Determining test interval strategies for clients undergoing preventive screening

Preventive screening using MRI in (private) healthcare is increasingly applied. Main reasons for individuals to perform preventive screening, is to be reassured about their health status, be able to manage potential risks to avoid the fear of having regrets when not applying for screening.

From government’s perspective and thus with regard to the greater community, screening programs they offer are to prevent people from developing a (chronic) disease. In addition, while using the strategy of a cyclic screening program, the goal of this public screening is to detect and diagnose to better cure or treat a certain disease in an early stage of development. Furthermore, an increase in frequency improves the sensitivity and specificity of the related outcomes as well. With these programs public health will be monitored more carefully, which can be profitable for future health provision; Eventually, when having the possibility to treat diseased individuals in an earlier stage of development, the amount of treating chronic diseases or other intensive cases can be reduced.

Aside from the screening of populations, individuals can also check or screen their own health status without having any complaints or reason for indications. Within the Dutch healthcare sector this preventive medical research is called “Preventief Medisch Onderzoek” (PMO). From an individual’s perspective PMO can be performed in several ways.

Prescan, a company originated in the eastern of the Netherlands, where most of the managerial and administrative departments are established in the headquarter of Hengelo, Overijssel, many of its private clinics are to be found just across the borders with Germany: Bottrop, Düsseldorf, Gronau, Rheine, Oberhausen and Ochtrup. Clients can also go to the relatively new private centres in Baarn, Schiedam, Amsterdam and Den Bosch.

Prescan is a leading organization in the provision of preventive MRI scans for individual screening. At Prescan, quality of healthcare services provided to their clients, is one of the main objectives they are striving for. Currently, planning a revisit to keep track of one’s health state is occurring more frequently. When clients receive advice to return for screening in the future, this currently is solely based on knowledge and experiences of the involved radiologists. To recommend an appropriate interval for a potential revisit, personalized for these specific clients, Prescan wants to have more insight in the estimation of risks in developing a clinically relevant finding. Based on data of comparable former clients and related (behavioral) risk factors, knowledge on the development of diseases can be gained.
PURPOSE - RESEARCH OBJECTIVE

Prescan provides their clients with a form of PMO in which bodyscans (MRI) are performed. By doing so, every individual in essence receives a kind of update about their health status. An insight is given in several relevant body regions, in which a selection of diseases and abnormalities can be diagnosed. Although in general it is unknown whether an individual will develop a disease, Prescan prefers to improve their advice for a potential revisit in future. Based on personalized risk profiles, knowledge in the development of diseases to potentially develop in future can be examined.

One of the main services within the possibilities of preventive screening techniques Prescan offers, is the Total Bodyscan (TBS), which is considered to be a set of MRI scans for different regions of the human body. To optimize the service towards existing and incoming TBS clients and thus provide better information and consultation, one of the objectives considers to scientifically proof and argue related risk factors and growth characteristics of several abnormalities and diseases. In this way, the goal is to come to a cyclic preventive screening strategy, with a personalized strategy for an incoming individual for revisiting Prescan. Based on retrospective data, some useful insights of the existing Prescan population will be given, to get to a more personalized strategy to revisit for screening for clients who underwent a TBS, without being diagnosed with an abnormality.

RESEARCH QUESTIONS

Therefore, the main goal of this study is to better specify and explain certain cyclic screening strategies and optimize the client’s experience and interval of their Prescan visits. Especially, when no findings are diagnosed during the first screening, it may be valuable to revisit later, in terms of repeatedly performing preventive MRI to update on their health status through this medical checkup. This can be a revisit for a TBS, or a selection of (one of the) focus areas Prescan offers. Main research objective is defined as:

- How can the time interval to a next potential screening moment be determined, for Prescan’s clients undergoing a Total Bodyscan, based on gathered and analyzed retrospective data?

Following from the definition of the core problem and provision of background information, several research (sub)problems have been developed in order to come to a solution for the main research question:

- What are current procedures and definitions within the topic of (private) preventive screening?
- What are current strategies and procedures used within Prescan’s organization for treating their clients?
• What are possible outcomes and clinically relevant findings of the concerned abdominal MRI within the TBS concept??
• Is it feasible to accurately determine the probability of developing and growing a clinically relevant finding based on currently available literature and data, and if so, can this be translated towards a personalized interval?
• How can the steps taken to solve the core problem of this research be improved to allow generalization to the other diagnostic tests offered by Prescan?

RESEARCH DESIGN

To determine a solution method for the core problem, a context investigation of preventive screening will be performed. To do so, current developments are highlighted. Relevant publications and background literature will be taken into account. In this way, this functions as required knowledge and preparation to develop further towards the report’s objective. In addition to the context of the topic, an internal analysis of Prescan’s organization procedures will be performed. By doing so, useful insights of responsibilities and data processing will be identified.

