24).

However, the TAM theory remains suboptimal for healthcare, even after several updates (TAM, TAM2 and UTAUT), since it is developed outside the healthcare industry (Appendix B figure 18) (YarBrough & Smith; Hu, Chau, Sheng & Tam; Hennington & Janz; Succi & Walter; Barker, van Schaik, Simpson & Corbett; Horan, Tulu, Hilton & Burton; Han, Mustonen, Seppänen & Kallio cited in Holden & Karsh, 2010; Davis, 1989; Venkatesh & Morris, 2000; Venkatesh, Morris, Davis & Davis, 2003). A comparative study of Holden & Karsh (2010) on twenty TAM studies shows that each study within healthcare added variables to the model to better understand the antecedents of acceptance of health IT (Holden & Karsh, 2010). Furthermore, other TAM related literature shows that perceived behavioral control (controllability & facilitating conditions) and compatibility with preferred work style has a strong significant relationship with IT acceptance (Maillet, Mathieu, & Sicotte, 2015; Holden & Karsh, 2010) (Appendix B table 24, 25 and 26). Based on this literature, it can be concluded that PU, PEOU, perceived behavioral control and compatibility are robust variables for health IT acceptance.

Next to the body of literature on TAM, HIS is also a frequently discussed topic by academics. HIS can increase efficiency, reduce costs and clynical errors, improve information management, support clynicians in remote care and continuity of services, and increase patients' access to health services (Ammenwerth, Iller & Mahler, 2003; Gagnon et al., 2012; Lapointe, Mignerat & Vedel, 2011; Li, Talaei-Khoei, Seale, Ray & MacIntyre, 2013; Black, 2011; cited in Sligo et al., 2017). This broad definition functions as a umbrulla term under which analytical CDSS can be categorized. A comparative study on the implementation of HIS determined several inhibiting factors for HIS implementation: user resistance, poor quality technology, organisational inflexibility and/or instability and lack of 'fit' between social, technological and organizational domains. These inhibiting factors and the accompanying references, shown in Appendix B table 27, are incorporated in table four.

Furthermore, a literature review on the application of big data analytics in healthcare incorporates the more technical challenges encountered when executing analytics such as inaccuracy and inconsistency of the data, data structure & standardization issues or semantic interoperability (Mehta & Pandit, 2018). These challenges are incorporated in table four due to this study its focus on analytics.

Table four shows the most robust barriers for implementation of IT in healthcare, the sequence is based on the number of times a certain barrier occurs in references. This is not the most reliable indicator of importance. Therefore, this sequence will be challenged by means of an assessment of the stakeholders' barriers for implementing an analytical CDSS within the qualitative part of this study.

Table 4: Most robust barriers for implementation of IT in healthcare from literature

Barriers	References
Compatability (lack of fit between social, technological and organisational domain; inappropriate IT infrastructure)	Cresswell & Sheikh (2013); Robert., Macfarlance & Peacock (2009); Tsiknakis & Kourabali (2009); Ammenwerth et al. (2006). Maillet et al. (2015); Holden & Karsh, (2010); Wang, Kung, Wang & Cegielski (2017); Fodeh & Zeng (2016); Costa (2014)
Concerns about patient privacy & confidentiality	Greenhalgh, Procter, Wherton, Sugarhood & Shaw (2012); Goroll, Simon, Ascenzo & Bates (2009); Costa (2014); Mohammed, Far & Naugler (2014); Huang, Mulyasasmita & Rajagopal (2016); Wang et al. (2017); Wu, Li, Cheng & Lin (2016); Weng & Kahn (2016)
Inaccuracy and inconsistency of data	Szlezák, Evers, Wang & Pérez (2014); Cox & Ellsworth (1997); Kruse, Goswamy, Raval & Marawi (2016); Geerts et al. (2016); Budhiraja, Thomas, Kim & Redline (2016)
User resistance (process change)	Gagnon et al. (2012); Hendy, Reeves, Fulop, Htchnings & Masseria (2005); Rivard & Lapointe, (2012), Takian (2012); Mohamed et al.(2014); Miller (2012)
Data structure & standardization issues	Raghupathi & Raghupathi (2014); Kruse et al. (2016); Huang et al. (2016); Geerts et al. (2016); Budhiraja et al. (2016)
Lack of skilled clinical scientists & managers to guide, process and interpret outcome	Asante – Korang & Jacobs (2016); Auffray et al. (2016); Fodeh & Zeng (2016); Wu et al. (2016)
Organisational inflexibility and or/instability	Avison & Young (2007); Ellingsen & Monteiro (2008); Harrison, Koppel & Bar-Lev (2007); Kaplan & Harris-Salamone (2009)

Semantic interoperability	Dinov (2016); Peek, Holmes & Sun (2014); Salas-Vega, Haimann & Mossialos (2015)
Analytics with siloed or fragmented data	Raghupathi & Raghupathi (2014); Szlezák et al. (2014); Dimitrov (2016)
Poor quality technology	Ancker, Kern, Abramson & Kaushal (2011); Powell – Cope, Nelson & Patterson (2008); Lorenzi & Riley (2003)
Perceived usefulness	Holden & Karsh, (2010); Althuizen et al. (2012); Sligo et al. (2017)
Perceived ease of use	
Perceived behavioral control (controllability & facilitating conditions)	Maillet et al. (2015); Holden & Karsh, (2010)
Concern about non-human supervised information processing information	Asokan & Asokan (2015); Grossglauser & Saner (2014)
Initial investment too high	Szlezák et al. (2014); Huang et al. (2016)
Limited observational data	Rumsfeld, Joynt & Maddox (2016); Huang et al. (2016)
Missing data and risk of false-positive relations	Rumsfeld et al. (2016); Mcnutt, Moore & Quon (2016)
Lack of knowledge about how to use data	Szlezak et al. (2014)
Transition from paper-based records to the use of distributed data processing	Peek et al. (2014)
Limited validation possibilities	Rumsfeld, Joynt & Maddox (2016)
Lack of knowledge to assess quality algorithm	Maia, Sammut & Jacinta-Fernandes & Chin (2017)
Lack of transparency within analytical systems	Raghupathi & Raghupathi (2014)
Integration of different structures of data (structured vs unstructured) from several resources	Auffray et al. (2016)
Reliability of data	Salas-vega et al. (2015)
Governance issues related to lacking data protocols and/or standards	Belle, Thiagarajan, Soroushmehr, Navidi, Beard, & Najarian (2015)

2. Methodology

This chapter describes the methodology utilized in this study. It specifies the research design per sub question, the respondent selection, design of the interviews, the data analysis method and assesses the reliability and validity of the research.

2.1 Analytical CDDS environment technology roadmap

Table 5 Research design sub question 1

	(1) What analytical CDSS are currently implemented in the Netherlands?		
Data need:	Assessment currently implemented analytical CDSS in the Netherlands		
Data collection:	Literature review	Fieldresearch: Presentations at Mobile health event	Fieldresearch: Semi structured interviews
Sources:	Literature on analytics in healthcare and the EHR	R1- R6 in table nine	R7 – R23 in table nine
Analysis:	Described below	Recording, transcribing and coding (section 2.4)	

The literature review (section 1.1.3 and 1.2.2) dissected analytics and determined the currently implemented analytical CDSS. This information enabled the construction of the preliminary roadmap as a sensitizing concept, hence an indefinite version which gives the researcher guidance in the preparation for the field research (Blumer, 1954). Furthermore, several presentations in relation to currently and to be implemented analytical CDSS at the 'Mobile health event', 8th of November 2018, were attended and transcribed afterwards by means of online available footage (Mobilehealthcare, 2018). The respondents at this event with a relation to implementing analytical CDSS were selected in advance as shown in table nine, which are R1 to R6. These respondents shared knowledge on what analytical CDSS are currently and will be implemented in the Netherlands. These results are specified by the results of the semi structured interviews with R7 to R23. The research design in table five enabled the description of the currently implemented analytical CDSS in the Netherlands for the roadmap.

This study utilizes the same methodology for the second sub question, except for the literature review, as shown in table six. This research design provided input for describing the to be implemented analytical CDSS within ten years in the Netherlands for the definitive roadmap.

Table 6: Research design sub question 2

	(2) What analytical CDSS will be implemented within 10 years in the Netherlands?	
Data need:	Assessment to be implemented analytical CDSS within 10 years in the Netherlands	
Data collection:	Fieldresearch: Presentations at Mobile health event	Fieldresearch: Semi structured interviews
Sources:	R1- R6 in table nine	R7 – R23 in table nine
Analysis:	Recording, transcribing and coding (section 2.4)	

2.2 BDFSB implementation plan

Table 7: Research design sub question 3

	(3) What are the stakeholders' barriers for implementing the BD4SB CDSS?		
Data need:	Explore stakeholders' barriers for implementing the BD4SB CDSS		
Data collection:	Literature review	Fieldresearch: Presentations at Mobile health event, AI assisted healthcare meetup, seminar digital health UMCU and SAS round table meetup	Fieldresearch: Semi structured interviews
Sources:	Literature on health IT implementation barriers	R1 - R6 in table nine	R7 – R23 in table nine
Analysis:	Decribed below	Recording, transcribing and coding (section 2.4)	

The literature review (section 1.4) assessed the available knowledge on stakeholders' barriers for implementing IT in healthcare consisting of the TAM, HIS and occurrence of big data analytics in healthcare literature. Firstly, the literature research route started with the TAM theory (Davis 1989, Venkatesh & Davis, 2000; Venkatesh et al., 2003). Subsequently, a Scopus query related to TAM healthcare articles "("TAM" AND "healthcare")" resulted in literature list narrowed down by only analyzing results from journals with an impact factor of two or higher led to relevant articles (Chen et al., 2017; Maillet et al., 2015; Schaper & Pervan, 2007; Venkatesh & Davis, 2000). Subsequently, these articles' citation patterns led to the comparative study of Holden & Karsh (2010). Secondly, the theory on the implementation of HIS was obtained via a Scopus query ("implementation" AND "health" AND "technology" OR "system "), limited to publication year 2016 – 2018. Thirdly, the theory of Mehta & Pandit (2018) was obtained via a Scopus query ("Big Data" OR "analytics" AND "health"), limited to publication year 2016 – 2018.

The results of the literature review accompanied with the results of the presentations concerning BD4SB, or other predictive analytical CDSS, at the following events: (1) AI-assisted healthcare meetup, 19th of June 2018, (2) Mobile health event, 8th of November 2018, (3) Seminar digital health UMCU, 6th of December 2018, and (4) SAS round table meetup, 18th of December 2018, provided guidance for executing the semi structured interviews with R7 to R23 and hence answering sub question three.

This study utilizes the same research design for sub question four except for the literature review as shown in table eight.

Table 8: Research design sub question 4

	(4) What are the proposed solutions for these stakeholders' barriers for implementing the BD4SB CDSS?	
Data need:	Explore solutions for stakeholders' barriers implementation BD4SB CDSS	
Data collection:	Fieldresearch: Presentations at Mobile health event, AI assisted healthcare meetup, seminar digital health UMCU and SAS round table meetup	Fieldresearch: Semi structured interviews
Sources:	R1 – R6 in table nine	R7 – 23 in table nine
Analysis:	Recording, transcribing and coding (section 2.4)	

2.3 Semi structured interviews

The units analysis of this research are the different stakeholders involved in IT implementation in healthcare as shown in the stakeholder analysis in section 1.3.2. Based on this analysis, the respondents shown in table nine were selected as the units of observation for this study. The respondents were directly approached, visited at an event or selected via purposive sampling, a form of non-probability sampling, based on advise of other respondents.

Table 9: Respondent description and categorization based on stakeholder analysis, section 1.3.2

Nr.	Respondent description	Groups from stakeholders analysis (section 1.3.2)
R1	Ex chairman of the board of AMC, ex-internist & current CEO hospital cluster, University College London Hospitals	Political & financial benificiary and normal operator
R2	Director ADAM and ambassador e-health & big data, UMCU	Political & financial benificiary
R3	Business development manager EHR data platform, CERNER	Political & financial benificiary
R4	Physician and clinical owner BD4SB, UMCU	Normal operator
R5	Professor & education director health informatics hospital, AMC	Political & financial benificiary
R6	Physician and clinical director, Vitaalpunt	Normal operator
R7	Healthcare director, SAS	Political & financial benificiary
R8	Senior technical consultant, SAS	Developer
R9	System engineer healthcare, SAS	Developer
R10	Ex-physician and senior sales executive healthcare, SAS	Political & financial benificiary and normal operator
R11	Ex-physician and data scientist, UMCU	Normal operator & developer
R12	Physician and clinical owner BD4SB, UMCU	Normal operator
R13	Program manager ADAM, UMCU	Political & financial benificiary
R14	CEO business intelligence organization healthcare, Vektis	Political & financial benificiary
R15	Managing partner CDSS developer, Finaps	Developer and political & financial benificiary
R16	Ethicist and member medical ethical commission, UMCU	Ethicist
R17	Business engineer CDSS developer, Finaps	Developer & maintenance operator
R18	Methodologist, UMCU	Methodologist
R19	Inspector e-health, inspection healthcare and youth Dutch government (IGJ)	Regulator
R20	Ex-physician and analytics entrepreneur	Normal operator & developer
R21	IT/ICT manager, UMCU	Operational support
R22	Clinical CEO notified body, Dekra	Regulator
R23	Projectmanager ‘registration at the source’, national federation academic hospitals (NFU)	Regulator

This research utilizes semi structured interviews which provide openings for a narrative to unfold while also applying questions based on the literature review (Galetta, 2013). This method is chosen since the current literature only supplies a limited amount of knowledge on analytical CDSS implementation. The unscripted narrative enables the researcher to explore the respondents' expertise. To guide this narrative the topic list shown in table ten was utilized. Not all the respondents stated in table nine are aware or involved with the BF4SB CDSS project, these non-involved respondents are questioned about implementing a predictive algorithm, as the BD4SB CDSS applies, to extract relevant knowledge on barriers and possible solutions for the BD4SB CDSS.

Table 10: Topic list semi structured interviews

Topic list semi structured interviews
Roadmap • Currently implemented analytical CDSS • To be implemented analytical CDSS within 10 years **Implementation plan BD4SB (non-BD4SB project members)** • Stakeholders' barriers for implementing analytical CDSS with a predictive algorithm • Proposed solutions to overcome these barriers **Implementation plan BD4SB (BD4SB project members)** • Stakeholders' barriers for implementing BD4SB CDSS • Proposed solutions to overcome these barriers

2.3.1 Laddering technique

To structure the questions in relation to the BD4SB implementation plan, this study applies the 'laddering technique'. This results in a categorization and content analysis of the connection between attributes, consequences and values experienced by stakeholders with the implementation of BD4SB CDSS or a predictive algorithm (Boundarouk, 2018; Jensen, 2005).

The laddering technique shows the means-end association by a focus on attributes, the consequences and values (figure nine) (Jensen, 2005). Skytte and Bove (2004) define 'attributes' as "attributes constitute the product, i.e. its features, and its components parts, process or activities" (p.6). According to Jenssen (2005), the 'consequence' level entails asking a respondent how an attribute or activity has or will influence his/her proceedings, Skytte and Bove (2004) define consequences as "consequences are the outcomes produced by the attributes" (p.5). Finally, the last stage of the hierarchy entails 'value' which Skytte and Bove (2004) define as "values are individuals their preferred end-states of existence" (p.5).

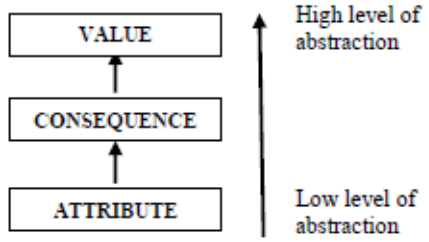

Figure 9: Laddering technique from attribute, to consequence to value (Jensen, 2005)

This research applies a form of the laddering technique to discover the hierarchies between specific BD4SB CDSS attributes, consequences and values. The aim is to discover the respondents' point of view on implementing the BD4SB CDSS and thereby creating a greater understanding of the demands of the stakeholders – based on their own frame of reference. To enable the utilization of this technique, the interviews with the R7 – R10 from table nine focused on describing the attributes of the BD4SB CDSS. These respondents were asked to describe features, components, processes or activities of the BD4SB CDSS in which the barriers for implementation occur. This qualitative approach will be supported by a literature review on the implementation of predictive algorithms (Hendriksen, Geersing, Moons & De Groot, 2013). Subsequently, the determined BD4SB attributes are distributed among the questionnaires for the respondents so that each interview focuses on the attributes related to the respondents' expertise. These respondents are asked to determine BD4SB implementation barriers (consequences) based on these attributes.

Furthermore, the laddering theory will not be copied exactly, the values are incorporated differently and the proposed solutions for barriers (consequences) are added. This study replaces the 'value' section by means of the corresponding, probably more abstract, barrier definition extracted from the literature review in 1.4 and will refer to it as a 'concept'. Moreover, this study includes the possible solutions to the stakeholders' barriers, and thus also partially for the concept extracted from literature, within the model. Hence, this study tailored the laddering theory to the goals of this study which resulted in the framework shown in figure ten.

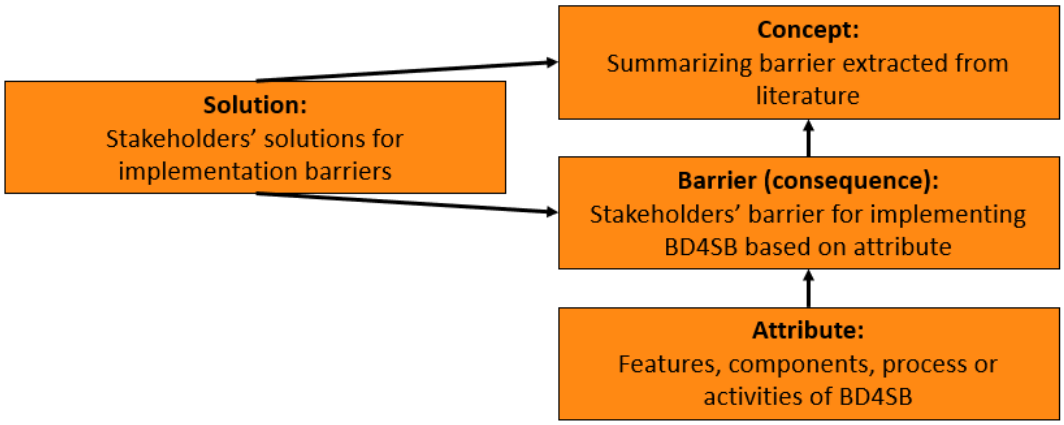

Figure 10: Customized laddering technique from Jensen (2005) tailored for this study

2.4 Data analysis

This study documents the data from the semi structured interviews and presentations at the events by recording and transcribing. Subsequently, the analysis is executed via coding with ATLAS.ti, a qualitative data analysis and research software. The codes are categorized within the following main topics: (1) current analytical CDSS in healthcare, (2) future analytical CDSS in healthcare, (3) stakeholders' barriers and solutions for implementing BD4SB for each attribute. The codes within the main topics will be collected within one network, these networks are shown in Appendix C. Within these networks the attribute is colored white, the barrier colored red, the solution colored green and additional contextual information colored purple. Furthermore, these networks provide the quotation numbers showing which respondents' statement is connected to which specific code. These networks function as a clarifying scheme which is beneficial for pattern recognition. This scheme can detect 'exception fallacy' whereas a single or small number of respondents share a certain opinion. However, this is less applicable to this study since the respondents are considered experts on the specific subject, hence attribute, discussed. An attribute/subject will often only be discussed with one respondent (e.g. ethicist, methodologist or e-health inspector) which almost always results in 'exception fallacy' since the statement cannot be supported by other respondents since they do not possess expert knowledge on the attribute/subject. However, there will also be attributes/subjects discussed with numerous respondents.

Therefore, the interpretation of the results will go as following. Within interpretation of the codes and the relationships among these codes, the reliability will be assessed via conformity of several respondents or via the expertise of the respondent on the attribute/subject (Becker, Bryman & Ferguson, 2012). Firstly, whenever two or more respondents who are considered experts on the attribute/subject share an opinion on a certain subject this will be considered as a reliable result. Secondly, whenever a result is based on the opinion of a single person, the result will be triangulated, a method for assessing the truthfulness of the result by comparing it with data from multiple investigators, research methods and theoretical perspectives (Denzin, 2009). This study applies data triangulation, hence comparing the results with different data sources, such as by fact checking the results of the semi structured interviews with literature or acceptable other sources such as government documentation. However, triangulation is not always possible and when this is the case, the result will be considered indicative which will be clarified in the text.

2.5 Assessment quality qualitative research

This section assesses the main quality indicators for this research which are reliability and validity (Babbie, 2015).

2.5.1 Reliability

The reliability of this study is mainly dependent on the qualitative section. To ensure the research reliability, as intensively as possible, the respondents are asked to sign an informed consent form explaining the context of the study among which the confidentiality as shown in Appendix D. Furthermore, the interviews are recorded, transcribed and sent to the specific respondents who are given the opportunity to supply feedback and corrections in relation to the transcript which will be incorporated in the definitive results by the researcher. Furthermore, reliability also depends on utilization of measurements that supply consistent results (Blumberg, Cooper & Schindler, 2005). This consistency is ensured by controlling the quality of the measurement device which are the constructs in the questions, hence the BD4SB CDSS attributes in this study which are selected by means of a literature review and semi structured interviews to ensure integrality. Furthermore, clearly defining the attributes, concepts and explaining the questions in the interviews minimizes misinterpretation (Babbie, 2015). Moreover, the reliability of the results of the qualitative research is ensured by means of triangulation as described in section 2.4.

2.5.2 Validity

Validity roughly entails, the extent to which a research measures what it intends to measure (Babbie, 2015). This will be assessed via the internal and external validity. Subsequently, the specific measurement quality is assessed by means of content and construct validity (Babbie, 2015).

Firstly, internal validity implies the credibility of the findings in relation to the measured phenomenon. This can only be determined by the participants of the study (Whittemore, Chase & Mandle, 2001). This study ensures internal validity by validating the transcripts with the respondents, clear instructions within the interviews and triangulation of the results. Secondly, the external validity implies the generalizability of the results (Babbie, 2015). This study creates generalizable results by incorporating a specific case, BD4SB CDSS, as well as the more general form, ‘predictive analytics’, within the qualitative section of this study. This enables to generalization of the BD4SB CDSS related results to the implementation of other analytical CDSS that also incorporate predictive analytics. Thirdly, content validity is the degree to which a measure covers the range of meaning from a concept (Babbie, 2015). The total meaning coverage of the used concepts within the interviews is assessed by cross checking the concepts in the questionnaires with healthcare & technology experts of SAS. Fourthly, construct validity describes the degree to which a measure is related to other variables as described within the theoretical relationship (Babbie, 2015). The overlapping relationship among measurements is mitigated by means of the selecting differentiating attributes within the qualitative section of this study.

3. Analytical CDSS environment roadmap results

This chapter provides the findings related to two empirical questions in relation to the analytical CDSS environment roadmap which describe the problem context for the BD4SB implementation plan. These questions function as the structure of this chapter: **(**SQ1) 'what analytical CDSS are currently implemented in the Netherlands?' and (SQ2) 'what analytical CDSS will be implemented within 10 years in the Netherlands?'. The first question assesses the current state of analytical CDSS, hence provides the starting point of the roadmap, and the second question explores the stakeholders' expectations and opinions on the future of analytical CDSS which provides input for the sequence of the components within the layers of the roadmap.

3.1 Current state of analytical CDSS

The analytics categorization as described in 1.1.3, descriptive and predictive, is assessed within the interviews to construct the analytics layer of the roadmap and determine which analytical CDSS are currently implemented for the CDSS layer.

3.1.1 Descriptive analytical CDSS

- **R9 (System engineer healthcare, SAS):** *"With the most hospitals it is descriptive, the operational proceedings are going to be predictive next."*

According to R7, R8, R9, R10, and R21, the current state of analytical CDSS is within the descriptive stage. R10, ex-physician and senior sales executive healthcare SAS, even suggests that the descriptive stage of analytics has room for improvement such as executing analytics quicker which is confirmed by the following statement:

- **R7 (Healthcare director SAS):** *"Sometimes the run time before a report is delivered that answers your question/query can take up to weeks or even months. This takes so much time, because you bring your query/functional question to a desk where several people must figure out if they did it before, which sources to use, if these sources are in the database, what kind of aggregation is needed. All of this has to be built which takes a long time before you get the report which shows trustworthy information that answers your question."*

This statement is also confirmed in section 3.2 on the EHR which shows that the speed at which historical medical data is made available is not from a preferred level. All in all, it can be concluded that the currently implemented analytical CDSS in healthcare mostly utilize descriptive analytics and still have some improvements to make, especially regarding timely data availability and integration.

3.1.2 Predictive analytical CDSS

R19, e-health inspector for the Dutch government, his expertise is to assess the implemented CDSS by means of the current WMH (law for medical devices) on the safety of the product and the safety of the product in use. He states that he has not has not encountered analytical CDSS with predictive analytics.

This statement from a single person is considered reliable since the frame of reference from the e-health inspector constitutes that of an expert for this phenomenon. This absence of implemented predictive analytical CDSS is confirmed by R13, program manager ADAM, who states that none of the predictive analytical CDSS within the ADAM projects is currently implemented.

However, predictive analytics is present elsewhere in healthcare according to R2, director ADAM, and R9, system engineer healthcare SAS. The predictive form of analytics is currently implemented within the non-clinical context of healthcare such as planning for intensive care, this is not within the scope of this research, however, as R9 states, this appliance of predictive analytics in non-clinical context might be the precursor for appliance in the clinical context:

- **R9:** *"I see predictive analytics more and more in the operational section and this is moving to the clinical section, patient safety for example with pain dashboards or decubitus dashboards."*

Additionally, clinical and technology experts on the Mobile health event, the largest conference on digital health in the Netherlands, presented their developed predictive analytical CDSS, however, all of these were still in the research & development environment and none were implemented (Mobilehealthcare, 2018). This signifies the state of the current analytical CDSS environment. R9 refers to this phenomenon as follows:

- **R9:** *"I think awareness on analytics is mainly coming now. The process of 'we can do something with analytics' is there. In the past years, hospitals were busy with solving other things and they saw analytics as a sort of science fiction in the future. Two years ago, there was nothing piloted with analytics and now you see there are several analytical CDSS pilots."*

It can be concluded that predictive analytics has made its way into healthcare, however, not yet in the clinical context with a CDSS, hence as a medical device, which is the focus of this study.

3.2 Utilization of the EHR by analytical CDSS

The assessment of the current analytical CDSS environment also discusses barriers and solutions for utilization of the EHR by analytical CDSS as a data source or as a mean to present the results of the CDSS because the EHR is considered the largest HIS which is also relevant for the BD4SB CDSS.

According to R7, healthcare director SAS, and R9, system engineer healthcare SAS, the EHR is implemented at all hospitals in the Netherlands. The EHR, which also functions as a data entry system, is a system through which users can view for example lab results, medical images, medication requests, however, it is not the direct source of all this information. This is a misconception that is made frequently according to R10, ex-physician and senior sales executive SAS. However, R10 also states that the EHR is the most important HIS that produces and saves data in healthcare.

3.2.1 Barrier EHR: Not user-friendly

R1 (ex-chairman board AMC, ex-internist and current CEO cluster hospitals in London) does not consider the EHR as not user-friendly. Additionally, R5, professor & education director health informatics hospital AMC, specifies that statement by emphasizing that the EHR does not enable user-friendly data registration without interrupting the workflow.

- **R1:** *"The current EHR still has a long way to go, clinicians see it as a trashcan where you can dump all your data and are not really interested what happens with the data which is confirmed by clinicians within academic studies. The benefits of the EHR do not outweigh the cons."*

R6, physician, and R7, healthcare director SAS, confirm that the EHR is not a user-friendly for registering data in a standardized method since the system does not have a user-friendly interface, does not work intuitive and interrupts the workflow. According to R7, R8 and R10, this is partially because the EHR originally was developed as a registration system for financial administration which purposes differ from those in within a clinical context

3.2.1.1 EHR Solution: Incorporate user feedback

- **R23:** *"If physicians do not share how they work, then I can understand really well that physicians are not satisfied about the EHR. How can you build a system for somebody if you do not exactly know what he/she wants?"*

According to R23, project manager 'registration at the source', the physicians and EHR suppliers should focus more on incorporating feedback. This is confirmed by Press et al. (2016) who determined that user satisfaction and EHR usability improves after periodic physician feedback assessments.

3.2.2 Barrier EHR: Integrability EHR

The two largest EHR (Epic & Hix) are considered as closed systems from which you can extract data, however, cannot upload data to without a large investment according to R15, managing partner CDSS developer. The integrability of the system with other data sources within healthcare leaves much to be desired as shown by the statement of R1, ex-chairman of the board of AMC, internist and current CEO cluster hospitals in London:

- **R1: "***It is hard to explain that we cannot upload results from the lab directly to our EHR."*
- **R15:** *"Hospitals want the EHR to be an open system to share data, this matter is currently discussed at the Dutch government."*

3.2.2.1 Solution EHR: Legislation 'Digitally exchanging healthcare information'

As R15 mentioned, the integrability problem is recognized by the Dutch government. The national federation for academic hospitals (NFU) started the 'registration at the source project', led by R23. This project aims to optimize uniform data registration that enables sharing of patient information among healthcare organizations which is achievable if the data is shareable and the systems "speak the same language", hence can connect with each other. The Dutch government noticed this impactful situation

and the minister of Healthcare, Welfare and Sports aims to construct a legal foundation called 'digitally exchanging information healthcare'. This will be done by a multiple year plan for digitizing healthcare in cooperation with healthcare insurers, hospitals, general practitioners and medical specialists, the plan will be assessed by the House of Representatives in April 2019 (Rijksoverheid, 2018).

The current bill for this legislation to the House of Representatives focuses mainly on standardization of data entry and on the unity of technology in which openness, accessibility, interchangeability is expected from all internal systems within healthcare where patient data is saved and exchanged. The goal is to develop norms among which the use API's is described, these are application programming interfaces, a collection of definitions whereby a system can communicate with another program or environment (Rijksoverheid, 2018). This bill benefits the integrability of the EHR, however, it remains unclear when it will convert to legislation and can be vindicated according to R23.

3.2.2.2 Solution EHR sharing information: Available API for sharing EHR data

- **R20:** *"FHIR enables sharing data from EHR between hospitals"*

R20, ex-physician and analytics entrepreneur, states that there is an API available for exchanging digital healthcare information from the EHR called: 'Fast Healthcare Interoperability Resources' (FHIR). This statement is confirmed by Nictiz, a healthcare information organization funded by the Dutch Ministry of Healthcare, Welfare and Sports (Nictiz, 2018).

3.2.3 Barrier EHR: Data quality

According to R1(ex-chairman of the board of AMC, internist and current CEO cluster hospitals in London), R2 (director ADAM) and R7 (healthcare director SAS), the information within the current EHR is not standardized enough, not available in the required uniform format to execute analytics. This can be categorized as insufficient data quality which refers to the accuracy, consistency and completeness of data according to Hazen, Boone, Ezell & Jones-Farmer (2014). All this implicates that the EHR data is not fit for the intended use of analytics. The following statement of R2 exemplifies this situation:

- **R2:** *"Once we asked clinicians if they always noted if a patient smokes or not. It turned out that only 60% submitted if the patient smokes yes or no. Then another problem, they submitted the data, however, on 80 different places within the EHR, this does not make it easy for us."*

R20 (ex-physician and analytics entrepreneur) also states that most clinicians use the free text section of the EHR within their registration proceedings which makes standardization substantially harder.

3.2.3.1 Solution EHR: Legislation 'Digitally exchanging healthcare information'

The legislation as described in 3.2.2.1 aims to optimize uniform data registration within healthcare in the Netherlands which should improve the data quality (Rijksoverheid, 2018).

