Feasibility study for the development of digital decision support systems for personalised medicine

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Contractor: Dr. Peeter Ross
Tel. +372 5635 3460
E-mail: Peeter.Ross@ttu.ee

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Team members of the Feasibility study for the development of digital decision support systems for personalised medicine:

**Coordinating team, affiliations and positions**
Dr. Peeter Ross – Team leader, Coordinator (Peeter.Ross@ttu.ee) – Tallinn University of Technology, Head of the Cardiovascular Medicine Institute eMedicine Laboratory.
Siim Läänelaid – Assistant to the coordinator – Todos OÜ, Member of the Board
Evelin Vanker – Technical support – Tallinn University of Technology, Faculty of Information Technology, Department of Informatics, Project Manager
Inge Pruks – Technical support – Tallinn University of Technology, Cardiovascular Medicine Institute, eMedicine Laboratory, Project Coordinator

**Clinical experts**
Dr. Margus Viigimaa – Cardiology – Tallinn University of Technology, Cardiovascular Medicine Institute, Chair of Cardiovascular Medicine, Chair and Professor; North Estonia Medical Centre Foundation, Chief Physician, Cardiology Center Head of Research
Dr. Peeter Padrik – Oncology – Director of the Tartu University Hospital Cancer Center
Dr. Ülle Jakovlev – Endocrinology – East-Tallinn Central Hospital, Clinic of Internal Medicine, Head of Center of Endocrinology

**IT architecture, design and data structure analysis experts**
Janek Metsallik – Tallinn University of Technology, Cardiovascular Medicine Institute, eMedicine Laboratory, Expert of e-health
Maarja Märus – Independent Design Consultant, Kontsept Disain OÜ
Jaak Kaevats – Design Consultant, Aspekt Labs OÜ
Kuldar Taveter – Tallinn University of Technology, Faculty of Information Technology, Department of Informatics, Chair and Professor of Software Engineering
Rein Kuusik – Tallinn University of Technology, Faculty of Information Technology, Department of Informatics, Chair and Professor of Foundations of Informatics
Erkki Leego – Hansson, Leego & Partner OÜ, Managing Partner
Kati Korm – Tartu University Hospital, Informatics Service, Head of Development Department
Liisa Parv – Tallinn University of Technology, PhD Student (Health Care engineering)
Raimo Laus - Estonian Health Insurance Fund, Head of IT Department

**International experts**
Heli Johanna Salminen-Mankonen – University of Turku, Director of Auria Biobank
Adam Benjamin Wilcox – Intermountain Healthcare, Director of Medical Informatics
Siew Hong Lam – Intermountain Healthcare, Medical Informaticist
Timo Haikonen – Duodecim Medical Publications Ltd., Director
Ilkka Kunnamo – Duodecim Medical Publications Ltd., EBM Guidelines & EBMeDS, Editor-in-Chief
Executive Summary

The current report has been composed by a team of experts (see page 2 for names and affiliations) in the framework of a procurement contract between the Estonian Ministry of Social Affairs and the Tallinn University of Technology. The aim of the study was to provide conceptual digital decision support solutions supporting clinical decision making following the principles of personalised medicine.

The feasibility study team has mapped health data available in different Estonian information systems. We also have identified standards and data formats that are used in each of these information systems. In parallel we have developed model scenarios for three clinical conditions (cardiovascular diseases (CVD), diabetes, cancer) covering a lifespan of a hypothetical individual with a hypothetical but realistic health data and medical history. These scenarios include several phases a person passes during his/her life, including prevention, treatment and follow-up/monitoring. From the clinical experts we queried full data which would be required at different phases to be able to intervene (independent of the type of intervention or the institution to intervene). The developed scenarios include both phenotype (incl. behavioural and environmental data) and genotype data. During the process, two scenarios (CVD and diabetes) were merged into one, leaving us a total of two scenarios to continue with: 1) breast cancer and 2) CVD and diabetes. Both are attached to the current report as Annexes 1.1 and 1.2. Both scenarios were analysed from the perspective of adding Digital Decision Support System (DDSS). The DDSS was added to the scenarios where the clinical experts advised, including a short description of the content of the decision support expected.

We investigated current clinical guidelines and DDSS-s existing in USA and Finland to identify existing personalised medicine (including genome data) digital decision support system scripts which could serve as examples for the DDSS-s applicable in Estonia. This information was added to the scenarios description (see chapter 8 for more information).

We have defined detailed data required for the DDSS in each of the prescribed points over the lifespan of the hypothetical individual in the two clinical scenarios. This is followed by the analysis and definition where (within the analysed nation-wide or healthcare providers’ health and medical information systems) this data exists and in which format it is stored. This, in turn, feeds into the IT architecture feasibility study work, so that this study group can decide which technical means are needed to collect and analyse this data, making a DDSS technically possible.

Based on the two scenarios we have developed a draft of the prototype, consisting of an individuals’ and healthcare professionals’ view on the digital health portal and electronic patient record, including decision support recommendations. For this, please extract the files from the attached Prototype1.zip file and execute the Start.html file.

Main findings and suggestions

We have defined that there is plenty of data in the Estonian Health Information System (EHIS), Estonian Health Insurance Fund (EHIF) and Estonian Genome Center of the University of Tartu (EGCUT) databases. Some of the data is collected in the structured way corresponding to existing standards but considerable amount of data is presented either as a narrative text or in non-compliant structures which is a challenge to the development of a nation-wide DDSS-s.

We have also established that the data required for Digital Decision Support System in Personalised Medicine is similar to the data required by conventional medicine in a vast majority of cases. As a major difference, it includes genome data and covers the whole lifespan of an individual rather than just random incidents. Based on the current knowledge of our team, genome data in the field of CVD and diabetes is not widely used for DDSS. The situation with cancer prevention and treatment is somewhat better. However, the research of genome data and calculations of risks for all mentioned conditions is evolving rapidly. Therefore it is our
suggestion to consider keeping two clinical fields – cancer and combination of CVD and diabetes – for the further development of the DDSS-s.

The DDSS-s concept and prototype from the current feasibility study will be applicable to personalised medicine as well as for conventional medicine, scalable to include more than Estonian population genotype and phenotype data and expandable/linkable to DDSS-s in other countries, as evidence-based personalised medicine evolves from research to everyday medical practice.

As a result of this feasibility study the strategy of implementation of DDSS in personalised medicine in Estonia was provided. This includes a) recommendation to establish an organisational and information technology framework for linking person’s genome, health and medical data for the processing with different DDSS-s during the whole life span depending on the user or quality goal; b) Audit and analysis of data existing in nation-wide and organizational (e.g. healthcare providers) medical and public health databases to agree about the sources of different data necessary for DDSS algorithms; c) Decide about the scope, scale and schedule of the development and implementation of DDSS applications; d) Establish an organisation responsible for already gathered genome, health and medical data normalization and distribution for the open use by different actors in health and care domains; e) Development and publishing of user friendly end user software and applications requirements for individual and professional use keeping in mind the DDSS functionalities and importance of the secondary use of data and implementation of new e-services in health and care spheres.
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# Abbreviations and Glossary

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<th>Abbreviation</th>
<th>Definition</th>
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<tbody>
<tr>
<td>ABPM</td>
<td>Ambulatory Blood Pressure Monitoring</td>
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<tr>
<td>AI</td>
<td>Artificial Intelligence</td>
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<tr>
<td>AOM</td>
<td>Agent-Oriented Modelling</td>
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<tr>
<td>AR</td>
<td>Augmented Reality</td>
</tr>
<tr>
<td>ATC</td>
<td>Anatomical Therapeutic Chemical (ATC)</td>
</tr>
<tr>
<td>BMI</td>
<td>Body Mass Index</td>
</tr>
<tr>
<td>BI</td>
<td>Business Intelligence</td>
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<tr>
<td>CDSS</td>
<td>Clinical Decision Support System - clinical application of digital decision support (mainly used in the USA)</td>
</tr>
<tr>
<td>CPRS</td>
<td>Computerized Patient Record System</td>
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<tr>
<td>CRC</td>
<td>Colorectal Cancer</td>
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<tr>
<td>CT</td>
<td>Computed Tomography</td>
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<tr>
<td>CVD</td>
<td>Cardiovascular Diseases</td>
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<tr>
<td>DDSS</td>
<td>Digital Decision Support System - computer-based information system that supports business or organizational decision-making activities, including at least the six different decision support systems outlined in chapter 4.2.2., Annexes 7 and 9.</td>
</tr>
<tr>
<td>DICOM</td>
<td>Digital Imaging and Communications in Medicine</td>
</tr>
<tr>
<td>DoI</td>
<td>Department of Informatics</td>
</tr>
<tr>
<td>DSIS</td>
<td>Decision Support Information Systems</td>
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<tr>
<td>EBMeDS</td>
<td>Evidence Based Medicine Electronic Decision Support</td>
</tr>
<tr>
<td>ECG</td>
<td>Electrocardiography</td>
</tr>
<tr>
<td>ED</td>
<td>Emergency Department</td>
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<tr>
<td>EeHF</td>
<td>Estonian eHealth Foundation</td>
</tr>
<tr>
<td>EGC/EGCUTC</td>
<td>Estonian Genome Center, University of Tartu</td>
</tr>
<tr>
<td>EHIF</td>
<td>Estonian Health Insurance Fund</td>
</tr>
<tr>
<td>EHIS</td>
<td>Estonian Health Information System</td>
</tr>
<tr>
<td>EPR</td>
<td>Electronic Patient Record</td>
</tr>
<tr>
<td>ELLIOT</td>
<td>Experiential Living Lab for the IoT</td>
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<tr>
<td>EMMeT</td>
<td>Elsevier's proprietary medical taxonomy</td>
</tr>
<tr>
<td>ENMG</td>
<td>Electroneuromyography</td>
</tr>
<tr>
<td>FAP</td>
<td>Familial Adenomatous Polyposis Coli</td>
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<tr>
<td>FHIR</td>
<td>Fast Healthcare Interoperability Resources</td>
</tr>
<tr>
<td>GD</td>
<td>Gestational Diabetes</td>
</tr>
<tr>
<td>GFR</td>
<td>Glomerular Filtration Rate</td>
</tr>
<tr>
<td>Goal Model</td>
<td>container of three components: goals, quality goals, emotional goals, and roles</td>
</tr>
<tr>
<td>GP</td>
<td>General Practitioner</td>
</tr>
<tr>
<td>GRS</td>
<td>Genetic Risk Score</td>
</tr>
<tr>
<td>GWAS</td>
<td>Genome-Wide Association Study (GWA study, GWAS)</td>
</tr>
<tr>
<td>HIS</td>
<td>Health Information System</td>
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<tr>
<td>HIM</td>
<td>Health Information Management</td>
</tr>
<tr>
<td>HIS</td>
<td>Hospital Information System</td>
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<tr>
<td>HL7 CDA</td>
<td>HL7 Version 3 Clinical Document Architecture</td>
</tr>
<tr>
<td>HSPC</td>
<td>Health Services Platform Consortium</td>
</tr>
<tr>
<td>ICD</td>
<td>International Classification of Diseases</td>
</tr>
<tr>
<td>IoT</td>
<td>Internet of Things</td>
</tr>
<tr>
<td>LOINC</td>
<td>Logical Observation Identifiers Names and Codes</td>
</tr>
<tr>
<td>LOV</td>
<td>Lists of Values</td>
</tr>
<tr>
<td>MDE</td>
<td>Model-Driven Engineering</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
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<tr>
<td>MEG</td>
<td>Truven Health Medical Episode Grouper</td>
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<tr>
<td>MeSH</td>
<td>Medical Subject Headings</td>
</tr>
<tr>
<td>ML</td>
<td>Machine Learning</td>
</tr>
<tr>
<td>MRT/MRI</td>
<td>Magnetic Resonance Imaging / Magnetic Resonance Tomography</td>
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<tr>
<td>NCSP</td>
<td>NOMESCO Classification of Surgical Procedures</td>
</tr>
<tr>
<td>NEHR</td>
<td>National Electronic Health Record</td>
</tr>
<tr>
<td>NGS</td>
<td>Next-Generation Sequencing</td>
</tr>
<tr>
<td>NIHD</td>
<td>National Institute of Health Development</td>
</tr>
<tr>
<td>NOMESCO</td>
<td>Nordic Medico-Statistical Committee</td>
</tr>
<tr>
<td>OID</td>
<td>Object Identifier</td>
</tr>
<tr>
<td>PACS</td>
<td>Picture Archiving and Communication System</td>
</tr>
<tr>
<td>PE</td>
<td>Physical Entity</td>
</tr>
<tr>
<td>PET</td>
<td>Positron Emission Tomography</td>
</tr>
<tr>
<td>PHR</td>
<td>Personal Health Record</td>
</tr>
<tr>
<td>PP</td>
<td>Patient Portal</td>
</tr>
<tr>
<td>RMRS</td>
<td>Regenstrief Medical Record System</td>
</tr>
<tr>
<td>RxNorm</td>
<td>RxNorm is a name of a US-specific terminology in medicine that contains all medications available on US market.</td>
</tr>
<tr>
<td>Scenario (Med)</td>
<td>An imagined or projected sequence of events, especially any of several detailed plans or possibilities:</td>
</tr>
<tr>
<td>Script (IT)</td>
<td>A simple program in a language that the computer must convert to machine language each time the program is run.</td>
</tr>
<tr>
<td>SDM</td>
<td>Shared Decision Making</td>
</tr>
<tr>
<td>SMART</td>
<td>Substitutable Medical Apps &amp; Reusable Technology</td>
</tr>
<tr>
<td>SNOMED</td>
<td>Systematized Nomenclature of Medicine</td>
</tr>
<tr>
<td>SNP</td>
<td>Single Nucleotide Polymorphism</td>
</tr>
<tr>
<td>SOAP</td>
<td>Simple Object Access Protocol</td>
</tr>
<tr>
<td>SPECT-CT</td>
<td>Single-Photon Emission Computed Tomography</td>
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</tbody>
</table>
1. Introduction

