# Semi-Automatic Matching for Inclusion and Exclusion Criteria in Clinical Trials

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# Abstract

The purpose of this paper is to investigate the possibilities improving the system for matching clinical trials with patients at the Department of Oncology at the Karolinska University Hospital. From investigating the current process we learned that the system used is mainly based on manual labor and paper based clinical trials. Therefore different computer based solutions such as: IBM Watson, Epic Beaker and SAP Hana were researched and a State of the Art analysis of IBM Watson is performed. Based on the State of the Art we decided that it would be most fitting to develop a new system for use at the Department of Oncology. With the use of parallel prototyping we created a prototype for managing clinical trials. In addition to the prototype, further contextual observations and interviews were performed in order to increase our understanding of the target environment. Furthermore, the prototype was updated in iterations based on feedback gathered during workshop sessions with the clients as well as an interview with a research nurse. The prototype created generated positive feedback overall during both the workshops and the interview. In the last sections of the paper, we discuss what needs to be researched further before this system could be implemented as well as how to test it's effectiveness. We also propose different areas to further investigate in order to expand the scope and possibilities of our proposed system.

# Contents

# 1

# Introduction

This section aims to introduce the reader to the prerequisites of the project. Section 1.1 is a brief introduction to the project. Section 1.2 provides the reader with a relevant stakeholder analysis. Section 1.3 describes the current processes the project was based on, while section 1.4 points out the issues within the current processes. Section 1.5 talks about the project scope and in section 1.6 the goals of the project are explicitly stated.

## 1.1 The Project

The project was carried out by students from Kungliga Tekniska Högskolan (KTH) within the courses Cooperative IT-design (DH2655) and Computer Science, Business and Management (DH2465). The project assignment was initiated by Rolf Lewensohn at the Department of Oncology at the Karolinska University Hospital in Solna. The project's scope was to develop a generic model of a patient filtering system for clinical trials (for more information on clinical trials, see section 2.1.4) and a contextual analysis of similar systems, mainly focusing on systems in the US. The project management can be found in Appendix E.

## 1.2 Stakeholders

Every project constitutes of stakeholders, which are "...those groups without whose support the organization would cease to exist." [FR83]. To better understand the problem space in which this project is embedded, a stakeholder map was created to show the involvement of different parties and their interest (Figure 1.1). The Stakeholder map helped the project team not only to identify each stakeholder, but also to unravel how the tasks, the workload and the information flows between the stakeholders.

The brief description in [HM12] was the basis for the decision on using the

stakeholder map method. A concise summary of the description: "Stakeholder maps help to visually consolidate and communicate the key constituents of a design project, setting the stage for user-centered research and design development."

Figure 1.1 shows the stakeholder map after many iterations and consolidation with our clients. So, for a clinical trial to happen, a sponsor needs to initiate and provide funding for a trial. Usually a sponsor is a producer of medicine with the interest to test a drug and its effects, or a medical institution such as Karolinska University Hospital with the interest to test a treatment. The sponsor appoints a principal investigator who is a specialist in the trial-related medical field and responsible for the medical procedures and the collected data.

The data is collected by the research nurse who plays a key role in clinical trials. The role of the research nurse is elaborated thoroughly in section 1.3. The patient's participation is obviously key to the trial, but that only happens after patient's consent. The research nurse is the patient's main contact point throughout a trial. In addition, a monitor maintains good clinical practice (GCP) [Gui11] during a trial.

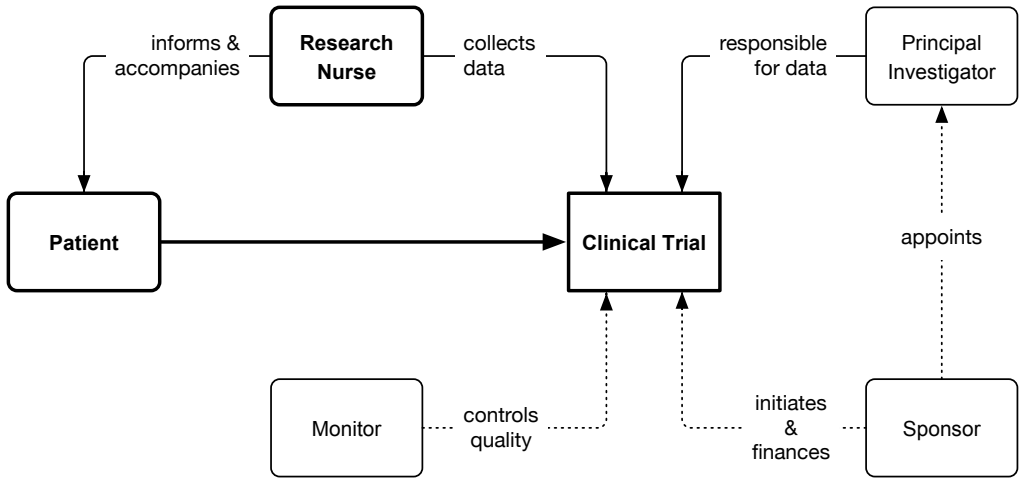



Figure 1.1: The stakeholder involved during a clinical trial

## 1.3 Current Patient Pathway

In order for a patient to participate in a clinical trial in the Department of Oncology at the Karolinska University Hospital in Solna, numerous steps have to be taken in advance, even before any participation can be considered.

The matching process – where a patient is matched to a clinical trial – may

look different in different institutions, but generally a patient will be screened by a research nurse according to the inclusion and exclusion criteria of a trial. For the research nurse to actually have the chance to screen a possible participant, the patient needs to enter the organization (in our case Karolinska University Hospital). There are numerous entry points for the patient, for instance by a referral from another hospital, a general practitioner at the same hospital or by the patient's own initiative.

In the TakeCare system (further described in section 2.1.2) the patient is registered for the Multidisciplinary Conference (MDC), which is a weekly meeting of specialists where several patients' treatment plans and diagnoses are discussed. To be considered as a participant in a clinical trial the research nurse – who is assigned to approximately ten clinical trials – has to pre-screen the patient's medical records for eligibility for a trial. The pre-screening entails a rough scan of the patient's condition and the medical records.

Pre-screening is an iterative process and therefore a patient can end up being discussed a few times at MDCs. The pre-screening helps, during the MDC, to decide if a patient should be informed about a possible trial(s) and eventually asked for a consent for more comprehensive screening and later on possible trial participation.

After the patient has given his or her consent, the research nurse carries out a detailed screening by going through all inclusion and exclusion criteria of all the trials the patient wishes to take part in and seems to be eligible for. If there are no complications the patient is eligible for one of the trials and can participate in it.

The current process of pre-screening and screening is very tedious, paper-based and labor-intensive and it requires the research nurse to recall trials, criteria and patients. A research nurse is usually integrated in many different daily activities and the screening for trials task is one with an immense workload, but a lower priority. Ultimately, however, clinical trials are of utmost importance for the Karolinska Institutet, not only financially through sponsored trials by a commercial partner, but also for possible advances in medical treatment.

## 1.4 Issues of Current Flow

The current patient flow (Figure 1.2) has several points that could be improved upon. First of, the trials are mainly kept in paper form in large binders. Unless the contents of all clinical trials are remembered by the doctors attending the MDC, all trials will not be considered. The process of finding patients for trials are entirely dependent on the doctor's and specialist's ability to remember clinical trials. Most of the MDCs are, however, visited by the research nurses who remember their assigned trials by heart. On the one hand, since research nurses are responsible for

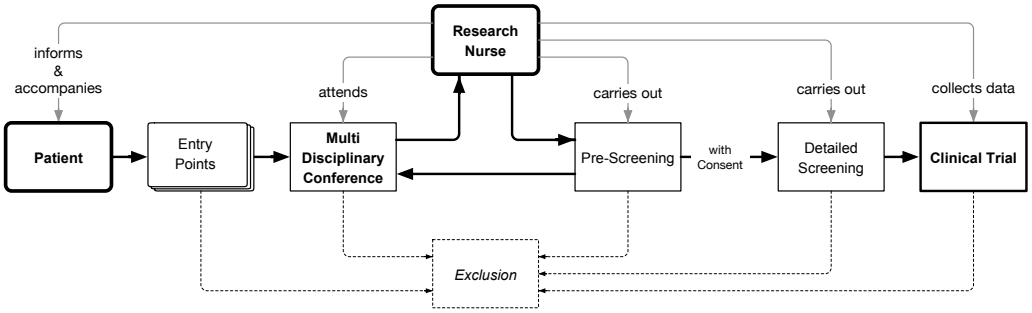



Figure 1.2: Patient's Pathway from entry to clinical trial

one or more trials they can provide the conference participants with information about them. There is, on the other hand, no guarantee that a research nurse will be attending a conference, nor is there a guarantee that the nurse attending is responsible for a fitting trial for the patients discussed during the conference.

The second problem with the current flow (Figure 1.2) and the current system for handling clinical trials is that there is no overview. There is no one place where every current ongoing trials are listed, with information about whether a trial has any participants or who is responsible for the trial. The inability to easily access relevant information considering the ongoing clinical trials make the first issue even larger.

## 1.5 Scope

As understanding the current flow has been a time consuming task. This project has focused on gaining an in-depth understanding of the current flow and how to design a system that best improves it. Therefore an implementation of the design has been deemed out-of-scope.

## 1.6 Goals

The purpose of the project has been to investigate the current work-flow and design a system that, when implemented, should achieve the following three goals:

- Reduce manual labor
- Improve overview of clinical trials
- Increase inclusion rate of clinical trials

To reach these goals we have focused on investigating the problems in iterations where each iteration has brought forth new information and feedback which

resulted in updates in our design. The detailed technical specifications of the system proposed in this report are to be considered in the future.

An implementation of the design is required to empirically determine if the goals have been reached. As implementing the design is out of scope, we must rely on the judgment of our clients for the success of the project. See section 4.3.2 and section 6.2 for discussion on performance indicators and testing the implementation.

# 2

# Background

The current section is divided into two sections, section 2.1 Domain and Section 2.2 Available Software Systems. The first section provides the reader with information on the relevant laws and some of the complexity areas of the domain. The latter section gives light background knowledge concerning existing software systems relevant for the project.

## 2.1 Domain

The current subsection provides the reader with relevant, but general information concerning the project's domain.

### 2.1.1 Patient Privacy in Sweden

The Patient Security Act regulates patient security within the health care sector. This legislation states a range of responsibilities where one of the most important obligations is confidentiality. In other words, unauthorized people should not have access to sensitive patient information that may jeopardize the patient's safety if this information is disclosed to a third party.

The Patient Data Act applies to caregivers' treatment of personal patient information. The very purpose of this legislation is that information should be managed keeping in mind the patients' health and safety. Furthermore, it is important that the personal information is managed in a way that respects the patients' personal integrity. Requirements are made so that the personal information is stored in such a way that the unauthorized people would not be able to access it. For more discussion on how our project fits into the frame of patient privacy legislation, see section 6.4. For a more thorough interpretation of the legislation, see appendix D.

### 2.1.2 Patient Records - TakeCare

One of the biggest patient record systems used in Sweden is the Take Care record system delivered by CompuGroup Medical, which is mainly used by Stockholms Läns Landsting (SLL). The Karolinska University Hospital utilizes the TakeCare system. Its approach is to offer a broad system taking care of more than just the act of keeping medical records. It has built-in modules to allow the customer to expand its usage [tak15b]. One ongoing problem in Sweden has been that of sharing medical records. Different caregiving units that utilize the TakeCare system are able to collaborate and share medical records through the system.