3.2.3.2 Solution EHR: Coding solutions

- **R6 (professor & education director health informatics, AMC):** *"There are a lot of projects for healthcare information standardization and integration such as Snomed CT or DHD. However, the implementation of these projects is seriously slow."*

This statement is confirmed by R20, ex-physician and analytics entrepreneur, who adds that physicians still mostly use the free text section of the EHR which cannot be coded by Snomed CT. Snomed CT is a medical standard to code and document which benefits sharing of clinical data from the EHR (Snomed, 2018). Furthermore, the Dutch hospital data (DHD) diagnose thesaurus can support the physician in data registration within the EHR (DHD, 2018).

3.2.3.3 Solution EHR: Natural language processing

R20, ex-physician and analytics entrepreneur, states that Google works on a speech to text solution for the EHR that can automate registration and coding. The paper of Chiu et al. (2017) confirms that Google built an NLP solution that can convert speech to text accurately which can be incorporated within the EHR and shows Google started a pilot study in 2018 at Stanford University. Furthermore, Amazon built the 'Amazon Comprehend Medical', an NLP system that utilizes machine learning to extract information from the EHR text and is currently piloted at Seattle's Fred Hutchinson Cancer Research Center (Bresnick, 2018; Amazon, 2018).

3.2.4 EHR Conclusion

Table 11: EHR related barriers & solutions for utilizing it as a source or a mean to present results of analytical CDSS

<table>
<tr><th colspan="4">Utilizing the EHR for analytical CDSS barriers & solutions</th></tr>
<tr><td>Barriers:</td><td>3.2.1 EHR not user friendly
Respondents: R1, R5, R6, R7 and R10</td><td>3.2.2 Integrability issues EHR
Respondents: R1 and R15</td><td>3.2.3 Data quality
Respondents: R1, R2, R7 and R20</td></tr>
<tr><td rowspan="4">Solutions:</td><td rowspan="4">3.2.1.1 Incorporate user feedback
Respondent: R23</td><td>3.2.2.1 Legislation 'Digitally exchanging healthcare information'
Respondent: R23</td><td>3.2.3.1 Legislation 'Digitally exchanging healthcare information'
(Rijksoverheid, 2018).</td></tr>
<tr><td rowspan="2">3.2.2.2 Available API for sharing EHR data
Respondent: R20</td><td>3.2.3.2 Coding solutions
Respondents: R5 and R20</td></tr>
<tr><td>3.2.3.3 Natural language processing
Respondent: R20</td></tr>
</table>

3.3 Future of analytical CDSS

It is too complex to give a specific prediction about the future of analytical CDSS according to R2, R7, and R9 as exemplified by the statement of R2:

- **R2 (Director ADAM): "***I have no idea where analytics will be in five years, it thought ten years ago that we would have been much further than we are now."*

Additionally, R20, ex-physician and analytics entrepreneur, claims that the implementation of predictive analytical CDSS could take ten years.

Next to this timespan prediction, the respondents were asked to think about which other techniques could be applied within a CDSS that would provide the CDSS layer within the roadmap with specific components for describing the analytical CDSS environment. However, according to R7, R8 and R9 there is no clear sequence in techniques.

- **R9 (System engineer healthcare SAS):** *"I do not think you can see techniques as natural language processing, machine learning and image recognition separately if they all incorporate a predictive model."*

This statement implies that there might be no distinction between techniques when there is a predictive model involved. However, R1 and R20 state that to be implemented analytical CDSS should be intuitive. According to R7 and R8, text analysis, an umbrella term for the appliance of analytics on free text among which natural language processing, is the most intuitive technology which is most likely to be implemented first

- **R7 (Healthcare director SAS)***: "Text analytics is the most transparent form of building a solution. This is most often the first step. This lies most closely with the understanding of the human and provides the required transparency which is beneficial for implementation."*

These results of the empirical part of the study confirm the results of the literature review in section 1.2.2 that showed that NLP is most the frequently applied analytical technology within clinical context (Mehta & Bandit, 2018). A CDSS with NLP has been developed by R7, R9 and R10 in the Netherlands called the 'Medic Miner', a system that can extract a diagnosis based upon the free text within the EHR by means of NLP which is comparable with the solutions of Google and Amazon described in section 3.2.3.3. According to R8, senior technical consultant SAS, the accuracy of the 'Medic Miner' was not from a preferred level and it only incorporated 30 from the 300 most frequent diagnostic terms. Additionally, to further develop the Medic Miner, the cooperation of EHR was needed.

- **R9 (System engineer healthcare SAS):** *"The conversations with the suppliers of HIX (EHR) resulted in problems because they do not appreciate it if you enter something in their system as an external party. Then they get the idea, this is something they should develop themselves which they subsequently do not do because this is not their expertise".*

The implementation of analytical CDSS such as the Medic Miner is dependent on the integrability of the EHR which is an obstacle as is discussed in section 3.2.2.

3.4 The analytical CDSS environment technology roadmap

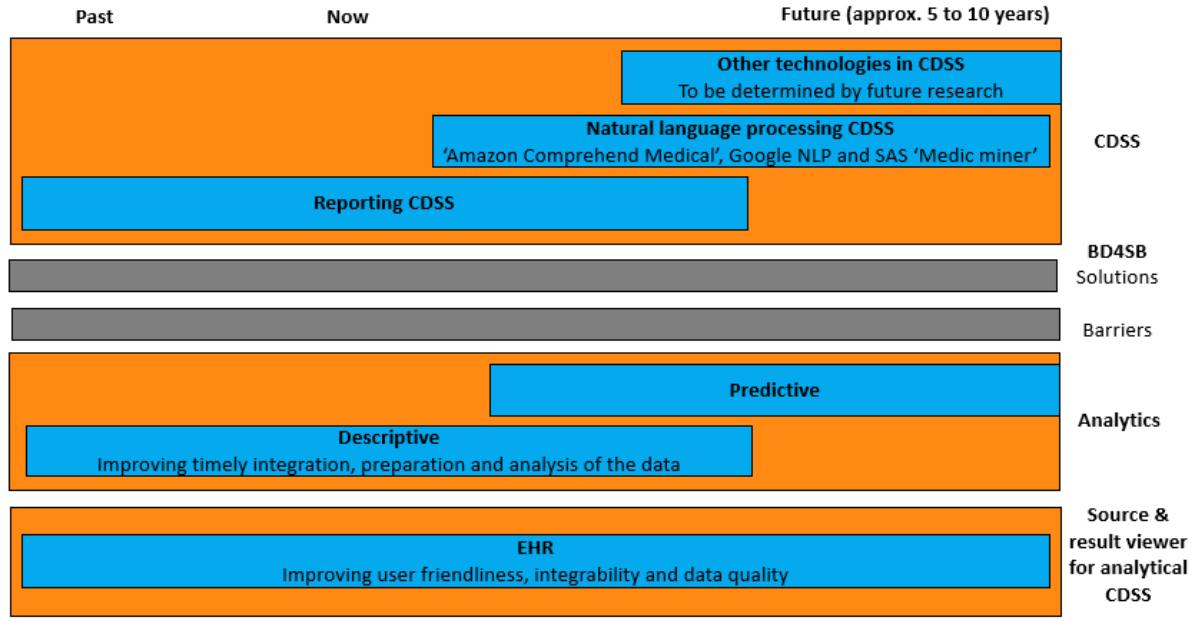

Figure 11: Definitive analytical CDSS environment technology roadmap

Figure eleven shows the analytical CDSS environment technology roadmap that describes the context of the BD4SB implementation plan, the grey layers consisting of the stakeholders' barriers and solutions, based on the literature review and qualitative results of this study.

This figure differs from the proposed roadmap in figure four by addition of new empirical findings. Firstly, the addition of the bottom 'source & result viewer for analytical CDSS' layer shows that the EHR functions an important source, also for BD4SB as shown in figure six, and a mean to present results to the user for analytical CDSS. However, the EHR can be better utilized by analytical CDSS if the EHR improves on user friendliness, integrability and data quality (accuracy, consistency and completeness of the data). Secondly, the 'analytics' layer implies that the current form of analytics applied within analytical CDSS is considered as descriptive which must improve on timely integration, preparation and analysis of the data. Furthermore, predictive forms of analytics within medical devices, as in the BD4SB CDSS, remain to be implemented. This implementation of predictive analytics can occur in parallel with the improvements within the descriptive realm as shown in figure eleven. Thirdly, within the 'CDSS' layer, reports describing historical healthcare information are considered as the currently implemented analytical CDSS. This study shows that the predictive CDSS that will be implemented first is probably the most intuitive one which refers to a CDSS with NLP. Organization as Amazon, Google and SAS developed NLP solutions to automatically extract information from speech or text which can kickstart analytics according to R20, ex-physician and analytics entrepreneur, however, currently, these CDSS remain within the research and development environment. Furthermore, it remains unclear what kind of predictive analytical CDSS will be implemented after NLP as shown in the unspecified 'other technologies' frame within the roadmap.

4. BD4SB implementation plan results

Within this chapter two empirical questions in relation to the BD4SB implementation plan will be answered: **(**SQ3) 'what are the stakeholders' barriers for implementing the BD4SB CDSS?', and (SQ4) 'what are the proposed solutions for these stakeholders' barriers for implementing the BD4SB CDSS?'. SQ3 identifies the stakeholders' barriers for implementing the BD4SB CDSS and SQ4 identifies the solutions for these stakeholders' barriers. This section starts with determining the attributes which categorize the stakeholders' barriers and accompanying solutions. Each of these attribute sections ends with a summary of the laddering technique consisting of the attribute, barrier(s), relevant concept(s) extracted from literature and proposed solution(s).

4.1 Attributes BD4SB

This section describes the attributes extracted from literature and semi structured interviews with R7 – R10 from table nine. These attributes in table twelve are the foundation for the laddering technique as shown in figure ten.

Table 12: Attributes BD4SB laddering technique

Attribute group:	BD4SB process	BD4SB peripheral business	Stages in implementing predictive algorithm attributes
Attributes:	Data availability	Ethics	Development
	Data integration	Legal	Validation
	Data preparation	Resources	Impact
	Analysis		
	Result		
	Utilization		

BD4SB process attributes

The data process attributes relate to the analytical process of the CDSS. Firstly, data availability implies to what extent the data is available as input for the CDSS when it is required, hence if the data can be extracted from the sources to execute analysis within the correct timespan. Secondly, data integration implies the ability of the BD4SB CDSS to integrate different data sources and formats. Thirdly, data preparation entails the ability of the CDSS to correct any data from inadequate quality before executing the analysis. Fourthly, analysis refers to the analytical process as shown in figure seven. Fifthly, the result attribute refers to the accuracy and reliability of the output. Lastly, the utilization attribute implies the implementation of the BD4SB CDSS by the physician within the healthcare process.

BD4SB peripheral business

Next to the attributes related to the BD4SB CDSS process, other peripheral business is essential for implementing a CDSS which consists of the ethical, legal and resource related aspects. The ethical attribute refers to the thought process of acting well or accordingly. For the BD4SB CDSS, this mainly

relates to how the CDSS can be incorporated within the decision-making process of the physician. The legal attribute refers to the influence of legislation on the implementation of the BD4SB CDSS. Lastly, the resources attribute entails the budget allocation for implementing BD4SB CDSS.

Implementing predictive algorithm attributes

Literature on the implementation of predictive algorithms distinguishes three distinct steps to become clinically valuable: development, validation and impact (Hendriksen et al., 2013). The development phase refers to the phase wherein the multivariable model is constructed. Within the validation phase, the model is tested by means of a new external set of patient data with the same variables/performance measures. This external validation is essential since the model often performs poorer due to case-mix or domain differences. The impact phase refers to the extent to which the model can be applied within patient management. The first two phases can be executed with a single cohort design whereas the impact phase requires comparative designs with multiple datasets, preferably by randomized designs. In this last phase, the clinical proceedings and the outcomes of the clinical process are compared with a control group not using the model, hence which applies usual care (Hendriksen et al., 2013).

4.2 Data availability (process attribute)

According to R12, clinical owner BD4SB CDSS, for the system to be clinical valuable, it must be able to extract data from different sources, as shown in figure six, execute the analysis and present the results within 24 hours to the physician. This is currently not possible for the BD4SB CDSS.

4.2.1 Data availability barrier: UMCU data warehouse unable to provide data timely

This inability to execute the BD4SB CDSS analytical process within 24 hours is partially due to the current UMCU data warehouse. According to R11, R12, R13, R15, R17 and R21, the current data warehouse of the UMCU is not designed to make data available within a short time span since it is designed for research which does not require data availability within a short time span. The following statement of R11, ex-physician and data scientist UMCU, specifies two causations of this phenomenon:

- **R11**: *"Some data producing machines within the UMCU are validated and CE approved for research and not for healthcare which is needed for BD4SB, a new CE approval of the data warehouse is required to realize this transition. Secondly, data source HIX (EHR) is currently updated once a day, however, only converted to usable input for analytics once a week."*

Hence, the data warehouse of the UMCU its inability to produce data at the required short notice is partially due to machinery not validated for healthcare and the EHR which converts the data to usable analytics only once a week.

4.2.1.1 Data availability solution: Single hospital wide critical data layer

A possible solution to execute the BD4SB CDSS analytical process within 24 hours would be a single hospital wide critical data layer according to R8, R9, R11, R12 and R17.

- **R12 (clinical owner BD4SB): "***The data can be extracted from the hospital wide critical data layer for analytical proceedings by means of API call, the data layer will recover the data from the sources by means of patient ID. We need this step or else we will still be looking at retrospective data. This is data layer is currently under construction, technologically feasible, however, realization depends on commitment and budget."*

UMCU currently develops this hospital wide data layer within the current data warehouse with data architects and data specialists according to R21, IT/ICT manager UMCU. This layer automatically collects, integrates and prepares the data from different data sources, this is a form of universal engineering. Subsequently, analytical CDSS such as BD4SB can extract the data for its analysis by firstly making sure the data meets the requirements and possibly perform additional preparation which can be considered as feature engineering. The framework for the data layer is shown in figure twelve. Additionally, R17 (business engineer CDSS developer) suggests that the eventual goal of this single hospital wide critical data layer would be to enable several analytical CDSS, however, it starts with the data for the BD4SB CDSS to eventually add other data sources for other analytical CDSS.

4.2.1.2 Data availability solution: EHR update

According to R11, ex-physician and data scientist UMCU, the inability of the EHR to present the data timely to the BD4SB CDSS can be solved by means of an update accompanied by a new server. This statement cannot be triangulated, however, is considered reliable since R11 is considered an expert on this specific phenomenon within the UMCU.

4.2.2 Data availability Conclusion

Table 13: Laddering technique 'data availability'

Attribute:	Data availability
Barrier:	**4.2.1 UMCU data warehouse unable to provide data timely** *Respondents: R11, R12, R13, R15 and R17*
Solutions:	4.2.1.1 Single hospital wide critical data layer *Respondents: R8, R9, R11, R12, R17 and R21*
	4.2.1.2 EHR update *Respondent: R11*
Concept:	• Compatibility: *Both solutions benefit an appropriate IT structure to execute analytics*

The inability of the UMCU data warehouse to provide the data to the BD4SB CDSS timely can be considered a pivotal barrier because the BD4SB CDSS can only be clinically valuable if it executes the analysis within 24 hours. Figure twelve visualizes the preferred solution. Firstly, update the EHR and CE approve the healthcare database so that the data can be supplied to the layer within the correct time span. Subsequently, bring the data quality to the required standard for the hospital wide critical data layer by means of universal engineering. Then the analytical CDSS, among which BD4SB, can retrieve the data by means of an API, perform additional data preparation (feature engineering) for the specific context, and execute the analysis within the correct timespan.

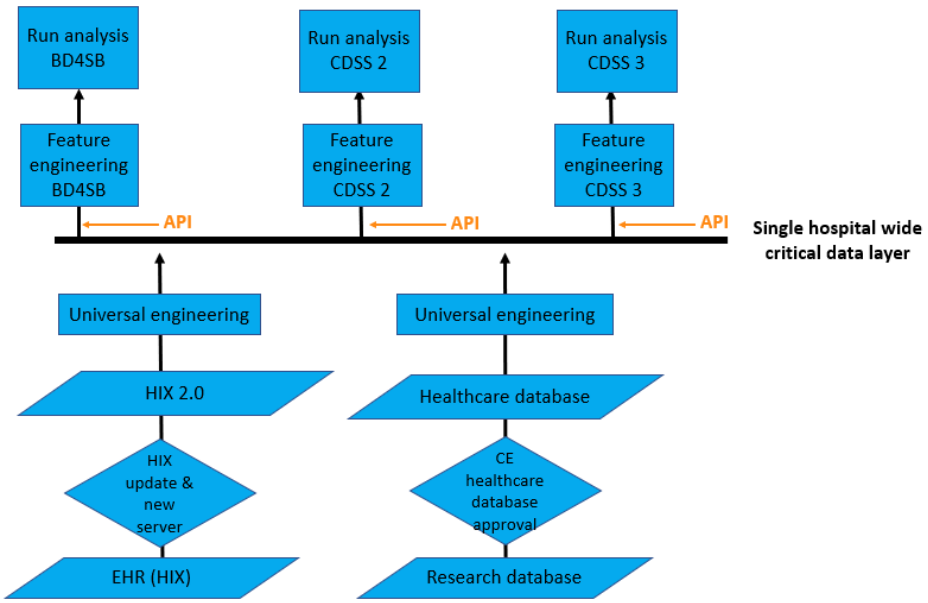

Figure 12 Solutions 'data availability' barrier with single hospital wide critical data layer

4.3 Data integration (process attribute)

According to R11, ex-physician and data scientist UMCU, there is no data integration hurdle apparent anymore with BD4SB CDSS anymore in the R&D stage. This hurdle is tackled as it can integrate different data as shown in figure six. However, the BD4SB CDSS is not implemented and therefore it is not certain that there will be no data integration hurdles when the CDSS is implemented.

4.3.1 Data integration barrier: Automating data integration

- **R12 (clinical owner BD4SB CDSS):** *"There is no automated process that collects data for analysis and makes it available to other solutions, all the data is still in it its original source and has to be extracted and integrated manually by somebody to enable the following analysis."*

As R12 states, currently there is no hospital wide critical data layer apparent which requires projects to collect and integrate their own data for the analytical CDSS within a R&D environment manually. Hence, the BD4SB CDSS functions well in the R&D environment, however, will encounter hurdles for implementation since the R&D and implementation environment differ according to R11, this creates a leap to implementation since data sources and the automation process are different.

4.3.1.1 Data integration solution: Single hospital wide critical data layer

The hospital wide critical data layer described in the previous section also functions as a solution for the data integration hurdle.

4.3.1.2 Data integration solution: Data managers

According to R12 and R15, clinical owner BD4SB and managing partner developer CDSS, including UMCU data manager in the BD4SB team can mitigate the data integration hurdles. These professionals are for example aware of any database permission hurdles and how these can be overcome which is also relevant to automate the process within the single hospital wide critical data layer.

4.3.1.3 Data integration solution: data protocols
R7 and R8 also determined that data protocols can benefit the data integration hurdle.

- **R7 (Healthcare director SAS):** "*Maybe they should work alongside a certain data protocol, XML was also discovered for a certain reason to be a certain format."*
- **R8 (Senior technical consultant SAS):** *"Data protocols describe among other things what data was used, where the algorithm was developed, which version it was and how it should be utilized. This increases the controllability and auditability. They are not used currently. Every system generates its own data in a way that is most easy for this system. Which is not wrong of course. Only when you come at a point when you use these systems you might realize that you should have done it in a different manner."*

A data protocol would bring uniformity with the utilization of data from several systems. This data protocol is part of healthcare information building block (HIBB) which will be further specified in section 4.4.2.1 & 4.4.3.1.

4.3.2 Data integration conclusion

Table 14: Laddering technique 'data integration'

Attribute:	Data integration
Barrier:	**4.3.1 Automate data integration** *Respondent: R12*
Solutions:	4.3.1.1 Single hospital wide critical data layer *Respondents: R8, R9, R11, R12 and R17*
	4.3.1.2 Data managers *Respondents: R12 and R15*
	4.3.1.3 Data protocols *Respondents: R7 and R8*
Concepts:	• Analytics with siloed data *Data that is isolated and/or under control of a department and requires permission to utilize which can be managed by data managers or described in data protocols.* • Integration of different structures of data (structured vs unstructured) from several resources *Integration of different data structures can be executed within the universal and feature engineering stage within the single hospital wide critical data layer*

The need for automated data integration, with the sources shown in figure six, can be considered as essential for implementing BD4SB CDSS as the data availability barrier because without automated data integration the CDSS fails to provide the result within the required 24 hours. The suggested solution concerning the construction of a single hospital wide critical data layer from the previous section also applies to this barrier, this construction can be supported by the data managers and data protocols stated within this section.

4.4 Data preparation (process attribute)

4.4.1 Data preparation barrier: BD4SB discovers & incorporates new relationships among variables

According to R17 (business engineer developer BD4SB CDSS) the data preparation for BD4SB is currently from a preferred level. However, according to R11, ex-physician and data scientist UMCU, and R12, clinical owner BD4SB, it seems to be an ongoing process as shown by the following example:

- **R12:** *"We collected all the data but did not know for sure if all the data was accurate. Let's take the rhesus factor. I asked our infections specialist about the variable and they told me it might be possible that a baby has more infections when he/she is rhesus positive. I asked for the data and found out that it was the rhesus factor of the blood donor instead of the patient that was influential. A baby who got a transfusion with red blood cells gets the infection more often, this is logical and hence not per definition a consequence of the rhesus factor. This shows that we continuously have to look carefully at the data we use in the CDSS."*

This shows that data preparation, interpretation of data input, is an ongoing process since the algorithm constantly detects relationships between different variables (e.g. rhesus factor and the blood infection).

4.4.1.1 Data preparation solution: continuously involve medical experts within the data science team

According to R11 and R12, it is impossible to fix all the data preparation hurdles in advance, it requires constant evaluation by medical experts. It is important to involve clinicians within the data science team to continuously assess the context and relations among variables as is confirmed by R2, director ADAM.

4.4.2 Data preparation barrier: Data quality suffers from inaccurate registration

- **R1:** *"Trash in and trash out is a serious problem within healthcare."*

The data quality in healthcare in general suffers from inaccurate registration according to R8, R11, R13 and R15. This makes is complicated to utilize historical data for analytics (R1, R12 and R13). This is also the case for the BD4SB case since the antibiotics, Augmentin, is submitted by clinicians in 42 different ways, from 'A' to 'Aum' according to R2, director ADAM, and R12, clinical owner BD4SB. This problem is solved at the UMCU by means of automated data preparation proceedings constructed by the BD4SB CDSS developers. However, it is likely that this inaccurate registration is still apparent at other hospitals which negatively influences the external validation proceedings for BD4SB as specified in section 4.12.1. R5, R6 and R13 state that the inaccurate registration is partially caused by the high registration load within healthcare and users' inability to see the benefits of registration.

- **R5:** *"I believe that a lot of professionals are not satisfied with the registration load whereas it still is not possible to benefit from this registration."*
- **R21:** *"The board of directors requires healthcare professionals to register things which might not be clinically valuable."*

R23, program manager ‘registration at the source’, states that this increasing registration load is caused by an increasing need for registration in healthcare for quality measurements, benchmarks, management information, research and epidemiological purposes.

4.4.3 Data preparation barrier: Dissimilar registration among hospitals

- **R1:** *“There is a tension between how we can standardize the systems input and how can we keep the input requirements user friendly, this is still not solved accordingly.”*
- **R12:** *“Submitting data in a pre-constructed list with questions would be perfect, however, this is very hard. The bottom section where you can enter free text which is not preferred is the most used section of the questionnaire.”*

The need for standardization of registration is apparent within healthcare and confirmed by R1, R2, R5, R6, R7 and R14. However, healthcare professionals are afraid of interruption of the workflow, loss of information and healthcare professionals have different registration preferences which makes it complicated to construct a uniform registration method according to R14, R21 and R23. This general registration uniformity inability of healthcare also influences the external validation possibilities for BD4SB CDSS which will be discussed in section 4.12.1.

4.4.2.1 & 4.4.3.1 Data preparation solution: Standardize registration via HIBB

- **R13:** *“New data entry forms should be a collaboration of the clinician and data analyst to determine what is user friendly to fill in and what is essential for the analysis.”*

R2, R12, R13 and R18 propose that hospitals join forces to make agreements on registration, these forces should consist of medical professionals as well as information professionals according to R13. These agreements would focus on only registering clinical valuable information. Aligned with this need, the NFU, national federation academic hospitals, started the project ‘registration at the source’ alongside with Nictiz, expertise Centre for e-health funded by the Dutch government, to develop and implement healthcare information building blocks (HIBB). According to R21, IT/ICT manager UMCU, the HIBB should remove hurdles experienced by different registration formats among hospitals. HIBB are described as following by R23 (program manager ‘registration at the source’):

- **R23:** *“Unambiguous agreements on aspects in healthcare, this could be a proceeding or a problem as alcohol misuse for example. If we talk about a proceeding, we register it in this and that way which is aligned with the agreements. For example, the blood pressure building block consists of the value, how it was measured and where. Another example is the postal code table building block which describes how we register postal codes.”*

Healthcare and information professionals developed 100 HIBB among which some are implemented (R23). The Dutch government supports HIBB by recognizing it as the healthcare information exchange standards for the Netherlands within the 2018 bill for the ‘digitally exchanging healthcare information’ legislation as discussed in 3.2.3.1. However, according to R23, it is unclear when the legislation will be

constructed and vindicated. Still, according to R21 and R23, this legislative support from the government would benefit the implementation of HIBB. Furthermore, the implementation of the HIBB is currently not obligatory and the responsibility fully lies with the hospitals and the EHR suppliers.

- **R23:** *"EHR suppliers and hospital clients have to determine together what, when and where the HIBB will be built into the HER. Here is a lot of improvement to make."*

This given freedom to the hospitals and the EHR suppliers might result in implementing the HIBB in a manner that is not preferred according to R23.

- **R23:** *"There will be a moment when we vindicate this method of registration with HIBB."*

This statement implies that there will be a moment when the method of registration will be monitored, however, until then the responsibility lies with the hospitals and EHR suppliers. Furthermore, the NFU, developer of HIBB, currently aims learn from the implementation procedures and optimize the product. The goal is to register 80% of the healthcare information from the academic hospitals, among which the UMCU, with HIBB by 2020 according to R23.

4.4.2.2 & 4.4.3.2 Data preparation solution: Standardize registration via coding solutions

The coding solutions (DHD and Snomed) mentioned in section 3.2.3.2 by R5 and R20 are also applicable to this barrier as is confirmed by R5 and R23.

4.4.4 Conclusion Data Preparation

Table 15: Laddering technique 'data preparation'

<table>
<tr><td>Attribute:</td><td colspan="3">Data preparation</td></tr>
<tr><td>Barriers:</td><td>4.4.1 BD4SB discovers & incorporates new relationships among variables
Respondents: R11 and R12</td><td>4.4.2 Data quality suffers from inaccurate registration
Respondents: R1, R2, R5, R6, R8, R11, R12, R13, R15, R21 and R23</td><td>4.4.3 Dissimilar registration among hospitals
Respondents: R1, R2, R5, R6, R7, R14, R21 and R23</td></tr>
<tr><td rowspan="2">Solutions:</td><td rowspan="2">4.4.1.1 continuously involve medical experts within data science team
Respondents: R2, R11 and R12</td><td colspan="2">4.4.2.1 & 4.4.3.1 Standardize registration via HIBB
Respondents: R2, R12, R13, R18, R21 and R23</td></tr>
<tr><td colspan="2">4.4.2.2 & 4.4.3.2 standardize registration via coding solutions (DHD & Snomed)
Respondents: R5 and R23</td></tr>
<tr><td>Concepts:</td><td colspan="3">• Inaccuracy and inconsistency of the data
Utilization of the HIBB and DHD/Snomed mitigate the inaccuracy and inconsistency of the data in healthcare.
• Data structure and standardization issues
Utilization of the HIBB and DHD/Snomed mitigate the data structure and standardization issues.
• Limited validation possibilities
HIBB benefit the uniformity of healthcare information and therefore make (external) validation more accessible.</td></tr>
</table>

BD4SB CDSS already involves the medical expert within the analytical process which it should do continuously. Furthermore, the undesirable data quality alongside the dissimilar registration among hospitals was also not that influential in the R&D stage of BD4SB, however, will be substantially influencing the (external) validation process of BD4SB CDSS as will be described in 4.12.1. Additionally, the success of the solutions depends on hospitals and EHR suppliers to implement the HIBB, the standardization (DHD) and sharing (Snomed) solutions.

4.5 Analysis (process attribute)

4.5.1 Transparency barrier: Auditable, traceable and trackable

According to R15 (managing partner developer BD4SB CDSS) the BD4SB CDSS must be auditable, traceable and trackable for implementation. The transparency of the analysis within this context is essential as is confirmed by R10 (ex-physician and senior sales executive healthcare, SAS):

- **R10:** "*The analytical process must be transparent. For example: which algorithm was used six months ago, which data was used and who entered or changed the data, where they entitled to do so, dot he data sources supply the required quality or how it was analyzed. If a physician stands in front of a judge, he/she must be able to exactly explain how the process was executed.*"

The BD4SB project team is aware of these requirements and can meet them according to R8, R11, and R17. However, it is not clear if this meets the standards for CE approval as will be discussed in section 4.10. Therefore, this section will discuss the solutions the BD4SB project team executed to meet the requirements shown in the statement of R10.

4.5.1.1 Analysis solution: Gradient boosting decision tree provides transparency

R17 (business engineer developer BD4SB CDSS) states that the gradient boosting technique within the BD4SB CDSS can show the decision tree which visualizes the decisions process within the analysis. Additionally, according to R11, ex-physician and data scientist UMCU, and R17, the model can quantify the impact of each variable by a Shably value for each of the 50 variables within the analysis of BD4SB CDSS by values ranging from -1 to +1. These features of the BD4SB CDSS gives it the required transparency for implementation according to R8, R11 and R17.

4.5.1.2 Analysis solution: Registration table

- **R17 (business engineer developer BD4SB CDSS):** *"We have a registration table that shows all used data with all operations over the data. So, you know what needs to happen with the data before the analytical process of a working model. This requires several different queries to be automatically executed but this is feasible."*

The current BD4SB project team develops a registration table that shows all the necessary proceedings for the required transparency for implementation according to R17. This statement cannot be triangulated and is not considered highly reliable since R17 is no expert on the transparency requirements of medical devices within the legislation which will be further discussed in section 4.10.

4.5.2 Conclusion Analysis

Table 16: Laddering technique 'analysis'

Attribute:	Analysis
Barrier:	**4.5.1 Transparency analytics** *Respondents: R10 and R15*
Solution:	4.5.1.1 Gradient boosting decision tree provides transparency *Respondents: R8, R11 and R17*
	4.5.1.2 Registration table *Respondent: R17*
Concept:	• Lack of transparency with analytical systems *Providing a decision tree and registration table benefit the transparency of an analytical system*

This BDFSB CDSS provides a decision tree and a registration table, however, it remains questionable if this meets the transparency requirements in the legislation for medical devices because these specific requirements of legislation remain unknown as will be explained in section 4.10

4.6 Result (process attribute)

- **R12 (clinical owner BDFSB):** *"The false negative predictive value of the algorithm meets the acceptable threshold, we chose a threshold of 75%. However, the system still misses some patients because they had other symptoms or something special, only 6 on the 500 children. This is not much, however, if all 6 babies die, this is hard to explain of course."*

Optimizing the accuracy of the CDSS remains an ongoing process. However, R7, R10, R11, R12, R17 and R18 state that the main discussion is not on the accuracy threshold, hence how safely somebody can incorporate the model in decision making since this is from an acceptable level as shown in the statement of R12. This is not something that withholds the BD4SB CDSS from implementation.