1.1. Digital Decision Support System (DDSS) concept – definition and background

Digital Decision Support throughout this report is considered to be a digital expert system supporting health behaviour and/or clinical decision-making (procurement No. 160141 terms and conditions paragraph 2.5.1.1.), except where it has been specified and widened to include other types of decision supports (see Annex 7 for possible options) or restricted to specific clinical fields (CVD, diabetes, cancer).

In the modern healthcare and health management the amount of data reflecting person’s health condition or disease process is increasing exponentially. This fact is accompanied by the paradigm shift where the volume-based healthcare is replaced with the value-based healthcare. Today the aim of the healthcare is to propose to the person the best care pathway depending on their individual genome, health and medical data. DDSS is considered as one of the most important tools to cope with ever increasing genome, health and medical data and to help person and healthcare professional to use this data meaningfully. DDSS is meant to improve health outcomes, reduce unneeded tests, eliminate drug-drug interactions and avoid unnecessary hospitalizations. Being accrued from evidence based publications, DDSS helps users to benefit from the collected genome, health and medical data and information in the most effective and efficient way. It is a tool to pre-analyse collected data and to give most appropriate recommendation for the next action.

1.2. Aims, materials and methods

Investigation of data, databases and their interrelations in the context of the implementation of digital decision support systems (DDSS) in personalised medicine.

The starting point of the current analysis is the construction of a hypothetical case study consisting of genome, health, behavioural and medical data existing or arising during the life span of a person, in an idealised situation from clinical perspective. Feasibility of the implementation of different decision supports is investigated from the health promotion and disease prediction, prevention, diagnosis, treatment and rehabilitation point of view for two health conditions – cardiovascular diseases (incl. diabetes) and breast cancer. The data and databases required for the DDSS are explored and listed keeping in mind the perspective that they would serve both as the input and source for the decision support algorithms. (See Annex 1.1 and Annex 1.2 for the layout of the scenarios for the CVD/Diabetes and Cancer)

In a nutshell, the research process we have been following makes up a bow-tie-shape, whereas the latter two developments are out of scope of the digital Decision Support System procurement team.
The first step done was an agreement about the clinical scenarios of personalised medicine which would benefit from the decision support systems in the future. This exercise was completed by prof. Margus Viigimaa, Dr. Ülle Jakovlev and Dr. Peeter Padrik with assistance of the whole team and in coordination with Clinical Feasibility Study group (See chapter 5 of the current document). Initially there were three clinical application fields (CVD, Diabetes and cancer). Based on the Management Team for the whole Personalised Medicine Project of Estonia, cardiovascular diseases (CVD) and Diabetes were merged into one case study and Cancer was still researched separately.

Secondly, both remaining (CVD/Diabetes and Cancer) clinical scenarios were decomposed into smaller episodes and events. These episodes were parsed into the data necessary for the decision making during the particular predictive, care or medical process and compared with specific DDSS algorithms (For data elements please see chapter 5).

Thirdly, we mapped the required data against different internationally accepted nomenclatures, terminologies, classifications and listed where the particular data is located or can be queried from (out of the different Estonian health and medical databases): Estonian Genome Center database (genotype and phenotype data combined), Estonian Health Information System, Estonian Health Insurance Fund, main hospitals’ databases and general practitioners’ information systems. The developed clinical scenarios revealed that for the development of a DDSS information from non-medical databases is also needed: e.g. data collected by the person with the help of mobile monitoring devices or collected/submitted/entered by the person him- or herself. Also over the counter medication data is sometimes mandatory for the decision making. Currently we are completely missing the collection and use of such non-medical data in Estonia. (See chapter 2)

Fourthly, an overview of commercially available digital decision support systems was made. At the first stage, Finnish decision support system EBMeDS (Evidence Based Medicine Electronic Decision Support) was evaluated and data compatibility with Estonian databases was tested.

As DDSS consists of hundreds of described and tested algorithms, the two clinical scenarios selected (CVD/Diabetes and Cancer) were described against the possible DDSS by the design

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1 Original contribution by the authors.
team. The two clinical scenarios were split between the perspective of different roles, e.g. person, nurse, general practitioner, specialty healthcare provider and specialist, and processes. (See chapter 7)

1.3. Results

Based on the current research and analysis, first findings of digital decision support system(s) feasibility for the personalised medicine in Estonia and initial steps for its implementation were written. (See chapter 6). The suggestion for the strategic plan for implementation of DDSS includes the following phases and actions:

- Establishment of organisational and information technology framework for linking persons genome, health and medical data for the processing with different DDSS during the whole life span depending on the user or quality goal.
- Audit and analysis of existing nation-wide and organizational (e.g. healthcare providers) medical and public health databases to agree about the sources of different data necessary for DDSS algorithms.
- Agreement about the schedule of acquiring of commercially available or development of new DDSS algorithms for the use in personalised medicine.
- Establishment of organisation responsible for collected genome, health and medical data normalization for the open use in context of DDSS by different actors in health and care domain.
- Development and publishing of user friendly end user software and applications requirements for individual and professional use keeping in mind the DDSS functionalities and importance of secondary use of data and implementation of new e-services in health and care spheres.

Actors and interrelations in the digital DDSS feasibility study.

Figure 2: Health and medical data are collected by healthcare professionals or individuals, stored in local databases and sent in standardised format to the nation-wide information systems and registries. Collected data should be normalized for the use of existing or under the development decision support algorithms. The results of the automatic decision support are presented according to the user or quality goal of care process in user application.²

² Original contribution by the authors.
2. List of classifications and taxonomies and description of data sources

From the Digital Decision Support Systems (DDSS) perspective, the data used to feed in decision algorithms should be only in the structured and standardized format. The spectrum of taxonomies accepted by different DDSS varies widely from locally generated lists (e.g. structures for entering patient complaints) to widely used classifications (e.g. ICD-10). For the time being, we have identified that vast majority of commercially available DDSS-s are using internationally accepted terminologies, classifications and nomenclatures.

Investigating Estonian situation, we have found that the Estonian Health Information System (EHIS), Estonian Health Insurance Fund (EHIF) and Estonian Genome Center University of Tartu (EGCUT) databases consist of substantial amount of structured and standardized data. The data is collected in the structured way corresponding to existing standards. However, considerable amount of data is presented either as a narrative text or in non-compliant structures which is a challenge to the development of nation-wide DDSS-s.

Data needed for the development of DDSS scripts could be divided in to several groups. To better understand the source and format of data, we use following list:

- Administrative data
- Measurements of common variables (Blood pressure, weight, height, BMI, etc.)
- Complaints
- Genome data, risk calculations
- Diagnoses
- Laboratory test results
- Medication
- Surgical procedures
- Reports of exams
- Images
- Patient visits

Besides of structured data also tracking of the start and end times of different medical events, treatment decisions or administration of medicines has great importance in proper functioning of DDSS scripts.

Standards and structures of different databases (EHIS, EHIF, EGCUT and healthcare providers) in relation to clinical scenarios were mapped. (Annex 2)

Brief summary of data structure research

The best situation is obviously with the administrative data. Once Estonia uses unique identifier, all Estonian residents' gender and age are available according to the identification number (ID). Moreover, ID enables linking the data of the same person in different databases easily.

Diagnoses are also well documented in ICD-10 classification in all databases. Though, in the planned pilot study some attention should be paid to the data quality and to the comparison of diagnoses from different sources. We assume that in some cases the same patient could have different ICD codes for the same condition as the coding could vary between databases according to the purpose of the activity, e.g. financial reporting vs. clinical reporting.

All investigated databases include measurements of common anthropometric and functional variables. However, the data structure varies substantially. Often height, weight, pulse and blood pressure are presented in free text. This demands aggregation of these data and normalization for DDSS use. The same concerns data describing individual habits (physical activity, smoking, alcohol consumption, etc.) and family history.
Prescribed medication is well documented in EHIF prescription centre database. Medicines are coded in ATC classification. For the DDSS more precise administration dates would be recommendable.

Laboratory test results are in LOINC classification in most of hospitals’ electronic patient records (EPR). However, for sending laboratory test results to EHIS they are often converted to free text. EHIS accepts LOINC codes from the year 2015 only. This is promising trend and it seems that laboratory test results are fully available for the DDSS in near future.

Surgical procedures are coded in NCSP (NOMESCO) classification in EHIS and EHIF databases. Also hospitals EPR-s include NCSP coding.

Genome data are stored in EGCUT and in rear cases, if the genetic test is indicated according to the clinical condition, in EHIS and hospital EPR-s. Risk calculators and potential genetic effect will be stored and generated in EGCUT. DDSS has to receive genome based personalised risk factors from EGCUT.

Data describing citizen’s health condition, complaints and other subjective information is mostly in narrative text. However, EHIS has health declaration structured report which is unfortunately used in very random or specific (e.g. application of bill of health for driving licence) cases only.

Images and image reports are stored in nation-wide picture archiving and communication system (PACS). Unfortunately the use of image reports and images for DDSS is very limited today.
3. Data structure and data quality assessment

Data quality in Estonian Health Information System (EHIS)
The data collected by the healthcare providers is often structured at the point of primary use, e.g. blood pressure, blood oxygenation, pulse, most of lab test, etc. This data is entered using international terminologies, classifications or standards. However, for the secondary use, hospital or general practitioners information systems compile a HL7 CDA document where initially structured data are converted into narrative text. This is necessary to send the document to Estonian nation-wide Health Information System (EHIS) and to share the information with other healthcare providers. From the digital decision support algorithms point of view it leads to the need to parse the document again back into data elements.

We have learned also about some promising trends. For instance, the documents that are used in EHIS to collect and share child health, behavioural and medical data are structured in HL7 document format. The document consists of structured data which could be unambiguously used in decision support algorithms. Unfortunately this is rather an exception than the rule in most of the documents collected in EHIS concerning adult health or medical data. The noted example shows that the data structure for weight, height, blood pressure, behaviour and organ systems status is in place but used only in limited number of documents in EHIS. (See Annex 2 for details)

Data quality in Estonian Health Insurance Fund (EHIF)
The situation with electronic prescriptions in EHIF database is relatively better than in EHIS because most of the data is well structured and medication filing is based on the ATC coding. Estonian Health Insurance Fund processes healthcare providers’ reimbursement claims, manages prescription centre (e-prescription data), deals with health promotion and prevention (incl. screening), and is responsible for disability insurance and sick notes. From the decision support system perspective the most important data collected about the persons health condition comes from the prescription centre (e-prescription data, incl. medication in ATC) and reimbursement claims (diagnoses in ICD-10, procedures in NCSP, number of appointments and hospitalisations, etc.). The data concerning health promotion and prevention could also be used for the decision support algorithms.