The Take Care patient record system offers structured record keeping in chronological order [tak15b] with templates in place allowing the user to browse and enter health metrics, medication history, previous diagnoses, etc. It also allows the caregiver to use standardized forms for any traditional paperwork required. Furthermore, other modules has other areas of use and can, for example, be used to schedule further appointments and surgery as well as keeping track of the day-to-day schedule of the user. TakeCare also enables third party software to interact with the system through the TakeCare Xchange module. Using a .net framework, other systems can integrate with the TakeCare server and in real time write, read and download data [tak15a]. For example, connecting to TakeCare and retreiving patient records can be done through TakeCare Xchange.

### 2.1.3 CE-marking

All medical devices are required to have a CE-marking to be released on the market. A CE-marking for a product is an insurance from the manufacturer that the product complies with the regulations and laws corresponding to that product. The mark does not mean that the product has been approved by an official authority. It means that the manufacturer takes responsibility that the product meets the needed requirements. For a product to be labeled as a medical device, the product's manufacturer has to state a purpose and area of use for the product corresponding to a set of laws regarding this. [Lä15]

All medical devices should be safe and the manufacturer is required to have necessary user and technical documentation. The manufacturer is obliged to continually monitor their products in practical use and is required to report accidents and incidents where there are suspicion that the medical device is the cause. [Lä15]

A standalone software with the purpose of influencing the patient's care is considered a medical device and must therefore be CE-marked. [eur12]

### 2.1.4 Clinical Trials

Clinical trials are research studies that involve people. They are the final step in a long process that begins with research in a lab. Most treatments we use today are the results of past clinical trials [cli15b].

Every trial has a person in charge, usually a doctor, who is called the principal investigator. The principal investigator prepares a plan for the trial, called a protocol. The protocol explains what will be done during the trial. It also contains information that helps the doctor decide if this treatment is right for a patient. The protocol includes information in different categories; essential (that all involved persons working with a study must follow), background, endpoints, study design (including types, phase, treatment, drugs and randomization), population (inclusion/exclusion criteria which defines Who can join the trials), effect evaluation, safety, statistics,etc. For more information, see appendix B.

## 2.2 Available Software Systems

The current section provides necessary knowledge on some available and widely used technologies relevant for the project.

### 2.2.1 IBM Watson

IBM Watson is a technology platform that uses Natural Language Processing (NLP) and Machine Learning (ML) to reveal insights from large amounts of unstructured data [wha15]. It uses cognitive computing, which involves self-learning systems that uses data mining, pattern recognition and NLP to mimic the way the human brain works in order to understand context and the real intent of the user's language [cog14].

Among a number of IBM Watson's offerings, Watson for Clinical Trial Matching (CTM) is an application aiming to help doctors narrow down a wide pool of available cancer trials and quickly identify potential matches for patients. Enabled with cognitive computing, Watson for CTM enhances clinicians' ability to more easily find the potential list of clinical trials for which the patient may be eligible, increase the likelihood that the patient is offered the option of a clinical trial as treatment, and help increase clinical trial fulfillment through effective patient recruitment [cli15a]. These characteristics of Watson for CTM are aligned with our first and third goals (section 1.6) and thus Watson is a reference to our system. The reader will find more detailed information about the functionality of IBM Watson for CTM in section 4.1.

### 2.2.2 SAP-HANA

SAP-HANA is a software that can handle large amounts of both structured and unstructured data and deliver the user real time analysis of both genomic data and clinical data. With the SAP-HANA software physicians can customize the treatment for each patient based on genetic markers that are specific for the patient [Sin13].

SAP-HANA is today used in different hospitals around the world. In a hospital in South Korea a study shows that using SAP-HANA has shorten the process of analyzing cancer patients from two days to twenty minutes [sap15b] and in a hospital in Austria, using the SAP-HANA software has lowered the total cost and shortened the time for reports, patient scheduling and clinical applications [sap15a].

Despite the positives, there are some serious issues with the SAP-HANA software. Several flaws in the security of the software has been found [Jer15]. Hackers can easily get hold on encrypted data[Kat15] and for a software that is meant to handle a lot of sensitive patient data, it is an issue that cannot be disregarded. Therefore it was decided to not use SAP-HANA in the clinical trials system presented in this report.

### 2.2.3 EPIC

Epic is one of the world's largest of Electronic Medical Record (EMR) software [epi13] and supplies 355 customers worldwide with health care software. Hospitals using Epic software hold the records for over 50 % of all patients within the US and 2.5 % of all patients globally [Gla15]. Epic supplies software solutions for all parts of the health care chain, including but not limited to hospitals, academic facilities and children's organizations.

Epic has its own system called Beaker for managing clinical trials. Epic's Enterprise EMR is integrated within Beaker in order to eliminate the need for multiple interfaces when working with trials. Beaker allows the user to both keep track of trials and patients within the trial system. It does not however provide any automated patient - trials matching [epi13]. There are two reasons to why we choose not to further investigate Epic Beaker as a reference to our system. First of all it does not provide the same functionality as our system does, and secondly Epic Beaker is only available for hospitals using the entire Epic Suite. It is not a stand-alone product.

# 3

# Method

This section describes the methods used to obtain data in this project. Section 3.1 describes the state of the art analysis done on IBM Watson. Section 3.2 describes contextual observations, interviews and the workshops conducted. Section 3.3 talks about the visualizations created and used, section 3.4 about the prototyping and section 3.5 talks about the focus to establish change within organizations.

## 3.1 State of the Art Analysis

The state of the art analysis aims at recovering the most advanced software technology used in connection to our problem, namely clinical trials. The state of the art was “accomplished by conducting what’s called a "literature search" of relevant documents” [sta12] in the area of technology and clinical trials.

Our state of the art analysis was done on IBM Watson. The other systems were not included as they were deemed not to be a perfect fit for our project. As IBM Watson was regarded the best fit time was focused on gaining an understanding of that system.

The literature search aimed at answering questions such as and similar to: How does the system work/look? Who are its main users? How does the system promote work with clinical trials? Is the system suitable for clinical trial management?

## 3.2 Contextual Observation, Interview & Workshops

The project’s complexity entailed a deep understanding of the hospital setting at the Karolinska University Hospital in Solna. After a first meeting with the clients where the project was introduced, several follow-up sessions were had where new information was presented.

### 3.2.1 Contextual observation

A contextual observation of a multidisciplinary conference was conducted at the Department of Oncology at the Karolinska University Hospital in Solna. The doctors and nurses at the conference were observed discussing treatments and diagnosis of 20 lung cancer patients. The duration of the observation was approximately two hours and the results of the observation was written down on paper. The aim of the observation was to get a better understanding of the part of clinical trials when deciding a treatment for a patient, see appendix C.

### 3.2.2 Interviews and workshops

In order to understand the role of a research nurse, get a better understanding of how the matching of patients and clinical trials is done and also to receive feedback on the current patient flow, an interview with a research nurse at the Department of clinical trials at the Karolinska University Hospital was conducted. To get reliable qualitative data and let the interviewee express her views in her own terms, a semi-structured interview was conducted[B06]. The interview was in the work environment of the interviewee. Nine questions, see appendix F, were defined beforehand and sent to the interviewee two days before the interview. During the interview, depending on the answer from the interviewee, follow up questions were asked in addition to the predefined questions.

The interview also included a user test were the interviewee tested a clickable prototype of the clinical trial system presented in this paper. The user test was a think aloud test where the user try to complete the task while loudly expressing her thoughts and views[Bar94]. The user test was recorded with Loopback - recording software [loo15].

Two workshops were held at the Oncology department of Karolinska University hospital. The aim of the workshops was to gather feedback on the process of the project and make sure that the project was heading in the direction that was in accordance with the wish of the stakeholders. The workshops[Boe02] were arranged as client meetings and consisted of presentations and feedback sessions.

## 3.3 Visualizations

Visualizations of processes and strategy are important since they resolve the issues of communicative misunderstandings, create a unified vision and appeal to our cognitive abilities [EP09]. Thus, visualizations played a big role in our project. All of the visualizations were done iteratively and were living documentation of the project's progress.

To communicate how our design impacts the current work process with clinical

trials a strategy map was created (see section 4.3.2). The map served two purposes; one internal and one external. The internal purpose was to provide the project group with an overview of how the project fits into the organization and to more easily communicate the project's goals and ambitions. The external purpose was to communicate to the client our view of how the project would impact the current processes and how that in turn would lead to achieving the project goals [WL13]. The strategy map was developed in iterations with feedback provided both from within the group and from the clients.

## 3.4 Prototyping

During the creation phase, we used the method of parallel prototyping [HM12] to create as many alternative solutions as possible. These solutions were created individually by each team member as paper prototypes which were shared in a follow-up meeting with the rest of the team. During the follow-up, the results were analyzed and synthesized into one solution which then was incorporated into an interactive prototype.

The interactive prototype is built with Axure RP Pro V7 and deployed through axshare.com (http://clx1mo.axshare.com/icdeep.html) which allows to view and interact with the prototype through most current browsers like Google Chrome, Apple Safari and Mozilla Firefox.

## 3.5 Bedding for Hand-off

As our project is in its nature short lived. The ambition of the group is to spark a fire of enthusiasm within Karolinska University Hospital so that our designed solution gets implemented when we are done. To do this we focused on the first four of Kotter's eight steps in establishing change within an organization [Kot96]. These four steps are about establishing a sense of urgency within the organization. Having a coalition of people that can drive the change. Creating a vision, and communicating it. The first two steps required little work initially as the project was set up with a coalition of people within Karolinska University Hospital that had a sense of urgency to change the current process of clinical trials. More discussion on this can be read in section 5.3.

# 4

# Results

This section states the result from the state of the art analysis of IBM Watson 4.1, the contextual observations and interviews 4.2, visualizations 4.3 and the proposed prototype 4.4.

## 4.1 State of the Art: IBM Watson

The matching process of IBM Watson Clinical Trial Matching (CTM) is partially automatic. Users first need to choose cancer type and input patient data (attributes) relevant to the cancer type selected. For pictures of the system with more explanation, see Appendix A.

In the first round of matching, potential clinical trials are listed with a breakdown of the percentages of trial criteria conditions (categories): Met, Action Needed, Unmet Modifiable Conditions, Not Met. This matching process provided by Watson is based on a comparison of the patient data provided and the relevant clinical trial criteria that were analyzed.

Users can check a potential clinical trial for details. In the detailed information screen, criteria (inclusion/exclusion) are listed as different categories. The user can read each passage in context by clicking "View Full Trial". Users can take further action to mark each criterion into proper category, by either drilling down into additional trial details and providing more patient data as needed (to let Watson evaluate matching) or doing it manually (to provide the user's own evaluation). Finally, users can add "Preferred" bookmark if they are interested in a certain trial and export trial information.

The whole matching process described above can significantly increase the efficiency of recruitment and inclusion rate of clinical trials. However, the clinical trials database used by Watson for CTM is from ClinicalTrials.gov, which is a

registry and results database of publicly and privately supported clinical studies of human participants conducted around the world [tri15]. Clients are not able to customize Watson for CTM by neither connecting it to another clinical trial database or by adding new trials.

Furthermore, Watson for CTM is just a supporting platform for general clinicians to match clinical trials for a certain patient. It does not meet specific requirements expected from multiple stakeholders in our project. For example, there is no storage function, which means research nurses are not able to view matching trials for certain patients and the principal investigator cannot check matched patients for certain trials.

To summarize, Watson for CTM is an excellent application for promoting matching process, but it cannot provide overview of certain clinical trials and is not fit for clinical trial management.

## 4.2 Contextual Observations, Interviews & Workshops

This section presents the results of our contextual observations, interviews and workshops.