4.6.1 Result barrier: Inconclusive format

R8, R12 and R16 state that it is not clear if the result should be shown as a percentage on the probability of blood sepsis, a red/green light or a notification that appears at a certain predetermined threshold.

- **R16 (Ethicist UMCU)**:*"There are theoretical sources that show clinical decision support systems that present the result of the algorithm in for example a red versus green light. This can lead to deskilling of the physician. Hence that the experts such as neonatologists lose their own feeling for when a baby needs antibiotics and make decisions based on the algorithm. This is a problem since the physicians become dependent on the algorithm and are unable to detect when the algorithm is wrong."*

This statement shows that selecting a certain result format is important and has consequences since it can make a physician more dependent on the CDSS which is not preferred.

4.6.1.1 Result solution: Expert meetings/interviews and case evaluation

Choosing the correct result format requires a study by means of expert meetings and interviews accompanied by retrospective case studies according to R11 (ex-physician and data scientist UMCU) and R12 (clinical owner BD4SB). These expert meetings or interviews will focus on the influence of the format on the users' decision making. The case evaluation method presents different cases with different BD4SB CDSS result formats to different physicians. By means of this retrospective method, the success rate of different result formats can be measured accompanied by evaluating how a user utilizes the result of the algorithm and his own knowledge within decision making.

4.6.1 Conclusion Result

Table 17: Laddering technique 'result'

Attribute:	Result
Barrier:	**4.6.1 Inconclusive format** *Respondents: R8, R12 and R16*
Solution:	4.6.1.1 Expert meetings, interviews and case evaluation *Respondents: R11 and R12*
Concept:	• Lack of skilled clinical scientists & managers to guide, process and interpret outcome *Within expert meetings, interviews and case evaluations knowledge is shared by which the skills of clinical scientists & managers could increase.*

The preferred result format for BD4SB CDSS remains unknown and should be determined by means of a study assessing the influence of different formats on the physicians' decision-making process.

4.7 Utilization barriers (process attribute)

4.7.1 Utilization barriers: User resistance due to high autonomy & responsibility physician

Physicians show resistance in using CDSS, among which BDFSB, within their clinical proceedings according to R8, R10, R11, R13 and R15. This study determined several reasons: (1) an algorithm intervenes with the physicians' right to exist which is based upon his/her knowledge, (2) the responsibility of a physician is high, and (3) physicians often distrust algorithms.

Intervenes with physicians' right to exist

An algorithm intervenes with the physicians' function description which is based upon his/her knowledge**.** Physicians are highly knowledgeable persons and are hesitant in taking advice from an algorithm providing external knowledge.

- **R20 (ex-physician and analytical entrepreneur):** *"New CDSS technology deprives the right to exist from the physician. Physicians want to work based on their own knowledge, want to have the feeling they are intelligent and the feeling that they are Dr. House. That is the essence of the problem, the psychology of the physician."*

This view on intervening with the physicians' right of existence is confirmed by R1, R7, R8 and R20.

High responsibility physician

- **R13 (Program manager ADAM):** "*If the algorithm says to intervene and the physician does not, he or she is responsible. If the algorithm says not to intervene and then he or she does not, he or she is still responsible. The physician is always responsible and therefore hesitant in using these systems*."

Next to the knowledge-based resistance, the physician profession is also one that comes with high responsibility (R8, R13 and R15). A physician is responsible for the care of the patient which implies that he/she must trust the CDSS before he/she will use it (R7: Healthcare director SAS).

Distrust in CDSS

- **R10 (ex-physician and senior sales executive healthcare SAS):** *"Trust is another important aspect. A physician must be able to trust the CDSS when something goes wrong. When a complaint is made, a hospital/clinician has to justify every step within the treatment process for which a certain extent of transparency is required."*

The trust in the CDSS must be from such level that the physician finds it a substantiated source to deviate from his own choice (R10, R11 and R20). According to R20, ex-physician and analytics entrepreneur, physicians used to trust their own emotional certainty for decision making and now must trust a machine. This is something a physician must accept for analytics to succeed in healthcare according to R10 (ex-physician and data scientist UMCU).

4.7.2 Utilization barriers: IT is too distant from physician

- **R7 (healthcare director SAS):** *"Hospitals have another problem. A cultural problem, the physicians are too distant from the IT department. I believe IT gets insufficient priority to realize these analytical projects."*

According to R7, the physicians are too distant from the IT department which implicates there is insufficient knowledge on utilization of IT by physicians which is confirmed by R1 (ex-chairman board AMC, ex-internist & current CEO hospital cluster, University College London Hospitals).

4.7.1.1 & 4.7.2.1 Utilization solution: Involve physicians within the development stage

According to R2, R11, R12, R13 and R14, involving physicians within the development stage of the analytical CDSS will be beneficial for trust and acceptancy of an analytical CDSS.

- **R11 (ex-physician and data scientist UMCU): "***We create awareness with physicians by expert meetings in which we discuss how we created a model. It is important to bring along a group of physicians within this process or else you will get the 'not invented by me syndrome'."*

Additionally, R1(ex-chairman board AMC, ex-internist & current CEO hospital cluster, University College London Hospitals) emphasizes to involve technical and non-technical savvy physicians. Usually, only technical acquainted physicians take part within these kinds of projects, however, it is essential to extract feedback from the less technically acquainted physicians. Furthermore, R1 suggests

that it is important to include the patients within the development process which is confirmed by R2, director ADAM, who states that the ADAM projects can only be realized by including the patient, data scientist and physician, furthermore, within the analytical CDSS development process the physician is the owner of the project since he/she is owner of the problem.

4.7.1.2 Utilization solution: Present BD4SB CDSS as a summary of the past 10 years

The neonatology section of healthcare is relatively small hence there is a low amount of research available and there are few to none protocols according to R11, physician and data scientist UMCU, and R12, clinical owner BD4SB. This could imply that neonatologists are more receptible to new information sources, this need could be utilized by presenting BD4SB as a summary,

- **R12:** *"the BD4SB CDSS should be interpreted as a summary of cases over the past 10 years tailored on a specific case at hand."*

4.7.1.3 Utilization solution: Build trust by showing added value use cases & process

According to R8 and R9, trust can only be obtained by showing improvements within the quality of care by use cases. Furthermore, according to R8, R9 and R12, trust is created by means of understanding of the decision process within the BD4SB CDSS.

- **R8 (senior technical consultant SAS): "***The user adoption process can be strengthened by using patient cases from the past and let a physician decide and the model decide, so they can compare results afterwards. These kinds of tests could benefit the physicians' trust in a CDSS."*

This methodology is normal procedure for introducing a new medicine and could also work for introducing an analytical CDSS as BD4SB according to R12, clinical owner BD4SB.

4.7.1.4 Utilization solution: Include BD4SB CDSS in a protocol

According to R11, R13 and R20 utilization of analytical CDSS could be kickstarted by incorporating the CDSS within a protocol. This would create a more trusted environment for usage of the analytical CDSS. Protocols require the physician to justify why he/she did not follow them because a protocol describes the standard proceedings that physicians usually apply according to R20, ex-physician and analytics entrepreneur. However, incorporating an analytical CDSS within a protocol is not something that is easily done because it requires a clinical trial according to R13 (program manager ADAM), as is the case in the CE approval process, and is time consuming since it requires publication of a scientific article on the appliance of the CDSS within a peer reviewed journal which can take up to years according to R11, ex-physician and data scientist UMCU.

4.7.2 Conclusion Utilization

Table 18: Laddering technique 'utilization'

<table>
<tr><td>Attribute:</td><td colspan="2">Utilization</td></tr>
<tr><td>Barrier:</td><td>4.7.1 User resistance due to high autonomy & responsibility:
Respondents: R1, R7, R8, R10, R13, R15 and R20</td><td>4.7.2 IT is too distant from physician
Respondents: R1 and R7</td></tr>
<tr><td rowspan="4">Solutions:</td><td colspan="2">4.7.1.1 & 4.7.2.1 Involve physicians in development analytical CDSS
Respondents: R1, R2, R4, R11, R12, R13 and R14</td></tr>
<tr><td>4.7.1.2 Present BD4SB CDSS as a summary
Respondents: R11 and R12</td><td rowspan="3">No other solutions extracted from interviews for barrier 4.7.2</td></tr>
<tr><td>4.7.1.3 Build trust by showing added value use cases & process
Respondents: R8, R9 and R12</td></tr>
<tr><td>4.7.1.4 Include BD4SB CDSS in a protocol
Respondents: R11, R13 and R20</td></tr>
<tr><td>Concepts:</td><td colspan="2">• User resistance (process change)
User resistance can be mitigated by user involvement, building trust by showing added value of use cases & process or including the CDSS in a protocol.
• Perceived usefulness
The perceived usefulness can be positively influenced by showing added value of use cases & process.
• Perceived ease of use
The perceived ease of use can be positively influenced by showing of use cases & process.</td></tr>
</table>

The utilization barriers are mostly applicable in the end of the adoption phase where the 'individual' user is apparent according to the IT adoption theory (Hameed et al., 2012). The user resistance barrier is considered as impactful since users' trust and acceptancy in the BD4SB CDSS determines utilization. The solutions within the laddering technique, table eighteen, show solutions for creating trust and support acceptancy of BDFSB CDSS by physicians.

4.8 Ethics (peripheral business attribute)

Without the approval of the 'medical ethical review commission' (METC), the BD4SB project team is not able to execute a clinical evaluation study which is required within the legalizing process. Hence, it is essential to focus on the ethical aspects next to the technical aspects.

- **R16 (Ethicist UMCU):** *"From an ethical perspective, we are not as far ahead as everybody claims."*

4.8.1 Ethical barrier: Developer algorithm holds a responsibility

- **R16:** *"If an algorithm makes a mistake or if a device makes a mistake, the developer is partially responsible since the algorithm has the mistake built into it, there is a causal link between the mistake and the algorithm. There is a difference between legal and moral responsibility. I do not know the legal side, but I know that the moral responsibility lies with the developer."*

Whereas the previous section described that the full responsibility lies with the physician, R16 states that there is a certain kind of moral responsibility that lies with the developer. Developers are hesitant within this area since society holds higher standards for technology than for humans which is remarkable since humans often make more mistakes which we forgive more easily than technology mistakes (R16).

4.8.2 Ethical barrier: third party within decision process

With the introduction of an CDSS such as BDSFB, the traditional decision process will change since the physician and patient are accompanied by a third party which moves the proportion of decision making. This shift and the exact consequences for decision making are still unknown and should be clear before implementing the BD4SB CDSS according to R16, ethicist UMCU, and R20, ex-physician and analytics entrepreneur.

4.8.2.1 Solution: Study on new authority routes for decision making with analytical CDSS

A study on the involvement of an CDSS as BD4SB within the decision process with the physician and patient could provide a greater understanding of the consequences for decision making according to R2, R16 and R20. Such a study should describe new authority routes within decision making with an analytical CDSS which could take years to implement according to R20, ex-physician and analytics entrepreneur. This study is already planned and initiated in January 2019 and can take up to a year according to R16, ethicist UMCU and the lead researcher of this study. The following statement shows the main subjects in the study:

- **R16:** *"How do the physician and patient experience care with the algorithm? Does the care change? Do conversations change? Do everybody trust the data? How should we factor the disagreement between a physician and an algorithm? How will a physician reason with the outcome of the algorithm? Is this a relief, does it offer support that will result in better care?"*

This study could be input for construction of new authority routes required for implementing BF4SB.

4.8.3 Ethics conclusion

Table 19: Laddering technique 'ethics'

Attribute:	Ethics	
Barriers:	**4.8.1 Developer algorithm holds a responsibility** *Respondent: R16*	**4.8.2 Third party within decision process** *Respondents: R9 and R16*
Solutions:	No solutions extracted from interviews	4.8.2.1 Study on new authority routes for decision making with analytical CDSS *Respondents: R2, R16 and R20*
Concepts:	• Concern about non-human supervised information processing information *The study on the new authority routes can provide a greater understanding of the concerns about non-human supervised information processing.* • Perceived behavioral control (controllability & facilitating conditions) *The study on the new authority routes also provides a greater understanding on the physicians' perceived controllability of the BD4SB CDSS*	

All in all, the ethical barriers can be considered just as important as the technical ones since legalizing BD4SB CDSS is impossible without the clinical evaluation study which requires approval from the METC which claims there is an insufficient understanding of the impact of BD4SB CDSS on the physicians' decision making. The planned study of one year could give more insight on this context, however, might also result in rejection of BD4SB CDSS.

4.9 Resources (peripheral business attribute)

4.9.1 Resources barrier: Unable to quantify business case BD4SB CDSS

Every medical device, as BD4SB CDSS will be, must have a business case in which it describes the financial added value and/or improvement in quality of care. BD4SB is not able to directly save costs since the antibiotics are not expensive, the added value is in improving the quality of care by (R17).

- **R17 (Business engineer CDSS developer):** *"It is not clear if the improvement of care is worth the costs of data scientists, medical trial, infrastructure and maintenance of the BD4SB project."*
- **R13 (Program manager ADAM):** *"The validation process for BD4SB is unclear which makes the budget for implementation unclear."*

As the BD4SB project approaches the implementation stage it becomes more important to quantify the business case which is complex since it is largely dependent on the validation design which remains unclear, this difference in validation designs will be further discussed in section 4.12.

4.9.2 Resources barrier: Allocating budget for implementing BD4SB CDSS

Allocating budget for implementing the BD4SB CDSS is a large barrier for implementation according to R13 and R17.

4.9.3 Resources conclusion

Table 20: Laddering technique 'resources'

Attribute:	Resources	
Barriers:	**4.9.1 Unable to quantify business case BD4SB CDSS** *Respondent: R7, R13 and R17*	**4.9.2 Allocating budget for implementing BD4SB CDSS** *Respondents: R13 and R17*
Solutions:	No solution extracted from interviews	No solution extracted from interviews
Concept:	• Initial investment too high *Quantifying the business case will not lower the investment, however, might benefit attracting external investors by clarifying business interest.*	

Without resources it is not possible to implement the BD4SB CDSS, hence it is an important barrier to overcome for which there are no solutions proposed.

4.10 Legal (peripheral business attribute)

BD4SB CDSS must be CE approved which shows that it meets the European requirements for software as a medical device. This CE approval process requires the following documents: (1) describing intended use, (2) medical device classification, (3) quality management system (QMS), (4) technical file, and (5) clinical evaluation report (CER). Then all the five documents must be assessed by a notified body to obtain the CE approval and ISO certificates required for a medical device. (Emergo, 2018)

4.10.1 Legal Barrier: METC has no yardstick in WMO for assessing algorithms

The METC assesses medical trial requests for the clinical evaluation report based upon the legal framework within the WMO (law for medical research). However, according to R16, ethicist and member METC, there is no clear legal framework for a predictive algorithm within the WMO.

- **R16:** *"It is actually almost irresponsible to implement predictive algorithms within a CDSS since there is no law for this in the WMO."*

The lack of related legislation within the WMO would require the METC to assess a medical trial requests outside the legal framework which makes it complicated and irresponsible according to R16. Furthermore, within this medical trial request, the requester must hand in a risk assessment.

- **R16 (ethicist UMCU):** *"We do not know enough to make a risk assessment, research concerning an algorithm versus a medicine research is very different."*
- **R11 (physician and data scientist UMCU):** *"CE approval requires description of risks when it goes wrong for which you need a test period. To execute this test period, you need to deliver a risk assessment to the METC, this is a vicious circle."*

This vicious circle implies that there is insufficient historical clinical research on predictive algorithms to construct a risk assessment. The BD4SB team currently aims to construct a risk assessment with retrospective patient data, however, it is not certain if the METC approves this. Also, legislation only states to execute a good risk assessment, there is no specification on requirements for predictive algorithms (R17, business engineer developer CDSS).

4.10.1.1 Ethical solution: Update WMO

R16, suggests that the WMO does not provide the legal framework for an approval for a medical trial from the METC. R16 is an ethicist and member of the METC and considered an expert on this phenomenon, therefore this solution is considered reliable.

4.10.1.2 Ethical solution: EU develops AI norms

According to R19, inspector e-health, the EU is currently developing norms for AI which are also applicable to analytical CDSS.

- **R19:** *"EU workgroups currently assess how to measure risks of clinical evaluation study with analytical CDSS"*

These norms could also give more foundation to the METC within the medical trial approval since it provides a greater understanding within a legal framework. R19 his profession requires him to stay up to date on these developments which makes him an expert on this phenomenon and therefore the solution is considered reliable.

4.10.2 Legal Barrier: MDR does not yet provide clear requirements

R19, R20 and R22 state that the legislation involved for the CE approval of software as a medical device is a grey area. According to R19, e-health inspector, the new legislation for medical devices in 2020 (MDR) gives more clarity on the requirements for software as a medical device to developers. However, R19 states that the concrete text within the legislation does not limit the incorporation of an algorithm as BD4SB as a medical device, however, the notified bodies interpret the text within the legislation to construct specific requirements and to apply within the CE approval process of these medical devices. These notified bodies generally do not share the specific requirements because these are government recognized organizations and no consultancy organizations. R22, global clinical director notified body, was only able to provide the following general recommendations concerning the CE approval process of an analytical CDSS as BD4SB: (1) you have to show the interaction between the variables, (2) how robust your algorithm is, (3) the risk benefit analysis has to prove that it is beneficial to the patient and this is often hard, and (4) a notified body looks at the investigator selection, hence the sources from which you retrieved your data for external validation, to determine the quality of the data, it will be taken into account if these data suppliers are friends or good clients for example.

In general, the specific requirements for the CE approval process of analytical CDSS remain vague to developers according to R22 as exemplified by the following statement:

- **R22 (global clinical director notified body):** "*In general it is very hard for developers to know what notified bodies want to see. Notified bodies work with internal or external clinicians. Together we conclude if there is enough data that provides us the required trust to give the CE approval. The data that a developer supplies should show that the product is safe, effective and has a place on the market."*

4.10.2.1 Specify MDR requirements

As stated earlier, R19, e-health inspector, stated that the interpretation of the MDR is still under construction. This is confirmed by R22 who states the following:

- **R22 (global clinical director notified body)::** *Dekra (NB) has adjusted it procedures to the new legislation on European level, the MDR, and send it to inspection healthcare and youth (IGJ). The IGJ and a couple European DEKRA colleagues visited us and looked at our new procedures, this is called a joined assessment. More than half of the time, especially in the first meetings, they were discussing with each other what this new MDR legislation exactly says. Hence, it took 7 years to write the new legislation, then you have a meeting with representatives*

of a notified body from several countries and the IGJ and they are still discussing what the MDR exactly says. The new legislation was hard to construct; however, they also want to keep the interpretation freedom because Germany wants something else then the Netherlands for example."

This statement exemplifies it is complex to extract specific requirement from the MDR, even for the notified bodies themselves for who it is core business, let alone for the developers.

4.10.3 Legal barrier: Clinical evaluation study is complex

According to R22, global clinical director notified body, the clinical evaluation within the CE approval process will play a large role in implementing predictive analytics and is the grey area since the remaining documentation are hard facts. This documentation concerns the intended use, qualification as a medical device, technical file and quality management system. Furthermore, R19, e-health inspector, states that software suppliers often do poor clinical evaluation:

- **R19:** *"Clinical evaluation entails the evaluation of what is known of the clinical functionality of the product, this can come from articles or from own research. We determined that this is often insufficiently executed by software suppliers. There is often not enough foundation for the findings, it can be based on a single study with few participants for example."*

The most optimal design for a clinical evaluation study is clear, a randomized control trial (RCT) as exemplified by R4:

- **R4 (clinical owner BDFSB):** *"The best way would be a randomized experiment where half will be exposed to the algorithm and the other half not. This is seriously hard, randomizing thousands of patients and the algorithm might be only suitable for our own population, we have to look at how we can show the clinical relevance without a randomized study."*

As stated by R4, the RCT is also hard to execute as confirmed by R11, R18 and R22 because it is timely, costly, patients might not approve and there is a saying 'One RCT is not RCT' according to R18, methodologist UMCU. Furthermore, R22, global clinical director notified body, states that they want to see more description of the long-term effects of a certain medical device in studies. Due to this fact, R18 states that the RCT is not the most suitable because the innovation changes over time.

<u>4.10.2.2 and 4.10.3.1 Legal solution: Include regulatory expert</u>

R22, global clinical director notified body, states that including a regulatory expert in the R&D team might be beneficial to the CE approval process preparation of the BD4SB project team:

- **R22:** *"A regulatory professional within a R&D team that is involved from step one can think of what a Notified Body or FDA wants to see for CE approval. Large companies see this and include a regulatory professional from the concept stage. "*
- **R22:** *"Regulatory consultancy agencies can write in the language a notified body wants to see, developers write in an engineering language."*

This implies that including more regulatory knowledge within the BD4SB project team would enable it to meet the notified body requirements based on the MDR easier. This statement from a single person is considered reliable since R22 is an expert on the CE-approval process for medical devices.

4.10.2.3 and 4.10.3.2 Legal solution: Udamed

R22 states that next to the MDR in 2020, a database will be made available to developers:

- **R22:** "*Udamed will be the European database that contains everything involved in the CE approval process (e.g. study protocols, approvals, side effects). Notified bodies and developers must upload all their data to this database. This database will give more transparency which helps the developers by looking at the CE approval process of other developers. The Udamed will officially become available to developers alongside the MDR in 2020.*

The database would give the BD4SB project team more reference points on how to prepare and execute the CE approval process which isneeded because the CE approval process of an analytical CDSS is new to the UMCU and developer of the CDSS, according to R17, business engineer developer CDSS. Furthermore, this solution is considered reliable since R22, global clinical director notified body, is an expert on the CE-approval process for medical devices.

4.10.3.3 Legal: Other options than RCT

- **R22 (global clinical director notified body**): *"RCT is not the only option, you only have to prove that it is good data."*

R11, R13, R18 and R22 confirm that there are other options than the RCT. However, according to R18, methodologist UMCU, there is no single answer to what methodology is best for the clinical evaluation study.

- **R18:** *"N=1 trials, clustered analysis or clustered trials are more suitable because you can incorporate the changes in the innovation in the analysis. Combinations are also popular now."*

Furthermore, according to R19, e-health inspector, and R22 it is possible to execute a clinical evaluation study by means of historical data if this dataset represents the current and future population. R17, business engineer BD4SB developer, specifies that R12, clinical owner BD4SB, approves the representativeness of the current dataset used by BD4SB in relation to the whole population, other physicians currently assess if all patients fit within the cohort. All in all, there are other possibilities stated for the design of the clinical evaluation study which could be considered more suitable.

4.10.4 Legal: Privacy

Privacy hurdles are frequently experienced when executing analytics on patient data. The BD4SB project team continuously executes a privacy assessment within the stages of the innovation funnel as shown in figure twenty Appendix B. Within this funnel there are no privacy issues encountered according to R13, program manager ADAM, for the BD4SB CDSS. Furthermore, R16, ethicist UMCU,

states that there is no separate informed consent form required for treatment with BD4SB CDSS since it will be incorporated within the general informed consent for clinical treatment within neonatology

4.10.5 Legal Conclusion

Table 21: Laddering technique 'legal'

Attribute:	Legal		
Barriers:	**4.10.1 METC has no yardstick for assessing algorithms** *Respondents: R15 and R16*	**4.10.2 MDR does not yet provide clear requirements** *Respondents: R19, R20 and R22*	**4.10.3 Clinical evaluation study is complex** *Respondents: R2, R11, R18, R19 and R22*
Solutions:	4.10.1.1 Update WMO *Respondent: R16*	4.10.2.2 and 4.10.3.1 Include regulatory expert *Respondent: R22*	
	4.10.1.2 EAA develops AI norms *Respondent: R19*	4.10.2.3 and 4.10.3.2 Udamed *Respondent: R22*	
		4.10.2.1 Specify MDR requirements *Respondents: R19 & 22*	4.10.3.3 Other options than RCT *Respondents: R11, R13, R18 and R22*
Concept:	No matching concepts extracted from literature review		

Without a CE approval for BD4SB CDSS as a medical device it is not possible to implement. The BDFSB project team is largely dependent on regulators within this area as shown in figure thirteen, the risk assessment adjustment by the EU, an update of the WMO, the introduction of the MDR and the Udamed would give more clarity on requirements within the CE approval process which is considered a grey area. The only solution that the BDFSB team can implement now is involving a regulatory expert in the BD4SB team to predetermine the requirements, eventually meet the NB requirements, and determine the adequate design for the clinical evaluation report, which is a dark grey area.

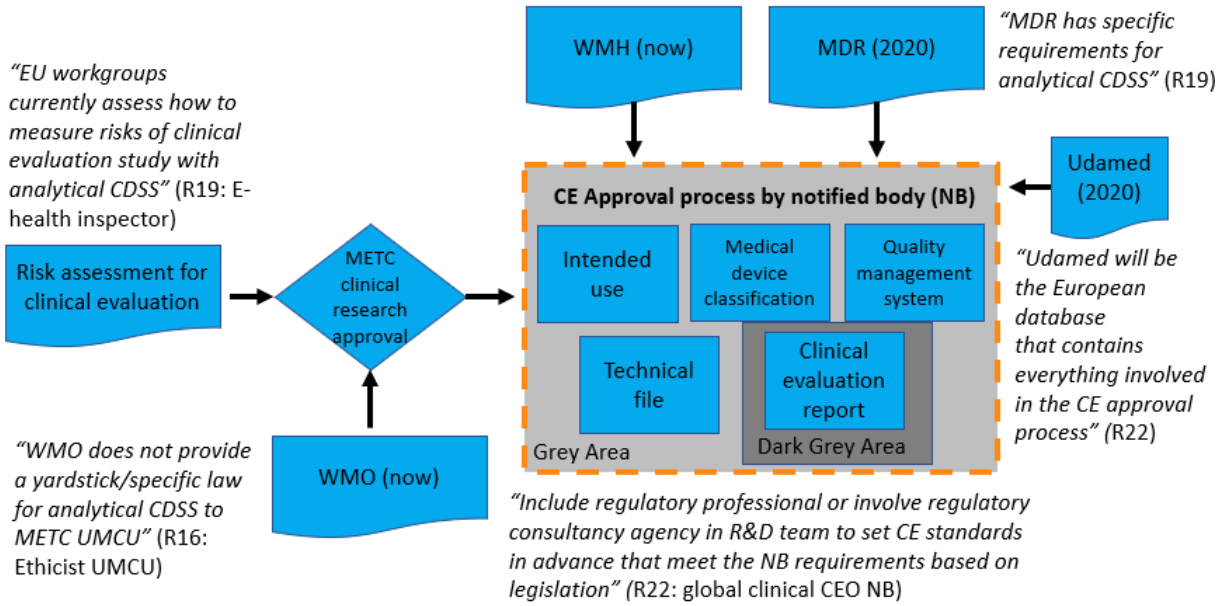

Figure 13: Influence of the WMO, WMH, MDR and Udamed on the legalization process

4.11 Development (Implementing predictive algorithm attribute)

The barriers connected to this attribute are dispersed over the other attributes.

4.12 Validation (Implementing predictive algorithm attribute)

4.12.1 Validation barrier: External validation

There is extensive discussion on the necessity and design of the external validation which is described within this section. R12, clinical owner BD4SB, questions if external validation is mandatory for CE approval and R18, methodologist UMCU, states that it is not mandatory, however, it remains the preferred design among methodologists since the patient spectrum outside the UMCU can differ a lot from the current UMCU spectrum. This external validation necessity is confirmed by R20, ex-physician and analytics entrepreneur. Hence the ideal situation would be to externally validate the model. This preference is strengthened by the high impact on the health of the patient by incorporating BD4SB CDSS within the healthcare process. According to R13, program manager ADAM, and R11, ex-physician and data scientist, this impact obliges the METC and notified bodies to be stricter on the validation process. External validation turns out to be complicated, especially for a relatively small field of study in healthcare as neonatology as exemplified by R4 (clinical owner BD4SB):

- **R4: "***Another problem is the validation. The best option is to do this externally, however, this is very hard. All relevant hospitals in the Netherlands, ten childcare departments in total, work with other systems and other variables."*

R17, business engineer developer CDSS, confirms this point of view and states that internal validation is hard enough. R18, methodologist UMCU, also recognizes this problematic situation, however, still claims that this is the preferred methodology even when there is a variable missing in the external dataset. When the data is sort of the same it is worthwhile looking externally.

- **R18:** *"The variables in the model are not required to have the same added value to the model in every dataset, this can differentiate, external validation shows you do not have to look for other variables. Let's say you have 5 items in your model, just look at these 5 items in another set and then it might be possible if the population is different that all these 5 items have another relation to the outcome. Then you should refit the variables in the model to that setting."*

Furthermore, R18 states that it is extra important for BD4SB to validate externally since neonatology is a relatively small field within healthcare, this implicates that the current UMCU dataset might not represent the whole population. Contradictory, R17 states that the current UMCU dataset consist of 1200 patients which should be most of the patient scenarios. R17, a business engineer, who develops the BD4SB CDSS is however a technical expert and has limited expertise on methodology regarding validation which is the expertise of R18, the methodologist. Hence the point of view of R18 on the preference for external validation is considered leading within this research.

4.12.1.1 Validation solution: Create omnipotent model

According to R12, clinical owner BD4SB, it could be possible to adjust the BD4SB model to enable external validation. This would require receiving datasets from other hospitals to execute the validation, this sharing of data for validation purposes is quite usual according to R13, program manager ADAM and R18, methodologist UMCU. This external validation can be executed if the model variables are adjusted so that they fit with datasets of other hospitals. This will result in a model that has a lower reliability for the UMCU and higher for all the external datasets on which it is validated according to R12. This downfall in reliability for UMCU can be mitigated by means of calibrating the model to the UMCU dataset after the external validation according to R18, methodologist UMCU. However, this calibration cannot be too impactful or else the model will be considered a different model and the external validation is not valid anymore within the CE approval process according to R22, global clinical director notified body.

4.12.1.2 Validation solution: Predictor definition research & dummies

R18, methodologist UMCU, encountered a similar external validation hurdle situation within a heart and vascular related case and utilized a predictor definition study:

- **R18:** *"A predictor definitions study focuses on comparing variables from dataset x with dataset y, variables can be measured differently or are related to something slightly or largely different. We expected that the impact on the model of these differences would be very large, however, the effect was not that large. A small difference in predictor definition was more permissible than we thought, it was negligible. However, this was for one model to this specific case, this can be different for another model but is seems to be not that impactful as we thought."*

The difference between the internal and external dataset for the heart and vascular related case was negligible, however, this does not imply that this will be the same for the BD4SB case. A predictor definition study would quantify the variable differences between the internal and external dataset which gives a greater understanding to what extent the model must be adjusted to enable external validation. Additionally, this adjustment can also incorporate dummy variables to create a more comparable set of variables according to R18. Furthermore, based on this adjustment, the BD4SB project team should be able to estimate what the calibration possibilities are after the external validation to tailor the BD4SB CDSS to the UMCU environment.

4.12.1.3 Solution validation: Change registration protocols other hospitals

Another solution to the external validation barrier would be to change the way other hospitals register their data. If BD4SB algorithm is of such a high quality, it might persuade neonatology departments of other hospitals to change their registration protocols to the same as neonatology UMCU to utilize the BD4SB CDSS according to R18. However, this solution seems ambitious since there is registration inflexibility within healthcare due to high registration load as explained in section 4.4.2.

4.12.1.4 Solution validation: internal validation

According to R22, global clinical director notified body, it is also possible to bypass the external validation barrier by only validating the BD4SB algorithm internally.

- **R22:** *"If you only want to use internal data, then you have to constantly compare your internal dataset with the new external data to ensure that the internal dataset is still representative."*

However, this requires constant comparison of the internal dataset with the external dataset to ensure the internal dataset is representative of the whole population. This solution from R22 is considered reliable since R22 is an expert on clinical evaluations studies within the CE-approval process.