Data structure & quality in Estonian Genome Center, University of Tartu (EGCUT)
With close to 52,000 participants, the biobank cohort represents 5% of the adult population in Estonia. All participants have gone through a standardized health examination; donated blood samples for purification of DNA, white blood cells, and plasma; and completed a questionnaire (Annex 4) on health-related topics, such as lifestyle, diet, and clinical diagnoses. High standards of phenotypic data are assured because the recruitment was conducted by medical professionals using computer assisted personal interviews, standardized coding has been used to record medical history (ICD-10) and medication use (ATC), and information was validated by electronic health records available to the recruiter.

The phenotypic data are continuously being updated by regular queries from Population Registry, Estonian Causes of Death Registry, Estonian Cancer Registry, Tuberculosis Registry, Estonian Myocardial Infarction Registry, Health Insurance Fund, Tartu University Hospital, North Estonia Medical Center and EHIS.

Biological samples were collected as 30-50 mL of venous blood into EDTA Vacutainers. Containers were transported to the central laboratory of the Estonian Biobank at +4…+6 C (within 6 to 36 hours) where DNA, white blood cells and plasma got immediately isolated and kept in aliquots in MAPI straws in liquid N2 for long-term storage.
A significant part of the cohort (n=20,000) has been genotyped using genome-wide single nucleotide polymorphism (SNP) arrays, and data from nuclear magnetic resonance spectroscopy (NMR) of blood plasma is available for 12,000 participants. All procedures are run according to ISO 9000-2008.

**Quality assessment**

According to the findings described above, the amount and availability of the data for the clinical DDS-s is considerably satisfying. However, from the quality perspective the credibility/reliability of collected data could be questioned. According to the recent feedback from pharma industry, the independent external audit of the quality of existing data in national databases (EGCUT, EHIS, EHIF, quality registers, etc.) would be very desirable. Also cross-matching of data in different databases gives valuable feedback about the data quality. This research is already initiated by the University of Tartu and Software Technology and Applications Competence Centre.

From the DDS application point of view, the structuring of the data is not satisfying. There are only few positive examples concerning structured data in the nation-wide databases. The situation in hospitals’ and general practitioners’ electronic patient records is somehow better. However, this allows the use of clinical DDS in the context of local information systems only and makes deployment of large-scale implementation of DDS complicated.

Currently there is no systematically stored data available for DDS algorithms using input from Personal Health Records (PHR) in Estonia. This hinders opportunity to apply health promotion algorithms. Health data entered or collected by the individual is available only from personal smart phones, web-sites or other mobile gadgets. However, Estonia is not an exception in this regard: systemizing health data is an issue all over the world.

Poor structuring of clinical data and almost non-existing structuring of health data is caused by the fact that the ontology and semantic interoperability is not agreed on the national level neither across different medical specialties. Future cooperation in this field between different stakeholders is mandatory. Also the use of DDS for data entering will support common semantics.
4. Best practice in digital decision support systems implementation and their suitability to Estonian context

Patient management decisions in healthcare have to be evidence-based and patient-centred unifying the best research evidence with clinical expertise and patient values and expectations. Digital Decision Support Systems (DDSS) in healthcare are designed to integrate a medical knowledge base, patient data and an inference engine to generate case specific advice. Recently also genome data and risk calculations based on the genome sequencing have become a part of the knowledge base. Digital decision support systems are a part of the genome, health and clinical knowledge management technologies to support the care and clinical processes and use of knowledge, from data capturing, diagnosis and investigation through treatment and long-term care. Additionally to DDSS developed for healthcare professionals use also advice systems for the citizen for his or her own health management and prevention purposes are emerging. Traditionally the decision support has been aimed only for the use of healthcare professionals. In addition to support healthcare professionals there has evolved a need for shared decision making (SDM). SDM is a process by which a healthcare choice is made jointly by the practitioner and the person him or herself. Shared decision making has a potential to reduce overuse of options not clearly associated with benefits for all, enhance the use of options clearly associated with benefits for the vast majority, reduce unwarranted healthcare practice variations, foster the sustainability of the healthcare system, and promote the right of patients to be involved in decisions concerning their health. In personalised medicine DDSS-s will use genome data as a new knowledge for scripts compiling and provides opportunity to help in decision making based on the molecular profiling of the particular individual.

4.1. Functional classes and examples of clinical digital decision support systems

The following table by Current Medical Diagnosis and Treatment shows the relations between DDSS functional classes and examples about it.

<table>
<thead>
<tr>
<th>Class</th>
<th>Function</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feedback</td>
<td>Provide feedback by responding to an action taken by the clinician or to new data entered into the system</td>
<td>Drug family checking results in alerts on allergies, drug-drug interactions, and other patient-specific conflicts. Parameter checking looks for dosing errors and other parameter discrepancies in patient-specific scenarios. Redundant utilization checking alerts physicians to duplicate test orders.</td>
</tr>
<tr>
<td>Data organization</td>
<td>Organization and presentation of disparate data into logical, intuitive schemas at the point-of-need</td>
<td>Aggregate data trending observes key indicators for large numbers of patients over time.</td>
</tr>
<tr>
<td>Proactive information</td>
<td>Provision of information to the clinician at the point-of-need (e.g. clinical pathways on different medical conditions, risk calculations based on the genome data, etc.)</td>
<td>Template and order sets can be provided to given situations.</td>
</tr>
<tr>
<td>Intelligent actions</td>
<td>Automation of routine and repeated tasks for the clinician</td>
<td>Template and order sets can be provided to given situations.</td>
</tr>
</tbody>
</table>
on a regular time schedule

Rule-based event detection allows users to create logical rules to be checked when triggering events occur. Time-based checks to post reminders when expected transactions have not occurred.

<table>
<thead>
<tr>
<th>Communication</th>
<th>Alert clinician and other providers who need to know about unusual data or communications regarding specific patients</th>
<th>Parameter alerts provide clinicians with key information on panic values. Automated e-mails send information to clinicians when provider-patient encounters occur.</th>
</tr>
</thead>
</table>

**Expert advice**

Diagnostic and therapeutic advice using a comprehensive knowledge base (incl. genome data) and a problem-solving method, such as probabilistic reasoning, neural nets, or heuristic rules

Differential diagnosis and suggestions for further testing generated from patient-specific data. Reducing uncertainty in test interpretation.

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### 4.2. Classification of digital decision support systems

#### 4.2.1. List of existing clinical digital decision support systems

Solutions were chosen from the reviews and articles about digital decision support systems. The information was taken from the vendors’/publishers homepages in May 2015. All these systems have got strong editorial policy about the content of the information. The analysis doesn’t focus on the quality of the content and editorial policy of the solutions.

<table>
<thead>
<tr>
<th>Nr</th>
<th>Name of the system</th>
<th>Vendor/Publisher (Country)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Alere Analytics CDS</td>
<td>Persivia (US)</td>
</tr>
<tr>
<td>2</td>
<td>Archimedes InDigo</td>
<td>Archimedes Inc., KAISER PERMANENTE Innovation (US)</td>
</tr>
<tr>
<td>3</td>
<td>Cortellis for Decision Support</td>
<td>Thomson Reuters (US)</td>
</tr>
<tr>
<td>4</td>
<td>EBMeDS</td>
<td>Duodecim Medical Publications Ltd (Finland)</td>
</tr>
<tr>
<td>5</td>
<td>ClinicalKey</td>
<td>Elsevier (US)</td>
</tr>
<tr>
<td>6</td>
<td>Instant Medical History</td>
<td>Primetime Medical Software (US)</td>
</tr>
<tr>
<td>8</td>
<td>MICROMEDEX®</td>
<td>Truven Health Analytics (US)</td>
</tr>
<tr>
<td>9</td>
<td>Up to Date / Provation Medical</td>
<td>Wolters Cluver Health (US)</td>
</tr>
<tr>
<td>10</td>
<td>Zynx Health</td>
<td>Zynx Health Inc. (US)</td>
</tr>
<tr>
<td>11</td>
<td>Symptify</td>
<td>Symptify LLC (US)</td>
</tr>
</tbody>
</table>

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4.2.2. Proposed classification

When conducting clinical expert interviews and mapping existing clinical processes (diabetes, hypertension, breast cancer), the design group mapped various opportunities for possible decision support system applications. DDSSs were mapped in different phases of the health promotion and clinical processes (health promotion and disease prevention, screening, diagnosing, treatment, monitoring and rehabilitation) as well as looking at the variety of actors of the personalised medicine process (general practitioner (GP), family nurse, clinical specialist, person, health coach, scientist, insurance fund, etc.). In each scenario integration of genome data as an enabler for personalised medicine approach was considered.

As a general finding, DDSS-s could be applied differently depending of the type of user, functions and data sources. Accordingly DDSS-s could be categorized as follows (Figure 3):

1. According to users
   a. Healthcare professionals (physicians, nurses, etc.)
   b. Individuals (healthy persons, patients, etc.)

2. Purpose of the use
   a. Data entering
   b. Receiving recommendations, reminders and alerts

3. Aim of the use
   a. Health promotion
   b. Disease management

4. According to the content source
   a. Evidence based medicine (peer reviewed publications, guidelines, etc.)
   b. Data driven research

![Figure 3. Categorisation of DDSS according to users, functions and data sources.](image)

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4 Original contribution by the authors.
In order to understand in more details the wide variety of possible digital decision support systems, the design group divided them into six main categories based on the area of application, maturity, nature of the processes and main users. It has to be emphasized that genome data similarly to health, environmental and medical data are integral part of knowledge source for all categories. Traditionally decision support systems have been understood as support tools mainly targeted for clinical specialist (here in category 4). The new personalised medicine process engages the patient in his or her health management and disease treatment in far greater extent than before. Therefore, also decision supports for patients, which could play a vital role in disease prevention but essentially in health promotion, and other new parties must be considered when implementing new personalised medicine processes.

We propose a decision support classification of 6 different subgroups (Annex 7 and Annex 9):

1. Improved data usage and visualisation
2. Health management
3. Patient monitoring supports
4. Clinical decision supports
5. Scientific gene research
6. Public health analysis tools

Digital decision support systems are analysed according to the business sector (giving the overview of different products in this field, because most of the vendors are offering complementary solutions); description of the system (rules, properties); methodology (methodology used and whether the solution is internet based or integrated solution); for whom the solution is directed to (administrators, general vs specialty physicians, other healthcare workers, patients and others); data management describing the inputs and data transfer standards.

More recently, advances in DDSS in the United States have been affected by trends beyond the software dedicated for healthcare professionals use only. Advances in genomic information have created a need for DDSS to help clinicians and other professionals appropriately leverage genomic data. This has affected the systems architecture of DDSS, since genomic information systems are typically independent of EPRs, so that DDSS must integrate data from both within and without the EPR. Increased understanding of the importance of patient-reported information is also affecting DDSS which will now need to both incorporate this new type of data, but also accommodate varying levels of trust for clinical decisions in data where the data types already exist but inferred quality may be different. These two data types are part of a broader trend towards personalised medicine, which is expected to advance the use of DDSS that can incorporate myriad data from multiple sources to assist the creation of an individualized plan of care.