### 4.2.1 Multidisciplinary Conference

The multidisciplinary conference consisted of doctors and nurses from different fields. The type of cancer patients that were discussed during the observed conference was lung cancer patients. The 20 patients that were discussed during the conference were printed on a paper sheet that had been handed to all the attending doctors and nurses. Each doctor and nurse had also been handed a short summary of each patient's medical condition. One doctor sat in front of a desktop computer and looked at the entire medical records of each patient through the TakeCare system. Another doctor showed CT-scans of each patient to all the other attending doctors and nurses. The patients were discussed one by one and each patient was discussed during approximately eight minutes. For each patient there was one attending doctor that was responsible for the patient. When a patient was discussed, the responsible doctor for that patient had to update the other doctors and nurses about the medical condition of the patient. By discussing the health condition of each patient, the doctors and nurses decided on adequate treatment or correct diagnosis for the patient. In some cases there were words misspelled in the medical records and this led to some confusion for the doctors and nurses. There was no research nurse attending during the observed multidisciplinary conference and clinical trials were never mentioned as a possible treatment for any of the patients.

### 4.2.2 Interview with Research Nurse

The research nurse explained during the interview that there is a list with name, diagnosis and personal number of patients who could be eligible for clinical trials. The list gets updated by doctors whenever a doctor thinks a patient could be a possible participant of a clinical trial. Except for looking at the patient list, the research nurse also attends multidisciplinary conferences a few times each week. In each conference different patients are discussed and the research nurse can through the conference find patients that could be eligible for clinical trials. Each conference takes two to four hours depending on the number of patients that are discussed. The research nurse is responsible for different trials and has them in mind when thinking if a patient could be eligible for a clinical trial or not. If a patient is in contention for a clinical trial, the research nurse looks at the criteria for the trial in mind and by looking at the patient's medial records. The research nurse looks if the patient is eligible for the trial or not. The matching is done manually and both the criteria and the medical records of a patient are printed out on paper. If a patient has been to the hospital for many years, the patient records is extensive and a lot of information about the patient's current and previous health conditions can be found. In some cases the patient has recently been enrolled to the hospital, in which case the medical records is very brief and a lot of information about the patient's health condition from the previous years missing. In general the research nurse thinks that the described process is very time consuming, but after doing the task for several years, the research nurse knows where in the medical records to look and to quickly attain knowledge of if a patient is eligible for a trial or not. In some cases the medical records does not have all the information that is required for finding out if a patient matches a criteria in a certain clinical trial and the patient has to undergo further examination. After the examination, the research nurse will do a second screening in order to see if the patient is eligible for a clinical trial or not.

The research nurse also gave feedback about the current patient flow (Figure 1.1). The original patient flow designed prior to the interview was mostly correct according to the research nurse. The only objection the research nurse had about the patient flow was that it should include a second screening of a patient when a patient's medical records does not have all the information needed and it is required to do further examination on the patient.

The interview with the research nurse also included a user test where the research nurse tested the clickable prototype of the clinical trials system that is presented in this report. The research nurse was told to perform a certain task and loudly say what things are understandable and what is confusing. Since it was only a prototype, some parts of the prototype where not as they would be in real life. This created an amount of confusion for the research nurse and could therefore not complete the task without help from the moderator. By receiving explanations of

the prototype and the thoughts behind the menus and buttons, the impression of the research nurse was that it was a system that could be useful and that it could make the workload easier for research nurses.

### 4.2.3 Workshops

The two workshops held at the Oncology department at the Karolinska University Hospital in Solna yielded in a better understanding of the hospital environment and how the clinical trial system presented in this report would fit in. By discussing solutions and receiving feedback from the clients it did not only increase the knowledge about how the different parts of the hospital are connected and the role of each person. The feedback received from the clients also helped to design a prototype of a clinical trial system that would be suitable and most importantly would lower the workload of the research nurses.

## 4.3 Visualizations

Here our visualizations are presented and described. They are a result of our interactions with the clients and iterations of understanding their needs.

### 4.3.1 Data & System Flow

Figure 4.1 and 4.2 visualize the data flow within the back end of the proposed system for trial matching. Figure 4.1 shows the data flow in the scenario when the principal investigator enters a new trail into our system. The assumptions in this scenario were that all clinical trials have inclusion and exclusion criteria, patient's target age (minimum and maximum age) and sex, and that the patient's target diagnosis can be expressed in ICD-10 format.

ICD-10 is a format that expresses all diagnosis as a code consisting of letters and numbers. For example, the diagnosis for malignant tumor in the frontal lobe has the ICD-10 code C71.1. ICD-10 is the 10th revision of the International Classification of Diseases [Org04].

As a new ICD-10 is entered the system should - in order to minimize human error - suggest the correct code and/or provide a list with all the existing ICD-10 codes. This can be achieved by having a local list of ICD-10 codes stored in a database or having access to the codes via API (the implications of the described entry of ICD-10 code are not shown in Figure 4.1).

The data in Figure 4.1 flows as follows: the principal investigator wants to enter a new trial into the system. Via an interface (which can be seen in section 4.4) the investigator enters each of the inclusion and exclusion criteria from the clinical trial separately (the criteria can be entered in English or Swedish, the significance

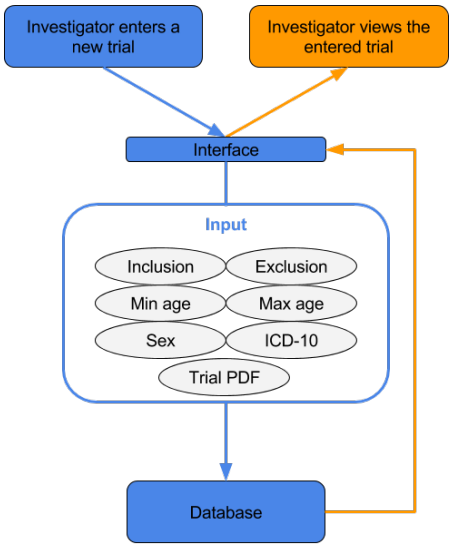



Figure 4.1: Data Flow Investigator

of language choice is briefly mentioned in section 6.2.1 Natural Language Processing and Machine Learning). The investigator also enters the minimum and maximum age for the participants in the trial, and also the participants sex. The investigator additionally provides the desired diagnosis(es) in the ICD-10 format - in this step the investigator is aided by the visual list of all ICD-10 codes and their meaning. All of the inputted information is then entered into a database, which is stored on the hospital's local server. The newly entered trial is then shown in the interface. The investigator is later on able to both delete and edit the trial.

Figure 4.2 shows the data flow in the proposed system in the situation when the research nurse wants to match a patient with available trials. The data flows as follows; the research nurse enters the patient's social security number into the system's interface (a prototype of which can be seen in Section 4.4). With the help of the social security number our system makes an API request to Take Care and as a response the system gets that patient's medical records. From the social security number the system gets the patient's age and sex and from the medical records the system gets the patient's latest diagnosis in ICD-10 format - a lot of the data in TakeCare, as mentioned in section 2.1.2, is unstructured, the diagnosis in ICD-10 format is however one of the structured fields within TakeCare. The system can now filter out the trials for which the patient is not eligible according to age, sex and diagnosis. The system then displays a list of trial for which the patient could be eligible.

From this list the nurse needs to go through all of the exclusion and inclusion criteria manually. The reason behind manual labor and not fully automated match-

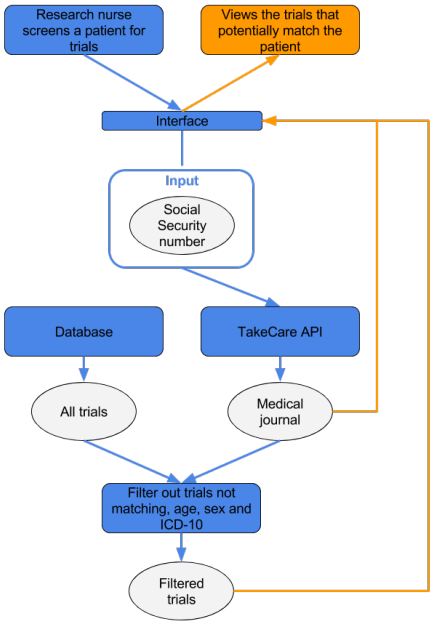



Figure 4.2: Data Flow Research Nurse

ing here is twofold. First of all, there is a notion that the research nurse wants to be in control of the data and see the full patient's medical records and second, there is a notion of distrust towards computers not being "intelligent" enough or being able to make decisions of the medical kind. Another reason behind manual labor is the fact that our state of the art analysis of IBM Watson for CTM (see Section 4.1) has revealed that there is yet to exist a system that can automatically match patients to trials. The system could be made more automatic and we propose some such extensions in Section 6.1.

In order to aid the cumbersome work of reading through all of the patient records - as the research nurse does currently - the system makes it possible for the nurse to search for words in the records. When a word is searched for the system highlights that word in the patient records. The system, however, never collapses the patient records into one or two entries - this is due to the need of control of the user (this feature is however not explicitly illustrated in Figure 4.2). Additionally, although Figure 4.2 displays the API as "Take Care" API our system should be able to connect to any other patient records system via API.

To summarize, Figures 4.1 and 4.2 show data flow in the proposed system within the scope of two scenarios: the investigator entering a new trail and a research nurse wanting to match a patient to a trial. The proposed system is not fully automatic due to both cognitive reasons and the information state of the art analysis revealed about IBM Watson for CTM.

### 4.3.2 Strategy Map

As described in section 3.3 a strategy map was created to communicate the impact of our project on an organizational level.

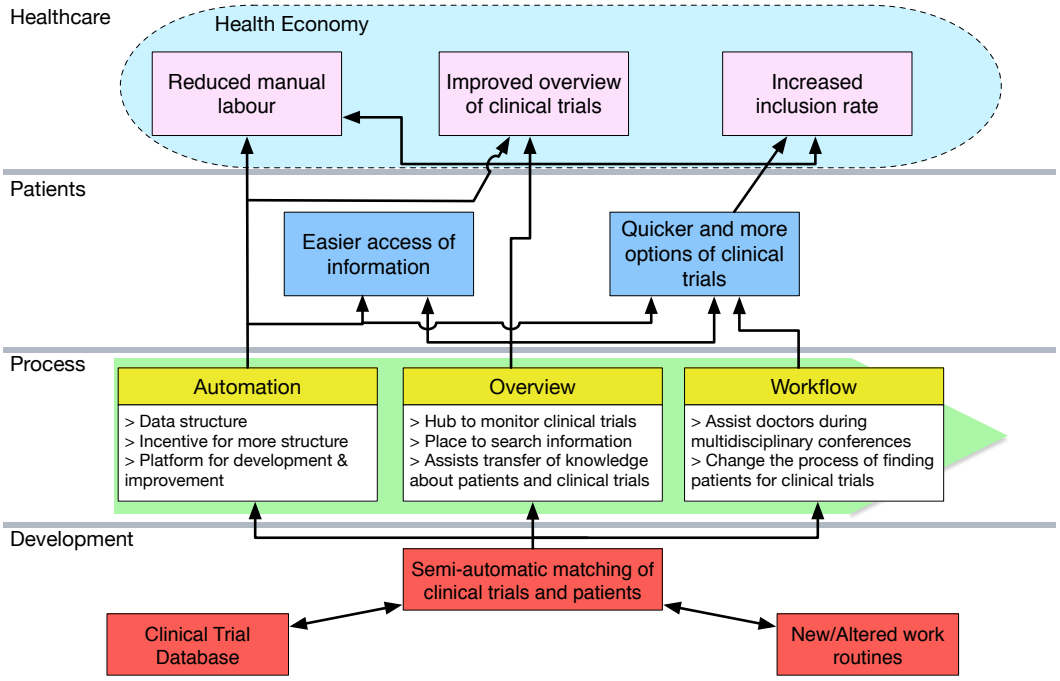



Figure 4.3: Strategy Map

Figure 4.3 shows the strategy map for implementation of our designed system that matches patients with trials. Development is what we have designed. Process is how our design change the current work at Karolinska. Patients is what our design will offer to the patients and healtcare is what the design offers Karolinska, our clients. The arrows between the elements encode dependencies and/or causality. The different entities on each level will be described from left to right. Thereafter the means to measure the goals (KPI:s) will be described and approximated.