4.12.2 Validation Conclusion

Table 22: Laddering technique 'validation'

Attribute:	Validation
Barrier:	**4.12.1 External validation** *Respondents: R2, R11, R12, R13, R17, R18 and R20*
Solutions:	4.12.1.1 Create omnipotent model *Respondents: R12, R13 and R18*
	4.12.1.2 Predictor definition research & use dummies *Respondent: R18*
	4.12.1.3 Change registration protocols other hospitals *Respondent: R18*
	4.12.1.4 Internal validation *Respondent: R22*
Concept:	• Limited validation possibilities *The limited validation possibilities would be mitigated when creating an omnipotent model, executing a predictor definition research & using dummies, by changing registration protocols at other hospitals or only using internal validation*

It can be concluded that external validation is the preferred option and valuable for the legalization process, however, external validation is currently complicated for BD4SB CDSS since there is a difference between variables used between internal UMCU dataset and the datasets of other hospitals, however, there are four solutions: (1) create a omnipotent model with internal and externally used variables, (2) the variable differences among the datasets can be quantified by means of a predictor definition research, the resulting differences can be incorporated in the omnipotent model, (3) change registration protocols at other hospitals so they use the same variables as in the model, or (4) continuously compare the UMCU database to the whole population alongside the BD4SB CDSS utilization to ensure constant adequate representativeness of the internal UMCU dataset.

4.13 Impact (Implementing predictive algorithm attributes)

4.13.1 Impact barrier: High variability measurement points impact assessment study

An impact assessment study is part of the CER for the CE approval. This requires quantification of the effects of implementing the BD4SB CDSS within the healthcare process which is complex due to high variability of the measurement points. Firstly, it is not certain if the physician will act on the BD4SB

CDSS and intervenes (R18, methodologist UMCU), secondly, it is impossible to know if the event that initiated the CDSS takes place afterwards (R18), thirdly, the physicians might be more critical on the algorithm result when it is introduced versus a couple months later (R16, ethicist UMCU).

4.13.1.1 Impact solution: (Automated) registration forms

To minimize the variability of the measurement points within the impact study, a registration form should be applied according to R18, methodologist UMCU. This should show if, when, why and how the physician used the CDSS. However, as discussed in section 4.4.2, healthcare experiences a high registration load, hence is not highly acceptant of new registration forms. Therefore, R18 suggests obligating the registration form or even better, use already (automatically) registered variables. This solution is considered reliable since R18 is an expert on impact assessment research methods.

4.13.2 Impact conclusion

Table 23: Laddering technique 'impact assessment'

Attribute:	Impact assessment
Barrier:	**4.13.1 High variability measurement points impact assessment** *Respondents: R16 and R18*
Solution:	4.13.1.1 (Automated) registration forms *Respondent: R18*
Concept:	No matching concepts extracted from literature review

The impact assessment is part of the clinical evaluation within the CE approval process, hence it is pivotal to overcome this barrier. This can be partially done by means of (automated) registration forms to quantify the impact of the BD4SB CDSS on the healthcare process and measure the short and long-term effects.

4.14 Timespan implementation BD4SB

Besides discussion on the barriers for implementing the BDFSB CDSS, the respondents were questioned about the timespan for implementing the system. There is no real consensus for this prediction as exemplified by the following statements:

- **R7 (Healthcare director SAS):** *"If the software is there I believe this could be done in months."*
- **R17 (Business engineer developer CDSS):** *"Implementation within months is technologically possible."*
- **R15 (Managing partner, developer CDSS):** *"Implementation should be possible within two years if there is enough budget."*

The prediction for implementation from a technological perspective, R7 and R17, has a relatively short time span. This is probably the case since technological hurdles are often relatively easy to grasp and solvable according to R21, IT/ICT manager UMCU. R15, managing partner developer CDSS, reasons from a financial perspective and suggests two years for implementation. This study considers the two-

year implementation prediction more realistic since the following proceeding must happen before implementation: (1) the new authority routes in decision making study which takes a year and started in January of 2019, (2) external validation, (3) clinical evaluation study, and (4) CE approval process. More specifically, the METC requires the authority routes study before approving the clinical evaluation study. This clinical evaluation study also incorporates long term effects which implies that the study cannot be finished in months. All in all, it can be assumed that the minimum period before the BD4SB CDSS will be implement is approximately 2 years, most likely more.

4.15 BD4SB implementation plan

The BD4SB implementation plan consists of the stakeholders' barriers, proposed solutions and stakeholders path analysis.

4.15.1 BD4SB implementation plan within the analytical CDSS environment roadmap

Appendix F table 33, 34 and 35 provide an overview of all the solutions, with a required timespan for execution based upon the results of the empirical data, that need to be executed to implement the BD4SB CDSS by categorizing the to be executed solutions per stakeholder based on the stakeholder path analysis shown in Appendix E figure 46 – 56.

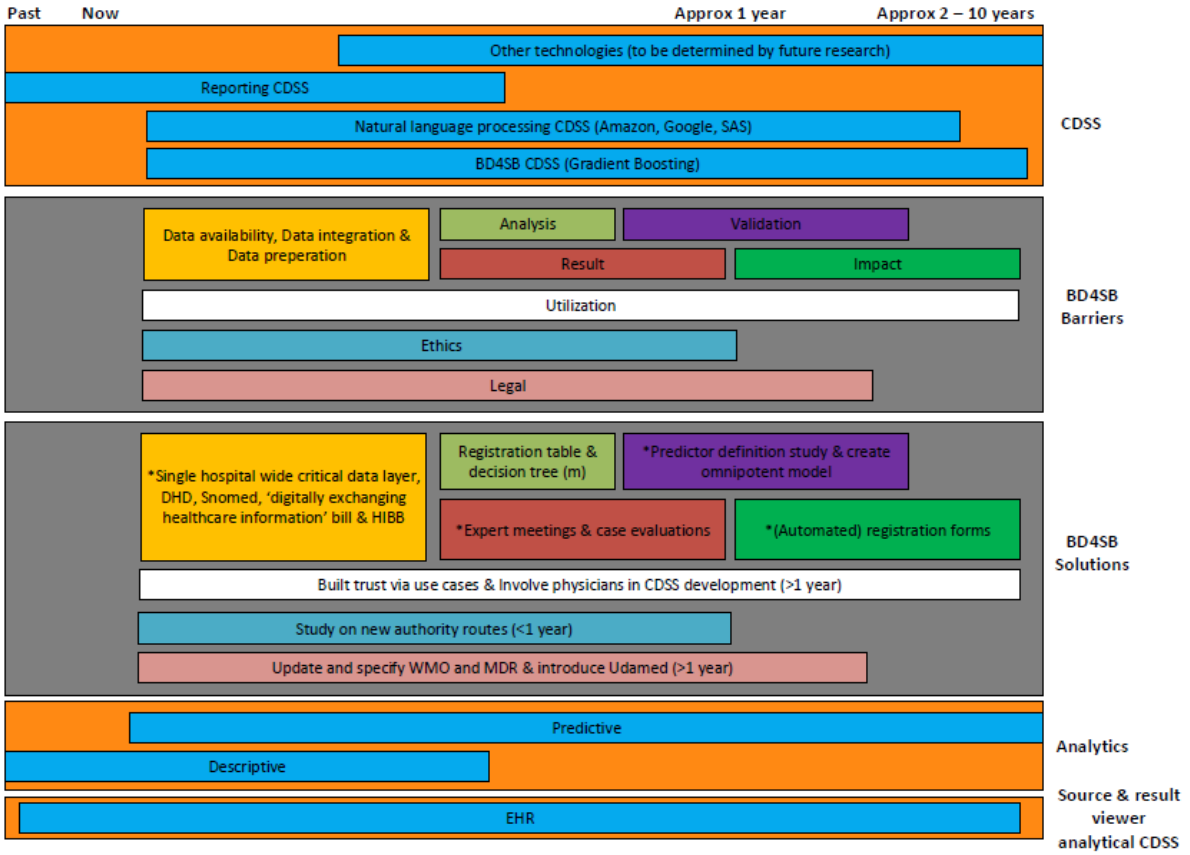

Figure 14: BD4SB barriers and solutions matched by color within the analytical CDSS roadmap

Figure fourteen shows the BD4SB stakeholders' barriers and solutions within the analytical CDSS environment roadmap. The solution and barrier layers are a summary of table 33, 34 and 35 from

Appendix F. Figure fourteen matches the stakeholders' barriers (summarized by the attributes) with the solutions by color and proposes a sequence for executing the solutions. This figure shows solutions that can be executed within months (m), less than a year (<1 year), more than a year (>1 year) or it remains unknown what times it takes to execute the solutions (*).

Based on the findings of this study, it can be concluded that the data availability, integration and preparation solutions should be executed first to enable analysis, produce a result, execute validation and the impact assessment for which all the accompanying solutions should be executed. Additionally, this study proposes to execute the legal, ethical and utilization solutions in parallel. Furthermore, the figure does not include the 'resource' attribute since this study found no solutions for this attribute.

4.15.2 Stakeholder path analysis

The results of the path analysis based on the to be executed stakeholders' solutions in Appendix F table 33, 34 and 35 are shown in figure fifteen. This section discusses which stakeholders have the most (time consuming) solutions to execute and are therefore most important for implementing an analytical CDSS as BD4SB.

Firstly, figure fifteen shows that the 'regulator' group, consisting of EU, notified body, CE-approval consultancy agency, Dutch Ministry of Healthcare, Sports and Welfare, NFU & Nictiz, has 7/10 solutions that will take more than a year to execute. Four of these seven >1-year solutions refer to specifying the MDR requirements, constructing the Udamed, update WMO and developing AI norms. These solutions must be executed by the European commission which makes it the most important member in the 'regulator' stakeholder group. The other members of the group must convert the 'digitally exchanging healthcare information' bill in to legislation, implement the HIBB or consult developers in CE approval process for analytical CDSS.

Secondly, the 'normal operator' concerning the UMCU physician neonatology is considered the second key stakeholder since this individual has ten solutions to execute from which two are executable within months. The physician plays an important role within the validation related solutions, should be involved in the analytical CDSS development process among which the expert meeting concerning the result format assessment of BD4SB and participate in the study on new authority routes within decision making with an analytical CDSS.

Thirdly, the figure indicates that the 'developers' group, containing SAS, Finaps and the UMCU IT department, has the most solutions to execute, however, from which 8/15 solutions are executable within months. Within this group, Finaps, developer of the BD4SB CDSS, has the most solutions to execute among which the validation related solutions (prediction definition research, creating an omnipotent model or bypass external validation by continuous comparison of the internal with external dataset to ensure required representativeness of the population) are considered most impactful. Furthermore, the UMCU IT also has an important role within the 'developers' stakeholder group with the construction of the single hospital wide critical data layer and implementation of HIBB.

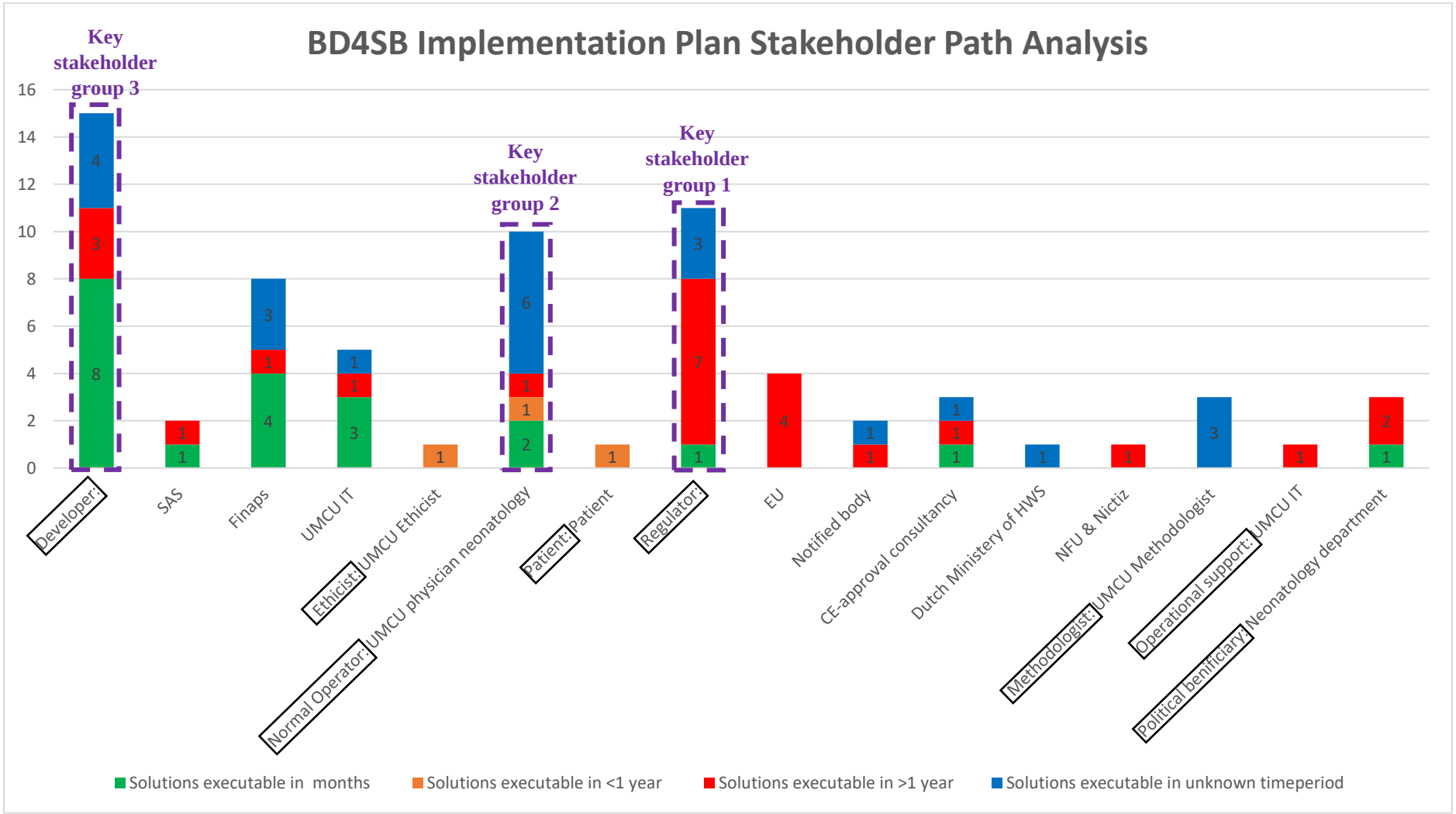

Figure 15: Results stakeholders path analysis; Purple boxes indicate the key stakeholders; Black boxes indicate the stakeholder groups which can consist of one or multiple members as stated after the ':' or on the right-hand side of the group indication

5. Conclusion & discussion

The chapter describes the conclusion, discussion and recommendations.

5.1 Conclusion

The developments concerning the appliance of analytics within healthcare have grown the past years. IBM claims to have created the new digital docter that is more accurate than the current human physician. Other organizations such as Apple, Google, Amazon and Microsoft are developing CDSS that can support the current physician. Several of these systems function upon analytics which is claimed to be the next best thing. Analytics could detect diseases, predict the development of the disease, identify deviation from preferred healthy state and changed disease directories (Mehta & Pandit, 2018). However, currently, healthcare has only seen improvement in quality of care by means of the more basic descriptive form analytics (Mehta & Pandit, 2018; Assante & Jacobs, 2016; Groves et al., 2013). There is an absence of evidence on the implementation of analytical CDSS with a form of more advanced analytics such as predictive analytics which is also incorporated in the BD4SB CDSS. It remains unclear what constitutes the analytical CDSS environment within the Netherlands and how an analytical CDSS such as BD4SB can be implemented within this environment. This study aimed to explore this phenomenon by means of the following research question:

"What are the stakeholders' barriers and possible solutions for implementing the 'Big data for small babies' clinical decision support system within the analytical clinical decision support system environment in the Netherlands?"

This chapter answers this research question by describing the most important outtakes of the analytical CDSS environment technology roadmap and the BD4SB implementation plan.

5.1.1 The analytical CDSS environment technology roadmap

5.1.1.1 **Creating awareness** of analytical CDSS

This study challenged the statement of Mehta & Bandit (2018) which implied that the current body of literature does not provide the adequate quantitative validation foundation healthcare needs for implementing analytical CDSS. This study confirms this statement since it determined that the implementation of analytical CDSS is very much within the embryonic stage. The implemented analytical CDSS in the Netherlands are very much within the descriptive stage, such as reports that describe historical patient information, and has not reached the predictive stage. Healthcare and IT related organizations are developing analytical CDSS at the predictive level, however, these systems remain in a R&D environment. Still, these projects show the possibilities of analytics and create awareness on the appliance of analytics among medical professionals and is a logical start for eventually implementing an analytical CDSS within the predictive level such as the BD4SB CDSS.

5.1.1.2 **Reinforcing** the foundation for analytics

This study found that mitigating several limitations apparent within the foundation for analytical CDSS concerning healthcare data can improve the implementation of analytical CDSS at a predictive level. This study examined the role and suitability of one of the most important HIS for analytics in healthcare, the EHR. This system provides data as input for the analytics and can display the results of an analytical CDSS, such as the BDFSB CDSS, to the physician. However, healthcare ICT developed independently from the EHR which resulted in integration issues that are also applicable to integrating analytical CDSS with the EHR (Michel-verkerke et al., 2015; Meyenhoefer et al., 2018). More importantly, this study found that the data quality (accuracy, consistency and completeness of the data) within the EHR is not from a preferred level required for implementing analytical CDSS.

This study proposes several improvements for the EHR that are important for implementing analytical CDSS. The Dutch minister of Healthcare, Welfare and Sports constructed a bill 'digitally exchanging healthcare information' to construct legislation which pleads for improving the integrability of HIS and uniform registration. This would improve the integrability and data quality within the EHR. These improvements can be realized by implementing HIBB, developed by the NFU and Nictiz, which give guidelines for uniform registration and improving integrability. Furthermore, there are other solutions available that can improve the data quality and integrability of healthcare information within the EHR such as the medical thesauruses (DHD) to standardize information, Snomed CT to code and share this information, and API's to enable integration of analytical CDSS with the EHR.

All in all, there are solutions available to reinforce the healthcare data foundation which is essential for implementing predictive analytical CDSS such as BD4SB.

5.1.1.3 **A look** into the future of analytics

The next step in analytics is obvious, from the current descriptive to predictive analytics, such as in the BD4SB CDSS. This study aimed to specify this evolution with a timespan and specific sequence of possible analytical CDSS to describe the change in the analytical CDSS environment. This study can only approximate the timespan for the transition from descriptive to predictive analytics at two years and most likely more. Furthermore, Metha & Pandit (2018) showed that there are numerous technologies applied within analytical CDSS such as machine learning, natural language processing, neural networks and image recognition. This study determined that CDSS incorporating these technologies remain within the R&D environment. Furthermore, giving a specific sequence for implementation these CDSS within the predictive analytics realm is not so obvious. The most robust outtake for a prediction of implementing a predictive analytical CDSS within the future is utilization of the most intuitive technology which would be a form of natural language processing. Organizations as Google, Apple and Amazon are developing these systems and have not been able yet to implement these, hence implementation of predictive analytical CDSS with natural language processing is also not so straightforward.

5.1.2 BD4SB implementation plan

The core of the emperical data of this study was focused on discovering the stakeholders' barriers and possible solutions for implementing BD4SB CDSS, a predictive analytical CDSS. This section shows the most important findings by discussing the barriers and solutions within three distinct steps to become clinically valuable for a predictive model, namely development, validation and impact (Hendriksen et al., 2013). Additionally, the key stakeholders extracted from the stakeholder path analysis concerning the execution of the solutions within the implementation are discussed.

5.1.2.1 Development

The development phase refers to the phase wherein the multivariable model is constructed (Hendriksen et al., 2013). To utilize the capabilities of predictive analytics, the velocity, the speed at which the data is obtained, stored, processed and analyzed, must be from a preferred level (Bedi et al., 2014). For BD4SB CDSS to be clinically valuable, it requires data from several sources to be available, integrated, prepared and analyzed within less than 24 hours which is currently not possible due to inappropriate IT structure of the UMCU. The proposed solution, a single hospital wide critical data layer would be able to integrate, prepare and make the data timely available as shown in figure twelve, this option is technically feasible, however, it remains questionable in which timespan this can be realized.

Within this datalayer, handling the veracity of the data is another important aspect which relates to assuring the quality (accuracy, consistency and completeness) of data in large dataset by data preparation (Sivarajah et al., 2017). This veracity hurdle is applicable to healthcare data in general as mentioned in section 5.1.1.2 and can be overcome by the implementing the HIBB, standardization (DHD thesaurus) and coding (Snomed) solutions which are supported by the 'digitally exchanging healthcare information' bill from the Ministery of Healthcare, Welfare and Sports.

When the BDFSB CDSS can utilize the single hospital wide data layer and execute the analytical process, the question remains in which format to present the result to the physician, as a percentage, number, red/green light or a notification at a certain threshold since each format affects the physicians' interpretation and therefore decision-making process differently. Interviews, expert meetings and case evaluations with several physicians can give a greater understanding on how each format affects the decision-making process and what the preferred format is.

Subsequently, when the result of the CDSS is available, it is up to the physicians if they will incorporate it within their proceedings. However, the physicians their right to exist consists of their knowledge which could be endangered by the introduction of an analytical CDSS such as the BD4SB CDSS in the eyes of the physician. Furthermore, the highly autonomous physician bears a high responsibility which results in slow acceptance and distrust in the BD4SB CDSS. This trust should be gradually obtained via showing the added value of incorporating BD4SB CDSS on retrospective cases to exemplify how it handles the case the physicians executed without the CDSS. Additionally, involving the physicans within the development process of these systems migitates the 'not developed by me'

syndrome which benefits acceptancy. These participating physicians should consist of technically and non technically savy ones to develop a CDSS that satisfies both parties' preferences.

When the physicians accept the BDFSB CDSS, it remains questionable how they will incorporate the third party alongside the patient's say within the descion making process. This shift in decision making proportions is considered an unkown phenomenon. This unexplored area can be clarified by a study on new authority routes within this decision making process with the physician and the patient, in the case of BD4SB, the parents of the premature born babies.

Next to the technical feasibility, utilization and exploring the influence on decision making, the BD4SB CDSS has to be CE approved as a medical device to enable implementation. However, current legislation for predictive algorithms is considered a grey area by developers, inspection e-health and notified bodies. Current legislation consisting of the WMO, for the clinical evaluation study (required for CE approval), and the WMH, for the CE approval process of medical devices, do not incorporate specific requirements for an analytical CDSS. The MDR, replacing the WMH, will be introduced in 2020 which will provide more specific requirements. However, the interpretation of this legislation is still being revised by workgroups within the European committee, hence the specific requirements are not definite. Furthermore, the Udamed, a European database containing all the documentation of CE approval processes of other medical devices, also software as a medical device, will become available to developers in 2020 which will give developers more reference points on how to prepare for and execute the CE approval process. Another possible solution to prepare for the CE approval process is to include a regulatory expert who is knowledgeable on the requirements within the new legislation and knows how to construct documentation required for the CE approval process of the notified bodies.

5.1.2.2 Validation

Another pivotal barrier for implementing the BD4SB CDSS, also relevant for the CE approval process, is the validation of the model/algorithm. According to Hendriksen et al. (2013), a model should be tested by means of a new external set of patient data with the same variables/performance measures. This external validation is preferred since models often perform poorer due to case-mix or domain differences. This study recognizes magnitude of external validation, however, the variables in the UMCU dataset that the BD4SB CDSS utilizes are not exactly like those of other hospitals, this complicates external validation. The proposed solution consists of executing a predictor definition study to determine how the internal and external datasets differ to determine to what extent the current BD4SB model must be adjusted, it might require creating an omnipotent model. After external validation, the omnipotent model can be calibrated to the UMCU dataset, however, this should not radically change the model as this will require new CE-approval since it is considered a different model/medical device.

Furthermore, it is also possible to bypass the external validation procedure by only validating the CDSS on internal data. However, this requires continuous comparison of the UMCU dataset with the external dataset to ensure that the UMCU dataset represents the population accordingly.

5.1.2.3 Impact

The impact phase requires a research by comparative designs with multiple datasets, preferably a RCT. The clinical proceedings and outcomes are compared with a control group not using the model, hence which applies usual care (Hendriksen et al., 2013). This study determined that the RCT is not the best option for the BD4SB CDSS since it is time consuming and does not allow changes in the model within the study which is required for the BD4SB CDSS. The impact study could incorporate other options as N=1 trials, clustered analysis or clustered trials which do allow changes in the model within the study.

Furthermore, the quantifying impact effect of the BDFSB CDSS on the healthcare process is complex since the measurement points are diffuse, it is not clear if the physician will act accordingly on the CDSS outcome, it is impossible to know if the event took place after the physician's intervention and the physician might be more critical on utilizing the CDSS when just introduced versus a couple months later. These quantification hurdles can be mitigated by obligating registration forms or even better, use available (automated) registration points from the healthcare process.

5.1.2.4 Key stakeholders

The ADAM projects at the UMCU determined that the physician, data scientist and patient are the key stakeholders within the development of analytical CDSS. This study found that this group definition is less optimal when the focus is on implementation instead of development. The stakeholder path analysis determines the following key stakeholder groups for implementing analytical CDSS: (1) 'regulator', (2) 'normal operator', the physician, and (3) the 'developer', among which the data scientist. These stakeholder groups have the most and/or time-consuming solutions to execute.

Firstly, the 'regulator' is the key stakeholder since the findings show that legislation is running behind. It seems that technology has surpassed current legislation. The European commission, notified bodies and Dutch Ministry of Healthcare, Welfare and Sports are currently making up lost ground by developing bills or implementing legislation for the CE approval process of medical devices and digitally sharing healthcare information. Secondly, the runner up key stakeholder is 'the normal operator', the physician, who must share his/her knowledge within the development of the CDSS and assess how he/she wants to incorporate CDSS within decision making. Lastly, the third key stakeholder group is marked as 'developer' consisting of the CDSS developer Finaps, SAS, and the UMCU IT department. This group must improve current data availability, integration, preparation and analysis of healthcare data to execute the CDSS process within the required timespan to be clinically valuable, for the BD4SB CDSS this is 24 hours.

Furthermore, the other stakeholder groups ('ethicist', 'patient', 'methodologist', 'operational support' and 'political beneficiary') have relatively few or quick executable solutions, hence are considered less as key stakeholders when compared to the 'regulator', 'normal operator' and 'developer'.

5.2 Discussion

The discussion section reflects on the findings of this study by a comparison with the available knowledge from the literature to assess what is confirmed, undervalued or undiscovered. Furthermore, this section describes the limitations of this study.

5.2.1 Contribution to the literature

5.2.1.1 Confirmation current analytical CDSS roadmap knowledge

The literature review on the analytical CDSS environment showed that: (1) healthcare currently utilizes descriptive analytics, (2) predictive analytics remains to be implemented and that (3) NLP is the most implemented technology within the analytics realm. This study confirms the first two findings and specified that NLP CDSS from organizations such as Google and Amazon remain in the R&D environment which suggests that NLP implementation is not so straightforward.

5.2.1.2 New analytical CDSS implementation knowledge

The barriers from literature, shown in table four, strongly focus on the technical aspect of implementing IT in healthcare with barriers related to compatibility, inaccuracy and inconsistency of the data or data structure & standardization issues. The new empirical results of this study confirm, specify and propose solutions to all these barriers, however, focused on analytical CDSS within the IT healthcare realm. The most pivotal barrier in literature and this study concerns compatibility which this study specifies with the EHR integrability hurdle and the inability of the BD4SB CDSS to integrate, prepare (ensuring data quality, hence the accuracy, consistency and completeness of the data) and analyze data from different sources within the required timeframe due to an inappropriate IT structure. Solutions proposed by this study related to compatibility are implementing the ‘digitally sharing healthcare information’ bill, HIBB, standardization (DHD) and coding & sharing (Snomed) solutions and a central data warehouse such as the single hospital wide critical data layer, figure twelve.

Furthermore, knowledge from literature also addresses the people aspect of implementing IT in healthcare with barriers related to user resistance, perceived usefulness, perceived ease of use and lack of skilled clinical scientist & managers to guide, process and interpret the outcome. The new empirical results of this study acknowledge, specify and propose solutions to these barriers. This study shows that there is user resistance from physicians because they are highly autonomous and bear a high responsibility which results in slow acceptancy and distrust in analytical CDSS. User resistance can be mitigated by means of involving physicians within the development of CDSS and showing the decision process of an analytical CDSS on the cases the physician handled in the past.

Next to these forms of barrier specification with the empirical findings, this study proves that there is an incomplete list of barriers within the literature of implementing IT in healthcare because all stakeholders’ perspectives are insufficiently incorporated. More specifically, this literature shows an absence or undervaluation of what this study calls the ‘peripheral business’ related barriers namely ethics and legal. This is also the case for validation and impact assessment related barriers. Firstly, the ethical

aspect remains undervalued by current literature, whereas, this study proves that a study on the ethical aspect of implementing CDSS is pivotal to obtain approval for a clinical evaluation study from the METC which is required for CE approval for analytical CDSS. Secondly, the legal aspect of implementing an CDSS as a medical device is undervalued in the implementing IT in healthcare literature whereas this study describes the barriers and proposes solutions related to the CE approval process for a CDSS as a medical device. Thirdly, within the literature review in table four, one reference mentions the barrier concerning limited validation options. This study shows that this barrier is undervalued since it is pivotal to execute external validation to detect shortcomings of a model, however, external validation is complicated due to differentiating datasets among hospitals. Proposed solutions are executing a predictor definition research and creating an omnipotent model. Fourthly, the implementing IT in healthcare literature does not show impact assessment related barriers such as, discovered by this study, the discussion on the inappropriateness of the RCT and the complexity of quantifying the measurements in the impact assessment study or measuring the incorporation of an analytical CDSS in decision making of a physician.

All in all, the findings of the BD4SB implementation plan contributed the following to the current literature: (1) solutions for and specifications of the known technical and people related barriers and (2) solutions for and specification of the absent or undervalued barriers related to legal, ethics, validation and impact assessment.

5.2.2 Limitations of the research

5.2.2.1 Analytical CDSS environment roadmap still a sensitizing concept

This study set out to discover and describe the analytical CDSS environment by means of a technology roadmap which describes the context of the BD4SB implementation plan. Current literature does not provide such an artefact and this study aimed to construct it by means of two particularly broadly asked sub questions: SQ1: ‘What analytical CDSS are currently implemented in the Netherlands?’ and SQ2: ‘What analytical CDSS will be implemented in the Netherlands in ten years?’’. These questions were intentionally broadly stated and not linked to a specific specialty in healthcare or other sort of demarcation of research context because preliminary investigation showed a lack of evidence on implementation of analytical CDSS as a medical device worldwide. Specific demarcation of the context of this analytical CDSS environment roadmap would have limited the research context of the analytical environment roadmap too much, however, this minimal demarcation also resulted in a generic artefact.

Within this roadmap, this study intended to clearly describe the current and future situation of the analytical CDSS environment with all the steps in between by means of layers concerning the type of analytics and the specific CDSS. However, this plan turned out to be too ambitious since the empirical data did not provide a thorough specification of the components within these layers. Therefore, the final version, concerning the orange layers in figure fourteen, of the analytical CDSS environment technology roadmap is considered as a sensitizing concept, hence an indefinite version. However, this version of

the roadmap is still considered as a valuable representation of the current analytical CDSS environment since it was partially based on interviews with respondents from e-health inspection and a notified body which both have a pivotal role in legalizing and monitoring analytical CDSS categorized as medical devices, hence are profoundly acquainted with the current and future implementation of analytical CDSS.