4.3. Description of the current and perspective decision support algorithms used in Finland

**Rationale and state of the art**

Recent advances in genomic, transcriptomic, proteomic, and metabolomic technologies have opened a whole new array of avenues towards the understanding of the molecular pathobiology of diseases. The information is bound to result is rewriting of the diagnostic taxonomy as the individual features within disease entities provide chances for better management of each patient. This personalised (or individualized or stratified) medicine, however, is only at its verge; and the most powerful set of tools to advance it is the unbiased, systematic analysis and data gathering from large repositories of disease-based resources of tissues and clinical information. By combining information from EPR’s and monitoring devices, outcome information and established prognostic markers with genomic, transcriptomic and biochemical data, it will be possible to identify digital phenotypes (digital fingerprints) for stratification of the patients within the current wide and often rather unspecific diagnostic entities. The current situation draws on
the – in this context as yet un-exploited, but quite obviously extremely powerful – amalgamation of presently available resources (biobank specimens and clinical data) from an extremely rich and highly mutually complementary set of extant resources – the biobanking efforts that have been underway for years/decades in Finland, and now set to a new level with the Finnish Biobank Act. Combining these resources to advance the understanding of disease biology has, in effect, been an almost obvious, but so far difficult-to-realize opportunity, given the federated nature of the resources within individual hospital districts. The current activities in Auria Biobank and Hospital District of South-west Finland thus appears to be a uniquely poised opportunity to realize the leveraging of a highly promising collaboration across these currently readily available, but disconnected, resources in Finland, to generate a set of values that will, indeed, exceed “the sum of the parts”. Currently, the utilization and/or leveraging of biobanking resources is difficult since both biobank specimens and the data from related EPRs are maintained in a "compartmentalized" fashion within individual hospital environments. It is therefore presently almost impossible to comprehensively even so much as assess the wealth of the resources available, let alone, to access and utilize them.

The broad spectrum of existing hospital biobanks is a hallmark of the potential of Finnish research that has been conducted over the last decades – strengths unrivalled in other parts of both the EU and the world at large. Millions of human diagnostic specimens with associated clinical data are stored in a number of existing (or to be established) biobanks in Finland; the good news is that on a collection-by-collection level, they are easily tractable. The challenges that to be addressed are the interconnectivity, including all appropriate data security and –privacy considerations. While in the context of personalised medicine, hospital integrated biobanks are the leading sources of data-driven medicine, they lack generic solutions for EPR interoperability and information harmonization. Unfortunately, the diversity of the hospital environment, in which the biobanks operate, has prevented their effective use so far in an integrated fashion. By overcoming these present limitations, Finland can establish itself as world leader in research & development related to digital phenotyping as well as its implementation, and could truly leverage the enormous potential of the resources. This position will increase the attractiveness of Finland for foreign investments, provide a fruitful soil for new start-ups/SMEs and generate tools modify the health sector leading to cost-effective ways to improve healthcare.

In particular, it will be possible to define and examine specific subgroups of patients, based on different phenotypes and/or genetic characteristics that are potentially particularly informative for allowing the generation of algorithms to predict clinical outcomes such as therapy response, relapse, and survival. The actual clinical outcomes among this subgroup can then be compared with the predicted ones, to determine if the predictions are clinically useful or not. In addition, the important, but largely unanswered question raise by the availability of digital health technologies and whether these will enable the opportunity to stratified patients for personalised treatment, based on novel digital phenotypic assessments as well. One of the future challenges is to test can digital health technologies provide new phenomarkers that are as informative as the molecular biomarkers used in oncology, so far.

Digital phenotype is the next frontier, and the technologies of digital health should enable profoundly improved measurement of the patient own experience. We are now able to assess and combine many different parameters, which should now be able to measure anywhere, anytime – not just the EPR based measures in hospital settings. The technologies of digital health offer powerful tools to inquisitive clinical researchers, whose challenge now is to leverage these technologies to provide information that is reliable enough, publishable, and most importantly -meaningfully for daily clinical care.

To provide optimal chances for such efforts to be truly successful, it is essential to have access to reliable, high quality patient record data, sufficiently large numbers of relevant patient records/examples, as well as access to the best possible digitally orientated tools for analysis. Because the format, quality, and degree of curation of data is often challenging (e.g., missing
values, measurement errors, censored values, unbalanced populations, skewed-multimodal distributions), only if tailored digital tools for analysis of this kind of challenging data are developed will a sufficient number of patient samples become accessible for selecting on a particular set of clinical features. Although many initiatives have been undertaken at national as well as the EU level, we are not aware of any other project that has successfully established the suite of research-accelerating environment or prerequisite tools and functionalities needed to develop a biobank-driven digital phenotyping source for improved clinical research, digital decision support system algorithm’s and therapy. We believe that we are in a unique position to create not only such a resource, but in doing so to pilot digital information platform and approaches that may be usefully deployed in other biobank-driven projects and thus create an important new set of resources and experiences for the research community.

Current situation on decision support algorithms used in Finland
Current Care Guidelines (Käypä Hoito) are independent, evidence-based clinical practice guidelines which are widely used in Finland. These national guidelines cover important issues related to Finnish health, medical treatment as well as prevention of diseases. Unfortunately, lack of phenotype/genotype associations are still missing. The guidelines are intended as a basis for treatment decisions, and can be used by physicians, healthcare professionals and citizens. The guidelines are developed by the Finnish Medical Society Duodecim in association with various medical specialist societies. They produce national, evidence-based clinical practice guidelines in support of healthcare decision making and for the benefit of the patient. Concise and easy-to-read guidelines support doctors' practical work and form a basis for compiling regional care programmes. The guidelines can be used to improve the quality of care and decrease inconsistencies between treatment practices.

The Current Care Board selects the topics covered by the Current Care Guidelines, mainly based on suggestions made by specialist associations. These specialist associations operate as the host association for the guideline in question, in partnership with Duodecim. PRIO-tool is used for prioritizing new guideline topics. First, an experienced professional information specialist conducts a systematic literature search. Current Care working groups (including approximately 1400 volunteer healthcare top professionals from a range of fields across Finland) produce guidelines in cooperation with Current Care editors, who operate as method experts. The guidelines are compiled based on the available evidence, and the most important recommendations are reasoned with evidence summaries. Prior to its completion, the guideline is circulated to specific interest groups for their consideration, after which any resulting comments are discussed and the guideline edited and specified, if necessary. Completed guidelines and updates are communicated as appropriate.

Another widely used clinical decision support tool is FINRISK-calculator produced by THL (https://www.thl.fi/en/web/chronic-diseases/vascular-diseases/finrisk-calculator). Using FINRISK calculator it is possible to calculate individual’s risk of acute myocardial infarction or acute disorder of the cerebral circulation within the next ten years. The calculator gives disease risk as a percentage.

Pharmacogenomic Database for Decision Support (by Abomics GeneRx) representing “next-generation” tools combining also medically relevant genetic information in the recommendations given. It is based on wide individual variations in drug response, based on genetic factors. Knowledge about these is available for several essential drugs. For example genetic polymorphism in genes CYP2C19 and CYP2D6 cause variation in metabolic rates of several drugs. In Finland these drugs are prescribed over 550 000 times annually. The Abomics GeneRx database includes information from genotypes that are associated with clinically relevant variation in drug responsiveness or drug-induced adverse effects. Database consists of following information: Active ingredient, ATC code(s), generic drug name, Genetic variations related to the drug, Information about the phenotype affected, e.g. metabolic rate, Recommendation texts, e.g.
dosing recommendations, References, Available genetic tests and their indications and Genetic
test providers, contact information and ordering instructions. In addition, Abomies GeneRx can
be integrated as a part of EPR drug database. In the integrated solution, the EPR system alerts
immediately in case of clinically significant genetic variation related to the drug prescribed for the
patient. Dosing recommendations, available genetic tests and their providers are all available.

4.4. Description of the current and perspective decision support algorithms
used in the USA
The next subchapter gives overview of DDSS development and implementation in practice in the
United States of America (US). Once the most advanced and utilized category in US is clinical
decision support for healthcare professionals, it is described in depth. For the reader it is
important to distinguish between clinical decision support systems (CDSS) and DDSS – CDSS is
a subcategory of DDSS and dedicated for clinical use only.
Clinical decision support systems (CDSS) have been used for half a century in the United States
healthcare system. Early systems were standalone, focused on models and automated systems for
diagnosis and therapy decisions and typically limited to a single area of clinical practice. These
systems would take input directly from users and then compute a recommended diagnosis or
therapy. Data were not accessed directly by the systems, nor were the actions more than
providing information back to the user. The HELP system was the first system that integrated
decision support with data in an electronic patient record (EPR). Its first use was in cardiology,
but over time it expanded use to a variety of clinical areas, and is currently used in most of
Intermountain Healthcare’s hospitals. Other systems followed, including the Regenstrief Medical
Record System (RMRS) in Indiana and the Computerized Patient Record System (CPRS) in the
Veterans Health Administration. These systems were known for their integrated decision support
rules that used data from the EPR without requiring separate data entry, and interruptive alerts.
Since these early systems, use of DDSS has grown substantially, with many published
demonstrations of their effect. As the use has grown, some have sought to find ways to share the
clinical decision support knowledge so that rules developed in one system could be easily be
transferred to another. Otherwise the development and validation burden of decision support
rules for a single institution would be unsustainable. To meet that aim, in the early 1990s the
Arden Syntax for Medical Logic Modules was developed, refined and validated. The Arden
Syntax was useful in defining the components of decision support rules, but the actual sharing of
the syntax or code was generally less successful. Sharing across institutions was difficult because
even if the logic was the same, the differences in the databases and the clinical concepts sufficed
for the rules to perform differently when imported. Other initiatives to share decision logic were
met with even more limited success.
Shortly after the turn of the century, enough CDSS had been developed, implemented, and
evaluated that the comparable impact in different clinical areas and for different clinical tasks
could have been measured in reviews. From 2004-2006, three different systematic reviews of
CDSS and health information technology were able to measure how these systems had been
effectively used. In 2004, Delpierre et al. demonstrated that CDSS had in general a positive effect
on preventive care, a mixed effect in practice and guideline compliance, and no demonstrated
benefit in outcomes. In 2005, Kawamoto et al. performed a sensitivity analysis on the systems
used in an earlier systematic review by Hunt et al. to define characteristics of the decision support

5 Wright A, Sittig DF. A four-phase model of the evolution of clinical decision support architectures. Int J Med Inf.
6 Evans RS, Pestotnik SL, Classen DC, Clemmer TP, Weaver LK, Orme JF, et al. A computer-assisted management
record systems and quality of care: more randomized clinical trials or a broader approach? Int J Qual Health Care J
systems associated with success\textsuperscript{8} \textsuperscript{9}. They found that the integration of decision support systems into clinical workflow as the most critical factor, followed by matching with the time of decision making, providing recommendations, and computer-based. In 2006, Chaudhry et al. studied health IT in general, though most systems reviewed incorporated CDSS\textsuperscript{10}. They found various benefits in quality and efficiency, though costs benefits were more elusive. More importantly, they noted that a sizeable proportion of the studies were done at just 4 benchmark institutions, and less than 4\% of the studies used commercially-developed EPRs. This was a critical finding, since by this time most institutions adopting EPRs were purchasing commercial systems, for which there was not a strong evidence base of effectiveness.

The adoption of commercial EPRs was accelerated significantly with the passage of the American Recovery and Reinvestment Act in 2009, which contained legislation supporting the development of incentives (and eventual penalties) for the adoption and “meaningful use” of EPRs. The Meaningful Use criteria required institutions to implement and use certified EPRs. This increased the use of EPRs from around 20-40\% of institutions to more than 80\% over a few years. While many argue that many of the goals of Meaningful Use have been missed due to various unintended consequences, it definitely had the effect of increasing EPR adoption, and with that the use of CDSS. The certification process ended up limiting the number of certified commercial EPRs available, so there has been significant consolidation of institutions with most using one of only a handful of EPRs. Meaningful Use criteria also included requirements for documentation of some standard clinical concepts, which the criteria defined in specific structured terminologies. An unintended consequence of the Meaningful Use program therefore was to reduce two significant barriers to sharing logic modules: by consolidating the number of EPRs used there could be more sharing across institutions using the same commercial EPR, and by requiring the use of specific coded data elements rules using those elements were more consistent.