On the development level our design offers semi-automatic matching of patients and consists of two sub-parts that can be used by other parties. A database with clinical trials that is available to all doctors and nurses and the creation of new work routines for the stakeholders.

The process level describes how our design impacts Karolinska and is something done over time, illustrated by the arrow in the background. The process level is categorized into three parts. Automation implies structured data within the clinical trial system, which in turn can work as an incentive for more data structure within other units at Karolinska. It also serves as a platform for further develop-

ment and improvement, not only of our system, but also for other systems. The overview represents that our system becomes a hub to monitor clinical trials and a place to search information. It can also assist the transformation of knowledge when a new doctor or research nurse is employed. Our design also changes the workflow of finding patients for clinical trials and offers support during multidisciplinary conferences.

For the patients, our design offers them easier access of information as information seeking is faster for employees at the hospital. Furthermore patient presentation systems can, in the future, connect to our system and potentially offer information directly to the patient. Furthermore our design makes the clinical trial process faster for the patients and can provides more options of clinical trials.

The last level, healthcare, refers to the health care system in general and the stakeholders within the field in particular. Its elements are our goals. Reducing manual labor is of course an outcome of a more automatic process. Improving overview of clinical trials offers more control to the stakeholders within the field. The last goal of increased inclusion rate refers to an increased number of patients participating in trials. The arrows leading to the goals are a representation of how our system will reach them. These three goals can be seen as parts of a unity - health economy.

Health economy is something that the clients lifted during feedback of the strategy map. It goes into every goal one way or another as health economy is a broad term ranging from the specific cost of treating a patient to the time spent by doctors with administrative tasks. One example of this is that our design offers the hospital a competitive advantage with its clinical trial process which can lead to more outside sponsors of clinical trials and thus more funding to the hospital.

As discussed in section 1.6 performance indicators have been identified in collaboration with the clients for every goal. The measurement of inclusion rate is quite trivial as one can measure the inclusion rate upon implementing the system. Regarding inclusion rate the clients has an expected increase of included patients of a 100 %, meaning a doubling of the number of included patients. The other two goals are a bit more intangible and will require surveys and interviews with the users of the system. One performance indicator here might be to look at the usage rate of the system although that should, according to the clients, reach a 100 % upon implementation. To successfully measure the success of the system qualitative interviews needs to be conducted.

## 4.4 Interactive Prototype

The created interactive prototype in this project is the common ground for discussion with the client and stakeholders. The prototype application of the clinical trial system enabled us to present, evaluate and iterate upon the ideas the team had. The application is split in 3 different parts which are based on the needs of the 3 key stakeholders, the research nurse, the principal investigator and the participants of the Multidisciplinary Conference derived from the stakeholder map (section 1.2) and the Patient Pathway (section 1.3).

The interface is divided into 3 panels which are shown in Figure 4.4. During the usage of the application, this layout never changes so that the user doesn't have to adjust to a new organization of information and knows what to expect in each panel.

The main navigation contains a tab navigation bar with the tabs Patients, Clinical Trials and Patient List. We based this selection on the key stakeholders and their main interactions.

The patient or trials are listed in the overview panel with the intent to show only the most important aspects of a patient or a trial for quick browsing. This section also includes a search and filter function.

The Content section is altered based upon the selection made in the overview panel. For example, the details to the patient and her relation to the trials, e.g., how many trials are matched and how high the inclusion rate is.

**Patient panel**

Figure 4.6 shows the interface which is used mainly by the research nurse during her screening process. In the overview panel are the search box which shows the currently searched patient by the social security number. The actual overview consists of the main attributes age, sex and diagnosis and followed by the selection list of matched and participating trials. In the content panel the matched trials are shown by default. Each trial shows the Short title, code, phase and short description of the trial. A bar graph helps to determine how many criteria are met, changeable, require action and unmet. These states are based on the IBM Watson for Clinical Trials (section 4.1).

In Figure 4.7 one of the matched trials is selected and shows the detail which are the inclusion/exclusion criteria list and the searchable patient record. The criteria state can be changed by pressing on the state button. This will show a list of the criteria states to select from as shown in Figure 4.5.

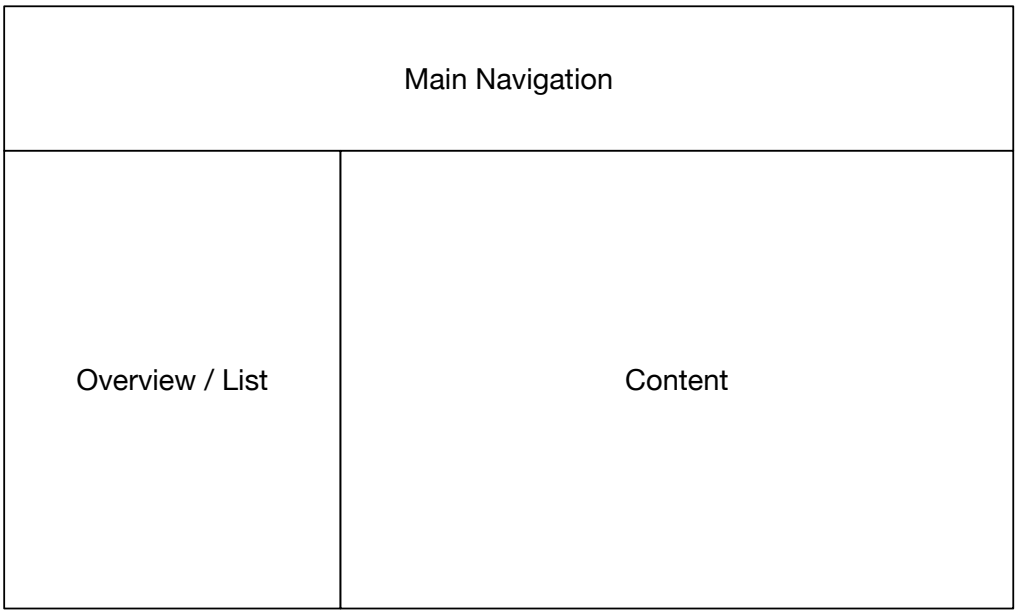



Figure 4.4: Application layout

The patient's full medical records is displayed and always will be because by filtering content, important data might be missing due to the ambiguity of medical records. Found search terms in the patient record is highlighted both in the records and in the time-line next to the scroll bar (to get a quick overview).

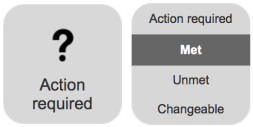



Figure 4.5: States of Trial criteria status button

### 4.4.1 Clinical trial panel

The clinical trial interface (Figure 4.8) follows the same layout as mentioned in section 4.4 and is mainly used by the investigator to maintain clinical trials. In the Overview panel is the list of all trials together with the search box and the "create clinical trial". The list item consists of the title and the code. By default a trial is selected and the details are shown in the content section. It is possible to edit or delete each trial by pressing the edit button or the delete button.

In the editing mode, shown in Figure 4.9, the layout of the content view stays the same, meaning the text fields appear at the same position as the static text in display mode.

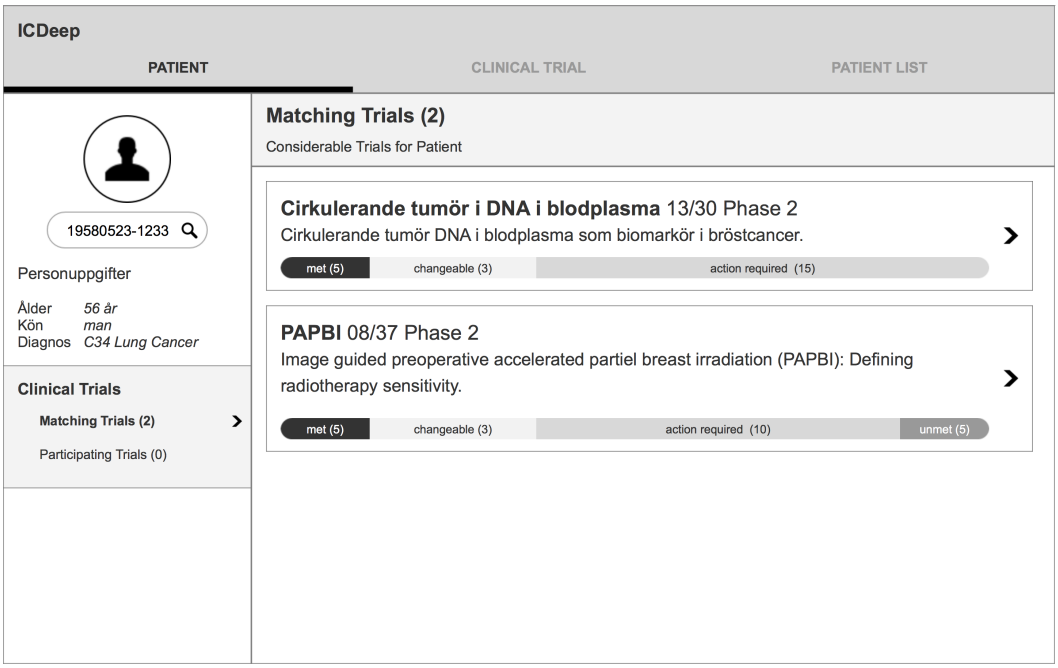



Figure 4.6: Prototype screenshot of patient interface

### 4.4.2 Patients list

The intention of the patients list interface (Figure 4.10 is related to the Multidisciplinary Conference. At the Karolinska University Hospital in Solna, this patient list is compiled before each conference meeting which consist of the patients up for discussion. This list is rather informal and compiled by the moderator. With our interface we want to create a common place for all participants of the conference which allows them to compile the list collaboratively and to have a history of past events.

The functionally are similar to the clinical trials section. In the overview panel is the list of the past and current MDCs, a search box with filtering and button to create a new list item. In the content panel is only a list of patients with a button to add more patients.

This prototype interface serves to show the functionality and not the design of the program.