5.2.2.2 Timespan and sequence solutions limitation

This study aimed to sequence the solutions for the stakeholders' barriers by means of the approximated time required for executing the solutions. However, several solutions could not be provided with such a timespan prediction because the respondents could not give an indication. These solutions are provided with an undetermined timespan for execution notification. Providing all the solutions with a timespan for execution would have made the analysis more valuable. Still, the current sequencing of the solutions and stakeholder path analysis provides a greater understanding on how to move towards implementation.

5.2.2.3 Reliability

This study selected the respondents within the described stakeholder group literature review from section 1.3.2. The respondents per stakeholder group often consisted of one respondent such as a methodologist or ethicist, which raises the question if some results of this study are reliable since they are based upon a single person's frame of reference. Therefore, this study assessed the expertise of the respondent on the subject and, if possible, triangulated the results by means of other data sources to ensure reliable results as much as possible. Furthermore, the units of observation in this study are considered representative for the units of analysis because a relatively small portion of the healthcare and IT professionals are involved in or aware of analytical CDSS implementation. I believe that the qualitative research with twenty-three respondents, consisting of eighteen interviews and five attended presentations, is substantial and provides the required reliability for this study.

5.2.2.4 Absence of the patient

The stakeholders group literature review determined that the patient is a stakeholder within the implementation process of analytical CDSS. Within the BD4SB CDSS case, the physician applies the CDSS within the healthcare process of the patient. Firstly, the physician must accept and trust the BD4SB CDSS to such an extent that he/she is willing to apply it within the healthcare process. Subsequently, the question remains if the patient accepts if the physicians' decision-making process is supported by an analytical CDSS such as BD4SB. Within the case of neonatology, the frame of reference of the parents of the patient would have added value to this study. More specifically, the concept of 'shared decision making', hence when physicians and patients collaborate in decision making enables the patient to have more say in his/her treatment, is becoming more popular according to R16, ethicist UMCU. However, this study was not able to incorporate this patient perspective because the researcher could not reach such a respondent and was limited by the time span of this study.

5.3 Recommendations & future research

Based on the findings in this research, the following recommendations are made to can benefit the implementation process of a predictive analytical CDSS such as BD4SB:

1. Use the analytical CDSS environment roadmap as a guideline for development, it shows the current and future state of analytics, what aspects of the healthcare data foundation need reinforcement and that NLP will most likely be in the next implemented CDSS.
2. Use the BD4SB implementation plan in communication with stakeholders. This plan shows thorough reasoning on implementing analytical CDSS from each stakeholders' perspective. The incorporation of each stakeholders' frame of reference seems to be vital in moving forward in the complex environment of implementing an analytical CDSS. In the past, the focus was more on development by only the developer instead of implementation with all stakeholders, this resulted in that the technological proceedings surpassed the legal and ethical required proceedings.
3. The requirements for analytical CDSS as a medical device are specified in the legislation of 2020. However, developers can be proactive by including a regulatory expert or regulatory consultancy agency within the CDSS R&D team to align the analytical CDSS with the new requirements.
4. Ethicists should also be involved within the development process because now they are lacking contextual knowledge and did not to study the impact of analytical CDSS on the physicians' decision making. UMCU has initiated a study on new authority routes within decision making that could have been initiated in an earlier stage if ethicists were more involved in CDSS development.
5. Data quality (accuracy, consistency and completeness) of healthcare data is from an unfavorable level. Data quality is a prerequisite for enabling predictive analytics. Improvements should start with the EHR, which is currently implemented at all hospitals, however, the next step is to ensure appropriate data quality in the EHR across hospitals. Guidelines for registration in the HIBB are supported by the 'digitally sharing healthcare information' bill and should be vindicated by the Dutch government organizations as NFU to accelerate improvements related to data quality.
6. Compatibility is a problem in healthcare, different HIS within or among hospitals complicate timely data collection, integration, preparation and analysis for analytical CDSS. There are solutions such as HIBB, API's, standardization (DHD) and coding & sharing (Snowmed) supported by the legislation mentioned in point five, again, implementation of these solutions should be vindicated.

Future research should focus on:

1. The analytical CDSS environment roadmap remains a sensitizing concept. It could be improved by empirical research with a larger and different pool of respondents, preferably outside the UMCU, with a health and advanced analytics profession.
2. This study focuses on implementing analytical CDSS, however, used available literature on implementing IT in healthcare and found that this literature focuses strongly on the technical and people aspect of implementing IT. Future research should focus more on the ethical, legal, validation and impact assessment aspects of this implementation process. More importantly, it should focus on combining these aspects to provide an in-depth overview of the implementation process. This can be executed by starting with a literature review assessing the specific fields of literature on ethics, legal, validation and impact assessment within a single study. Furthermore, this theoretical approach can be supported by an empirical study focused on stakeholders with expertise in ethics, legal, validation and impact assessment to further specify the available knowledge from the literature review.

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Appendix

Appendix A: SAS

SAS started as a project called ‘statistical analysis system’ (SAS) started in 1966 in North Carolina. Nowadays it is a company that supplies analytics software and has 165 offices in 58 countries, from which the headquarters is located in Cary, US. Furthermore, it has 14052 employees and $3.2 billion in revenue as of 2016. Its vision is to transform the world of data into a world of intelligence. SAS envisions a world where everyone can make better decisions, grounded in trusted data and assisted by the power and scale of SAS analytics. When decisions happen at just the right moment, advancements are set in motion and the word moves forward. Additionally, SAS its mission is to empower and inspire with the most trusted analytics.

Appendix B: Literature review

In each industry, artificial-intelligence demand will depend on market size, pain points, and willingness to pay.

	Market size	Pain points		Willingness to pay
	Global industry size, $ trillion	Artificial intelligence (AI) use cases, #	Start-up equity raised,[1] $ billion	Average AI economic impact,[2] %
Public & social sector	25+	50+	1.0+	5–10
Retail	10–15	50+	0.5–1.0	5–10
Healthcare	5–10	50+	1.0+	15–20
Banking	15–25	50+	1.0+	<5
Industrials	5–10	50+	0.5–1.0	10–15
Basic materials	5–10	10–30	<0.5	15–20
Consumer packaged goods	15–25	10–30	0.5–1.0	5–10
Automotive & assembly	5–10	10–30	0.5–1.0	10–15
Telecom	<5	30–50	<0.5	20+
Oil & gas	5–10	30–50	<0.5	<5
Chemicals & agriculture	5–10	10–30	<0.5	5–10
Pharmaceuticals & medical products	<5	10–30	<0.5	20+
Transport & logistics	5–10	30–50	<0.5	5–10
Insurance	<5	30–50	<0.5	15–20
Media & entertainment	<5	10–30	<0.5	15–20
Travel	<5	10–30	<0.5	5–10
Technology	<5	10–30	<0.5	10–15

[1]For cross-industry start-ups, equity amount was assumed to be distributed based on global industry size.
[2]Economic impact is the sum of value related to all use cases divided by global industry size.

Figure 16: AI potential per industry (Batra et al., 2018)

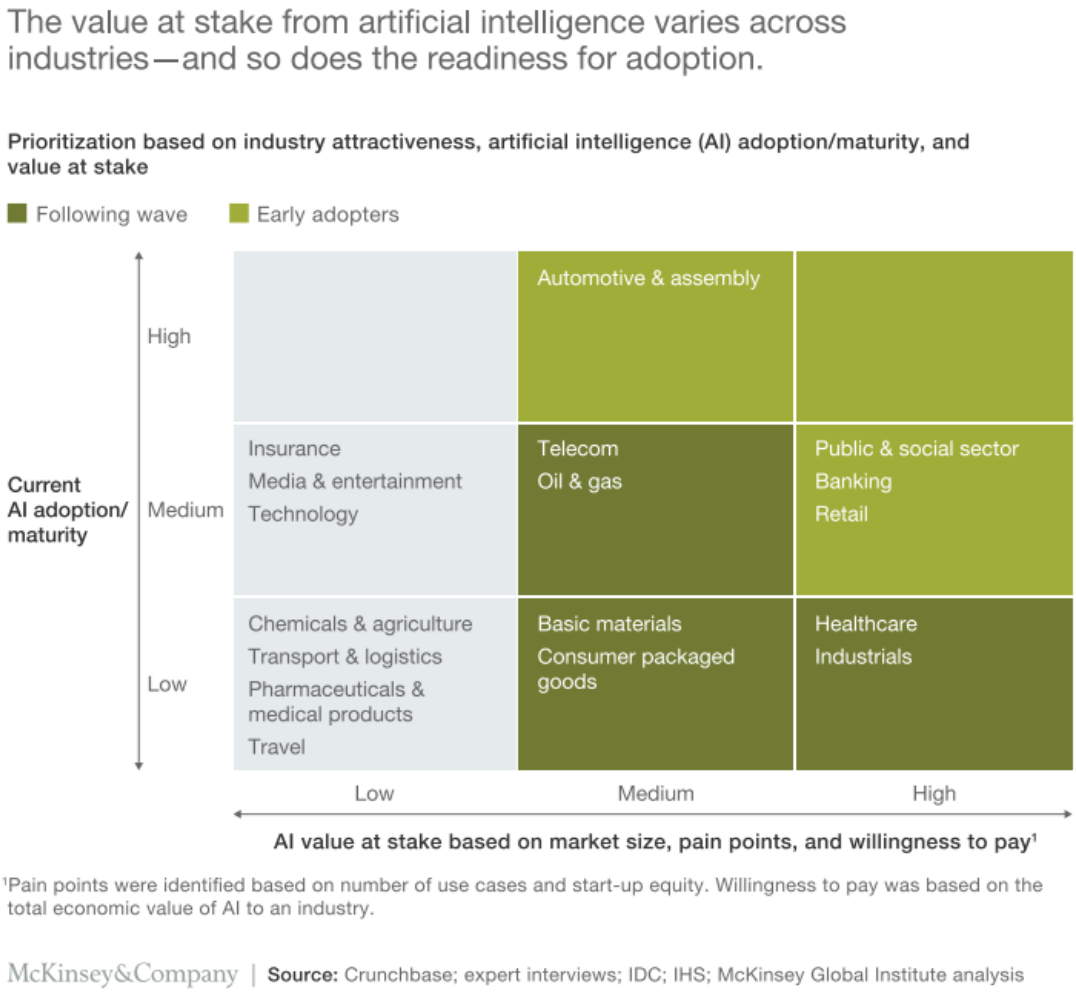

Figure 17: AI potential per industry (Batra et al., 2018)

Table 24: Measures of key constructs TAM part one (Holden & Karsh, 2010)

Table 4
Measures of key constructs use by reviewed studies.

Construct	Measurement dimensions of construct	Studies using measure
Perceived usefulness	Useful for job (or task)	[32,96,97,99,100,103,104,106,107,109]
	Increases productivity	[32,96,97,100,103,106–108]
	Enhances effectiveness of job (or work)	[32,96,97,99,104,106,107,109]
	Allows tasks to be accomplished more quickly	[32,99,100,106–108]
	Improves job performance	[99,103,104,107,109]
	Makes it easier to do job/work	[32,100,106,107]
	Increases quality of care	[97,106]
	Increases quality of work	[106]
	Improves work efficiency	[103]
	Allows tasks to be done more accurately	[104]
	Allows tasks to be done more objectively	[104]
	Supports critical aspects of job	[96]
	Increases chance of getting a raise	[108]
	Allows greater control over work	[106]
	Enables decisions based on better evidence	[104]
	Improves patient care and management	[32]
	Not enough information on measurement	[98,101,102,105,110]
Perceived ease of use	Easy to use	[32,97,99,100,103,104,106,108]
	Clear and understandable	[32,96,97,99,103,104,107,108]
	Easy to become skillful with system	[32,100,104,106–109]
	Easy to get it to do what you want it to	[32,96,97,99,104,106,109]
	Easy to learn to operate	[32,104,107–109]
	Flexible to use/interact with	[32,100,104,106]
	Low mental effort	[96,97]
	Easy to do what I want	[103,107]
	Easy to do tasks with system	[96]
	Clear	[106]
	Understandable	[106]
	Does not demand much care and attention	[103]
	Navigation is easy	[107]
	Easy to remember how to perform tasks with system	[99]
	Not enough information on measurement	[98,101,102,105,110]

Table 25: Measures of key constructs TAM part two (Holden & Karsh, 2010)

Social influence/subjective norms	Pediatricians who influence my behavior think I should use system	[97]
	Pediatricians who are important to me think I should use system	[97]
	People who influence my behavior think I should use system	[108]
	People who influence my clinical behavior think I should use system	[49]
	People who are important to me think I should use system	[108]
	People whose opinions I value think I should use system	[99]
	People who are important to my health care services think I should use system	[49]
	People who are important in assessing my patient care and management think I should use	[49]
	Senior management of hospital has been helpful	[108]
	Hospital supported use of system	[108]
	Colleagues who are important to me think I should use system	[99]
	Superiors at work think I should use system	[99]
	Subordinates at work think I should use system	[99]
	Not enough information on measurement	[102,105,110]
Perceived behavioral control/facilitating conditions	Have necessary resources to use system	[49,99,108]
	Have knowledge to use system	[49]
	Compatibility with other systems	[108]
	Availability of technical assistance	[108]
	Able to use system at work	[99]
	Able to use system for patient care and management	[49]
	Using system at work is wise	[99]
	Using system entirely under my control	[49]
	Not enough information on measurement	[102,105,110]

Table 26: Definitions constructs TAM (Holden & Karsh, 2010)

Perceived usefulness	Perception that using system leads to enhanced personal performance (original TAM definition [39,40])	[96,99–101,103,104,106,107,109]
	Perception that using system will help user attain gains in job performance (UTAUT definition [51])	[108,110,111]
	No formal definition given	[32,97,98,102]
Perceived ease of use	Perception that using system will be free from physical or mental effort (original TAM definition [39,40])	[96,99–101,103,104,106,107,109]
	Perception of the degree of ease associated with using system (UTAUT definition [51])	[108,110,111]
	No formal definition given	[32,97,98,102]
Social influence/subjective norms	Perception of important (or relevant) others' beliefs about person's use of system (TAM2 [50], UTAUT [51], and TPB [42] definition)	[49,97,99,108,110,111]
	No formal definition given	[102]
Perceived behavioral control/facilitating conditions	Perception that organizational and technical infrastructure exists to support using system (UTAUT definition [51])	[108,110,111]
	Perception of internal and external resource constraints on performing behavior (adaptation of TPB [42] definition)	[99]
	Perception of availability of skills, resources, and opportunities necessary for using the technology (adaptation of TPB [42] definition)	[49]
	No formal definition given	[102]

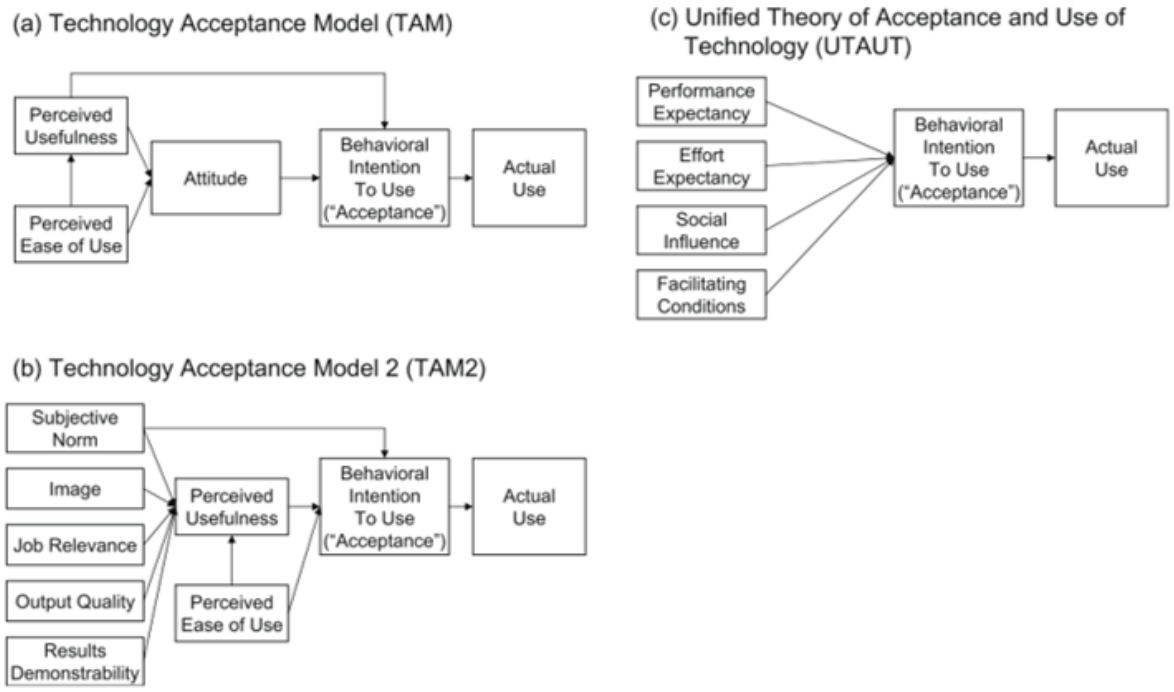

Figure 18: The evolution of technology acceptance model (Holden & Karsh, 2010)

Table 27 Inhibiting factors implementation HIS (Sligo et al., 2017)

Inhibiting Factor	References
User resistance	Gagnon [3], Hendy et al. [169], Rivard and LaPointe [170], Takian et al. [168]
Poor quality technology	Ancker et al. [165], Lorenzi and Riley [162], Powell-Cope et al. [166]
Organisational inflexibility and/or instability	Avison [21], Ellingsen and Monteiro [57], Harrison et al. [92], Kaplan and Salamone [163]
Lack of 'fit' between social, technological and organisational domains	Ammenwerth et al. [129], Cresswell and Sheikh [10], Tsiknakis and Kouroubali [39] Robert [30]

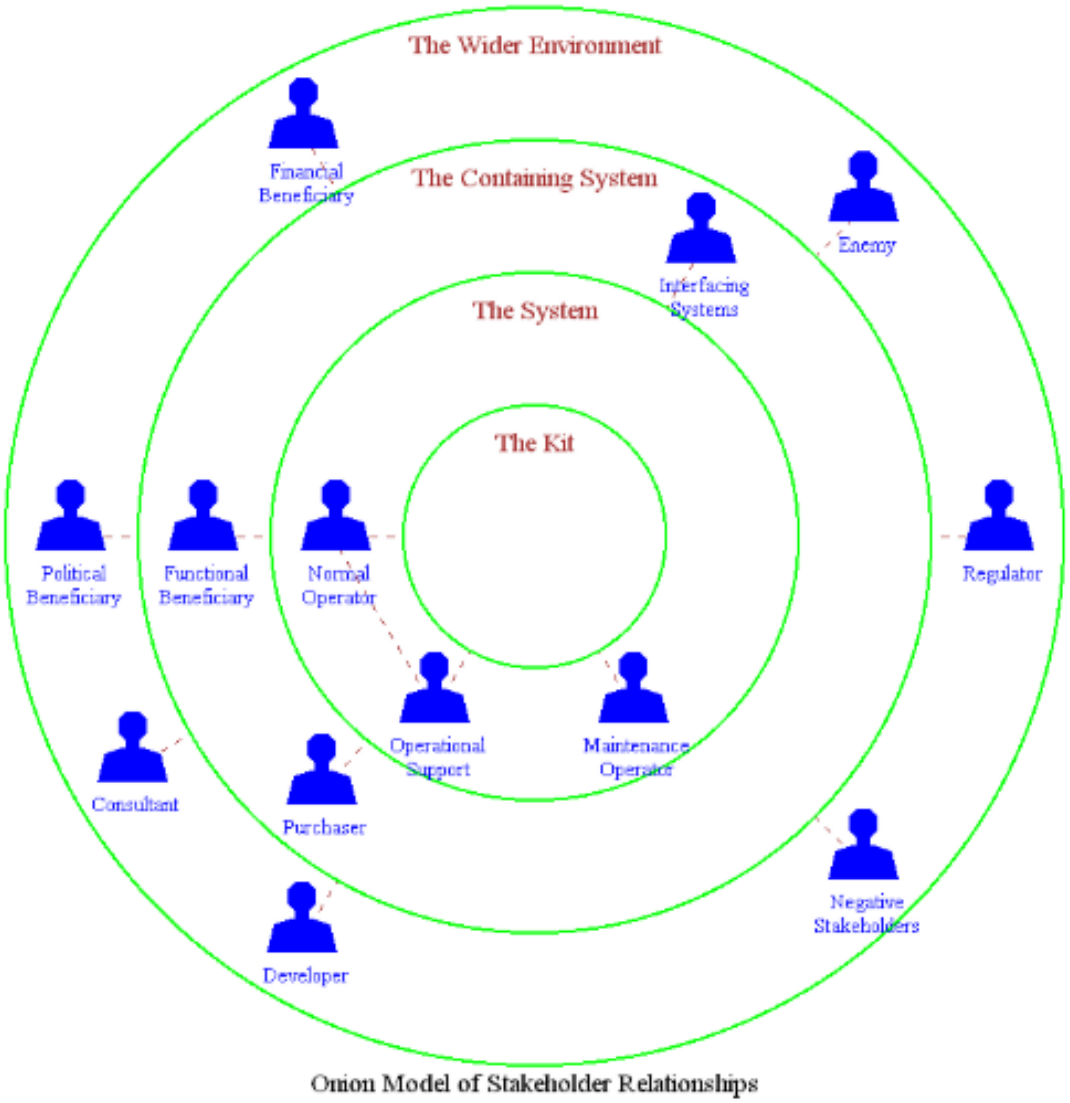

Figure 1: Onion Diagram of Product Stakeholders

Figure 19: Stakeholders within the development of information systems (Alexander, 2005)

Table 28: Stakeholders within the development of information systems part 1 (Alexander, 2005)

Onion Model tailored for Volere	All 37 Stakeholder roles defined in Volere.co.uk template	Volere Row No.
The Wider Environment		
Financial Beneficiary	— *none* —	
Negative Stakeholder		
	Opponents of project/product	38
	Public Opinion	41
Developer		
	Packaging Designer	28
	Manufacturer	29
	Project Management	32
	Business Analysts	33
	Requirements Engineers	34
	Technical Designers	35
	Technical Systems Architect	36
	Organisational Architect	37
	Testing Specialists	42
Consultant		
	Business/Subject Experts	11
	Future Ideas Specialists	12
	Current System Specialists	13
	Sales Specialist	17
	Marketing Specialist	18
	Aesthetics Specialist	19
	Graphics Specialist	20
	Usability Specialist	21
	Safety Specialist	22
	Security Specialist	23
	Cultural Specialist	24
	Legal Specialist	25
	Environmental Specialist	26
	Standards Specialist	40
	Financial Specialists	44
	Negotiation Specialists	45
Regulator		
	Auditors	43
Political Beneficiary	— *none* —	

Table 29: Stakeholders within the development of information systems part 2 (Alexander, 2005)

Interfacing System	— *none* —	
Purchaser		
	Customer	10
Functional Beneficiary		
	Client	9
Champion / Sponsor		
	Protectors of Project/Product	39
Our System		
Maintenance Operator		
	Product Installer	30
	Maintenance Specialist	27
Normal Operator		
	Clerical User	14
	Technical User	15
	Potential User	16
Operational Support		
	Training Staff	31

Table 30: Stakeholders checklist (Panyard et al., 2018)

Health System IT
- ☐ Decision support team
- ☐ Ambulatory team
- ☐ Orders team (inpatient)
- ☐ Results team
- ☐ Clinical documentation team
- ☐ Outpatient department team
- ☐ Radiology team
- ☐ Imaging warehouse team
- ☐ Cardiology team
- ☐ Anesthesiology team
- ☐ Surgery team
- ☐ Medication team
- ☐ Patient portal team
- ☐ Patient identification team
- ☐ Health information team
- ☐ Coding team
- ☐ Long-term & home health team
- ☐ Internal messaging team
- ☐ Hospital billing team
- ☐ Physician billing team
- ☐ Interface team
- ☐ Network team
- ☐ Security team
- ☐ Environment manager
- ☐ Server team

Health System Administration
- ☐ Ambulatory/inpatient leadership
- ☐ Clinical division/department chair
- ☐ Clinician champions
- ☐ Pharmacy leadership group
- ☐ CMIO/clinical informatics
- ☐ Purchasing director
- ☐ Medical board/delegation
- ☐ Health system legal team
- ☐ Clinic staffing manager
- ☐ IT resource allocation group

Reporting
- ☐ Reporting team

Training
- ☐ System education/training team

Other Health System Teams
- ☐ Laboratory

External
- ☐ Community health partner

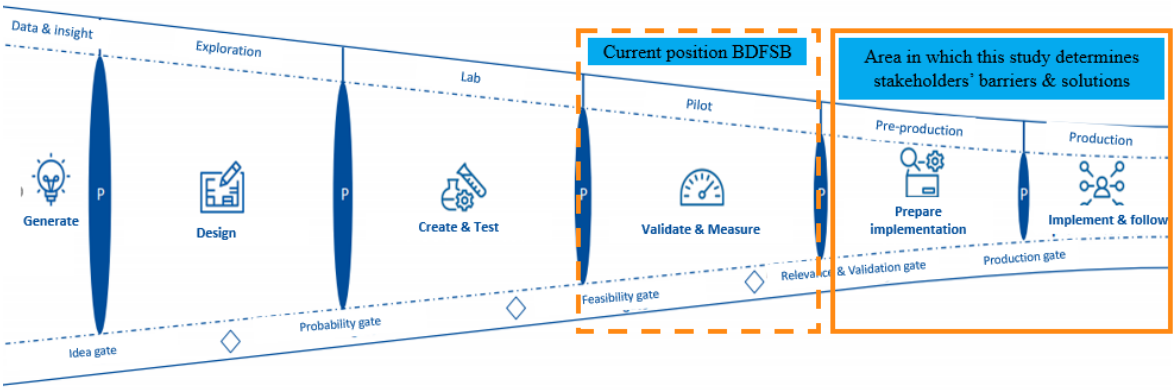

Figure 20: Implementation plan BD4SB within innovation funnel UMCU

Appendix C: Coding Schemes

The respondent numbers used in the text differ from those within the coding trees in this section since the results of several respondents' presentations that were initially incorporated turned out to be invaluable for this study and were eliminated from the results. This elimination of several respondents interrupts the consecutive numbering of respondents. Table 31 is a conversion table which shows the consecutive numbering used in the text and the numbering used within the coding trees visualized in this section.

Table 31: Respondent number conversion table to coding schemes

Respondent number in text	Respondent number in coding trees	Respondent description:
R1	R2	Ex chairman of the board of AMC, ex-internist & CEO hospital cluster, University College London Hospitals
R2	R4	Ambassador e-health & big data and director ADAM, UMCU
R3	R5	Business development manager EHR data platform, CERNER
R4	R6	Physician and clinical owner BDFSB, UMCU
R5	R7	Professor & education director health informatics hospital, AMC
R6	R8	Physician and clinical director, Vitaalpunt
R7	R11	Healthcare director, SAS
R8	R12	Senior technical consultant, SAS
R9	R13	System engineer healthcare, SAS
R10	R14	Ex-physician and senior sales executive healthcare, SAS
R11	R15	Ex-physician and data scientist, UMCU
R12	R17	Physician and clinical owner BDFSB, UMCU
R13	R18	Program manager ADAM, UMCU
R14	R19	CEO business intelligence organization healthcare, Vektis
R15	R20	Managing partner CDSS developer, Finaps
R16	R21	Ethicist and member medical ethical commission, UMCU
R17	R22	Business engineer developer BDFSB CDSS, Finaps
R18	R23	Methodologist UMCU
R19	R24	Inspector e-health, inspection healthcare and youth Dutch government
R20	R25	Ex-physician and analytics entrepreneur
R21	R26	IT/ICT manager, UMCU
R22	R27	Clinical CEO notified body, Dekra
R23	R28	Projectmanager 'registration at the source', national federation academic hospitals (NFU)

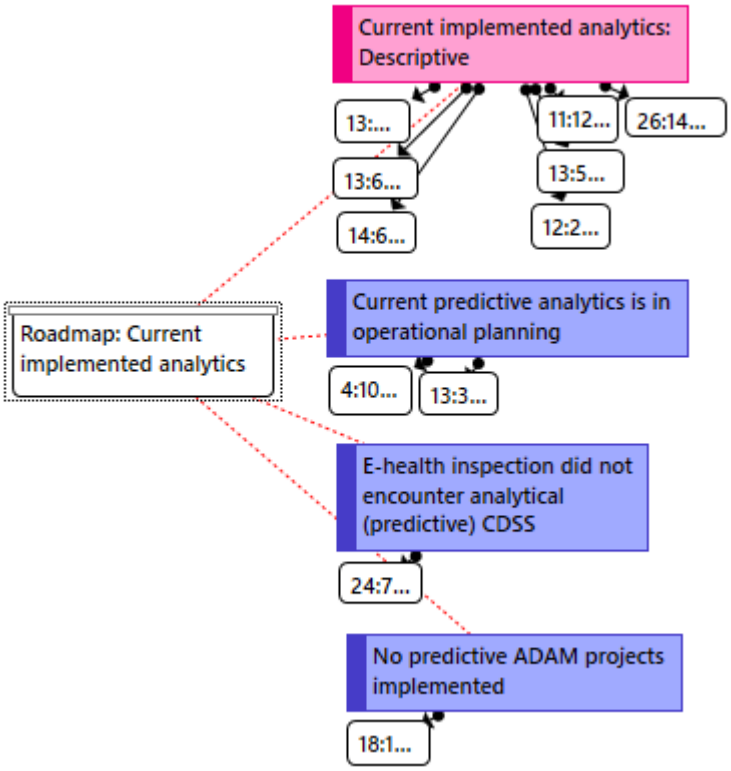

Figure 21: Coding scheme 'current implemented analytics'

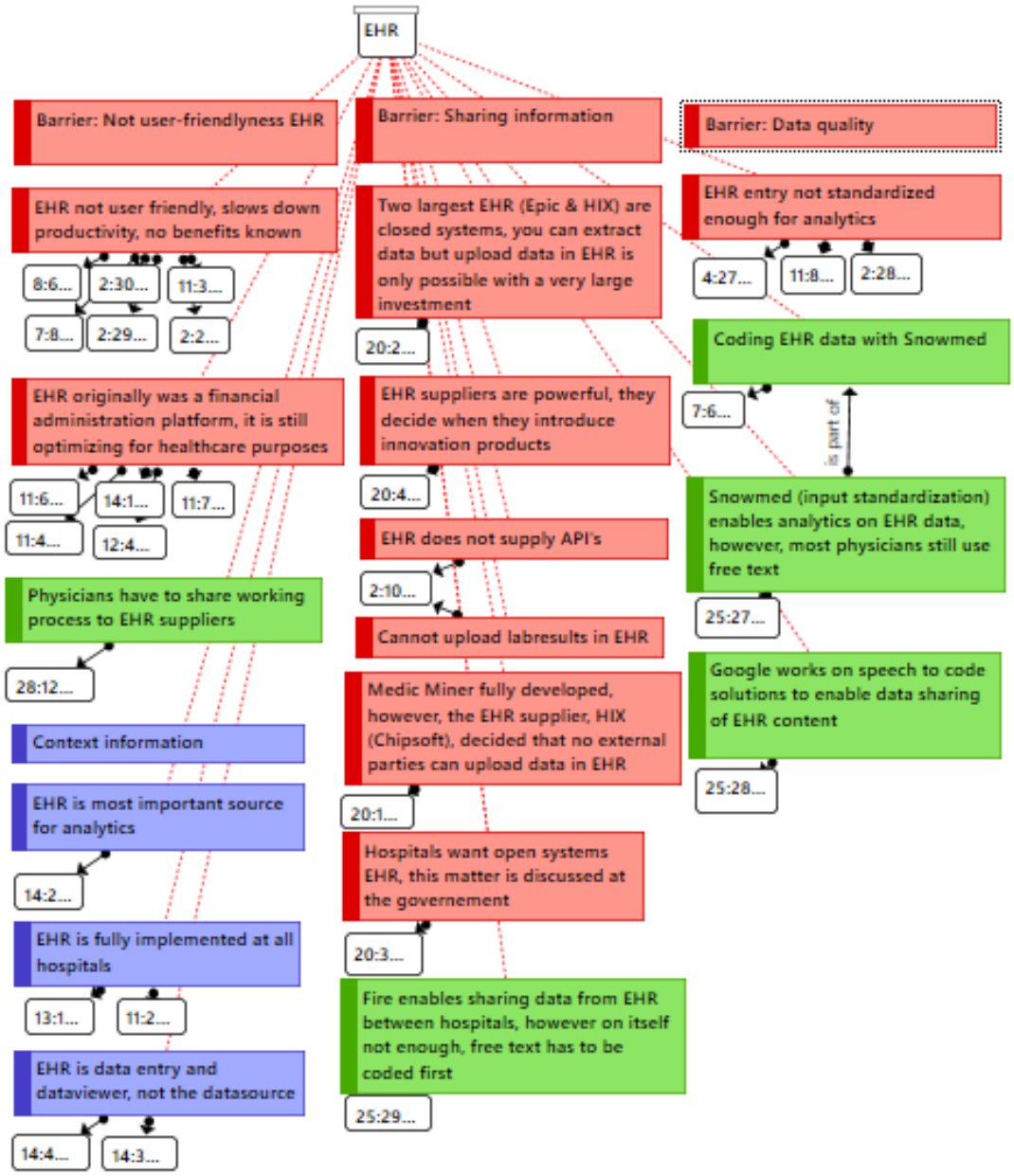

Figure 22: Coding scheme 'EHR utilization for analytical CDSS barriers & solutions'