During the site visits to US health plans Kaiser Permanente (Oakland, California) and Intermountain Healthcare (Salt Lake City, Utah) in June 2015 the study group team had opportunity to learn about personalised medicine programs in the aforementioned organisations. Both health plans are paying a lot of attention to apply DDSS in the context of exploiting recent advantages in genomics and next-generation sequencing technology to integrate genomic information into routine medical use. Both health plans are integrating their DDSS into their existing EPR systems: Kaiser Permanente into Epic; Intermountain Healthcare integrates Syapse Precision Medicine Data Platform to provide actionable data to oncologist into HELP2 system. The studied software are excellent examples of DDSS integration into clinical and health management pathway. Cooperation with both organisations would benefit Estonian personalised medicine pilot implementation. Syapse for instance states that “Intermountain Healthcare uses Syapse software to examine multiple, complex sources of patient data, interpret incoming tumor sequencing results in the context of a patient’s medical history, and formulate a clinical action plan to be conveyed to the patient’s oncologist\textsuperscript{4}. However, once the DDSS-s used by both health plans are integral parts of local EPR, Estonia cannot implement those applications directly into Estonian health information system.

\textsuperscript{8} Kawamoto K, Houlihan CA, Balas EA, Lobach DF. Improving clinical practice using clinical decision support systems: a systematic review of trials to identify features critical to success. BMJ. 2005 Apr 2;330(7494):765.


4.5. Conclusions and suggestions

At this moment there does not exist one certain DDSS software that would solve all specific scenarios of this feasibility study from the personalised medicine implementation perspective. Different software solutions from various providers (incl. software developed in Estonia) are to be used in different stages of a process to get a holistic solution. The categorization of DDSS and perspective timeline for personalised medicine implementation presented in Annex 7 outlines a DDSS-s implementation scenario for Estonia, proposed by the authors of this study.

We have to take into consideration that we need several decision support services to cover different services at different stages for personalised medicine implementation. To do that we need to normalize the data collected and stored by healthcare professionals and possibly also by individuals, which means aggregating structured data into a form that this data could be shared among the variety of users and then retrieve data to be processed by different decision support engines. The authors of this study have had more experience with the EBMeDS (Duodecim Medical Publications Ltd., Finland) system and this could also be implemented most efficiently in Estonia, compared to all other already existing systems. This software also enables, for example, to assess the family doctors’ actions by their patient against treatment guidelines. It should also comply with the scope of interest of the Estonian Health Insurance Fund. To achieve this goal it is important to integrate laboratory data with family doctors’ health information systems. Without the availability of the laboratory data in health information systems none of the decision support systems will actually work.

With regard to the genome data the existing decision support systems are very basic. We could not find any DDSS which includes scripts that exhaustively take into consideration genome, health and medical data. DDSS software tends to be either EPR specific (e.g. Kaiser Permanente’s Epic; Intermountain Healthcare’s Syapse, etc.) or function specific (e.g. EBMeDS for clinical data mainly). At this point the investigated DDSS-s give mainly links and suggestions to perform particular gene test or present risk score. However, Duodecim has already started to compile EBMeDS scripts which are based on the genome test findings and risk calculations. In Estonian perspective the development strategy of new scripts by Duodecim is very appealing because it allows creating country specific algorithms based on the collected evidence. The idea of this kind of DDSS script development is that EBMeDS users can benefit from established technology, generate own scripts, register them in Duodecim database and implement in the local information system. In this context, the exploitation of the Estonian Genome Center of the University of Tartu (EGCUT) knowledge in genome research, combining it with the existing script development and maintenance rules established by Duodecim would be very rational for Estonia.

Architectural approaches to DDSS can be divided into four separate types. The first is standalone, similar to the earliest CDSS-s but currently implemented in structured documentation forms in EPRs. These have the simplest forms of decision support, applied to data as they are entered into the forms. Common examples are calculations and range checking.

Systems of the second type are similar to the integrated CDSS-s like HELP or RMRS, that exist within an EPR, use data from the EPR, and perform actions within the EPR user interface. Common examples are alerts, reminders and drug interaction checks. The third type includes the more advanced systems of today, which integrate data from multiple sources, can include genetic and patient-reported data, and may exist outside the EPR. These systems are extremely flexible in the data they can use and their logic structures, though they may have difficulty integrating with the user interfaces of the workflow systems, like EPRs. The final type is a recent innovation, supported by initiatives like the Substitutable Medical Apps & Reusable Technology (SMART) at Harvard, Fast Healthcare Interoperability Resources (FHIR) from HL7, and the Health Services Platform Consortium (HSPC). Rather than existing outside the EPR and integrating data from multiple sources, these support a model where standard applications can exist as “apps” within an EPR, and use
services to connect to different data sources. **The biggest advantage to this approach is that the entire decision support application – user interface, data services, and logic – are distributed as a group, increasing the likelihood they can be both shared and maintained successfully.**

Based on the knowledge above we recommend to start the DDSS implementation for personalised medicine in Estonia with the localisation and implementation of two DDSS categories – clinical decision support system (e.g. EBMeDS) and scientific gene research decision support (e.g. STACC with EGCUT). This can be followed by health management, patient monitoring and improved data usage and visualisation decision support systems development later on.
5. Model use case scenario descriptions for the three clinical fields (cardiovascular diseases, diabetes, malignant tumours), their data structure description and decision support application feasibility analysis

The current chapter describes the use case scenarios selection and principles applied in the three predefined clinical fields. The first two (CVD and Diabetes) were merged during the 2\textsuperscript{nd} project period and hence in the Chapter 8 where we describe the prototype, we only address two clinical fields, their user scenarios and Digital Decision Support System (DDSS) prototypes. The references to the genotype data necessary for the implementation of the DDSS, is also added to the scenarios in chapter 8.

5.1. Cardiovascular Diseases (CVD)

1. Patient specification in the field of cardiovascular diseases

Uncomplicated patients with essential hypertension (ICD code I 10) 50 years of age. The group size will be 50 patients.

2. Main clinical data set for diagnostics, treatment and follow-up of the patients with essential hypertension

2.1. Prevention of essential hypertension

2.1.1. Data about lifestyle, education, environmental factors from the Estonian Population Register, Declaration of Health. Lifestyle advise and risk factor management.

2.1.1.1. Abdominal obesity (waist circumference: men ≥102 cm; women ≥88 cm)

2.1.1.2. Obesity [BMI ≥30 kg/m\textsuperscript{2} (height\textsuperscript{2})]

2.1.1.3. Fasting plasma glucose >5.6 mmol/L

2.1.1.4. Abnormal glucose tolerance test

2.1.1.5. Dyslipidaemia: Total cholesterol >4.9 mmol/L (190 mg/dL), and/or Low-density lipoprotein cholesterol >3.0 mmol/L, and/or High-density lipoprotein cholesterol: men <1.0 mmol/L, women <1.2 mmol/L, and/or Triglycerides >1.7 mmol/L

2.1.1.6. Smoking

2.1.1.7. Sedentary lifestyle

2.1.1.8. Elevated salt consumption

2.1.1.9. High alcohol consumption

2.2. Diagnostics of essential hypertension.
2.2.1. Sex, weight and height of the patient.
2.2.2. Family history concerning hypertension.
2.2.3. Stroke/myocardial infarction family history in age less than 65 years.
2.2.4. Exclusion of main reasons of secondary hypertension (TSH, T3, T4, ultrasound investigation of kidneys).
2.2.5. Associated cardiovascular risk factors (smoking, dyslipidemia, metabolic syndrome).
2.2.6. Pre-treatment blood pressure readings: systolic and diastolic blood pressure.
2.2.7. Pre-treatment pulse rate.
2.2.8. Pre-treatment ambulatory blood pressure monitoring (ABPM) data (mean 24-hour, daytime and night-time systolic and diastolic blood pressure, nocturnal blood pressure fall (%), mean 24-hour heart rate).
2.2.9. Indicators of kidney damage: creatinin plasma level (fP-Crea), estimated glomerular filtration rate (eGFR).
2.2.10. Indicators of heart damage: left ventricular hypertrophy based on ECG and echocardiography.
2.2.11. Metabolic disturbancies: blood glucose, HbA1c, total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, uric acid).

2.3. Treatment of essential hypertension
2.3.1. Drugs and dosages according to the ATC classification. Use of fixed drug combinations.
2.3.2. Compliance to medication according to electronic prescription database (number and proportion of purchased antihypertensive drugs during last 6 months).
2.3.3. Lifestyle modification (body weight lowering, decrease in salt consumption).
2.3.4. Number of general practitioner and specialists visits during last 12 months.

2.4. Follow-up of essential hypertension.
2.4.1. On-treatment blood pressure readings: systolic and diastolic blood pressure.
2.4.2. On-treatment pulse rate.
2.4.3. On-treatment ambulatory blood pressure monitoring (ABPM) data (mean 24-hour, daytime and night-time systolic and diastolic blood pressure, nocturnal blood pressure fall (%), mean 24-hour heart rate).
2.4.4. Blood pressure control according to office blood pressure measurements (BP<140/90 mm Hg).
2.4.5. Blood pressure control according to home blood pressure measurements (BP<135/85 mm Hg).
2.4.6. Blood pressure control according to ABPM (BP<130/80 mm Hg).
2.4.7. Creatinin plasma level (fP-Crea), estimated glomerular filtration rate (eGFR), blood glucose, HbA1c, total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, uric acid.
2.4.8. Reminders to the patient
   - blood pressure lowering drugs need to be purchased regularly (in case of non-compliance)
   - time of the next visit to the doctor
   - regular positive lifestyle alerts
2.4.9. Reminders to the general practitioner
   - patient is non-compliant to antihypertensive medication
   - patient has not come to visit in time

5.2. Diabetes (DM)

1. Patient specification in the field of Diabetes
Woman 50 y, Type 2 Diabetes, without complications (compensated)
Diagnosis code (ICD 10) E11.9 – group of patients for analysis: 50
Analyzed period unclear 10 years
5 years before the diagnosis and 5 years after the diagnosis of Type 2 Diabetes

2. Main clinical data set for diagnostics, treatment and follow-up of the patients with Type II Diabetes

2.1. Prevention

2.1.1. BMI\textsuperscript{11} (weight kg/ height x height m) dynamics – when (first time during lifetime) > 25 kg/m\textsuperscript{2}, and when > 30 kg/m\textsuperscript{2} \(\rightarrow\) information available in digital medical history (weight changes during the investigated period)

2.1.2. Data about life habits, education, environmental factors \(\rightarrow\) Estonian Population Register, Declaration of Health

2.1.3. Gestational diabetes diagnosis in women (O24.4) \(\rightarrow\) digital medical history

2.1.4. Family history \(\rightarrow\) digital medical history (in future the connection with Genome Centre)

2.1.5. Comorbidities: Hypertension (I10) \(\rightarrow\) digital medical history

2.1.6. Diabetes Risk Questionnaire (copy of Finnish Diabetes Risk Questionnaire)

Recommended is the use of materials of Finnish Diabetes Prevention Study:

A genotype score based on diabetes risk alleles which may predict new cases of diabetes in not in use today – there is not enough knowledge about this area.

There are a lot of genetic markers but the connection with clinical manifestation is not clear.

\[\text{Figure 4: Example of genes under the investigation}\textsuperscript{12}\]

According to American Diabetes Association the risk of developing type 2 diabetes is:

- One in 7, if one of your parents was diagnosed before the age of 50
- One in 13, if one of your parents was diagnosed after the age of 50
- One in 2, if both your parents have diabetes

It is difficult to separate lifestyle risk from genetic risk. Not everyone who carries a mutation will get diabetes, some people carry several mutation.