Since the objective is to improve recommendations for future follow-up towards the clients, it is important to know what experienced (dis)advantages are within preventive screening. Psychosocial factors and preferences can contribute to shared decision making of the screening frequency. Therefore, relevant articles are included within the investigation of the topic, before further focus of the report is determined.

After performing this context analysis where relevant insights and perspectives are treated, the company’s available data is gathered. When gathered and analyzed, all included data is prepared in a way that the intervals of all retrospective clients can be presented. Since a lot of clients perform preventive screening with multiple possible outcomes, a certain delimitation will take place. Subsequently, a literature search will be conducted focusing on current status of incidence, progression and other disease-related information. With a focus on screening strategies, relevant information can be used on the database conducted within the case of Prescan.

After establishing the previous steps, the intention of this study is to eventually generalize the setup and model for overall preventive MRI findings, and thus for clients performing preventive screening in general. The execution of this step will be, logically, completely depending on the results following from all these steps and the extent to which the subproblems could have been answered.

LITERATURE REVIEW
The literature search give insights in answering the first part of research question 4, “Is it feasible to accurately determine the probability of developing and growing a clinically relevant finding based on currently available literature and data?” To do so, literature is used to gather information and see what current trends and knowledge are. In this way, insights and strategies are used to relate to Prescan's situation and data.

Since screening techniques are improving and become more capable in detecting several abnormalities, the number of these outcomes and incidental findings are increasing. Although these advanced techniques nowadays cause a higher incidence or detection of new abnormalities, it ensures early diagnosis and thus the possibility to treat this finding. In all three selected "cases" in this report, early asymptomatic diagnosis often yields a better prognosis for this specific person. An interesting comparison when thinking of all abnormalities not screened at all. However, a new challenge arises of managing the appropriate follow-up and surveillance for all different sorts and behaviors within the diagnosed incidentalomas. Percentages from researches in Japan for example, add up to a prevalence of abnormalities found in approximately 40-50% of the population (slightly more in men; 44.5% against 34.2% in females). Consequently, the relevance increases of managing these findings and select or filter all potential malignant ones requiring follow-up.

In line with results from this literature search, some scientific thresholds and guidelines are gathered and analyzed in a report of the American College of Radiology.

Initially, a literature search was conducted focusing on indicators for disease development and screening trends from the perspective of the selected abdominal MRI findings. Since this gave relevant insights but was not sufficient in information provision to take further steps in the estimation of risks in developing clinically relevant findings in future, a second search was performed, with a better focus on solely strategies for follow-up determination. By applying these methods extra insights in both directions were discussed.

**SOLUTION DESIGN**

Findings of MRIs performed at Prescan are analyzed and registered in a report by the involved radiologist. To compare and validate the outcomes of the gathered data, in this report these findings will be categorized. This is based on the most relevant characteristics per finding, following from the conducted literature search. In addition, categories used within the Aftercare department and the earlier conducted research are partly used as well.

Within the potential AAA group of findings, age, sex and size of the detected dilatation were labeled as important risk factors in developing an AAA. According to literature and the ACR, development in size is a relevant risk factor to track over time as well.
For the second group, this includes pancreatic lesions like a cystic mass. Of these findings, it's important the following risk factors are identified: size, contour and location, and whether the mass can evolve to a more malignant stage like BD-IPMN, SCN, MCN or PDAC.

When renal masses are considered, its categorization is mostly based on the behavior of the specific abnormality, where a hemorrhagic cyst or calcification of it are good indications for their stage in the Bosniak classification system. Furthermore, size is partly taken into account, where cysts from 30mm are included for follow-up.

After the data analysis performed, all the client's ages and their development through multiple researches have been visualized, in which several selections of findings were highlighted. Characteristics of the selections with all findings were presented separately. Afterwards, all findings were generalized into the definition of a clinically relevant finding, for which follow-up has been advised by the treating care providers.

With these visualizations, an overview is given of what the ages per related research moments were, and what the personalized care path has been per client at Prescan.

To come to an estimation for new clients’ potential revisit recommendations, a model will be produced to estimate the risk of developing a clinically relevant finding. This will be done by the use of the available and prepared data, for several selections of client groups. Furthermore, the fact that this report considers research in the field of health care technology and management, must be taken into account as well. Therefore, some assumptions are made tending towards this field of knowledge, which can slightly influence the clinical appropriateness in some situations.

In the working field of healthcare research, the medical term prevalence refers to the proportion of persons in a population who have a particular disease or attribute at a specified point of time, or during a period. It gives information of the amount of people having a certain disease, and for example how widespread it is.

To estimate the risk for developing a clinically relevant finding of a returning client at Prescan, data from comparative clients will be analyzed to come to a recommendation for follow-up. Since this data already exists over a large population, initially the research moments of all included clients are sequenced. Of each of the individuals it is known per corresponding scan moment, whether they had been diagnosed with a finding or not.