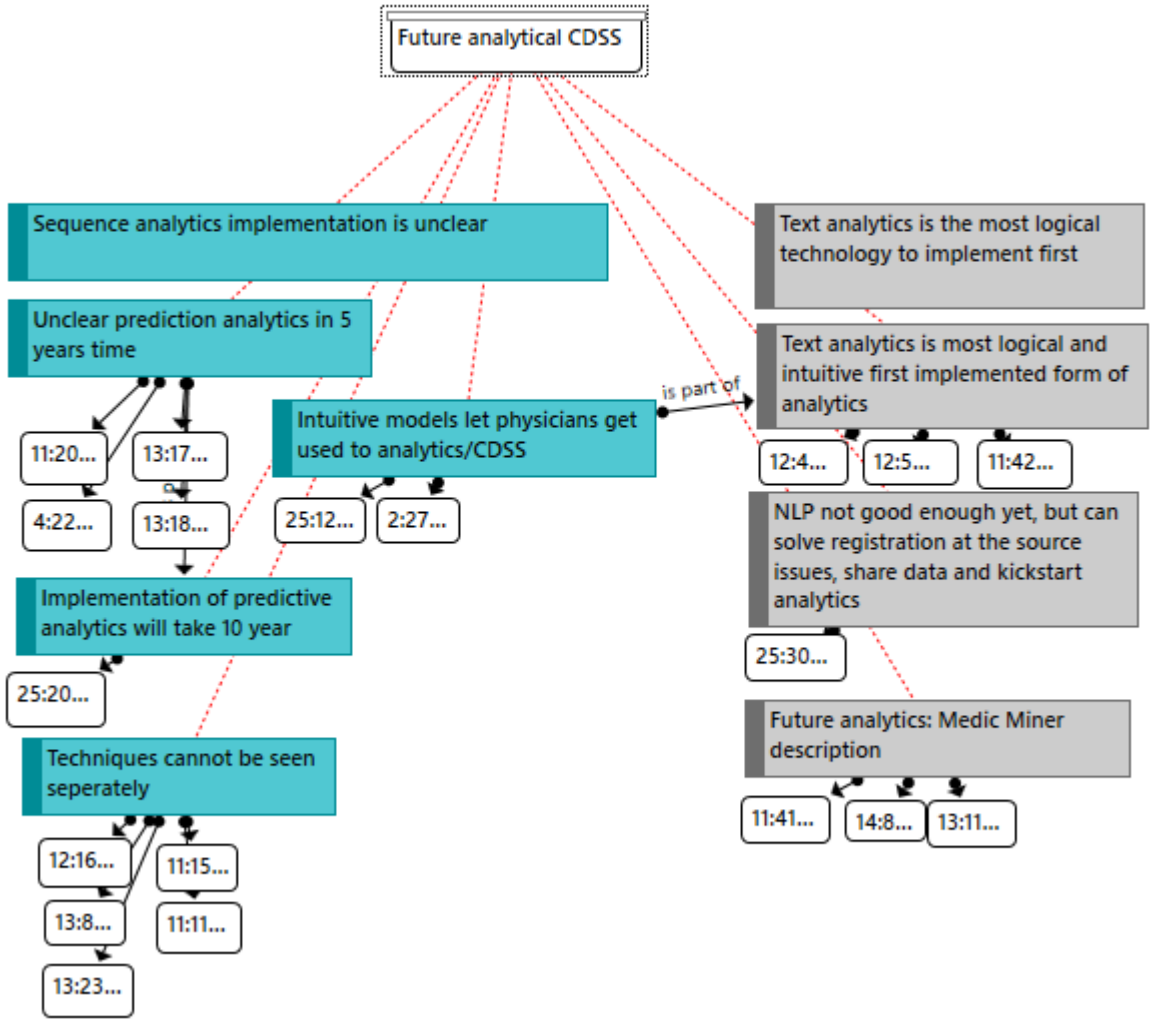

Figure 23: Coding scheme 'future analytical CDSS'

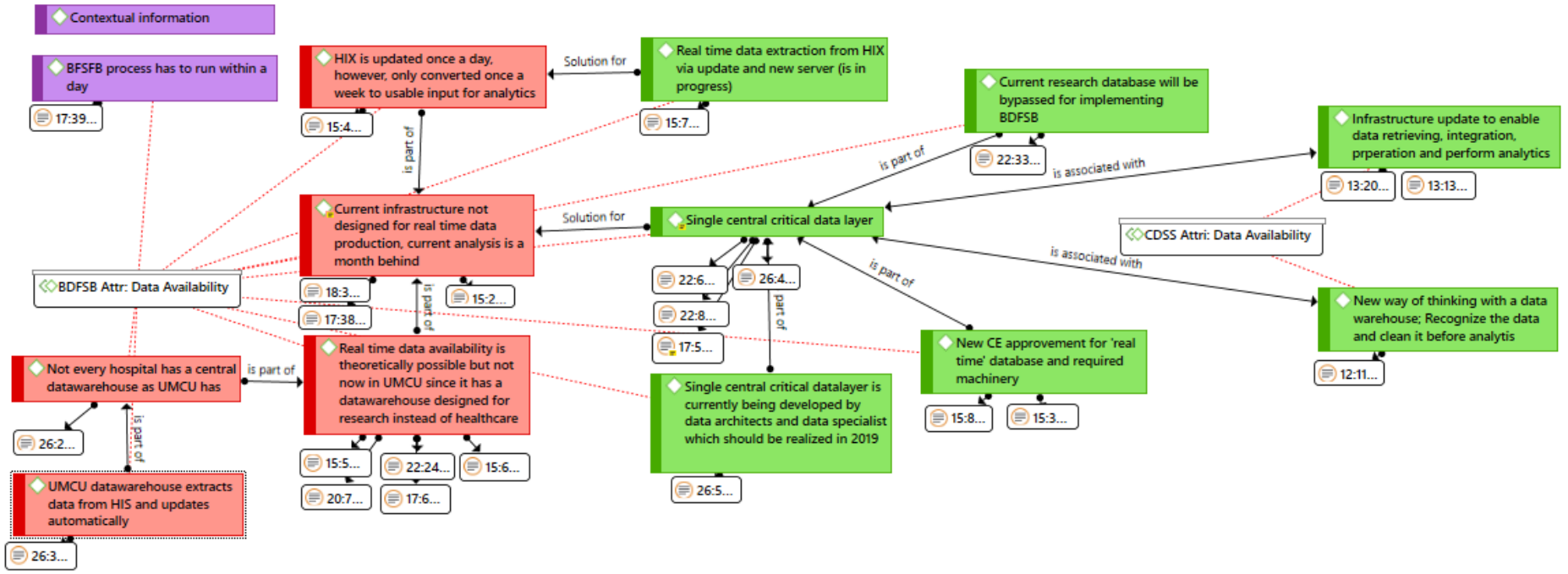

Figure 24: Coding scheme barriers & solutions 'data availability'

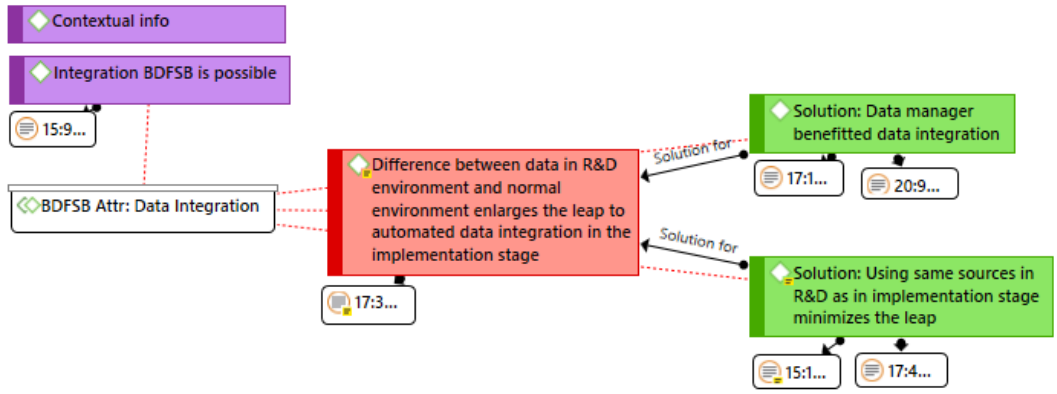

Figure 25: Coding scheme barriers & solutions 'data integration' BD4SB

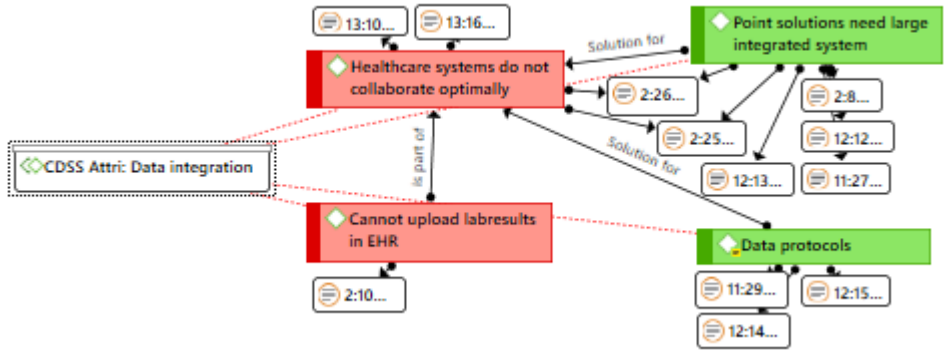

Figure 26: Coding scheme barriers & solutions 'data integration' non-BD4SB

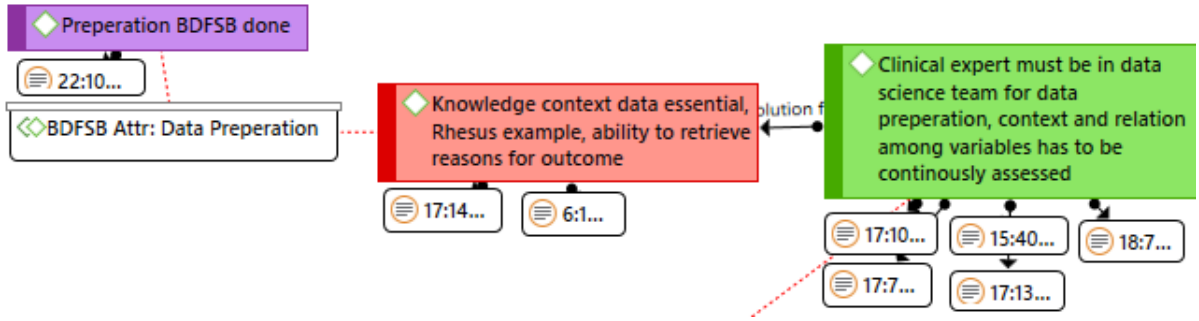

Figure 27: Coding scheme barriers & solutions 'data preparation' part 1

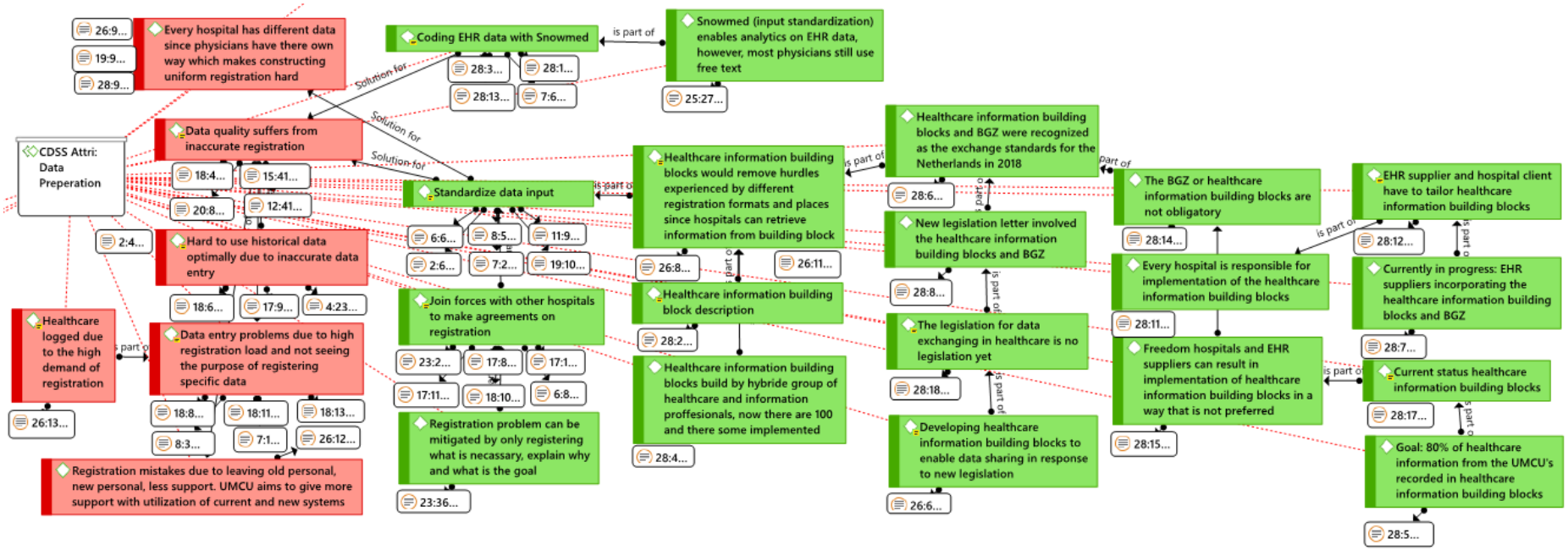

Figure 28: Coding scheme barriers & solutions 'data preparation' part 2

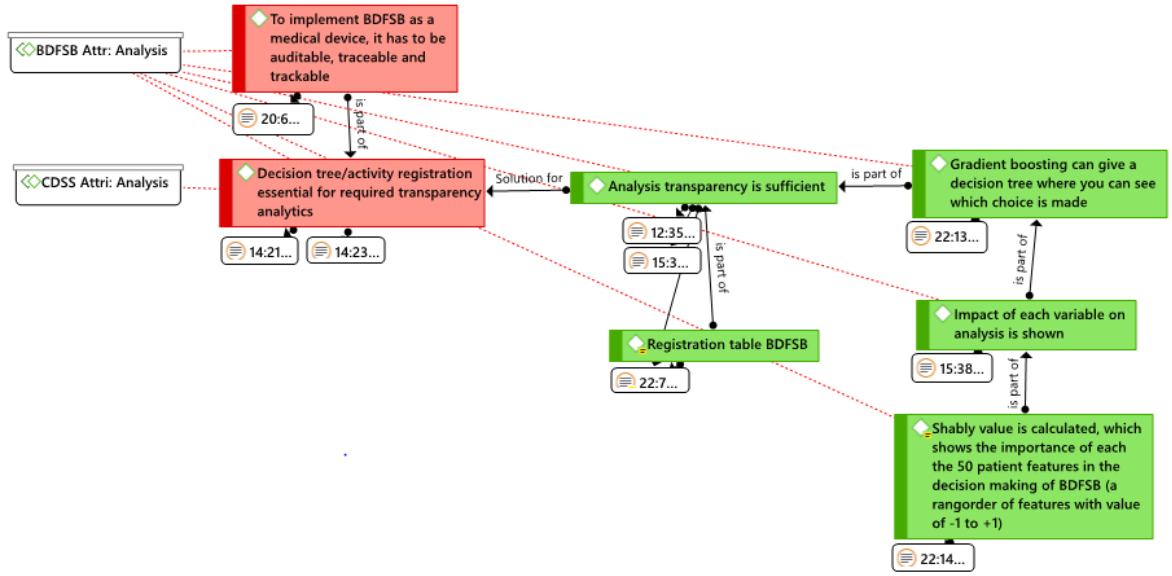

Figure 29: Coding scheme barriers & solutions 'analysis'

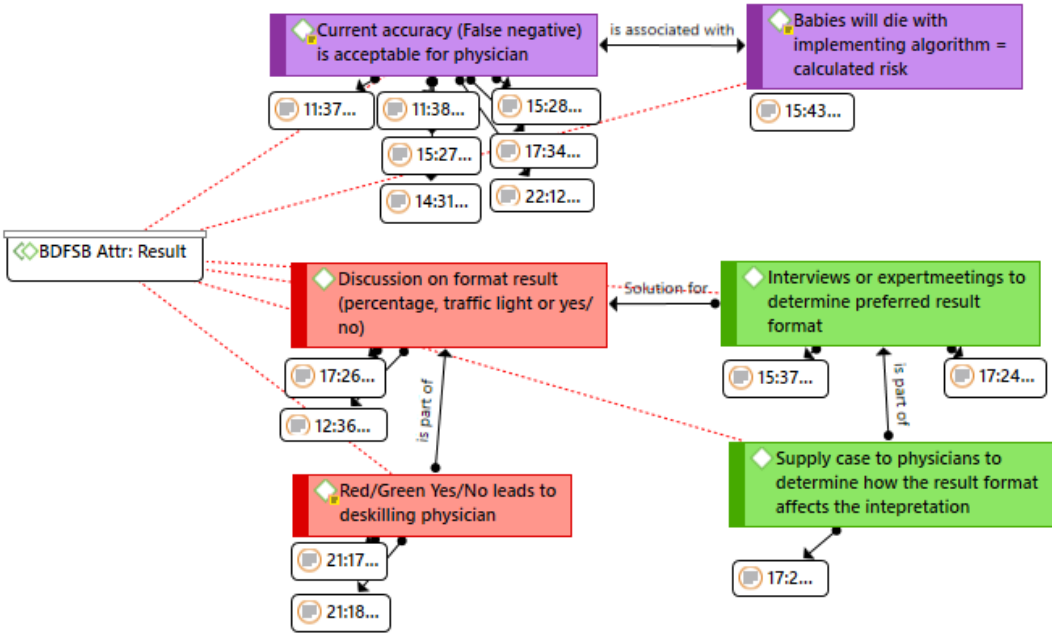

Figure 30: Coding scheme barriers & solutions 'result'

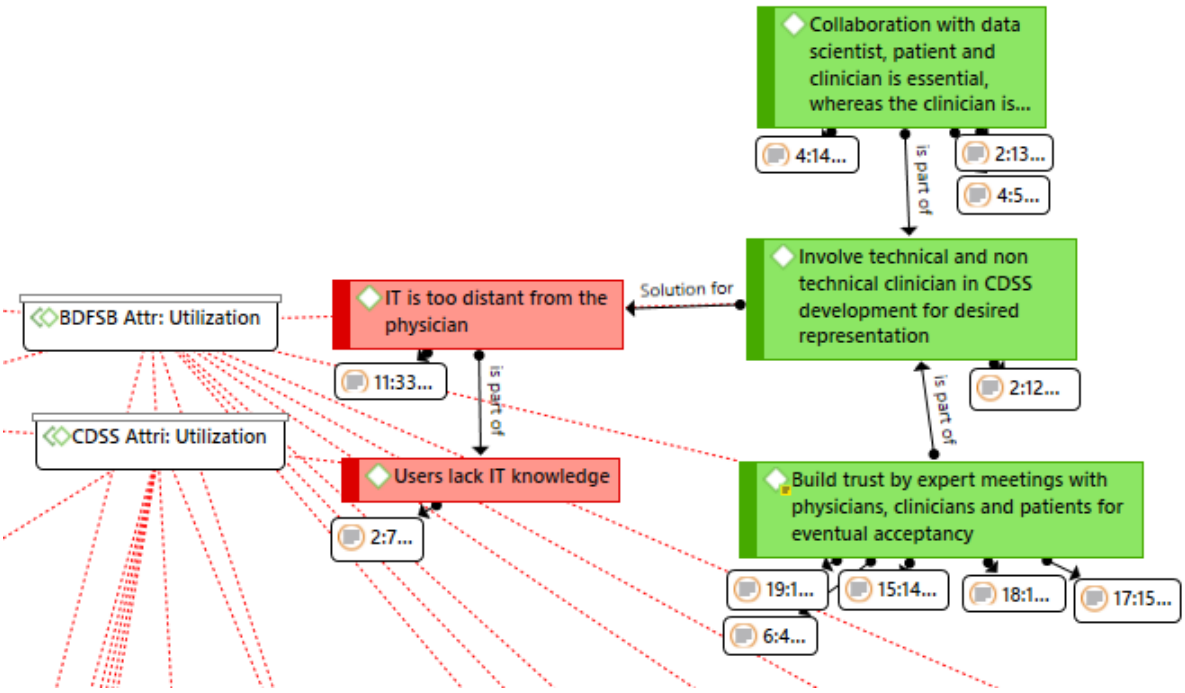

Figure 31: Coding scheme barriers & solutions 'utilization' part 1

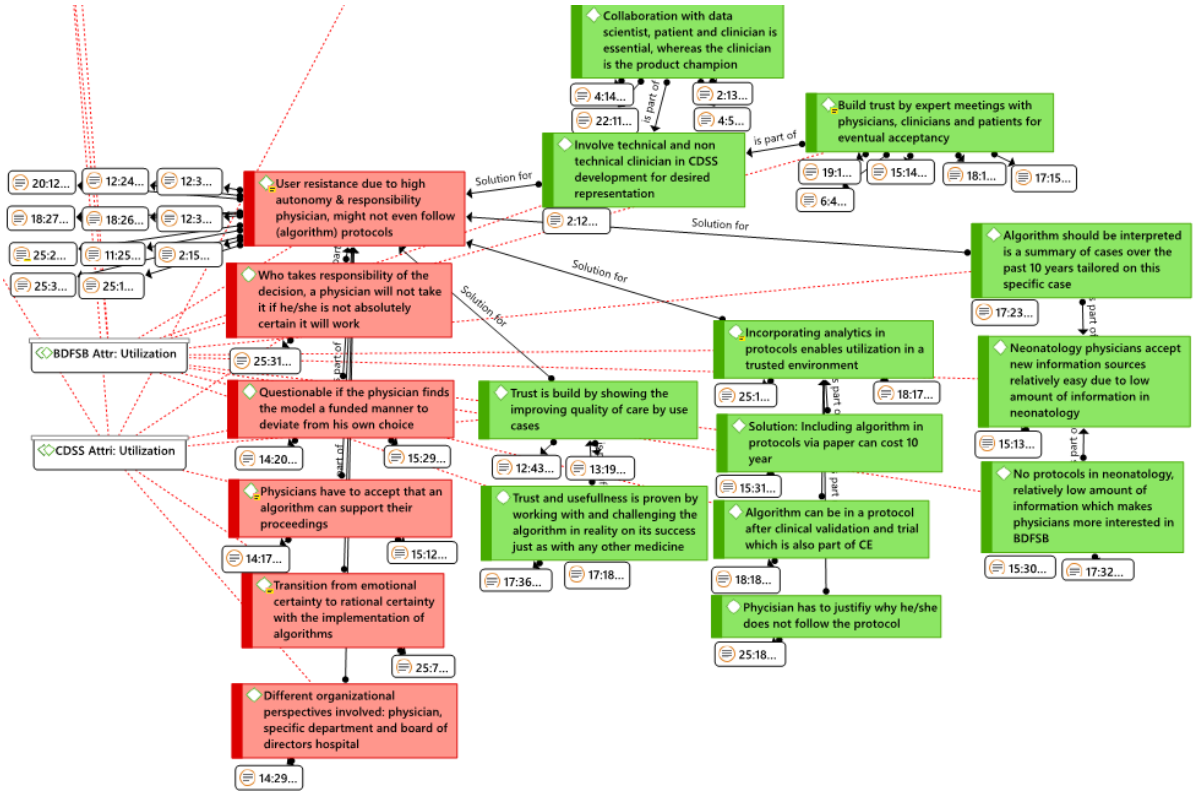

Figure 32: Coding scheme barriers & solutions 'utilization' part 2

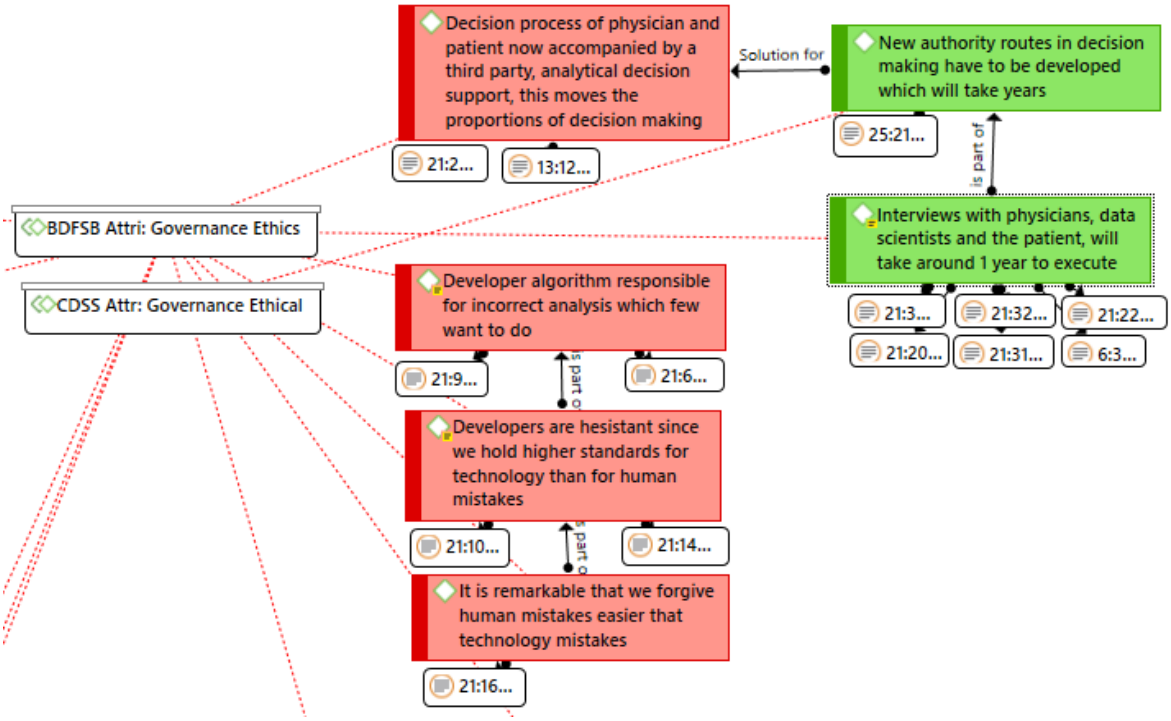

Figure 33: Coding scheme barriers & solutions 'ethics'

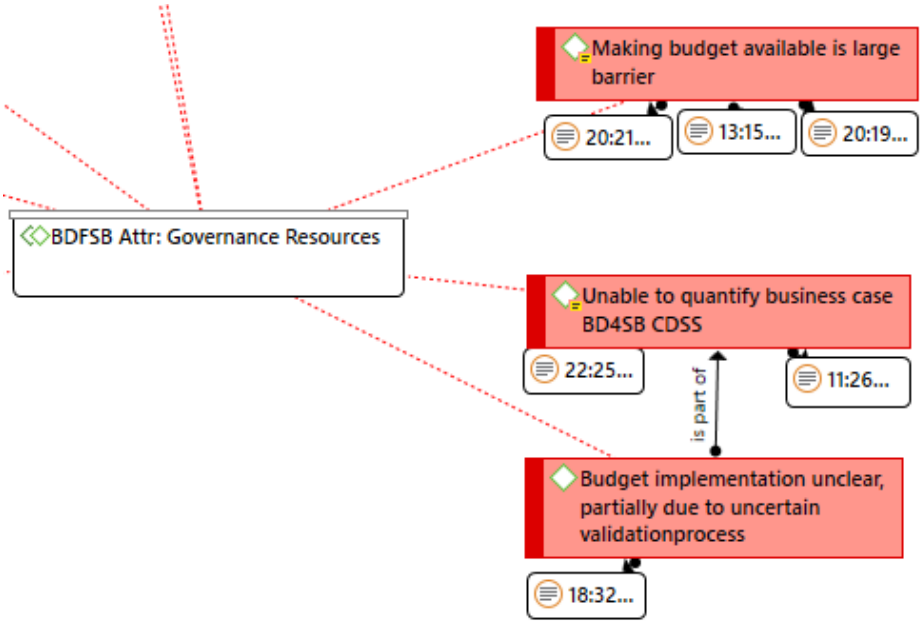

Figure 34: Coding scheme barriers & solutions 'resources'

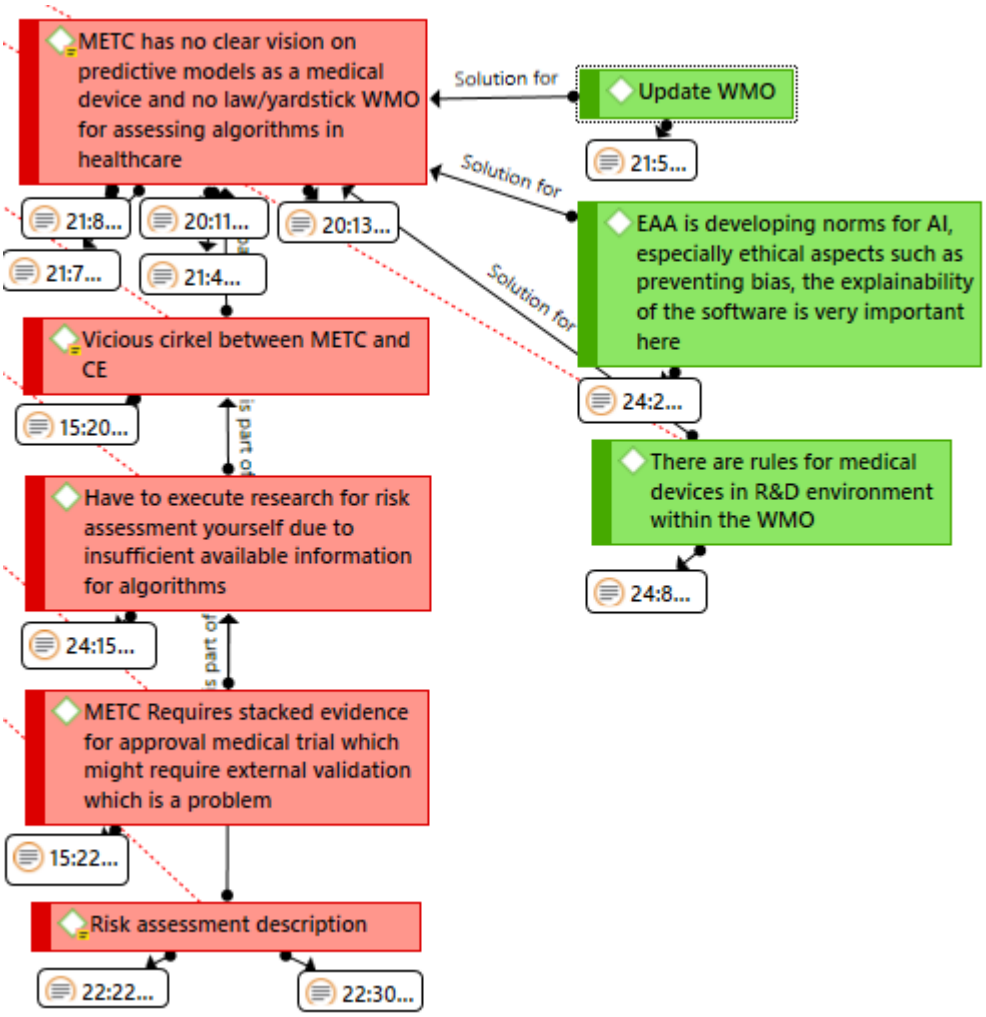

Figure 35: Coding scheme barriers & solutions 'legal' (METC & WMO)