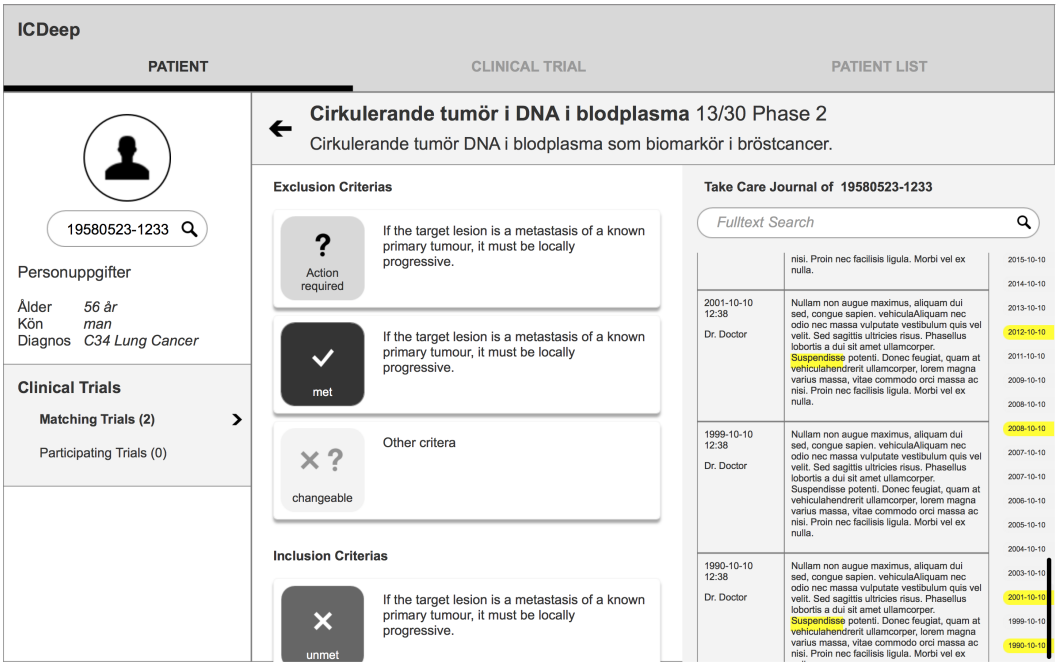



Figure 4.7: Prototype screenshot of patient interface with criteria and medical records view

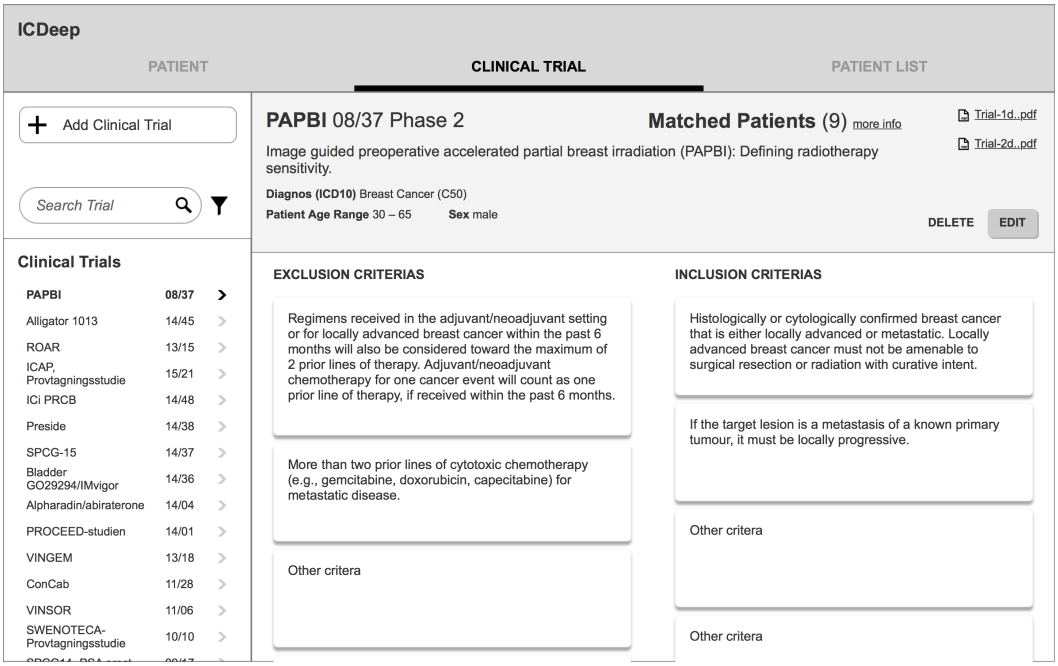



Figure 4.8: Prototype screenshot of clinical trial interface

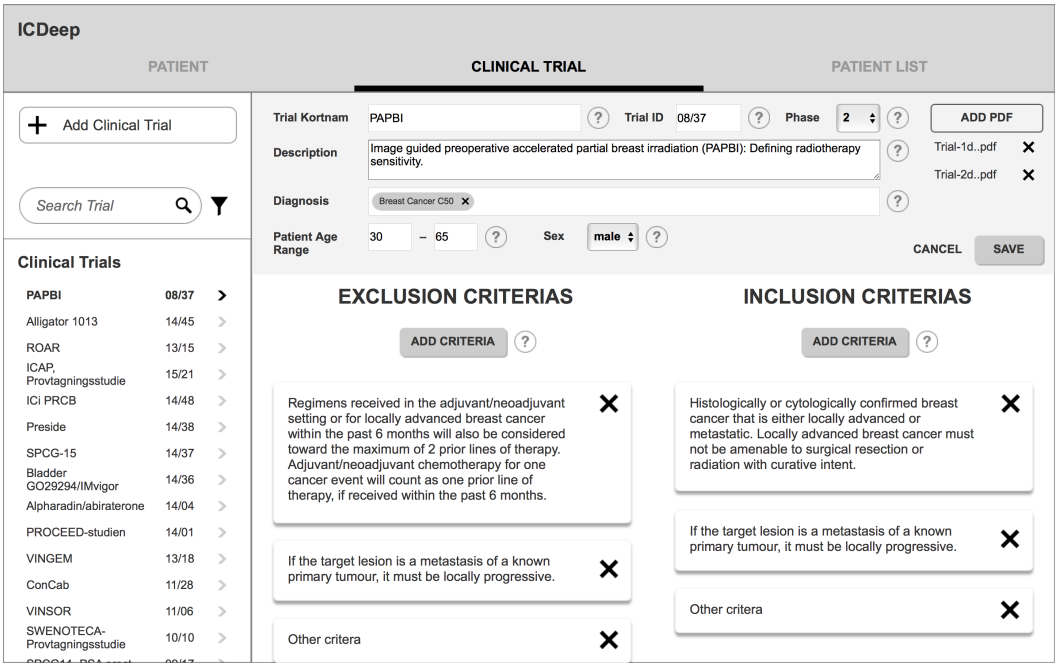



Figure 4.9: Prototype screenshot of clinical trial interface in edit mode

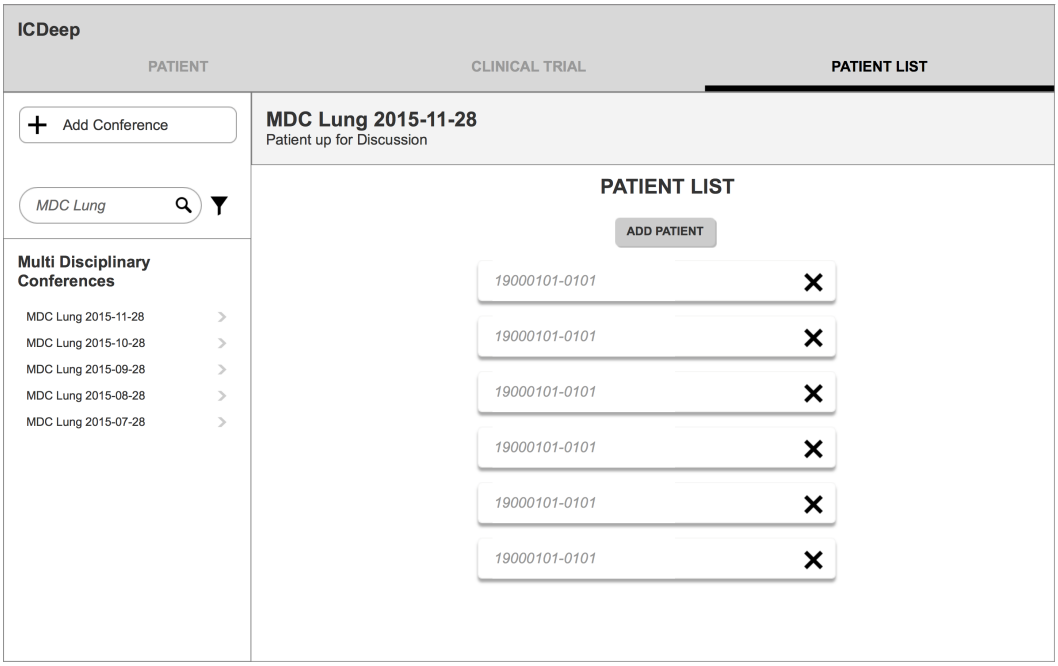



Figure 4.10: Prototype screenshot of patients list

# 5

# Discussion

## 5.1 Application

The solution that we came up with attempts to utilize the best features of IBM Watson. Using the integrated patient records present in Watson as well as the exclusion/inclusion classifications. In contrast to how work is done today at the Oncology department, our solution allows them to digitize and streamline much of the clinical trial management. Since there currently is not any system for overview clinical trials our system easily fills a void in that aspect.

There are however other aspects of our application that may have a negative impact if it were to be implemented. Our application requires a change in their work routine, there is a risk included in changing a work routine, even if the new routine would be an improvement when it is established. It can cause mistakes because some employees are not used to the new routine. This is further discussed in section 5.3

## 5.2 Prototype

The created prototype has a compact packaging and enables us to convey our ideas and intentions to the client and involved stakeholders. The content of the prototype is specific yet leaves room to explore more options and ideas. Due to the interactive features, the users could understand the behavior of the application quickly.

Although there are some negative aspects which appeared during the development and testing of the prototype. The states of parts of the interface are not well chosen, e.g. the patient interface (see Figure 4.7) had no default state where the user could start the search, instead the search was shown as completed. This in between state confused the user and prohibited her to explore the interface (see section user testing). Adding a default state with an empty search box would remove

the user's confusion.

Also there are inconsistencies in the overview panel between the patient and clinical trial interface. In the patient interface (see Figure 4.7) there is additional patient information shown and intertwined with the searchbox. This is in contrast to the clinical trial interface which makes a clearer separation of search and shown information. Also, some states are overwhelming to the user because there is too much information displayed (e.g. edit mode trial). A redesign of the layout according to the clinical trial interface would solve that. Also a redesign of the creation of a clinical trial could be simplified by nesting information and not by displaying all at once, e.g. by applying the user interface pattern "Wizard" [Tid10].

The state button (see Figure 4.5) with an integrated drop-down button confused the user because it didn't look like an interactive element and also the switch between states was not familiar. As an alternative a simple radio button group or a regular dropdown should lift the confusion.

All these suggestions should be tested again with a larger group of research nurses from Karolinska Hospital University in Solna and Huddinge.

## 5.3 Bedding for Hand-off

As the ambition is that our clients will continue our work and implement our design we have utilized Kotter's theories about establishing change in organizations. The approach from the beginning was to focus on the first four steps as rushing through the steps seldom leads to good results [Kot96]. The first two of the four, establishing a sense of urgency and forming a guiding coalition came natural as the project was defined by our clients and they already had a sense of urgency. The latter two, creating a vision and communicating it, proved to be much bigger challenges as the project turned out to be complicated in terms of understanding the problem itself. This was something that was continuously worked on with visualizations in form of flow charts and the strategy map, which was discussed in section 1.4, 3.3 and 4.3.2

# 6

# Future Work

## 6.1 Natural Language Processing and Machine Learning

As mentioned in section 4.3.1, the state of the art analysis has revealed that there currently does not exist a system that matches patients to trials automatically. IBM Watson for CTM uses however, as mentioned in section 2.2.1, natural language processing (NLP) - a field within computer science and artificial intelligence that deals with understanding natural language.

A further extension/improvement of our system would be to use NLP in order to automatically match some of the inclusion and/or exclusion criteria to content in a patient's records. Another possibility for the system is, with the help of NLP, "understand" the inclusion and exclusion criteria and highlight the entries in the patient records that are related to the criteria. A problem that will need to be addressed if such an extension were to be implemented is that all documentation for clinical trials is in English while all the patient's medical records are in Swedish.