Considering the objective of these prospective risk estimations, it is even more interesting and required to look at the risk of developing a disease in future. According to Witteveen and Otten, probabilities of state transition from the initial state (healthy) to the next (diagnosed finding) have to be known. But, in this situation, asymptomatic clients aren't screened every now and then, and certainly not all of them performed a screening multiple times. This occurrence of having unknown parts of information within
the research population, is often called censoring. To account for this, health scientists got to use a more adequate way of describing this estimation of developing a disease; the incidence. The incidence rate conveys information about the risk of contracting the disease, whereas prevalence gives an indication of how widespread it is. It determines a probability of developing a specific disease over a stated period of time. Therefore, it can be seen as an estimate of risk.

A model for estimating risks of developing findings is conducted, based on the second part of the literature search insights. By doing so, all findings found are included, for both the revisiting clients and those who visited Prescan once during the research period determined.

To come up with the number of cases (events) as ratio of all person years, initially the period in which will be searched is determined. When a client is for example 62 at moment of screening, this person is included when the initial period of lower bound (LB) and upper bound (UB) of ages equals [60-70].

Since the LB and UB determine which clients are included in this calculation, it means that every client within this selection visited Prescan at least once in between this period of [LB,UB]. However, this does not mean their whole period of their screening path is in between these bounds. Therefore, their share is calculated based on reframing their path and deciding to which extent this part is taken into account.

To actually calculate this, the second step is using the distinction made between the characteristics of the selected clients: whether they were diagnosed with a clinically relevant finding during their screening visits at Prescan, determines which procedures to call. In the preparation of the dataset this characteristic was included, so a simple check can confirm whether a client belongs to the "non-finding" or "finding” group.

**VALIDATION OF THE DESIGN**

Looking at the validation of a model, it is related to verification in a way that verification can be seen as subset of the wider issue of validation. A key concept of this broader validation is the extent to which it serves the specific purpose, or objective of the setup. With the use of these definitions, this report makes a distinction between concept and data validation, and validation of the solution.

First, the concept validation in this report's situation is different compared to standard validations of simulation models for example. This is, because this model's objective is solely to dynamically determine incidence rates over different subgroups selected. To show sensitivity of the outcomes and influence of using the definition of IR, multiple scenarios are considered.

In conclusion, this report's model can be considered valid, due to the fact that the model serves the objective to present incidence rates aligned with its definition and calculation. On the other hand, it also is completely depending on its data input. For example, next chapter shows results with [LB,UB]
differences of two years, because a smaller bin size would be too dependent on events occurring by chance. With an average disease prevalence of 1% for example, outputs can easily differ too much, when a small amount of clients are included in the subgroup (n=50 for example).

Validating the solutions of the model based on outcomes is achieved by comparing these outcomes to real system measurements and experts' intuition. For example, when looking at the incidence rates of diseases calculated between zero and 25 per 1000 person years as first results will show, this means over a period of one year zero to 25 out of 1000 subjects will be diagnosed with this specific disease. These solutions can be considered as reasonable values.

Strengthening these statements, can be accomplished by feeding the subgroups and related calculations with more and different data. For example, when we want to improve the confidence of the model to proof validation, data of other findings and body regions can be gathered and used as input of the same model. By comparing differences in incidence rates and fitting these outcomes to existing data on disease incidence, external validity of the model can be shown.

RESULTS, CONCLUSIONS / RECOMMENDATIONS

Of all clients within the research population considered, about a fifth revisited for preventive screening. A preferred selection of these clients undergoing a Total Bodyscan was made, based on interviews held and their expert’s opinion. Therefore, within client selections of the abdominal body region, all aortic, pancreatic and renal findings out of the research population were identified during a 20-month period. As expected, of all revisiting clients the average in-between period of screening revisits was shorter for clients of whom a finding was diagnosed in their first moment of screening.

By selecting clients out of the research population based on their age, the most personalized results were achieved by the model calculations. Especially when comparing subgroups with starting ages 30, 40, 50, 60 and 70, incidence rates are higher when the clients’ ages increase. For different age categories and corresponding estimation of the related risk, the period recommended for a potential revisit is presented. These insights can be used as support tool in the shared decision making between radiologists at Prescan and present clients.

When using these estimations in the determination of client advise, it is recommended to point out these indications are based on retrospective data of comparable clients. Furthermore, this study focuses solely on a selection of relevant findings, which cannot be used as generalized estimations for potential development of clinical findings directly. For further research it seems valuable for Prescan to keep track of more (behavioral) risk factors of their clients, to achieve a more individualized recommendation to revisit for preventive screening. When the amount of data increases, or retrospectively other body
regions and stages of clinically relevant findings are included in the analysis, it seems possible to indicate personalized predictions of developing potential threats in future.