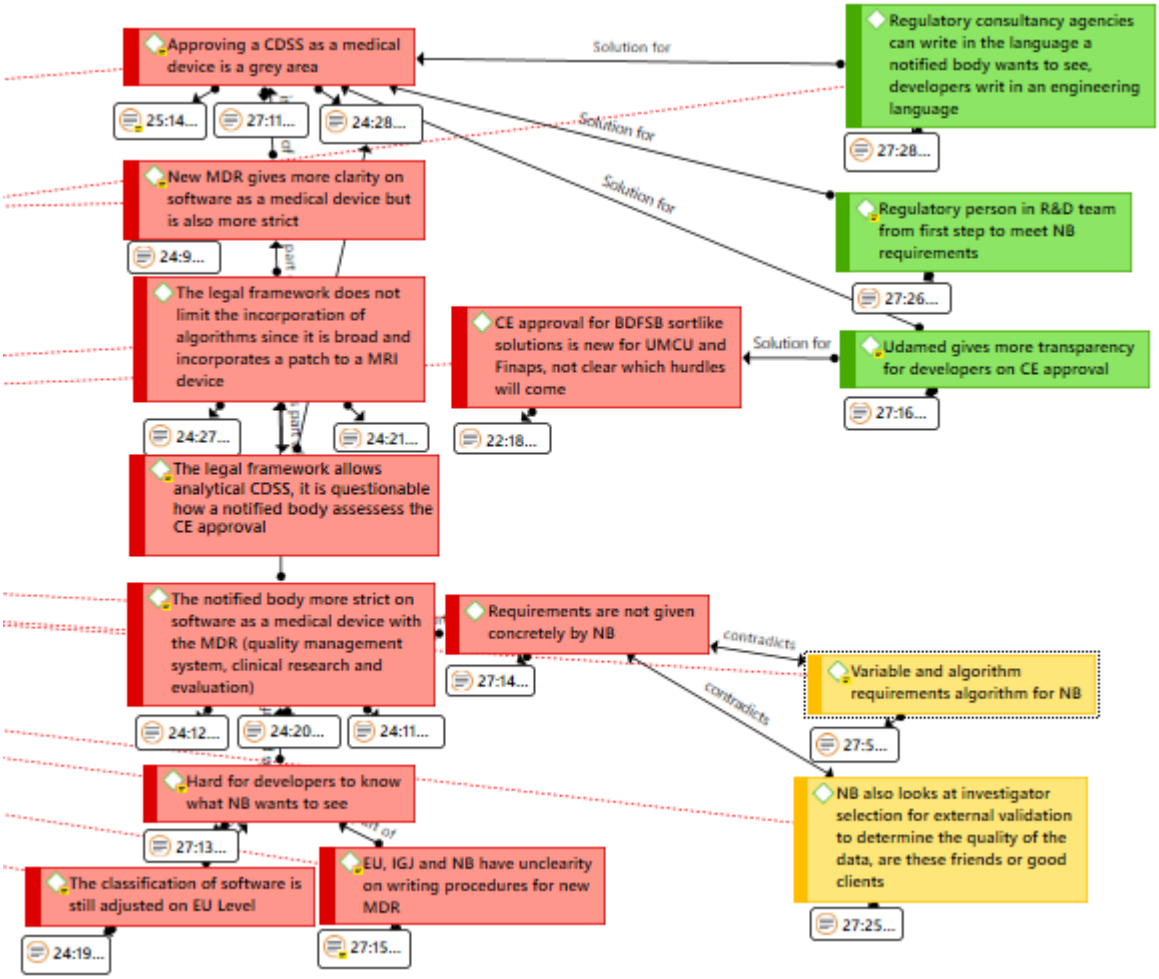

Figure 36: Coding scheme barriers & solutions 'legal' (MDR requirements)

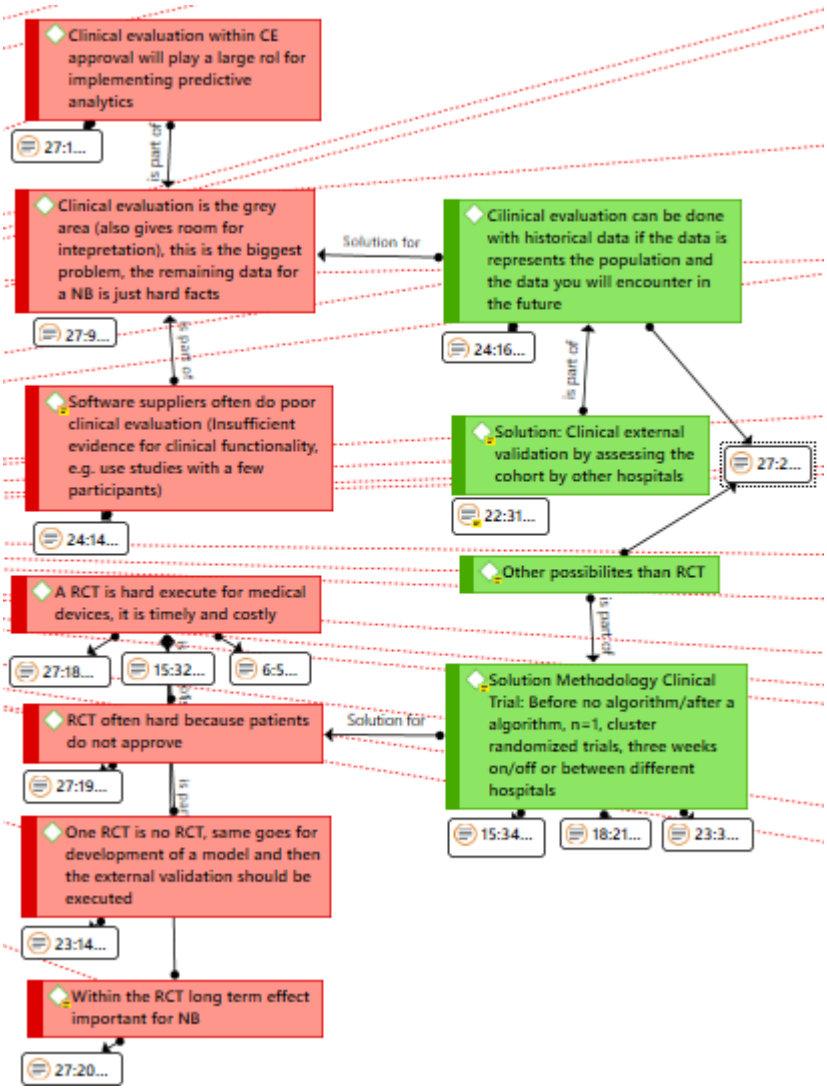

Figure 37: Coding scheme barriers & solutions 'legal' (Clinical evaluation study)

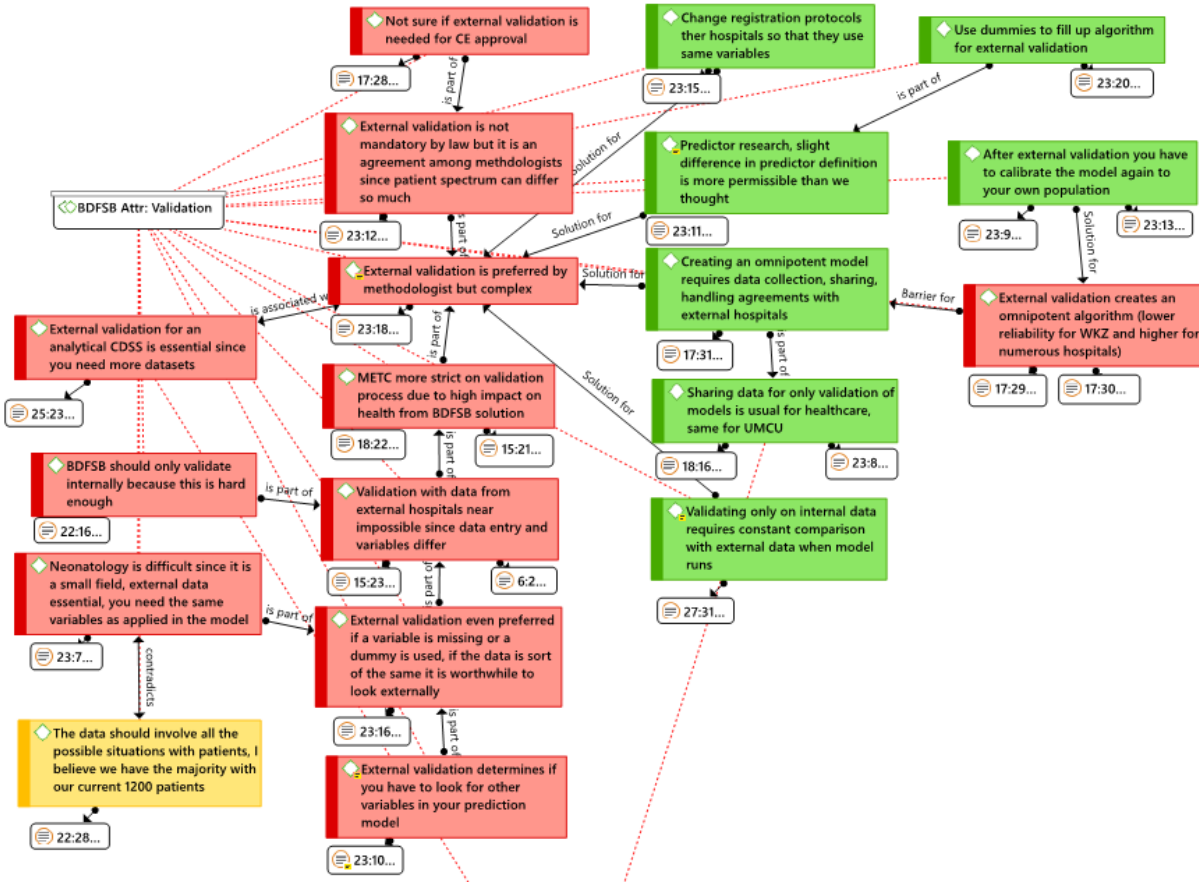

Figure 38: Coding scheme barriers & solutions 'validation'

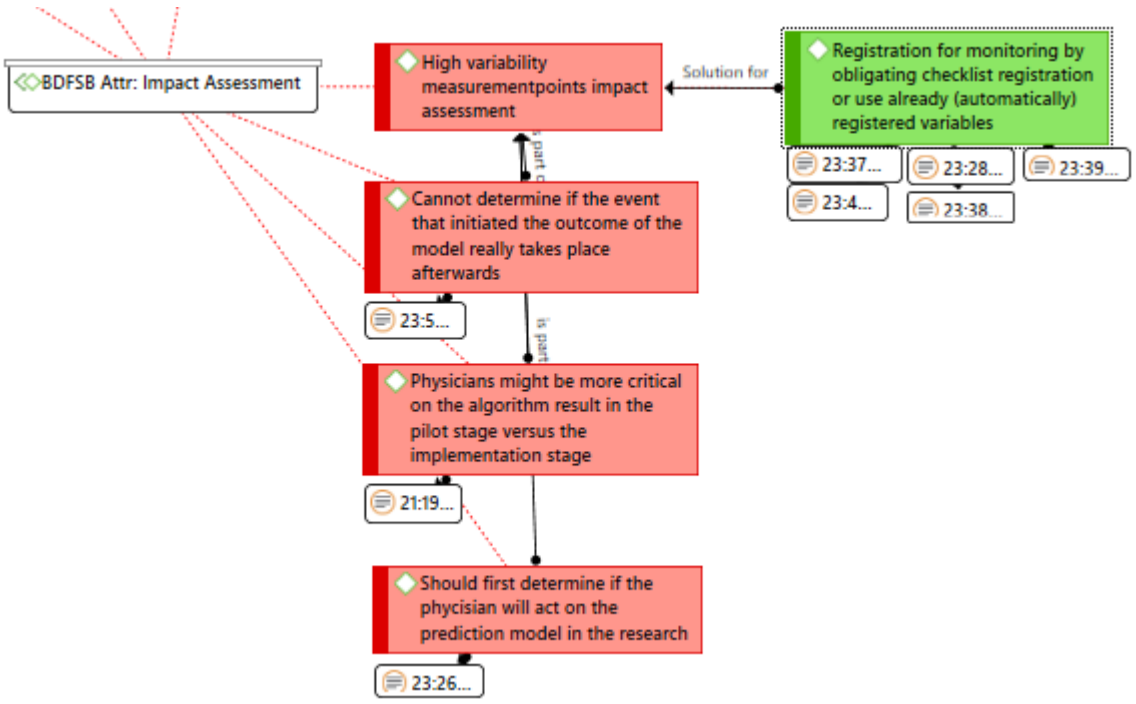

Figure 39: Coding scheme barriers & solutions 'impact'

Appendix D: Informed Consent Form

INFORMED CONSENT FORMULIER

Naam van het onderzoeksproject
The road to implementing analytical clinical decision support systems (CDSS).

Doel van het onderzoek
Dit onderzoek wordt geleid door Rick Klein Koerkamp. U bent van harte uitgenodigd om deel te nemen aan dit onderzoek. Het doel van dit onderzoek is het beschrijven van de barrières van belanghebbenden in het implementatieproces van CDSS en een implementatieplan voor het big data for small babies CDSS.

Gang van zaken tijdens het onderzoek
U neemt deel aan een interview waarin aan u vragen zullen worden gesteld over het implementeren van analytische CDSS. Een voorbeeld van een typische vraag die u zal worden gesteld: “Wat zijn de barrières voor het implementeren van ‘Big data for small babies’ CDSS”.

U dient tenminste 16 jaar te zijn om deel te nemen aan dit onderzoek.

Tijdens het interview zal, aan de hand van een topic list, dieper worden ingegaan op uw ervaringen met het implementeren van analytische CDSS. Van het interview zal een audio-opname worden gemaakt, zodat het gesprek later ad-verbum (woord voor woord) kan worden uitgewerkt. Dit transcript wordt vervolgend gebruikt in het verdere onderzoek.

Potentiële risico's en ongemakken
Er zijn geen fysieke, juridische of economische risico's verbonden aan uw deelname aan deze studie. U hoeft geen vragen te beantwoorden die u niet wilt beantwoorden. Uw deelname is vrijwillig en u kunt uw deelname op elk gewenst moment stoppen.

Vergoeding
U ontvangt voor deelname aan dit onderzoek geen vergoeding. Door deel te nemen aan dit onderzoek zult u meer inzicht krijgen in hoe gezondheidszorg analytische CDSS kan implementeren.

Vertrouwelijkheid van gegevens
Uw privacy is en blijft maximaal beschermd. Er wordt op geen enkele wijze vertrouwelijke informatie of persoonsgegevens van of over u naar buiten gebracht, waardoor iemand u zal kunnen herkennen.

Binnen het onderzoek worden uw gegevens **anoniem** gemaakt: uw naam wordt geanonimiseerd. In een publicatie of presentatie zullen of anonieme gegevens of pseudoniemen worden gebruikt. De audio-opnamen, formulieren en andere documenten die in het kader van deze studie worden gemaakt of verzameld, worden opgeslagen op de beveiligde (versleutelde) computer van de onderzoeker.

Meest relevante punten dataverwerking voor deelnemer:
- De data wordt opgeslagen op de drive van de onderzoeksleider welke niet toegankelijk is voor andere personen
- Respondenten kunnen de gegevens in januari 2018 opvragen, nadien is dit niet meer mogelijk gezien de gegevens dan volledig anoniem verwerkt zijn in het onderzoek.
- De originele data wordt weggegooid zodra deze geanonimiseerd zijn.

Vrijwilligheid
Deelname aan dit onderzoek is geheel vrijwillig. Je kunt als deelnemer jouw medewerking aan het onderzoek te allen tijde stoppen, of weigeren dat jouw gegevens voor het onderzoek mogen worden gebruikt, zonder opgaaf van redenen.

Dit betekent dat als je voorafgaand aan het onderzoek besluit om af te zien van deelname aan dit onderzoek, dat dit op geen enkele wijze gevolgen voor jou zal hebben. Tevens kun je tot 10 werkdagen (bedenktijd) na het interview alsnog de toestemming intrekken die je hebt gegeven om gebruik te maken van jouw gegevens.

In deze gevallen zullen jouw gegevens uit onze bestanden worden verwijderd en vernietigd. Als je tijdens het onderzoek, na de bedenktijd van 10 werkdagen, besluit om jouw medewerking te staken, zal dat eveneens op geen enkele wijze gevolgen voor je hebben. Echter: de gegevens die u hebt verstrekt tot aan het moment waarop uw deelname stopt, zal in het onderzoek gebruikt worden, inclusief de bescherming van uw privacy zoals hierboven beschreven. Er worden uiteraard geen nieuwe gegevens verzameld of gebruikt.

Als u besluit om te stoppen met deelname aan het onderzoek, of als u vragen of klachten heeft, of uw bezorgdheid kenbaar wilt maken, of een vorm van schade of ongemak vanwege het onderzoek, neemt u dan aub contact op met de onderzoeksleider:
Rick Klein Koerkamp: r.m.kleinkoerkamp@student.utwente.nl

Toestemmings-verklaring
Met uw ondertekening van dit document geeft aan dat u minstens 16 jaar oud bent; dat u goed bent geïnformeerd over het onderzoek, de manier waarop de onderzoeksgegevens worden verzameld, gebruikt en behandeld en welke eventuele risico's u zou kunnen lopen door te participeren in dit onderzoek

Indien u vragen had, geeft u bij ondertekening aan dat u deze vragen heeft kunnen stellen en dat deze vragen helder en duidelijk zijn beantwoord. U geeft aan dat u vrijwillig akkoord gaat met uw deelname aan dit onderzoek. U ontvangt een kopie van dit ondertekende toestemmingsformulier.

Ik ga akkoord met deelname aan een onderzoeksproject geleid door Rick Klein Koerkamp. Het doel van dit document is om de voorwaarden van mijn deelname aan het project vast te leggen.

1. Ik kreeg voldoende informatie over dit onderzoeksproject. Het doel van mijn deelname als een geïnterviewde in dit project is voor mij helder uitgelegd en ik weet wat dit voor mij betekent.

2. Mijn deelname als geïnterviewde in dit project is vrijwillig. Er is geen expliciete of impliciete dwang voor mij om aan dit onderzoek deel te nemen.

3. Mijn deelname houdt in dat ik word geïnterviewd door een onderzoeker van de Universiteit van Twente. Het interview zal ongeveer 45 tot 60 minuten duren. Ik geef de onderzoeker toestemming om tijdens het interview opnames te maken en schriftelijke notities te nemen. Het is mij duidelijk dat, als ik toch bezwaar heb met een of meer punten zoals hierboven benoemd, ik op elk moment mijn deelname, zonder opgaaf van reden, kan stoppen.

4. Ik heb van de onderzoeksleider de uitdrukkelijke garantie gekregen dat de onderzoeksleider er zorg voor draagt dat ik niet ben te identificeren in door het onderzoek naar buiten gebrachte gegevens, rapporten of artikelen. Mijn privacy is gewaarborgd als deelnemer aan dit onderzoek.

5. Ik heb de garantie gekregen dat dit onderzoeksproject is beoordeeld en goedgekeurd door de ethische commissie van de BMS Ethics Committee. Voor bezwaren met betrekking tot de opzet en of uitvoering van het onderzoek kan ik me wenden tot de Secretaris van de Ethische Commissie van de faculteit Behavioural, Management and Social Sciences op de Universiteit Twente via ethicscommittee-bms@utwente.nl .

7. Ik heb dit formulier gelezen en begrepen. Al mijn vragen zijn naar mijn tevredenheid beantwoord en ik ben vrijwillig akkoord met deelname aan dit onderzoek.

8. Ik heb een kopie ontvangen van dit toestemmingsformulier dat ook ondertekend is door de interviewer.

Naam deelnemer	**Handtekening**	**Datum**
Rick Klein Koerkamp		17-12-2018
Naam Onderzoeker	**Handtekening**	**Datum**

Appendix E: Stakeholder path analysis in ArchiMate

ArchiMate is an enterprise architecture modelling language that can be used for designing the architecture of a CDSS. This language consists of four layers (business, application, technology and motivation) from which this study utilizes the motivation layer to model motivations, or reasons that are related to the design or change of an Enterprise Architecture (The Open Group, 2017). This motivational layer is used to describe the barriers, solutions, involved stakeholders, outcome and goal for each attribute assessed in this study within figure 46 – 56 by means of the concepts in figure 40 – 45.

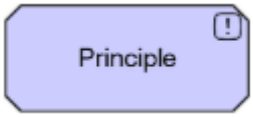

Figure 40: Principle element ArchiMate language

Principles are general properties that apply to any system in a certain context (The Open Group, 2017). This refers to the attributes in this study.

Figure 41: Constraint element ArchiMate language

A constraint is a restriction in the route of the realization of a system which is the stakeholders' barrier related to the attribute within this study (The Open Group, 2017).

Figure 42: Requirement element ArchiMate language

A requirement refers to a statement of aspect that must be realized by a system (The Open Group, 2017). This refers to the solution for a certain barrier within this study.

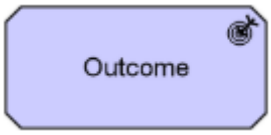

Figure 43: Outcome element ArchiMate language

The outcome within the ArchiMate language implies the result of a certain system which is the outcome of the execution of the solution in this study (The Open Group, 2017).

Figure 44: Goal element ArchiMate language

The goal refers to the end state that stakeholders intend to achieve with a system. This refers to the end state that the execution of the solution enables within this study (The Open Group, 2017).

Figure 45: Stakeholder element ArchiMate language

The stakeholders figure refers to the individual, group or organization involved within the architecture (The Open Group, 2017). This refers to the stakeholders involved in executing a certain solution within this study.