Type 2 diabetes is caused by both – genetics and environmental factors.

http://www.healthline.com/health/type-2-diabetes/genetics#Overview1

2.2. Diagnosis

\textsuperscript{11} BMI – body mass index

2.2.1. Data about the time of diagnosis → (GP’s summary, visit to Emergency Unit → data in electronic medical history
2.2.2. The basis of diabetes diagnosis; HbA1c and/or Glucose Tolerance Test (high diagnostic glucose values measured in plasma 2 times)
2.2.3. HbA1c changes (dynamics) during investigated period
2.2.4. Diagnosis of long term complications

2.3. Treatment
2.3.1. Visits to diabetes nurse/GP’s nurse (first, repeated visits/consultations)
2.3.2. Oral treatment – monotherapy, dual therapy, triple therapy → Digital Prescription Center
2.3.3. Injectable treatment – insulins, GLP-1 R<sup>13</sup>, insulin pump → Digital Prescription Center
2.3.4. Combination of oral and injectable treatments → Digital Prescription Center
2.3.5. Treatment change is suggested after every 3 month if HbA1c is not on goal
2.3.6. Concomitant medications – statins, hypertension treatment
2.3.7. Data from Digital Prescription Centre to evaluate the treatment compliance: purchased medication „realized“, not purchased medications „expired“
2.3.8. Digital Prescription Center gives possibility to follow the use of Medical Facility Card (meditsiiniseadme kaart) – did patient purchase the test stripes for glucometer, needles for pen-syringes and lancets

2.4. Monitoring – yearly checkup and laboratory tests, home glucose monitoring
2.4.1. Yearly checkup
   – Number of visits/consultations to doctor
   – Number of visits/consultations to diabetes nurse/GP’s nurse (first, repeated visits/consultations)
   – Height (cm) Weight (kg) BMI (kg/m2) Blood pressure (mmHg)
   – Comorbidities: Obesity (E66.0), Hypertension (I10),Chronic urinary tract infection (N39.0) → digital medical history

2.4.2. Laboratory testing
   – Hematology
   – Blood Glucose
   – HbA1c
   – Creatinin + GFR
   – Lipid profile: Cholesterol; LDL; HDL; Triglycerides
   – Albumin/creatinin ratio in urine
   – Ophthalmological examination of eye fundus or photography of eye fundus,
   – Periferal pulses on leg (Doppler of arteries on leg)
   – Neurological sensitivity investigation (physical examination, ENMG<sup>14</sup>) → digital medical history
   – Pictures of ulcers on leg

2.4.3. Blood glucose home-monitoring:
   – Diabetes diary on paper (older patients)
   – Continues glucose monitoring with sensor
   – Glucometer connected to smartphone
   – Physical activity – step counter in smartphone

2.5. Possible notifications/Recommendations/Alerts/Reminders
All notifications, recommendations, alerts and reminders can be switched off or ignored.

<sup>13</sup> GLP-1 RA – glukagon-like peptid – 1 receptor agonist
<sup>14</sup> ENMG – electroneuromyography
2.5.1. For the patient

- Woman – with diagnosis of Gestational Diabetes (GD\textsuperscript{15}) – notification after every 3 year for screening of diabetes
- Questionnaire to evaluate diabetes risk for everybody and especially if BMI > 25 kg/m\textsuperscript{2} and/or age > 45 y;
- (Questionnaires of Quality of Life)
- Notification about BMI\textsuperscript{16} – when the BMI first time during lifetime is higher than 25 kg/m\textsuperscript{2} and 30 kg/m\textsuperscript{2}
- Notification if patient did not visit GP more than 1 year
- Notification from Digital Prescription Center – medications not purchased – for example „the receipt expires after one week“
- Notification from Digital Prescription Center – test stripes for glucometer, lancets or needles for pen-syringes not purchased – the card expires after one week

2.5.2. For the nurse/doctor

- High blood glucose (> 11.1 mmol/l) without diabetes diagnosis
- Overweight/Obese patient not screened for diabetes
- Age over 45 y but not screened for diabetes
- Woman with Gestational Diabetes – screen for diabetes after every 3 year
- Add statin to the treatment of type 2 diabetes
- Patient has not visited the doctor more than one year
- Pathological laboratory findings:
  - HbA1c is not on goal > 7% - change treatment
  - Impaired kidney function (GFR\textsuperscript{17} < 45 ml/min/1.72m\textsuperscript{2}) – change treatment
- Patient was hospitalized through Emergency Department (ED\textsuperscript{18}) – notification to GP
- Patient is visiting several doctors of same specialty in different hospitals at the same time
- Prescription is in conflict with discount rules
- Combined medications are in conflict

5.3. Cancer

**Personalised medicine is considered as the future of cancer care:** medicine aiming at giving patients the best treatment according to their personal medical history, their physiological status, and the molecular characteristics of their tumours\textsuperscript{19}. A majority of cancers are driven by genomic alterations that dysregulate key oncogenic pathways influencing cell growth and survival. (Annex 6) However, the ability to harness tumour genetic information for its full clinical potential has only recently become manifest. Over the past several years, the convergence of discovery, technology, and therapeutic development has created an unparalleled opportunity to test the hypothesis that systematic knowledge of genomic information from individual tumours can improve clinical outcomes for many patients with cancer.

The direction of travel is clear – precision diagnosis and treatment of cancer at the molecular level – and this change in paradigm has profound implications, from preclinical definition of

\textsuperscript{15} GD – Gestational Diabetes
\textsuperscript{16} BMI – body mass index
\textsuperscript{17} GFR – glomerular filtration rate
\textsuperscript{18} ED – Emergency Department
mechanism of action to the development of molecular taxonomies of cancer, and from genome
diagnostics to trial design.
Both the mutation profile of a tumour and germline mutations – heritable aberrations found
within the individual – may influence disease outcome and/or response to therapy.
As cancer treatment evolves from stratified to personalised cancer medicine, there remain major
challenges in information and communication technology (ICT) and bioinformatics. Large-scale
genomic data will need to be integrated with health and clinical data, analysed and translated into
information to serve as guidance for clinical decisions. Furthermore, the vast amount of
information generated from translational research initiatives and ‘big science’ projects, like the
cancer genome projects, need to be translated and interpreted, with effective information flow
between laboratory and clinical researchers a prerequisite. Despite present concerns about this
complexity, automation of much of the analytical and interpretive processes is likely to develop
alongside the genomic technologies and drive understanding to a new level. However, this
suggests that a new focus on healthcare knowledge engineering is needed to facilitate this
knowledge transmission across the research-healthcare gap.
It seems clear that available technologies for genome characterization are fast becoming equipped
to meet the demands of precision oncology. The analytic challenges that accompany
comprehensive genomic data have proven more problematic. The somatic and germline
alterations that are relevant to each cancer must be identified with high accuracy, and clinically
actionable, so-called driver events must be distinguished from the much larger set of passenger
alterations that are present in tumour DNA. Rigorous analysis and astute clinical interpretation of
comprehensive genomic data is impossible without the assistance of computational algorithms to
support clinical-grade data interpretation. Although numerous aspects of clinical computational
biology remain in their infancy, a variety of resources and approaches have already emerged that
may assist clinicians as they prepare for the unprecedented flow of tumour and germline genomic
information.

We can separate two concepts in personalised cancer medicine:
I Prevention and early detection on the basis of germline cancer hereditary susceptibility testing
with personalised preventive strategies (Figure B; Annex 10)
II Personalised cancer therapy on the basis of cancer tissue molecular profiling (+/- germline
assessment) (Figure C)
Figure 5: Challenging the traditional model of cancer genetic counseling. (A) Traditional model of clinical cancer genetics. (B) Incorporating next-generation sequencing (NGS) into genetic cancer risk assessment. (C) NGS of tumors with incorporation of incidental germline findings. WGS, whole-genome sequencing.

I Prevention and early detection on the basis of cancer hereditary susceptibility testing with personalised preventive strategies

The last three decades have witnessed significant strides in our understanding of the genetic basis of cancer susceptibility. In the 1980s and 1990s, rare but highly penetrant cancer predisposition genes were identified by studying cancer-prone families showing Mendelian modes of inheritance. These investigations successfully implicated genes such as BRCA1 and BRCA2 in hereditary breast-ovarian cancer syndrome, DNA mismatch repair genes in Lynch syndrome, p53 in Li-Fraumeni syndrome, and APC in familial adenomatous polyposis. Identification of the genetic basis of such syndromes has had a powerful impact on the practice of preventive oncology. The incorporation of cancer genetic testing into oncology marked one of the first applications of personalised genomics in medicine, because it allowed tailored cancer screening, prevention, and, in some cases, therapeutic measures. Recently, the applications of next-generation sequencing (NGS) technology have led to multiplex gene-panel testing (Annex 5) and genome-wide sequencing, posing broad new challenges to clinical oncologists.

A cell with normal DNA develops into a cancerous cell through the accumulation of genetic changes. Some of these alterations are sporadically acquired and others are inherited in the form of cancer predisposition genes. The identification of cancer predisposition genes has led to the development of screening programmes to identify patients “at-risk” of developing cancer and helps them make decisions on individual risk-modification behaviours. However, an essential part of any screening programme is to have an appropriate accepted therapeutic intervention that can alter the natural history of the disease.

Given the modest effect size for most risk variants identified, the clinical utility of genomic profiling for risk stratification based on GWAS data has been limited for most common cancers. However, the clinical utility of common genetic variants in risk assessment continues to evolve. For example, as a result of large international consortia studies, 49 new loci were recently identified for breast cancer, 26 for prostate cancer, and eight for ovarian cancer. With such additional discoveries, the incorporation of genetic susceptibility into models of risk stratification for public health programs and cancer screening may eventually be feasible.

Data needed for digital decision support

- precise sequencing data of each patient's predisposition genes
- interpretation of gene analysis findings
- familial history
- personal clinical history
- risk factors exposure history
- the latest knowledge and approaches from all available open sources and databases for personalised preventive strategies

II Personalised cancer therapy on the basis of cancer tissue molecular profiling

In recent years, advances in molecular biology, genomics, and related technologies have resulted in greater understanding of the mechanisms of cancer at the molecular level. It is now possible not only to identify the genetic and molecular variations in each patient's cancer cells, but also to apply in many cases the results from the tumour profiling for treatment strategies that target the
molecular underpinnings of the specific disease in each patient\textsuperscript{24} \textsuperscript{25}. Therefore, systemic cancer treatment is undergoing a fundamental change. This change is based on moving away from a paradigm in which histologically defined disease is treated primarily with cytotoxic chemotherapy, toward the use of molecularly targeted drugs prescribed to selected subsets of patients across multiple tumour types. In other words, the treatment decision should be based on the molecular signature of tumour. As genotyping costs continue to decrease, and computational abilities improve, there will be increasing demand for all patients with cancer to undergo tumour genome sequencing to guide targeted therapies.

The scale of tumour genomic profiling is rapidly outpacing human cognitive capacity to make clinical decisions without the aid of tools. New frameworks are needed to help researchers and clinicians process the information emerging from the explosive growth in both the number of tumour genetic variants routinely tested and the respective knowledge to interpret their clinical significance\textsuperscript{26}. The science of computational cancer medicine is still in its infancy; however, there is a clear need to continue the development of knowledge bases, best practices, tools, and validation experiments for successful clinical implementation in oncology.

The answer probably is the artificial intelligence/machine learning (AI/ML) built into clinician-friendly tools, the ultimate goal of which is the personalised oncology improving patient outcomes. The challenges listed above can be met by a systemic approach integrating the advanced analytical capacities with the (1) existing, and rapidly differentiating human disease genomics and clinical research data, (2) user-friendly clinical informatics tools, (3) the latest advances in the high throughput genomics and expression profiling tests. Most importantly, such an integrated system must offer the real access to the proposed therapy options.

**Vision for digital decision support for personalised cancer therapy**

The extreme genomic complexity and mutability of cancer is analysed with the use of comprehensive sequencing and gene expression platforms as well as with analysis of functional protein pathway activation patterns.

Using developed big-data analysis platform, it is possible quickly distinguish clinically meaningful and important genetic alterations from non-important ones and match them with recommended targeted drugs, their combinations and availability.

Conceptually: first, the genomes of the patients’ tumours are characterized using state-of-the-art technologies; second, the genomic data is analysed through a knowledge base of existing and emerging anti-cancer drugs and presented to the treating oncologists into clinical decision making. Third, corresponding targeted therapies are available to patients as standard therapies, expanded access programs, or in the reachable clinical trials.