Another improvement of the system could be to use Machine Learning (ML), which is a field within Computer Science that deals with learning from available data and making predictions on new data. ML could be used for recognizing patterns in matching of clinical trials to patients. For instance, as was mentioned in the interview with a research nurse (section 4.2.2), some of the inclusion criteria make it rather hard to match patients to clinical trials and the research nurses often starts off by matching these criteria. With the help of ML, the system could learn which criteria are hard to match and begin matching a patient to that specific criteria - making it less time consuming to screen a patient, which might turn out not to be eligible for a trial.

In short, both NLP and ML have the potential to radically improve the proposed system, and so more research needs to be conducted within this area in order

to implement such improvements.

## 6.2 Future Testing

At the current stage, the prototype is in need of several iterations where the design and functionality is updated. This is followed by an implemented version into the current system that can be tested in efficiency. One way of testing this is to implement the new process with the prototype application at Karolinska University Hospital in Solna and not in the Karolinska University Hospital in Huddinge. The difference of change can then be investigated to see if there's a basis to implement the system in a full-scale. An investigation into the hospital adapting the new process can be done individually as well by comparing things like the inclusion rates before and after the integration. Something to keep in mind is that integrating a new process along with a new application might not achieve results in the short run. When there's many users and stakeholders involved it usually takes time for everyone to adapt, and thus, to see the results of the new process.

The testing process needs to be closely monitored and updated and cannot be prematurely rejected for it's real rate of success to be known. Another important part of the testing would be to have focus groups and interviews. The program can help give an overview of clinical trials and procedures and relieve stress for the users by not having to individually keep track of patients and clinical trials. These factors cannot easily be seen and evaluated through numbers but needs qualitative evaluation methods such as interviews and focus groups.

## 6.3 Implementation Suggestions

The project group believes that designing the application for the web would have several benefits. In a hospital setting, a web application would fit in very well to the many different devices and screens involved in the daily work of the staff. We also saw that the research nurse has a dense daily schedule and is often on the move. Considering devices like tablets and smartphones supports the case of a web-based application.

In the fields of web applications, Google showed a plethora of work which could be a vast resource of inspiration for this project. Many ready-to-use frameworks and guidelines like the "Polymer Project" [Pro14] or the "Material Design Guidelines" [goo14] are a good starting point for further investigation and evaluation.

## 6.4 Security Issues and Patient Privacy

It is difficult to foresee what legal challenges this project could entail because the law is not able to define everything in the health care sector and this project falls

within a gray area. The law is constantly changing and evolving but the progress is not fast enough because areas like health care and IT are moving much faster. Professional legal input is required to be able to determine if the project is feasible. See appendix D for some discussion on the matter.

## 6.5 Management and Means of Measurement of Goals

### 6.5.1 Performance Indicators

As some performance indicators are intangible, qualitative evaluations need to be conducted upon implementation. Furthermore in discussion with the clients they have shown a belief and enthusiasm in the project and thus pressuring the clients for clear numbers of performance indicators yielded what can be too high numbers (inclusion rate to rise with 100% and usage of 100%). This is related to expectation management, discussed below.

### 6.5.2 Expectation Management of the Clients

During the project it was from time to time challenging to manage the expectations of the clients. On the one hand, the project consisted of evaluating the current processes and proposing a solution for the problems identified within the learned processes. On the other hand, however the project were to take into account data systems that are in the making, but yet do not exist. If we were to make a similar project in the future a possible solution to problems of expectation management would be to introduce new stakeholders and their requirements. That way some of the requirements would cancel out and some others would win due to majority vote.

As Kotter [Kot96] explains, it is rather important to be a part of a powerful guiding coalition when implementing change in an organization. During the project our guiding coalition consisted only of our clients, but we would have needed to have the support of a few research nurses. It is the research nurses who would mostly use the system we here propose and thus they are in a certain sense the most important stakeholder. Their involvement in the project would have made it more rooted within the organization and would thus provide support to our project and spread the vision of change.

### 6.5.3 Time Allocation for Visualization

Visualizations that were produced during the project all functioned as living documents. That is, all of the visualizations have been iterated through during the duration of the project and updated numerous times, especially after the client meetings. Visualizations have proved to be an important tool in creating a common vision of systems, processes and strategies. The only downside to the visualiza-

tion was that they were rather time consuming. The benefits of the visualizations however outweigh the downside of the time consuming task of creating them.

The strategy map and KPI:s proved to be invaluable in the communication of the goals of the project both internally, within the project group, and externally, to the clients. The strategy map was created rather late in the project and it should perhaps have been made earlier on and been iterated through diligently as the project unfolded.

# 7

# Reflection

## 7.1 What We Have Learned

During the course of this project we have learned a lot about designing for the health care sector and what implications that has for the design. In contrast to many other fields we quickly learned the overarching goal for any project within health care and medical technology: 'Improve care for patients'. We also learned that there is an inherent risk with designing a system that makes decisions or aids in decision making. This is why we put our focus into making it easier for the doctors to make decisions, without affecting their routines significantly. This was mainly learned through communicating with our client.

Furthermore, doing this project has also increased our appreciation of proper project planning. We created our plan during the first week of the project and we have kept up with it for the most part. It has been a great help to us, reminding us when it is time to do things and making sure everyone is up to date with where we currently are in the project.

One lesson learned is to start user testing at an earlier stage. This would have helped us get a better picture of the problems and the current process early on. We would also have liked to do more observations and interviews but due to the project's time limitation it was very hard to be able to do this. We have learned the value of putting more emphasis on interviews and user testing as early as possible.

## 7.2 Challenges and How We Worked Through Them

The largest challenge for us during the entire project was to get a clear picture of how things worked today at the oncology department; how they handled clinical trials, how participants were chosen, where and how they moved through the system etc. Our solution to this was a lot of iterative work with flow charts and schema

depicting patient- and work-flows.

As for the administrative work in the group we soon found ourselves with a Google Drive folder that was too cluttered with different files and folders, something that we could have, and should have, put more effort into structuring from the beginning. While at first glance our documents appear to be very well structured due to large amount of folders, it just an illusion due to the group not being entirely clear about what goes into what folder.

Another big challenge of this project has been its scope. We have had roughly 8 weeks from where we were first informed by the client and until the final deliverables. During this time we have worked in iterations where we have gathered feedback and updated our suggestions of solutions and design accordingly. Much more work and time is needed, both to fully grasp the problems and to find solutions, in this very complex area. We are not stating that we are near a finished product but we believe to be in an early iteration process where we have rooted out the problems and have a suggestion which is up for both debate and testing. The detailed technical specification of this suggestion is redundant due to the fact that it is in the early process where more testing is required.

# References


[B06] Cohen D. Crabtree B. Qualitative research project. http://www.qualres.org/HomeSemi-3629.htm, July 2006.

[Bar94] A C Jacobijn. V Someren W Maarten Barnard, F Yvonne. Sandberg. *The Think Aloud Method - A Practical Guide to modelling Cognitive processes.* " Academic press, London.", 1994.

[Boe02] Viveka Boettege. Workshop02. Lecture, Nov. 11 2002.

[cli15a] Watson for clinical trial matching. http://www.ibm.com/smarterplanet/us/en/ibmwatson/clinical-trial-matching.html, 2015.

[cli15b] What are clinical trials. http://www.cancer.gov/about-cancer/treatment/clinical-trials/what-are-trials, 2015.

[cog14] What is cognitive computing? http://whatis.techtarget.com/definition/cognitive-computing, Jan 2014.

[EP09] Martin J Eppler and Ken W Platts. Visual strategizing: the systematic use of visualization in the strategic-planning process. *Long Range Planning*, 42(1):42–74, 2009.

[epi13] Epic: Departments and ancillaries. http://www.epic.com/software-ancillaries.php, 2013.

[eur12] Medical devices: Guidance document. http://ec.europa.eu/health/medical-devices/files/meddev/2_1_6_ol_en.pdf, 2012.

[FR83] R. Edward Freeman and David L. Reed. Stockholders and stakeholders: A new perspective on corporate governance. *California Management Review*, 25(3):93–94, 1983.

[Gla15] Jeff Glaze. Epic systems draws on literature greats for its next expansion. http://host.madison.com/news/local/govt-and-politics/epic-systems-draws-on-literature-greats-for-its-next-expansion/article_4d1cf67c-2abf-5cfd-8ce1-2da60ed84194.html, 2015.

[goo14] Material design - google design guidelines. https://www.google.com/design/spec/material-design/introduction.html, journal=Google design guidelines, 2014.

[Gui11] ICH Harmonised Tripartite Guideline. Guideline for good clinical practice e6 (r1), june 10, 1996. *Available at:. Accessed June*, 20, 2011.

[HM12] Bruce Hanington and Bella Martin. *Universal methods of design: 100 ways to research complex problems, develop innovative ideas, and design effective solutions*. Rockport Publishers, 2012.

[Jer15] Kirk Jeremy. Dangerous bugs leave open doors to sap hana systems. http://www.computerworld.com/article/3002666/security/dangerous-bugs-leave-open-doors-to-sap-hana-systems.html, Nov 2015.

[Kat15] Noyes Katherine. Sap hana users warned about security vulnerablity. http://www.computerworld.com/article/2937978/malware-vulnerabilities/sap-hana-users-warned-of-security-vulnerability.html, June 2015.

[Kot96] John P Kotter. Leading change, harvard business school press. *Boston, MA*, 1996.

[loo15] Understand users with lookback. https://lookback.io/, 2015.

[Lä15] Läkemedelsverket. Ce-marking. https://lakemedelsverket.se/, Sep. 22 2015.

[Org04] World Health Organization. *International statistical classification of diseases and related health problems*, volume 1. World Health Organization, 2004.

[Pro14] Polymer Project. Polymer project. https://www.polymer-project.org/, 2014.

[sap15a] Sap business warehouse powered by sap hana. http://hana.sap.com/content/dam/website/saphana/en_us/PDFs/ebooks/SAP%20Business%20Warehouse%20powered%20by%20SAP%20HANA.pdf, 2015.

[sap15b] Sap hana use cases. http://hana.sap.com/content/dam/website/saphana/en_us/PDFs/SAP%20HANA%20Use%20Case%20Map%20V2.pdf, 2015.

[Sin13] Enakshi Singh. Sap hana platform for healthcare: Bringing the world closer to real-time personalized medicine - sap hana. https://blogs.saphana.com/2013/10/15/

sap-hana-for-healthcare-bringing-the-world-closer-to-real-time-personalized-me
2013.

[sta12] Discovering the state of the art. http://guides.library.iit.edu/scitech_research, 2012.

[tak15a] Bruksanvisning takecare version 13.4. http://www.shvab.se/PageFiles/2096/Bruksanvisning%20TakeCare.pdf?epslanguage=sv, 2015.

[tak15b] Takecare broschyr. http://www.cgm.com/media/cgm_se/documents_10/takecare_1/TakeCare_broschyr.pdf, 2015.

[Tid10] Jenifer Tidwell. *Designing interfaces*. " O'Reilly Media, Inc.", 2010.

[tri15] Clinicaltrials.gov | search for studies. https://clinicaltrials.gov, journal=Search for Studies, 2015.

[wha15] What is ibm watson? http://www.ibm.com/smarterplanet/us/en/ibmwatson/what-is-watson.html, 2015.

[WL13] Carl Åke Walldius and Ann Lantz. Exploring the use of design pattern maps for aligning new technical support to new clinical team meeting routines. *Behaviour & Information Technology*, 32(1):68–79, 2013.