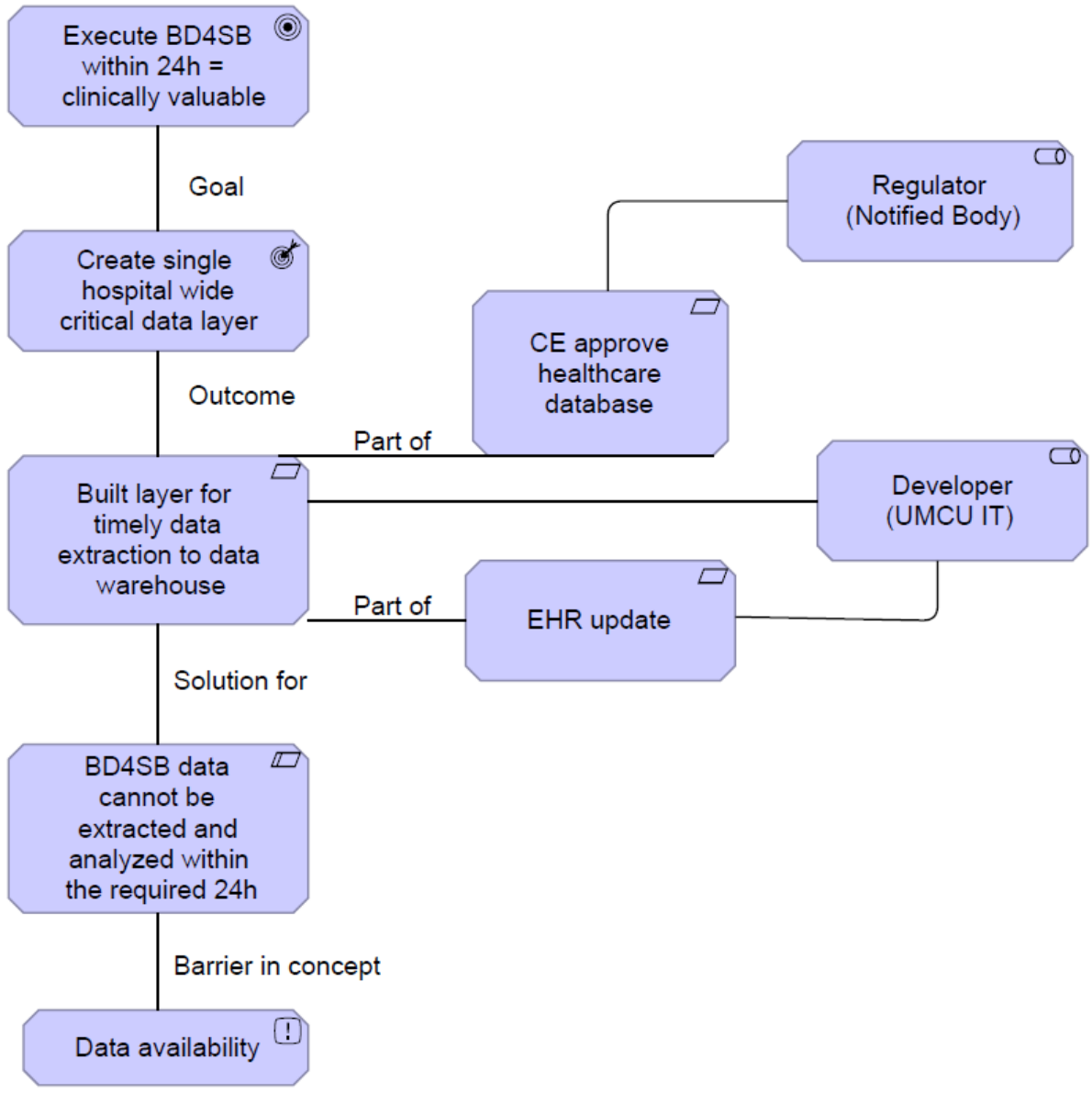

Figure 46: Process flow attribute: 'data availability' BD4SB

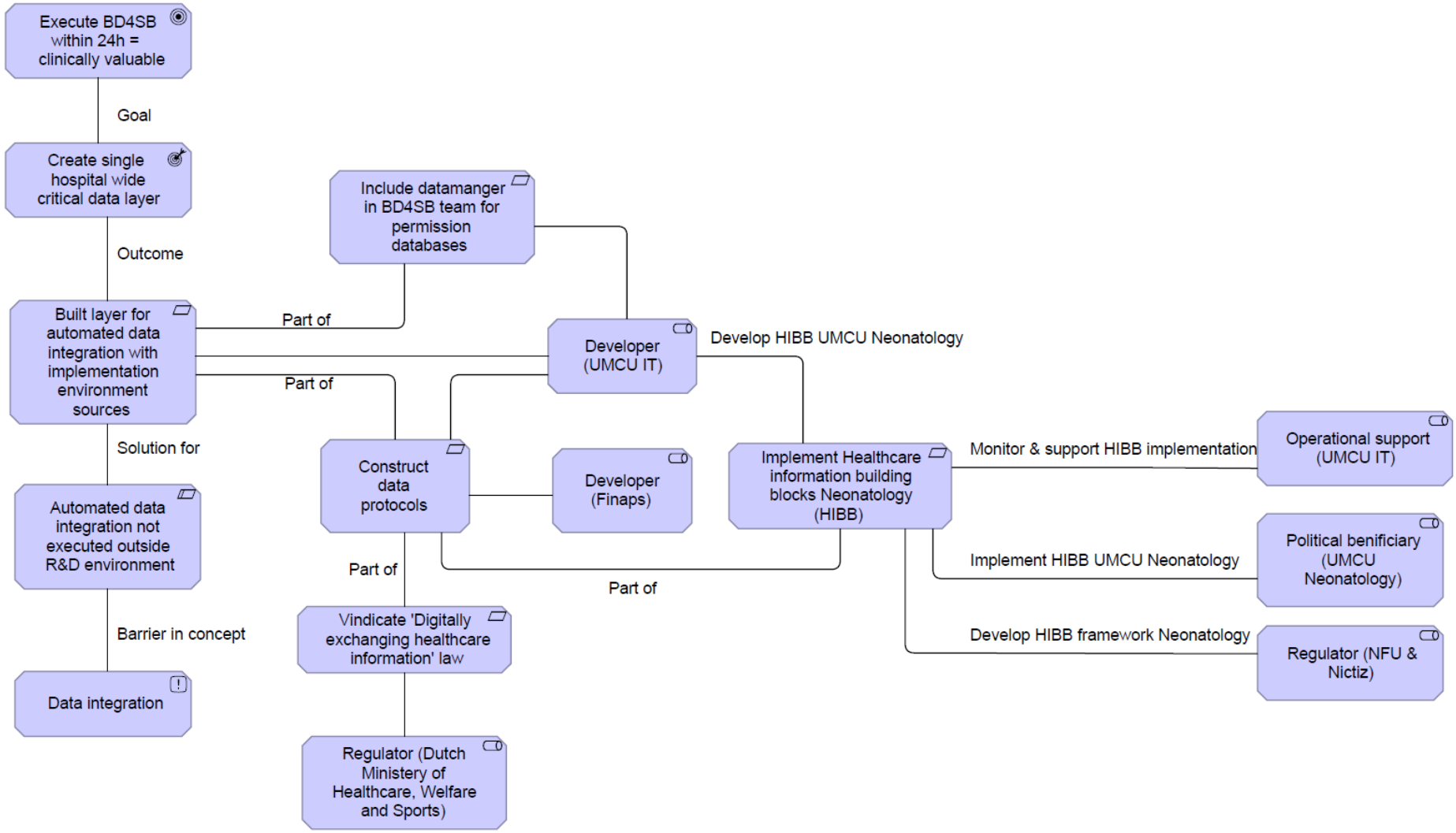

Figure 47: Process flow attribute: 'data integration' BD4SB

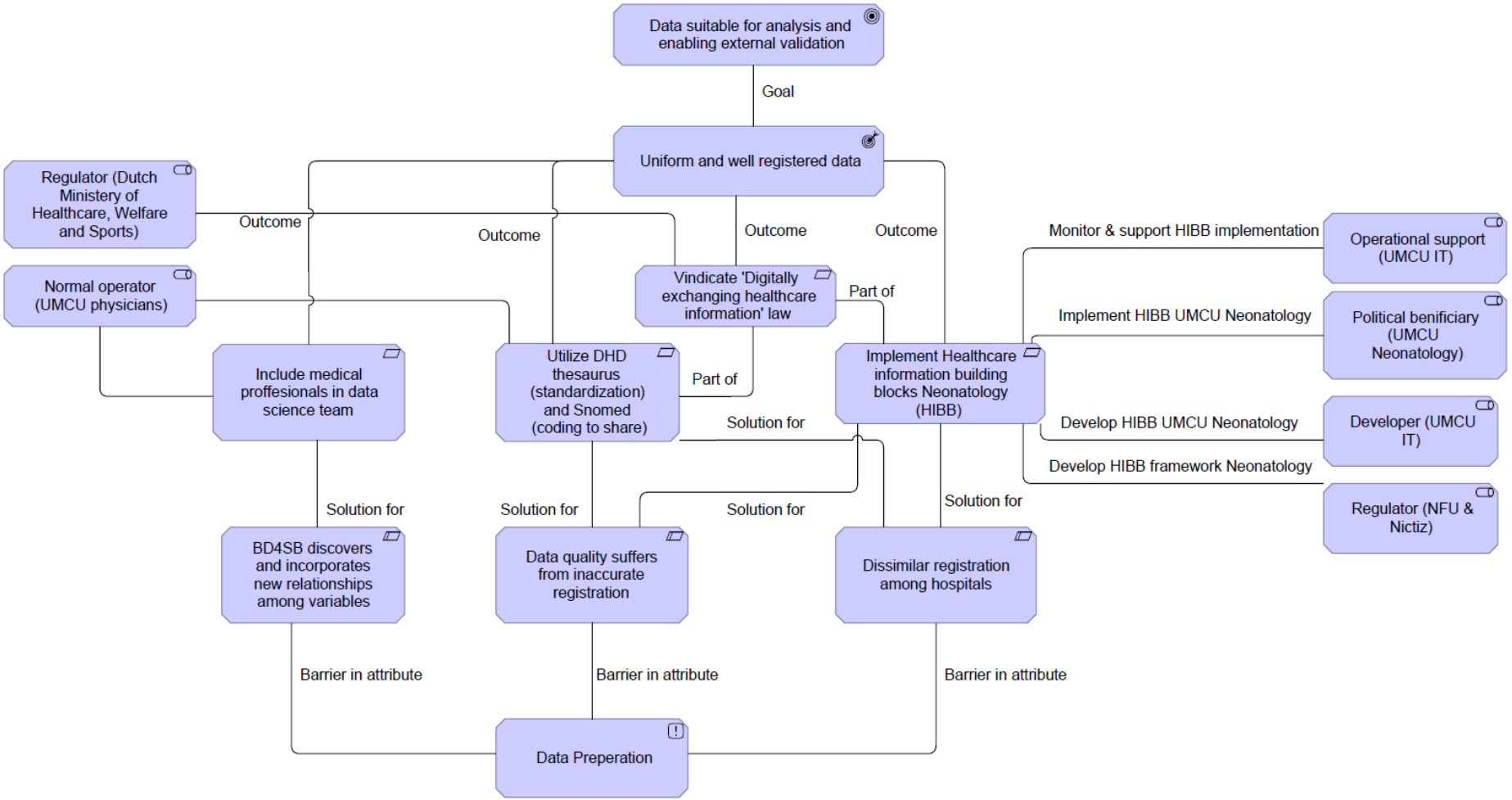

Figure 48: Process flow attribute: 'data preparation' BD4SB

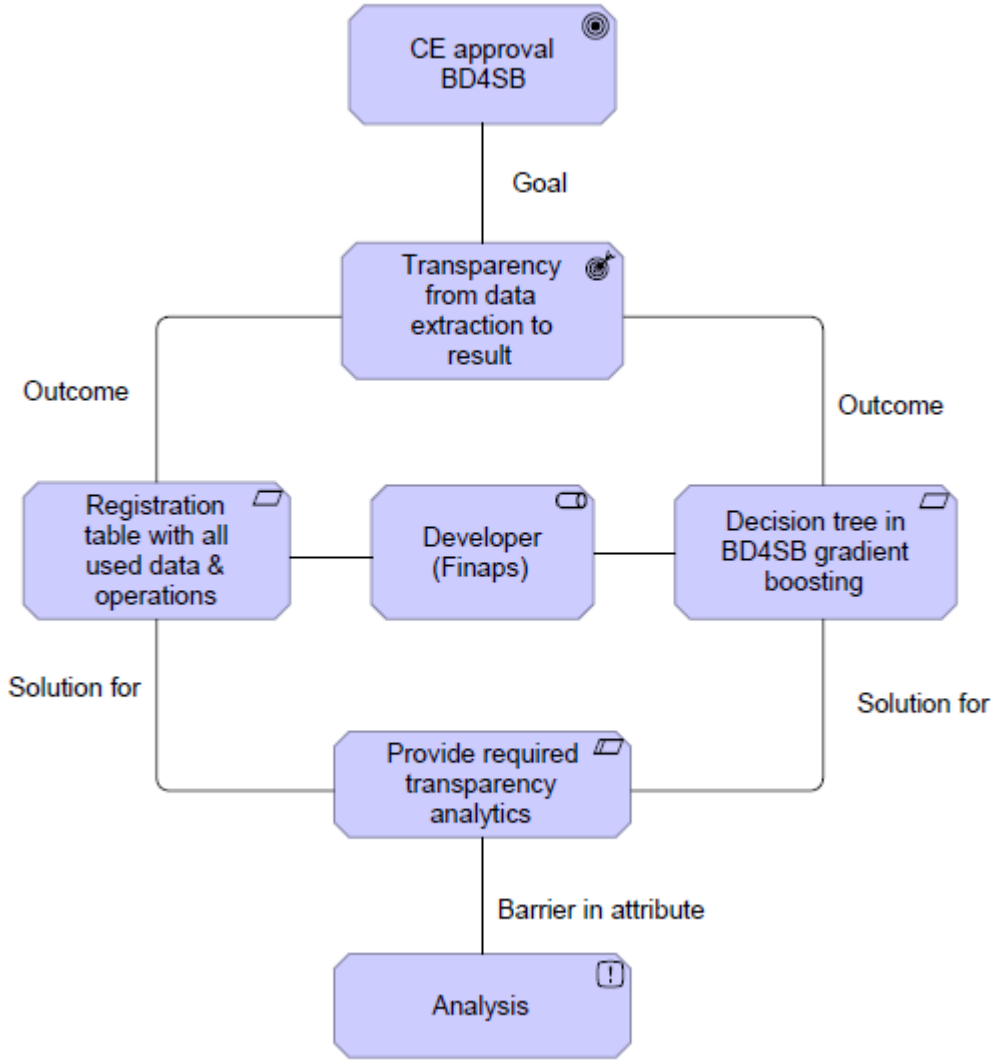

Figure 49: Process flow attribute: 'analysis' BD4SB

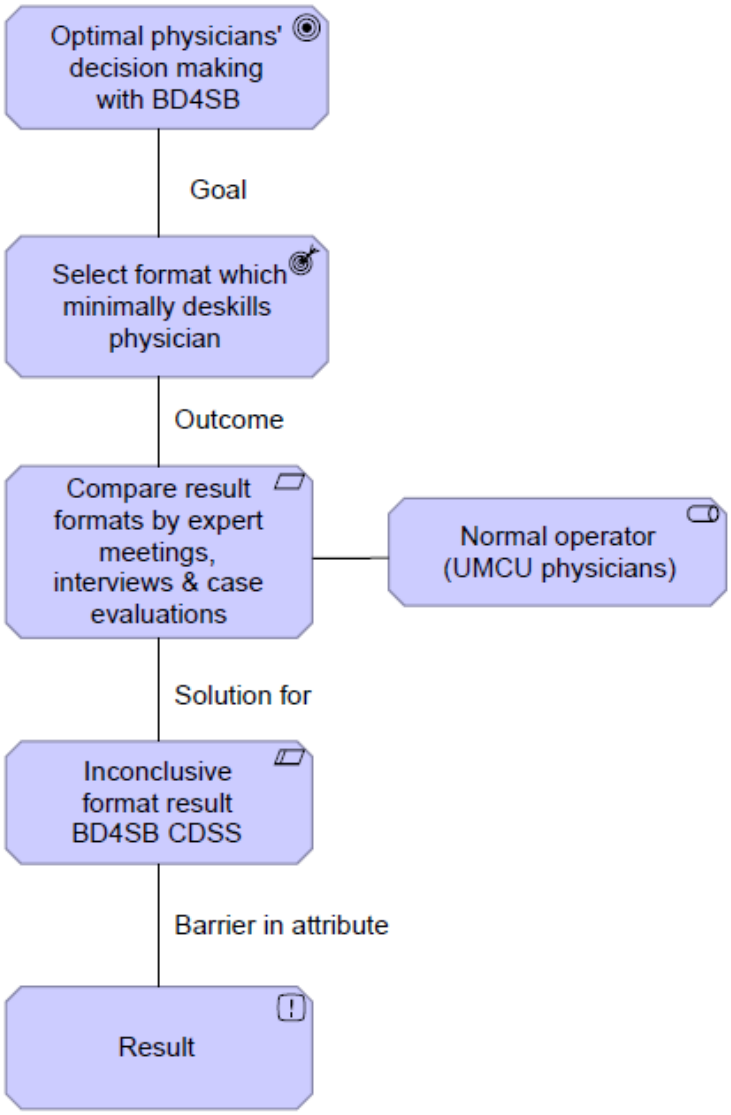

Figure 50: Process flow attribute: 'result' BD4SB

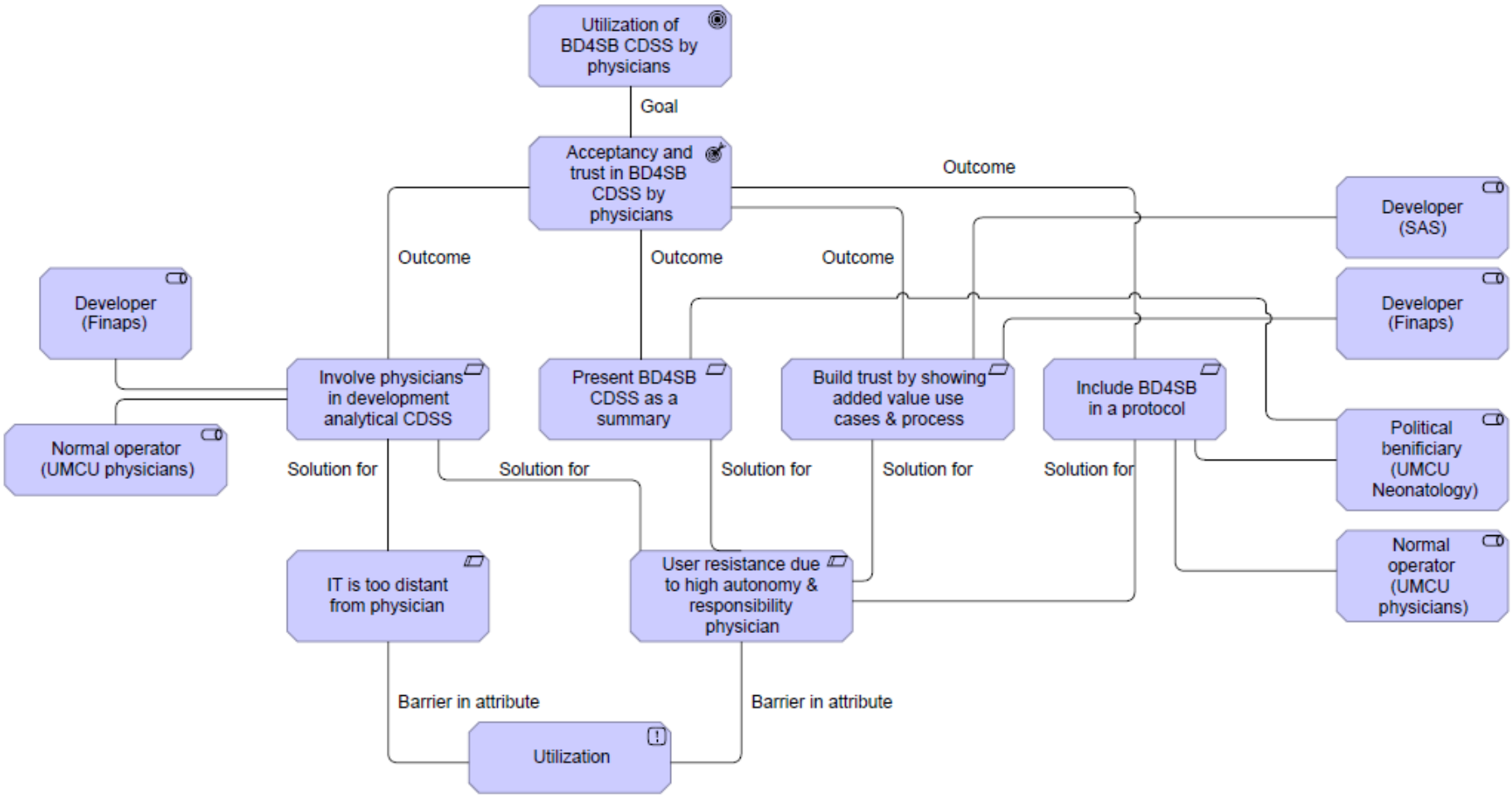

Figure 51: Process flow attribute: 'utilization' BD4SB

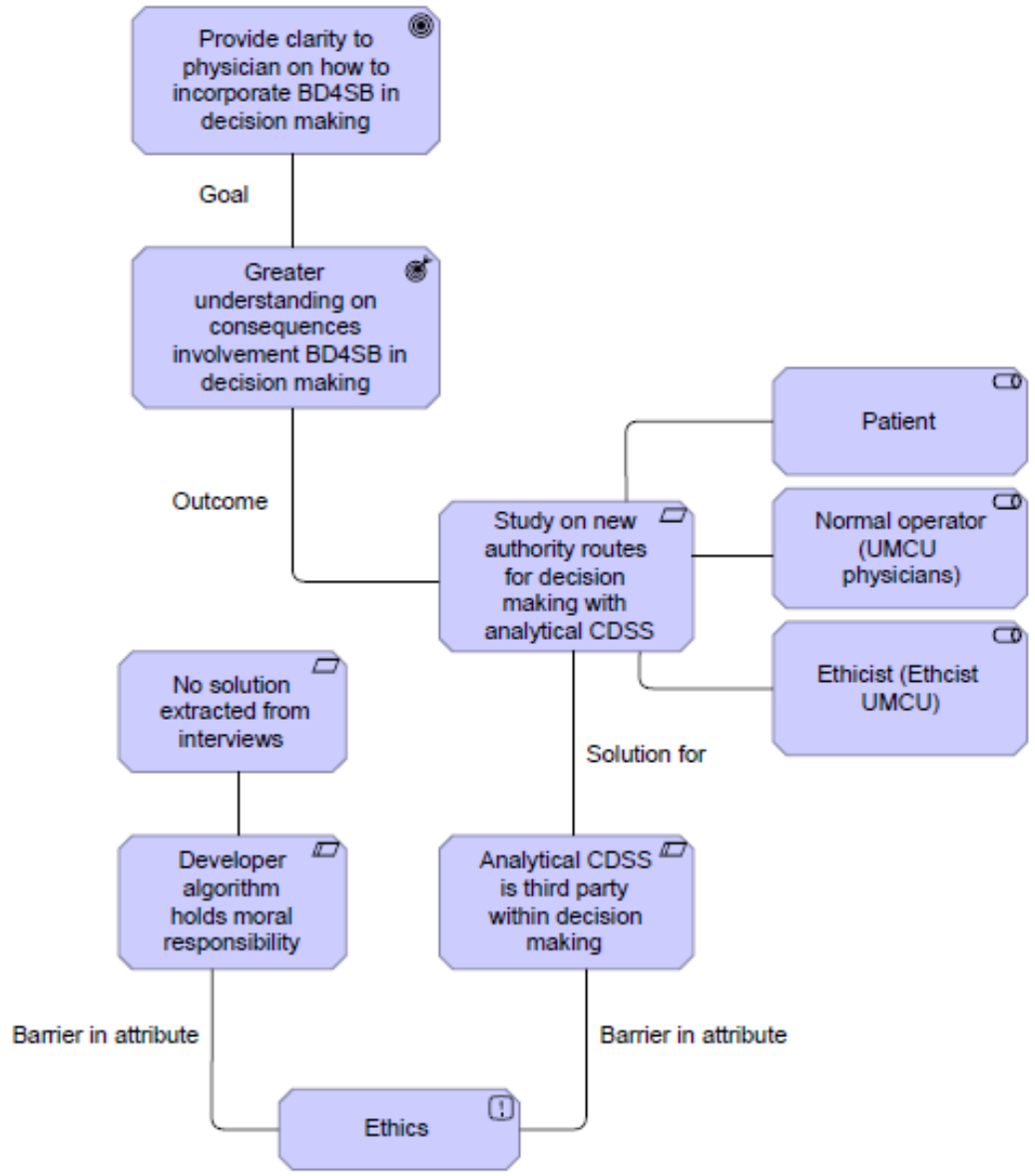

Figure 52: Process flow attribute: 'ethics' BD4SB

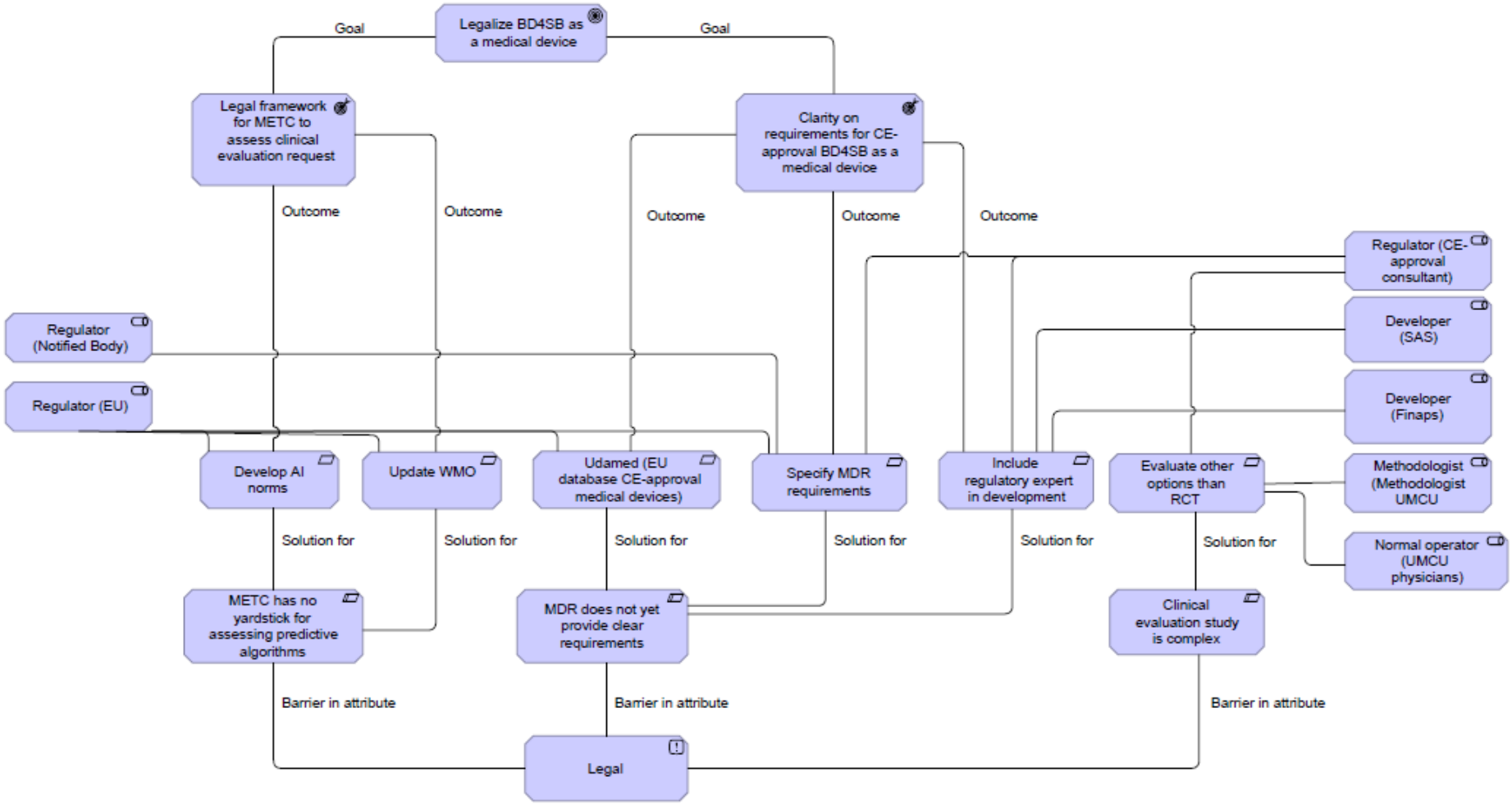

Figure 53: Process flow attribute: 'legal' BD4SB

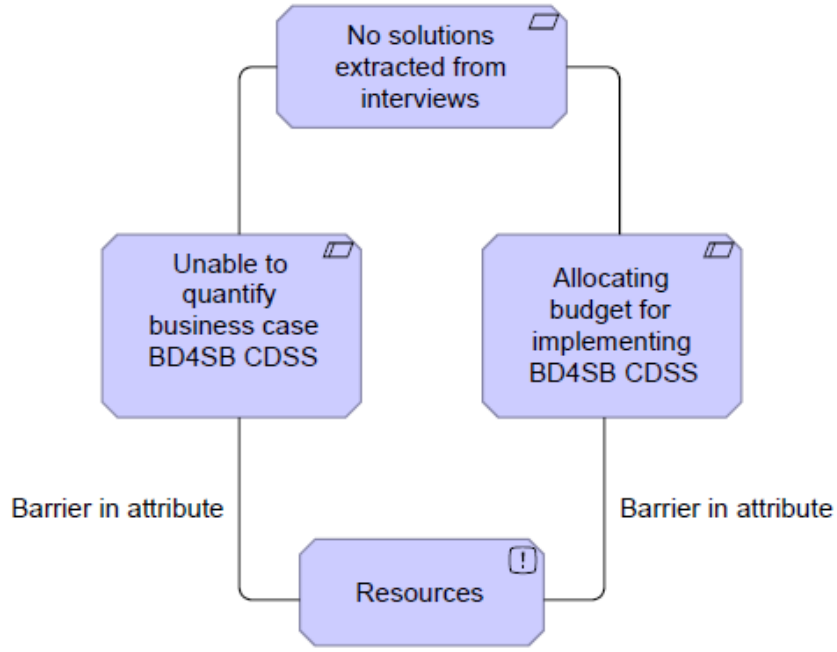

*Figure 54**:** Process flow attribute: 'resources' BD4SB*

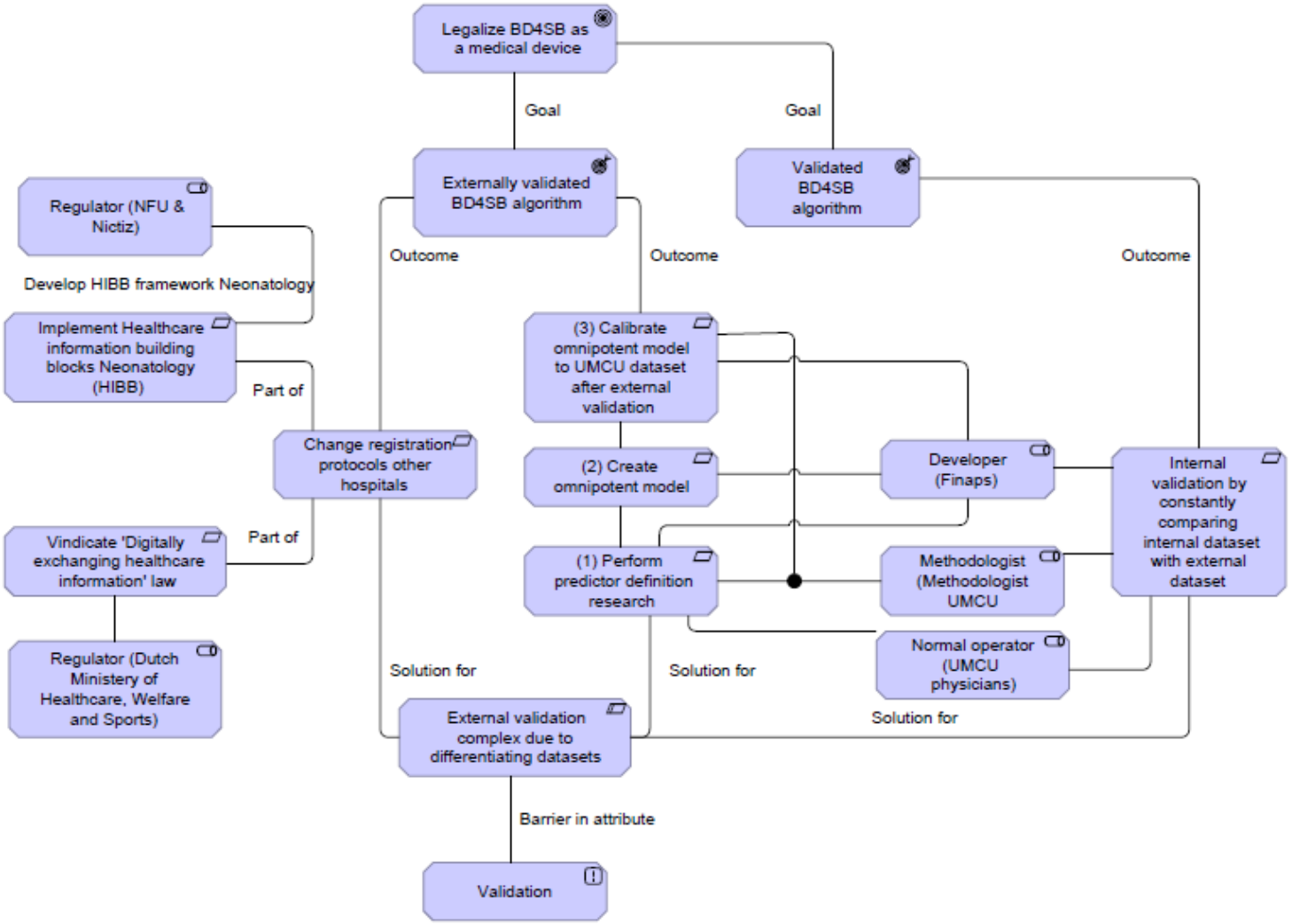

Figure 55: Process flow attribute: 'validation' BD4SB

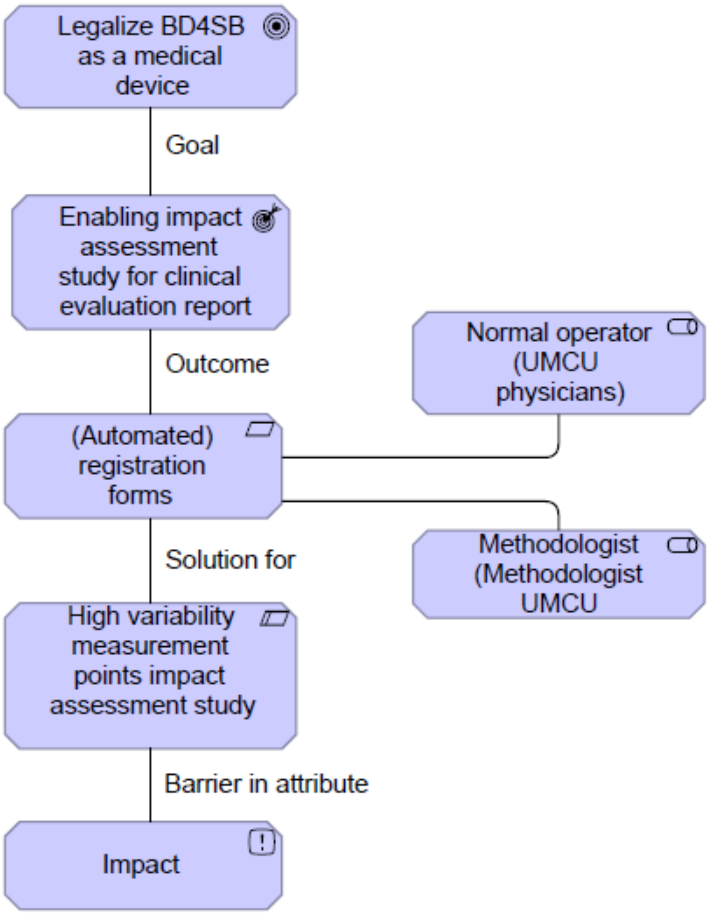

Figure 56: Process flow attribute: 'impact' BD4SB

Appendix F: Stakeholder path analysis specification

Table 33, 34 and 35 visualizes the stakeholders' barriers, solutions and which stakeholders can execute the solution accompanied with an approximated timespan categorized by the attributes. Green refers to solutions executable within months, orange refers to solutions executable within less than a year, red refers to solutions which require more than a year to execute and blue refers to solutions for which there is no approximated timespan determined by this study. The abbreviations within these tables are specified within table 32.

Table 32: Abbreviations in total stakeholders' barriers & solutions specification (table 33 – 35)

Abbreviation	Meaning
SHWDL	Single Hospital Wide Critical Data Layer
DM	Data Managers
WMO	Wet Medisch Onderzoek
AI	Artificial Intelligence
MDR	Medical Device Regulation
R&D	Research & Development
RCT	Randomized Control Trial
DEHI law	'Digitally exchanging healthcare information' law
HIBB	Healthcare Information Building Blocks

Table 33: Stakeholder path analysis part 1

Attribute:	**Data availability**			**Data integration**					**Data preperation**			
Barrier:	Cannot extract & analyze data within required 24h			Automated data integration not executed outside R&D environment					discovers new relationships	Data quality poor due to registration	Dissimilar registration	
Solutions general:	Construct single hospital wide critical data layer (SHWCDL)			DM for database permission	Construct SHWCDL	Construct data protocols			Include medical proffesionals	Utilize DHD and Snomed	Vindicate 'DEHI' law	Implement HIBB
solution specification:	Construct SHWCDL	EHR Update	CE approve database			Vindicate 'DEHI' law	Implement HIBB	Construct protocols				
Stakeholders:												
Developer												
SAS												
Finaps												
UMCU IT												
Ethicist												
UMCU Ethicist												
Normal Operator												
UMCU physicians												
Patient												
Patient												
Regulator												
EU												
Notified body												
CE-approval consultant												
Dutch Ministery of HWS												
NFU & Nictiz												
Methodologist												
UMCU												
Operational support												
UMCU IT												
Political benificiary												
UMCU Neonatology												

Table 34: Stakeholder path analysis part 2

Attribute:	**Analysis**		**Result**	**Utilization**					**Ethics**
Barrier:	Provide required transparency		Inconclusive format	User resistance				IT too distant from physician	Third party in decision process
Solutions general:	Registration table	Decision tree	Expert meetings & case evaluations	Present BD4SB as summary	Built trust via use cases & process	Include BD4SB in protocol	Involve physicians in development CDSS		Study on new authority routes
solution specification:									
Stakeholders:									
Developer									
SAS									
Finaps									
UMCU IT									
Ethicist									
UMCU Ethicist									
Normal Operator									
UMCU physicians									
Patient									
Patient									
Regulator									
EU									
Notified body									
CE-approval consultant									
Dutch Ministery of HWS									
NFU & Nictiz									
Methodologist									
UMCU									
Operational support									
UMCU IT									
Political benificiary									
UMCU Neonatology									

Table 35: Stakeholder path analysis part 3

Attribute:	**Legal**						**Validation**					**Impact**
Barrier:	METC no yardstick		MDR has no clear requirements			Clinical evaluation complex	External validation					High variability measurement points
Solutions general:	Update WMO	Develop AI norms	Specify MDR requirements	Udamed	Include regulatory expert in R&D	Evaluate other options than RCT	Predictor defintion research	Create Omni-potent model	Internal validation via constant comparison internal with external data	Change external registration protocols		(Automated) registration forms
solution specification:										Vindicate 'DEHI' law	Implement HIBB	
Stakeholders:												
Developer												
SAS												
Finaps												
UMCU IT												
Ethicist												
UMCU Ethicist												
Normal Operator												
UMCU physicians												
Patient												
Patient												
Regulator												
EU												
Notified body												
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