**Data needed for digital decision support:**

- precise sequencing data of each patient's tumour molecular profile
- precise sequencing data of each patient's health tissue genes (+/- predisposition genes)
- interpretation of gene analysis findings
- familial history


personal clinical history, including relevant disease (cancer therapy) history
risk factors exposure history
the latest knowledge and approaches from all available open sources and databases for personalised preventive strategies (all available clinical evidence, from specific databases and also by global research big-data analysis)
practical recommendations for the access to therapies, including suitable clinical trials

DATA ANALYSIS & INTERPRETATION
A. The Process of Genome-scale Variant Identification
1st step: Sequence alignment
- targeted sequencing
- exome
- transcriptome
aligning the raw data to the reference human genome to better understand variations. Multiple tools exist for this process.
2nd Variant Identification and Tumour/Germline Comparison
3rd Molecular Annotation of Variants

B. The Process of Clinical Interpretation of Tumour Variants
Classifying the Clinical Effects of Genomic Variants
1. Classification of the type of clinical effect
   predict risk of disease
   confirm a diagnosis
   predict prognosis
   predict response or resistance to treatment
   measure response to treatment
2. Classification of the strength of evidence

Prioritizing targets for precision cancer medicine
Level evidence scale for target prioritization

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>Clinical implications</th>
</tr>
</thead>
</table>
| I: Molecular alteration validated in several robust early phase trials or at least one phase III randomized trials | Alteration validated in the disease under consideration, targeted therapies have shown to be ineffective in patients who are lacking the genomic alteration | No evidence that the therapy does not work in the absence of the molecular alteration | Level I molecular alteration, but not in the disease under consideration | A/B: Patients must be treated with the targeted therapy
C: Patients should be considered for clinical trials |
| II: Efficacy of targeting molecular alteration suggested in single and underpowered phase I/II trials | Alteration validated in the disease under consideration, targeted therapies have shown to be ineffective in patients who are lacking the genomic alteration | No evidence that the therapy does not work in the absence of the molecular alteration | Level I molecular alteration, but not in the disease under consideration or anecdotal evidence of response to targeting molecular alteration in single patient case reports | Patients should be considered for clinical trials testing the targeted therapy |
| III: Target suggested by preclinical studies | Preclinical studies include human samples, cell lines and animal models | Preclinical studies that lack either cell lines or animal models | NA | Inclusion in clinical trials is optional |
| IV: Target predicted but lack of clinical or preclinical data | Genomic alteration is a known cancer-related gene | Genomic alteration is not known as cancer-related gene | NA | Inclusion in clinical trials is optional |

Data for Breast Cancer clinical scenario

Diagnosis: Breast carcinoma

Personal data:
Woman
Age
Race
Menstrual status: premenopaus/perimenopaus/postmenopaus
Age at menarche
Age at menopause
No. of pregnancies
No. of deliveries
Age at first live birth
Weight
Height
Body mass index
Hormonal agents used: contraceptive pills/ estrogen replacement /
Family history: known malignancies in biological relatives, by degrees of relatives
  • Personal history: previous breast diseases (Presence of atypical hyperplasia, lobular carcinoma in situ), biopsies, other malignancies

Tumour characteristics:
Histologic type of the carcinoma
Stage
T
N
M
G
Preferably pTNM, if not possible, then cTNM
Estrogen receptor status
Progesterone receptor status
HER2 status

Diagnostics performed:
Mammography
Ultrasonography: breasts
Ultrasonography: abdomen, pelvis
X-ray: thorax
MRT breasts
MRT: brain
MRT: abdomen, pelvis
CT brain
CT thorax
CT abdomen
CT pelvis
PET
SPECT-CT

Therapy:
Established Risk Factors for Breast Cancer: Fixed Factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (female vs. male)</td>
<td>100</td>
</tr>
<tr>
<td>Age (less than 50 vs. over 50)</td>
<td>6.7</td>
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<tr>
<td><strong>Endocrine factors:</strong></td>
<td></td>
</tr>
<tr>
<td>Age of menarche (less than 10)</td>
<td>1.4 to 1.9</td>
</tr>
<tr>
<td>Age at first birth (more than 35)</td>
<td>1.7</td>
</tr>
<tr>
<td>Nulliparity</td>
<td>1.4</td>
</tr>
<tr>
<td>Age at menopause (more than 55)</td>
<td>1.3</td>
</tr>
<tr>
<td>Benign breast disease</td>
<td></td>
</tr>
<tr>
<td>ADH, LCIS</td>
<td>4.0 to 5.0</td>
</tr>
<tr>
<td><strong>Family history:</strong></td>
<td></td>
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<tr>
<td>First-degree relatives</td>
<td></td>
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<tr>
<td>BRCA1/BRCAl mutation</td>
<td>10 to 30</td>
</tr>
<tr>
<td>P53 (Li-Fraumeni)</td>
<td>1.5 to 6.0</td>
</tr>
<tr>
<td>Cowden syndrome</td>
<td>2.0 to 4.0</td>
</tr>
<tr>
<td>Therapeutic radiation</td>
<td>35</td>
</tr>
<tr>
<td><strong>Modifiable Factors:</strong></td>
<td></td>
</tr>
<tr>
<td>Exogenous hormones:</td>
<td></td>
</tr>
<tr>
<td>Oral contraceptive pills</td>
<td>0.9 to 1.0</td>
</tr>
<tr>
<td>Estrogen replacement (more than 10 years)</td>
<td>1.1</td>
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<tr>
<td>Estrogen and progesterone</td>
<td>1.4 to 3.0</td>
</tr>
<tr>
<td>Obesity (BMI more than 30)</td>
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<tr>
<td>Exercise (more than 3 hours per week)</td>
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<tr>
<td>Alcohol use</td>
<td>1.1 to 2.2</td>
</tr>
<tr>
<td>Diet</td>
<td>1.0</td>
</tr>
<tr>
<td>Mammographic density</td>
<td>2.2 to 5.3</td>
</tr>
</tbody>
</table>

Risk Assessment Models:
- Modified Gail Model: [www.cancer.gov/bcrisktool](http://www.cancer.gov/bcrisktool)
- Claus Model

Risk factors used in these models are:
- Age
- Body mass index
- Age at menarche
• Age at first live birth
• Age at menopause
• Number of breast biopsies
• History of atypical hyperplasia
• Number of first-degree relatives with breast cancer
• Number of second-degree relatives with breast cancer
• Number of third-degree relatives with breast cancer
• Race
• Age of onset of breast cancer in a relative
• Bilateral breast cancer in a relative
• Ovarian cancer in a relative
• Male breast cancer in a relative
• Hormone replacement therapy use
• Presence of atypical hyperplasia, lobular carcinoma \textit{in situ}
6. Decision support application feasibility analysis for CVD, DM and Cancer

6.1. Approach
One of our aims is to suggest the most feasible clinical condition for the decision support system piloting in the upcoming period of 2015-2018. During phase two of the study we have narrowed the clinical fields down from three to two: CVD+diabetes and breast cancer.Preferring one clinical scenario over the other is complicated yet. We have found out that even though most of the clinical information related to selected clinical cases is collected and shared in the standardized document format, the data itself is mostly in narrative form and needs pre-processing and aggregation before it could be used in decision support systems. Data representing person’s health behaviour, over the counter medication or data entered by the person itself is lacking almost completely in Estonian healthcare databases. Even more, in the current phase we have done profound analysis of genotype data for decision support systems for cancer and CVD and diabetes patients. We have found out that commercially available decision support systems cover only part of the goals posed for this personalised medicine feasibility study. This means that at least partly we have to design decision support systems based on the specific aims arising from the Estonian pilot.

6.2. Interoperability
DDSS-s automate knowledge about health related information. The knowledge formalization is based on certain understanding of causal relationships between health related facts (information). A DDSS takes health (related) information as input and generates new health information. The information is represented in some form of data (e.g. bits on a computer disk or in computer memory) and the facts are revealed by a processing system (by a DDSS). Obviously, a DDSS has to understand the data to be able to apply the knowledge it represents.
In real life, the information systems used in the health related domains use many alternative ways to encode information into data. For example, some medical diagnostics systems use insurance services or price list based encoding of laboratory orders, some others use LOINC based encoding of laboratory orders. A health record system (EPR) and DDSS must understand the facts the same way to be engaged in cooperation. They must be interoperable. How big is the overlap in the way the data is interpreted by EPRs and potentially applied DDSSs in Estonia?

![Health Records Domain and Decision Support Domain](image.png)

Figure 6: Health records data and decision support data may be defined differently.

A network of systems may interoperate on many levels. Lowest level of interoperability is some form of shared data; the data can appear in the form of common data storage or a transmitted message. An article in Wikipedia proposes 6 capability levels of interoperability.

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28 Original contribution by the authors.
Application of decision support assumes clear understanding of the meaning of the input data. It is essential that both data collector (EPR developer and user) and data interpreter mutually understand the concepts the data represents.

Data definition domains of EPRs (also electronic medical records) used in Estonia have presumably some overlap with data definition domains of prospect decision support systems. These overlaps may be large enough to enable application of certain DDSS, or some extra effort is needed to increase the potential of use.

**Meaning of EHIS data**

The data being collected into the National Health Information System (EHIS) is defined by centrally published standards, by documentation of the systems integrated, and by end users entering the data. Big part of the collected data is structured and encoded according to the standards published by the Estonian E-Health Foundation (EeHF).

1. EeHF standards contribute to the meaning of the data via:
   a. Defined data exchange services (message types), and exchanged document types – these artefacts enhance interpreter understanding by providing some context of data processing methods and events.
   b. Defined data structures (templates) – these artefacts provide interpreter with syntactic relationships between various data items. For example, from a particular template definition one can understand that encounter period, diagnosis code, diagnosis type, and patient id can be all part of a same expression of main diagnosis of a care case of a patient.
   c. Published lists of values (LOV) provide constraints to template fields and reference to codes entered. LOV-s published by EeHF are based on various ontologies either of international coverage or locally developed.

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30 Original contribution by the authors, based on Wikipedia article.
d. Extension mechanisms/structures for parties integrating to EHIS. These mechanisms include possibilities to apply own identification systems, or alternative encodings. The parties register their definition through OID register.

2. Integrated systems contribute to the meaning of the data via generating presentation-focused content into narrative sections of the templates. The generated content can be interpreted only by knowing the source system behaviour. Human readers apply their contextual knowledge to facilitate interpretation of the generated narratives.

3. End users entering the data into free text fields electronic health records (and medical records) are the owners of the meaning the entered data. The data can be interpreted by computer agents (DDSS) only in wider statistical/cultural contexts. Also human interpreters can understand the data only by adding some wider context to the free text data, or by double checking the meaning with the author or the subject.

EHIS data, to be made available for decision support needs possible interoperability advancement in the following areas:

1. Technical interoperability – on needs legal physical access to EHIS data. EHIS provides services over Estonian governmental service bus (X-Roads) in the form of SOAP message exchange.

2. Syntactic interoperability – EHIS templates have to be translated to decision support syntax. This is most probably lossless translation. For example, if EHIS has a record saying “patient X has diagnosis Y”, but DDSS needs the data in the form “diagnosis Y has been observed for subject person X”.

3. Semantic interoperability – there is coded, narrative (structured text), and free text data in EHIS
   a. coded data is tagged for semantic interoperability;
   b. narrative data is mostly generated for human reader and needs some form of supplementary specification to be developed to enable semantic interoperability, one can catalogue the source systems of narrative data, and build a map of generation models used by these systems;
   c. free text data is meant to be written by human authors, it is not expected to be available for machine processing.

4. Pragmatic interoperability – the data collected into EHIS has clear definition of document types and message types, also the requirements of the content have been defined in accordance with the present requirements of medical and statistical records. However, one has set no explicit requirements for clinical digital decision support system yet, the data collection and distribution process is not necessarily designed for DDSS processing.

5. Dynamic interoperability – the EHIS data includes valuable timing data for the purpose of statistics and direct, document based use in medical care mostly. There have not been explicit requirements on data availability timing and status from the clinical digital decision support system perspective. For example, clinical digital decision support system may require information about person’s current and coexistent diagnosis to be available, EHIS only records diagnosis data in regards to encounter (care case) and documentation timings, however.

6. Conceptual interoperability – designers of the EHIS and DDSS must understand the information shared the same way. There must be mutual understanding of the meaning of the health facts recorded into EHIS and the facts interpreted by a DDSS. From the conceptual interoperability perspective the EHIS data falls into the following categories:
   a. Facts encoded according some internationally recognized ontology. There is high probability that a prospect DDSS will interpret the facts the way they were understood by the author or source system (e.g. laboratory diagnostics).
b. Facts encoded according to locally developed list of values. It is not possible to feed these facts into common DDSS, and also it is not possible to apply evidence based decision rules on these facts directly. These facts have to be mapped to some widely accepted ontology, and this is often lossy, generalizing translation.

c. Facts encoded into narratives are to be enriched with semantic tags for decision support. No other system can interpret the narratives directly.