# Appendix A

# IBM Watson screenshots

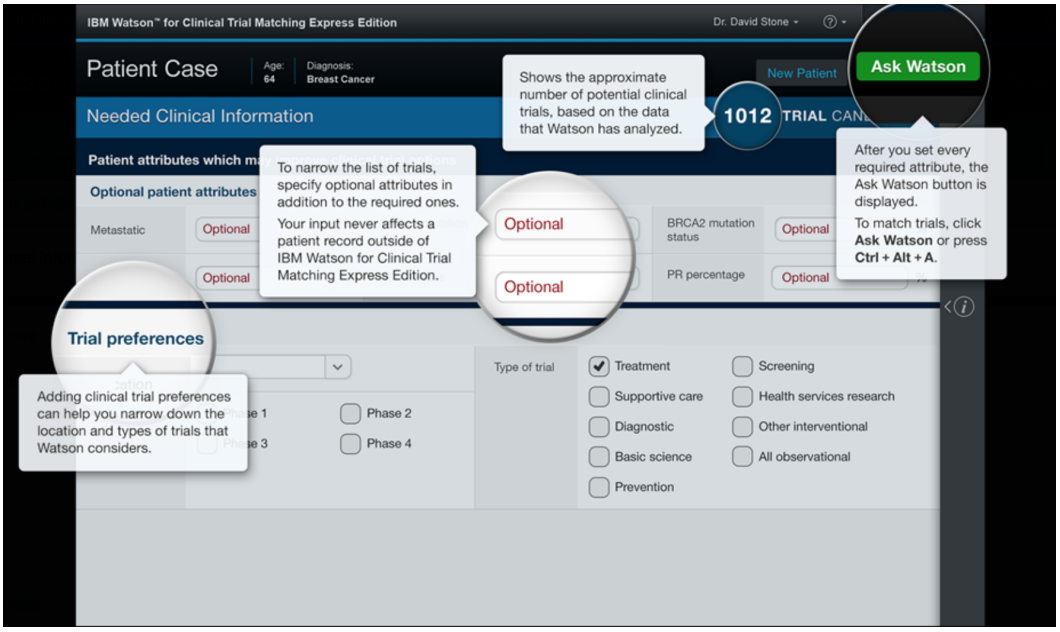



Figure A.1: Watson for Clinical Trial Management / Patient attributes detail

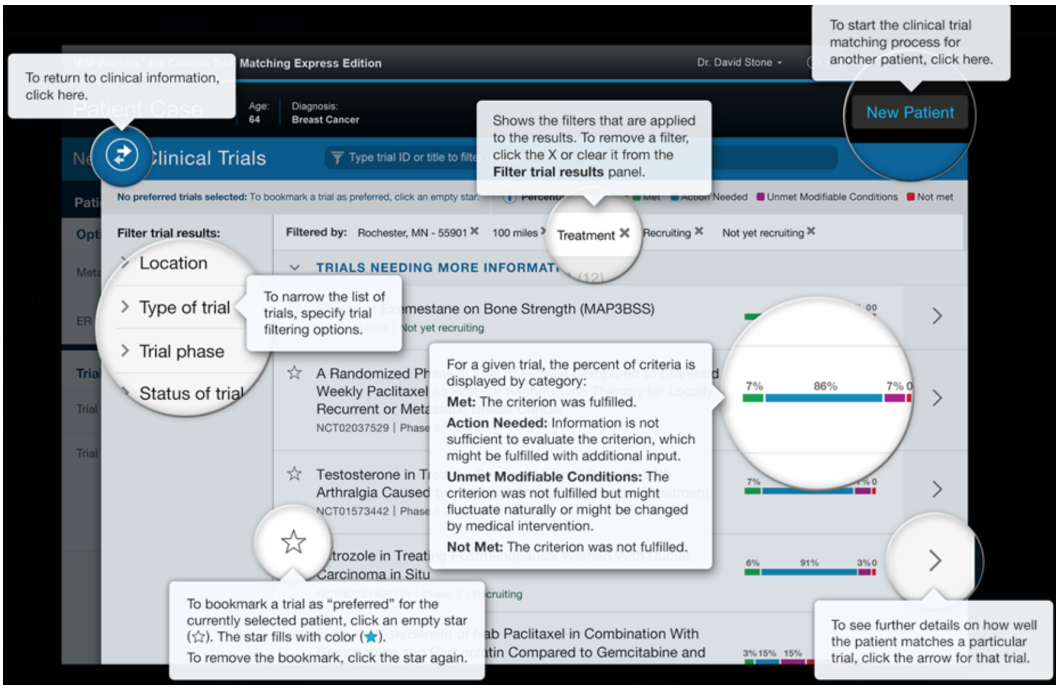



Figure A.2: Watson for Clinical Trial Management / Matched Clinical Trials


Figure A.3: Watson for Clinical Trial Management / Matched Clinical Trials

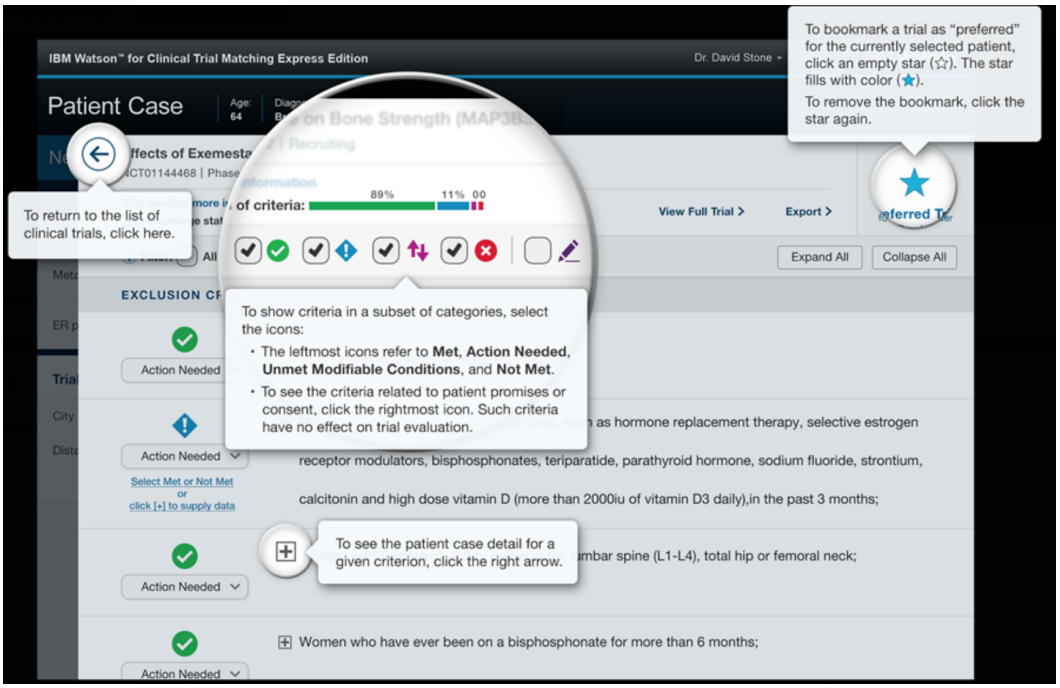
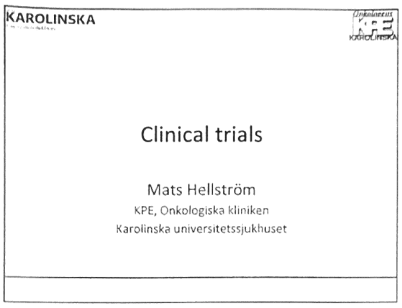


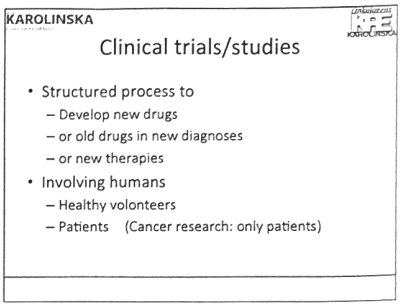

Figure A.4: Watson for Clinical Trial Management / Trial Criteria

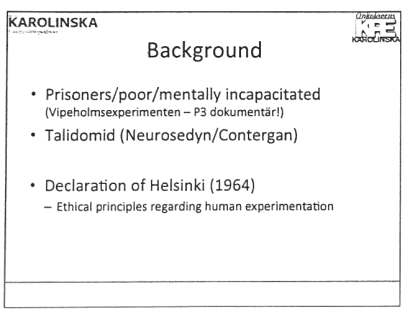
# Appendix B

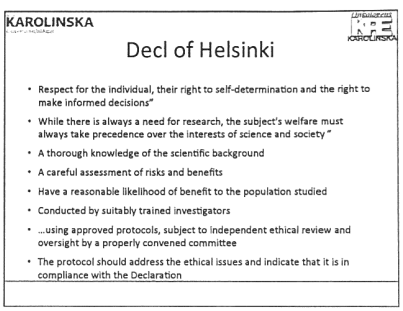
# Mats Hellström clinical trial presentation slides

20.10.2015



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## GCP!

- Ensure that the studies are scientifically authentic and properly documented.
- Standards on how clinical trials should be conducted
- Defining the roles and responsibilities of sponsors, investigators and monitors
- Comprehensive documentation for the clinical protocol, record keeping, training, and facilities, including computers and software.
- Quality assurance and inspections ensure that these standards are achieved.

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## GCP

Positive:
- High standard
- Audit trails
- Trace data
- Trust results
- Ethics
- Clear roles
- International

Negative:
- Paper
- Resources
- Burocratic
- Expensive

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## Regulations

- EU Directive 2001/20/EC and later

Sweden:
- **Läkemedelsverkets föreskrifter om kliniska läkemedelsprövningar på människor** (LVFS 2011:19)
- **Läkemedelslagen** (SFS 1992:859)
- **Läkemedelsförordningen** (SFS 2006:272)
- **Lag om handel med läkemedel** (SFS 2009:366)
- **Sekretesslagen** (SFS 1980:100)
- **Arkivlagen** (SFS 1990:782)
- **Arkivförordning** (SFS 1991:446)
- **Patientskadelagen** (SFS 1996:799)
- **Personuppgiftslagen** (SFS 1998:204)
- **Lag om biobanker i hälso- och sjukvården m.m.** (SFS 2002:297)
- **Lag om etikprövning av forskning som avser människa** (SFS 2003:460)
- **Patientdatalagen** (SFS 2008:355)
- **Offentlighets- och sekretesslagen** (SFS 2009:400)
- **Utsättning av genetiskt modifierade organismer i miljön** (2002:1086)

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## Types of studies

- Lab
- Phase 1 – dose (max dose) 20-100 persons
  - First in man (phase 0)
- Phase 2 – effect, safety profile 100-300 pers
- Phase 3 – effectiveness, compare 300-3000+

Approval
- Phase 4 – safety, new markets

Time: 12-18 years

20.10.2015

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## The Protocol

- Essential. All involved persons working with a study must follow it.
- Background
- Endpoints
- Study design Type, phase, treatment, drugs, randomisation
- Population - Inclusion/exclusion criteria
- Effect evaluation. Respons
- Safety
- Statistics
- Div: Source data. QA/QC. Database. Finance. Publication...

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## Patient information and consent

- Oral and written information
- Layman language
- Separate consent form
- Procedure:
  1. Information, questions
  2. Time
  3. Consent
- The consent may be withdrawn at any time

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## Organisation

- The Sponsor: Initiates and finances
- The Monitor: Quality control at site.
- The Principal Investigator: Specialist, medically responsible. Responsible for data.
- The Research Nurse: Sees the patient, keeping order, data collecting...
- Statistician, datamanagers

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## Inclusion/exclusion criteria

- To find the study population
- Specific for each study
- Common:
  - Age
  - Status: Other diagnoses, blood values, PS, survival, able to participate etc
  - Diagnosis
  - Tumour status

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# Appendix C

# Contextual Observation at the multidisciplinary conference

Multidisciplinary Conference - 3rd of november

The purpose of the meeting was to meet with doctors from different departments and together declare a diagnosis for each patient on the agenda. The agenda of the day consisted of around 20 patients, and none were eligible for clinical trial treatment.

The discussion of every patient started with a doctor reading the referral (english word?) for the patient which summarized why the patient was there and what the purpose was. This included basic information such as health condition (FEV for example) and information on what has been found on scans etc. The doctor reading the referral was as far as it was possible the doctor in charge for treatment of the patient.

After reading the remiss all the doctors discussed on what the diagnosis was using medical records as well as looked in microscopes of cell tests and using the scans. If a cancer type could be classified the doctors jointly agreed upon how to treat the cancer and what the next steps could be. If a diagnosis could not be decided further steps for analysis was agreed upon and scheduled. The doctor in charge of the patient took responsibility of notifying the patient and actually schedule the next appointment of the patient. If the doctor responsible for the patient was not present, that doctor should be notified.

Afterwards, in discussion with Simon (who was the doctor responsible for us on our visit) Simon explained that the main problem is that it is hard to find participants for the trials mainly due to the trials required the patients to be in a generally healthy condition. Furthermore he confirmed that there is a lot of manual

labour required in this process and thought that our idea of having a CT database and matching for patients before the conference would help them keep trials in mind when discussing patients.

He also mentioned that something they decide on during the conference is the staging of the cancer (the cancer type) and is necessary information for almost every clinical trial. See picture below.

The remiss contains a summary of why the patient is discussed at the conference and can be found under letters in takecare.

On two occasions the journal contained misleading information where the person inputting the information simply had misspelled a word causing confusion among the doctors.

Simon also thought that our idea of manually inputting the trials seemed like a good idea and was doable. However, Simon did not have any technical knowledge.

Simon also mentioned that there is an app in norway that does something like we try to do and knew the doctor in charge of that project. He would email information about the app this afternoon and also provide contact details for the doctor in charge.

At the conference there were two people sitting in front of computers - one person sitting with patient journals and one person sitting with CT-scans and showing all the scans to the other doctors at the conference.

# Appendix D

# Patient Privacy Legislation

There is a connection between the Patient Data Act and Personal Data Act (1998:204) concerning the processing of the personal data in health care. It is necessary to take this into consideration if the information is going to be automated and structured and made available for searching in an organized database.

The statute comment to the Bill 2007/08:126 states that Patient Data Act is a ”regulation of the internal confidentiality”. This means that only certified people within health care, e.g. a doctor, are able to access confidential patient information. There are some keywords in the Patient Data Act that are important to understand to be able to interpret the law correctly. In this context, the word ”caregiver” is an important expression that needs to be defined. 3§ of the Patient Data Act states that ”caregiver” means a natural person or legal person that is professionally involved in health care. This legislation provides some loop holes for personal data to be used considering the restrictions that are made on the information and who has access to it. For example, 2§ in chapter 2 of the Patient Data Act states that it is allowed to process personal data even if the individual patient objects to it. The individual's right in this case is solely the right to have the opportunity to object, but it is still allowed to a certain extent to process personal data. The case may also be so that the patient demands that his or her information is processed in a way that is not specified in the Patient Data Act. The main rule in Chapter 2 focuses on the individual's expressed consent to a particular personal data process, which opens up a leeway for situations that the law has not literally expressed.

The basis to access information derives from the Freedom of Press Act and Public Access to Information and Secrecy Act. The Patient Safety Act, Patient Data Act and Personal Data Act limit the ability to share and take part of information within health care.

The legislation that is most relevant in this case is the Patient Data Act

(2008:562), however the Patient Safety Act is important to take into consideration due to the confidentiality aspect. The paragraph which is applicable to our project is 4§ in chapter 2 in the Patient Data Act where the health cares primary purpose of processing patient data is declared. It states that patient personal data may be processed if it is needed to fulfill the obligations set out in chapter 3 (duty to keep patient records), set up documentation required for patients or the administration related to patients, help in providing the right health care for the patient in each individual case or for statistical reasons. Here one can argue that our project falls within the scope of providing the best health care for the patient. 2§ in chapter 3 states the purpose of patient records. It says that the purpose of documenting the patients personal information and keeping a patient's medical records is primarily to facilitate and contribute to good a safe care of the patient. Such medical records are needed for patient monitoring, development of health care, research and such records are also good information sources. The aspect that is most important in our case is keeping in mind that the patient information provided is to be able to better the health care for that specific patient and that the patient can receive the most beneficial and optimal health care for him or her. Furthermore, this project can be seen from a research point of view and research work is allowed according to Swedish law. However it is difficult to foresee what legal difficulties may arise in connection with patient data processing because the law is not crystal clear in its definition of how the law should be interpreted because there are many circumstances to take into consideration. One must take precaution when spreading the sensitive patient information so that unauthorized people do not take part of it and that the information is stored in a safe way including hard copies of information and electronic copies. Not taking this into consideration would mean going against a series of provisions on privacy and personal data. The statute comment states that the reason for specifying the primary purposes of the Patient Data Act is so that a framework is created where personal data may be collected and processed as long as it is within the limitations of the framework. The premise is therefore that processing of patient data is allowed if it falls within the framework. A further assessment is however needed by the caregiver and how detailed or precise such an assessment should be may vary from case to case.

5§ in chapter 2 is somewhat difficult to interpret but the statute comment helps in shedding light on what the law actually says. It states that in certain cases it is allowed to use personal data that is already available in the business even if such personal data has been collected for another purpose. If special circumstances demand that information is provided to another authority it may be done in accordance with the Public Access to Information and Secrecy Act (2009:400). The statute comment further states that the so called "Finality principle" also applies to the processing of personal data under the Patient Data Act. This means that personal data that is already available in health care may be processed for another purpose than the purpose it was collected for, provided that the information's new objective is consistent with the previous purpose. It further states that information

collected may be used for historical, statistical or scientific purposes and that use of information for research purposes is allowed without having to state any specific reason. However here one must take into consideration the Act (2003:460) on Ethical Review of Research Involving Humans and the Personal Data Act.

# Appendix E

# Project Management

Agile management with weekly iterations was used for this project. The group had at least one meeting a week with the primarily agenda to present what had been done, things in need of discussion and what the focus for the coming week should be. The project group met their supervisor, Marie Sjölinder, on a weekly basis and the supervisor provided the group with feedback on the ongoing work.

In order to be able to conduct work in parallel and work more efficiently the project group was divided into six well-defined responsibility roles (Table E.1).

| **Tasks / Responsible** | Niklas | Aydin | Marcus | Elizaveta | Huiting | Charles | Gustav |
|---|---|---|---|---|---|---|---|
| Project Leader | | | | | | | |
| Prototype | | | | | | | |
| Report | | | | | | | |
| The system/tool | | | | | | | |
| Website | | | | | | | |
| Workshop/Interviews | | | | | | | |

**Table E.1.** Responsibility Matrix

A Gantt chart was created to keep the project on track (Figure E.1). The focus of the chart was the most important deliverables - marked as red diamonds, which include the prototype iterations, the website and the report. The chart was created to provide a quick overview of the project phases and the work that comes with it.

A risk analysis matrix was also created (Figure E.2) along with appropriate measures (Figure fig:measures-risks) for each risk. The matrix had the potential to help the project group prepare for potential risks and to indirectly avoid the risks by knowing about them.

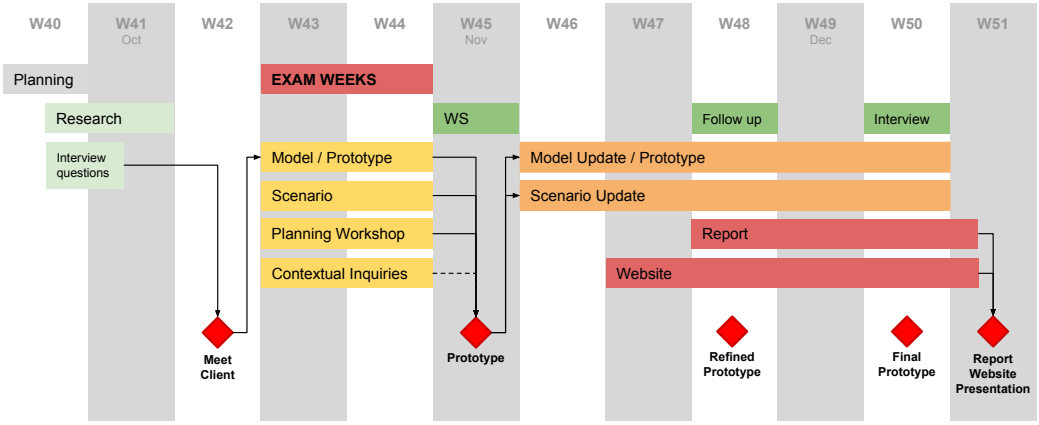


Figure E.1: Gantt chart providing an overview of the project

| | | | | Impact | | |
|---|---|---|---|---|---|---|
| | | Very Low | Low | Medium | High | Very High |
| | Very High | 1.1 Some people not turning up for meetings | 1.2 | 1.3 Stressed at the end -> lower quality report | 1.4 | 1.5 Forgetting a major area |
| | High | 2.1 | 2.2 Not keeping up with our initial plan | 2.3 Not agreeing on things | 2.4 Group members not doing their job | 2.5 Not enough stakeholders for interviews/work shops |
| Likelihood | Medium | 3.1 | 3.2 | 3.3 Not starting to write the report on time | 3.4 Not enough documentation during the process | 3.5 |
| | Low | 4.1 | 4.2 A group member gets sick during final presentation | 4.3 Group member gets sick for a long period of time | 4.4 Not enough feedback from our supervisor | 4.5 Bad group dynamic |
| | Very Low | 5.1 We run out of coffee | 5.2 | 5.3 | 5.4 Losing all of our documents | 5.5 Not being able to meet with Mats/Rolf and/or supervisor |

Figure E.2: Risk Analysis Matrix

| | |
|---|---|
| 1.1 | People who do not show up for meetings will be punished by bringing Fika |
| 1.2 | |
| 1.3 | Make sure we keep up with the schedule |
| 1.4 | |
| 1.5 | Recapture on meetings |
| 2.1 | |
| 2.2 | Weekly meetings and iterating the plan continously (going through it) |
| 2.3 | Compromise/Vote |
| 2.4 | Talk to the person who's not doing his/her job. Go to Björn if things don't change. |
| 2.5 | Plan ahead/Early invitation |
| 3.1 | |
| 3.2 | |
| 3.3 | Stick to the schedule / Recap |
| 3.4 | Keep track of your source / Summary after research finished |
| 3.5 | |
| 4.1 | |
| 4.2 | Divide that part amongst us |
| 4.3 | Divide his/her part among us |
| 4.4 | We will try to get information from another source (maybe Björn or Mats) |
| 4.5 | Clear division of work |
| 5.1 | Buy more |
| 5.2 | |
| 5.3 | |
| 5.4 | Keep a backup |
| 5.5 | Find some other relevant person to talk to |

Figure E.3: Measures for risks

# Appendix F

# Questions - Interview with Research Nurse

**app** How does a normal day for you as a research nurse look like?

Can you show us how you evaluate/screen a patient's journal?

How do you document the screening?

When do you attend a multidisciplinary conference? How are you informed?

How do you find patients for the clinical trials?

Is there anything you would like to change within the current process of finding patients for clinical trials that could make your workload easier?

Are there any documents that need to be printed? For what purpose?

Is there any communication between the different research nurses?

How do you match inclusion/exclusion criteria for a patient?

**User Test**

Scenario

Try to look for a patient → explore Interface → explore trial → change criteria status → browse journal

During all steps: Explain what you see