Figure 8: Mutual understanding of concepts is prerequisite of effective communication

Improvement of conceptual interoperability is often affecting the whole value-chain of information processing. Conceptualization process on wider scale requires human learning, communication, and this requires time.

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31 Original contribution by the authors.
Figure 9: Not all EHIS standard lists of values are backed by widely accepted ontologies.\footnote{Original contribution by the authors.}
7. Description of suggested algorithms and concept of the decision support solution

7.1. Approach
The Decision Support feasibility study has gone through the health data needed for digital decision support based on idealised case-studies – processes for health promotion and disease prevention, diagnosis, treatment and follow-up (Annex 1.1 and 1.2) – and detailed both the possible origin of the data, as well as the potential users of the decision support over the lifespan of an individual. The genome data were considered in all phases of DDSS algorithms evaluation. Therefore we know the format of the data now and the intervention of the digital decision support system. We have also outlined the existing international and principal (Estonian) architecture of digital decision support systems. Where we left off, is:

– where the data needs to be taken and organized to digital decision support system format, suggested by the IT architecture feasibility study and;
– where the organization to support this architecture should be suggested by the leadership and management feasibility study.

Reference 1:
The Leadership and management feasibility study has suggested the implementation of the Digital Decision Support system in Estonia will be the responsibility of the non-profit organization to be established by the Ministry of Social Affairs. The target is to organize and grant access to all relevant databases in Estonia (see chapter 11 in the management study).

Reference 2:
The Information architecture and data management study outlines alternative solutions for the DDSS to be implemented, of which some take more and some less resources, in correlation with the expected gains. (see chapter 8 in the Information Architecture report).

7.2. Architecture Concept
Understanding the Digital Decision Support Systems
Digital Decision Support Systems (DDSS) are designed to assist human user in health-related and clinical decision making activities. One of the promises of DDSS is the ability to generate case-specific advice based on the available information and knowledge about information relationships. The knowledge can be explicitly defined via rules or scripts, or the knowledge can be automatically derived from the contextual information (big data, machine learning, etc.). The knowledge enables a DDSS to propose new facts (new information) that would exist, if a decision was made by the assisted human user. For example, a patient needs to take a correct dose of medication and a DDSS proposes the correct dose, though no one has taken any medication yet.

The same set of decision rules that enable prediction of possible human decisions is available also for simulation of consequence of already made choices. For example, a DDSS can suggest alternative diagnosis after physician has selected a diagnosis already, or propose additional medication to a drug being prescribed. In simulation situation, a DDSS takes user a step further by showing the consequence of the planned action.

Besides providing direct advice to users, a DDSS can also present the existing information in a way that stimulates a user to find possible patterns or relationships. The visualization is a crucial tool for new knowledge elicitation during scientific studies, but the same techniques can also be helpful for physicians and patients (incl. healthy people). For example, a physician may be in a search for possible cause for a certain disease among a group of patients; by showing the patients’ living locations a map can give a hint about environmental factors causing the health issue.
Application of the visualization techniques directly on practitioners’ and patients’ end-user-devices opens the e-health ecosystem for broad-based knowledge acquisition, helps to preserve the context of acquired knowledge as specific as possible, feeds scientific research and decision support development with new potential rules, speeds up the feedback loop between data collection and knowledge management, and eventually improves healthcare.

**Process Viewpoint**
During the study several clinical scenarios were analysed for the possible applicability of a DDSS. The scenarios included prevention, cure, and rehabilitation phases of clinical intervention. The same time patient (or a healthy person) centric life-long view on health related events was considered, and also scientific research view on the health information. All scenarios are taking into account the advantages of genome research and available data in EGCUT. This study proposed six focus-areas where specific decision support mechanisms could be further analysed (Annex 6).

Even though the DDSS application focus-areas need further detailed research, some general implications of DDSS on health processes can be proposed. In general health processes have included decision points all the time, patient and doctor have reached to an understanding of the next action of care process. The digitalization of the health information just provides for more knowledgeable decisions. DDSS improves to handle effectively and efficiently large datasets of genome and phenotype data. This is the place where decision support systems enter the scene. The changes the study is focusing are in the way the information moves between the agents of the health process, how the information is presented, and how the information processing systems can help to see relationships in the information.


**Figure 10: Health Process and Management Process**

Health processes are gradually matured with decision support. There is a suggestion to use six-sigma originated DMAIC improvement cycle also for maturing the use of information in health processes.

maturity framework for decision processes in health can be pictured as matrix of process and maturity dimension.

![Maturity framework for decision processes in health](image)

**Figure 11:** Maturity framework for decision processes in health

The health processes will be iteratively improved via introduction of better information processing methods and tools. The improvement process cannot succeed on the healthcare as a whole, there must be something graspable to work with. One key to the effective process improvement is management process that is able to govern both the high-level goals and small-scale updates scenario by scenario.

Architecture blueprint of the personalised medicine initiative must support implementation of changes iteratively during a longer period.

**Functional Viewpoint**

A DDSS is still an information system. Experience of building information systems is valid with DDSS-s. DDSS has some functional characteristics that other systems may lack. These functions are:

1. explicit decision rules/scripts (explicit knowledge)
2. data analytics system (implicit knowledge, explicit context)
3. machine learning (implicit knowledge, implicit context)

In the healthcare domain the above functions may all be elaborated. Explicit decision rules, due to more strict human control over the algorithm, is often applied in a situation with direct influence to one’s health; only evidence based rules are allowed in these situations by policy. Data analytics systems are often sources of scientific studies that enable design of new decision algorithms. However, the distinction is not absolute, and decision support combining all these functions may enable most comprehensive advisory to a user.

The discussion functional viewpoint uses a 5-zone reference architecture. The image below depicts the reference architecture zones with sample building blocks for the zones.

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34 Original contribution by the authors based on: [https://en.wikipedia.org/wiki/DMAIC](https://en.wikipedia.org/wiki/DMAIC).
Examination of the reference architecture from the point of view of the decision support reveals possible areas of change. Considering the 5-zone functional architecture of an information system the allocation of new functions could be as follows.

1. Interaction Zone represents components or subsystems for information exchange with the environment of the system. This exchange includes user interfaces, and messaging interfaces or gateways. For example, one can find patient portal and practitioner workbenches from the interaction zone. In regard to decision support the following ideas for change come up.

   1.1. User interfaces must present advice generated by decision support. This should also include genomic information. The advice may appear in integration with other datasets like work lists (highest priority, highest urgency), or the advice can be presented as separate data on its own (e.g. a reminder flag).

   1.2. User interfaces should present decision rationale and source data that motivates the advice (e.g. genetic risk score evidence source(s)).

   1.3. Interaction modules (message adapter, user interface) may include implementation of decision rules to enable operative advice that includes current input (or message) as a source data.

   1.4. User interfaces need most probably adjustments in data collection as decision support works best on well-coded data. Genome data could be retrieved from Biobank (in Estonian case EGCUT) to different end-user applications.

2. Processing Zone represent components or subsystems for data validation, transformation, routing, inference, enrichment, etc. These components take care of transporting data between various data storage locations in other zones. For example, a system in the processing zone may query couple source systems for patient data, apply decision support rules to the transferred data to generate advice, and insert the advice for later retrieval into a target data store. This also applies to the individual molecular profiling which could be done automatically in this zone. An application of DDSS could bring the following changes to the processing zone.

   2.1. More data integration systems will be deployed. Efficient DDSS needs specialized data sources; the data sources will be fed by the new integration processes. For example, personalised genetic risks can be prepared for risk based decision support.

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35 Original contribution by the authors.
2.2. Integration systems that apply decision rules to generate advice data. Such advices will be prepared asynchronously to simplify central decision rules management, to save time during interactive presentation phase, and to enable parallel and secondary use of advices.

2.3. The quality of data being transported via existing data processing streams needs improvement. For example, the EHIS input validation is being improved potentially rising the quality of decision support too.

3. Storage Zone represents components or subsystems dealing with shared data stores. The data stores of this zone are shared between many processing and interaction elements. For example, digital medical documents are collected into EHIS document store and shared between many hospital or primary care systems; or images in diagnostics archive can be retrieved by many users. An advancement of decision support will depend on the possible changes like:

3.1. New data stores will be created to keep advice data, related decision rationale, and copy or links to source data that motivated the advice.

3.2. Decision support, to be timely and efficient, may need source data to be rearranged possibly into a new derivative storage. For example, person’s medical record, environmental data, and lifestyle data can be collected into one storage to support interactive decision support.

3.3. Person’s genomic data and other omics data could be stored in separate repository.

4. Reference Zone collects components or subsystems that represent data required for the information system to operate, but the data is provided by external systems or processes. In contrast to the storage zone, where the data is maintained by other parts of the information system. For example, data validation and processing rules can be installed into the system in the form of decision tables, message templates, lists of values, etc. Implementation of the decision support certain new elements appear in the reference zone.

4.1. Explicit decision rules that are applied in other parts of the system will be installed as components of the reference zone.

4.2. Interoperability between decision support components and other parts of the system may need additional enabling data definitions (message/document standards, common taxonomies) to be deployed

4.3. DDSS-s references, rules and releases are listed in this zone. New rules based on the genome research are added.

5. Control Zone represents components or subsystems that provide feedback about the system operations and support management decisions about system improvement. Typical activities performed on components of the zone are data analytics (business intelligence) and monitoring. A system may require analytics and monitoring from many viewpoints including business, process, usage, and technology viewpoints. Implementation of decision support brings in additional requirements that fit into the control zone.

5.1. Data quality surveillance will need to be improved as decision support is more sensitive on quality of data than existing human user oriented functions.

5.2. Business intelligence mechanisms (data mining) can be applied on stored data to find new decision patterns. The discovered patterns may be then analysed further against medical evidence to change decision rules base.
Technical Viewpoint
An information system consists of various build technical blocks. In abstract sense there are components and transports. Components are application elements that provide and consume services. Transports are agreements that enable collaboration of the components.

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Figure 13: Change management

Figure 14: Technical viewpoint

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36 Original contribution by the authors.
37 Original contribution by the authors.
The components implement the functions discussed via functional viewpoint above. For example there are components dealing only with interaction, integration, data storage, etc. Also there can be components with combined functionalities, like an HIS can provide user interface, integrate hospital data with EHIS, and also store medical records. ECGUT stores genome data but also updates phenotype data. The components are hosted and maintained by various organizations.

Figure 15: Components

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38 Original contribution by the authors.
8. Description of a functional prototype exemplary application and its visualization

8.1. Mapping Existing Processes Through Clinical Expert Interviews

8.1.1. Mapping Clinical Processes and Finding Opportunities for Possible Digital Decision Support System Applications

For creating a description of the exemplary DDSS prototype application, the design group started with analysing existing clinical processes of the three selected clinical fields (diabetes type II, hypertension, breast and ovarian cancer) in collaboration with the respective clinical experts. The clinical processes were mapped during workshops with Dr. Ü. Jakovlev (diabetes type II), Dr. M. Viigimaa (hypertension) and Dr. Peeter Padrik (breast and ovarian cancer). Existing clinical processes were divided by parties involved (GPs, clinical specialists, patients, third party) and phases (health management, prevention, diagnosing, treatment, follow-up monitoring) to better understand the application possibilities for a wide variety of DDSS-s. Furthermore, the design group, in collaboration with clinical specialists, brainstormed and came up with new possible processes for disease prevention and patient monitoring enabled by the application and wider spread of new supportive technologies in the near future. Working closely with clinical and IT specialists, the design group aimed for coming up with an exemplary DDSS concept, which was realistic to implement as well as being a valid pilot for gathering new insight and provide added value for both clinicians and patients alike.

8.1.2. Conclusions and Findings from Clinical Expert Interviews

Poor usability of information systems is an obstacle in current decision making

When conducting expert interviews, the design group found that poor usability of medical information systems was seen as the main obstacle in current decision making. Gathering patient data from the poorly designed interfaces is currently fairly ineffective and takes a significant amount of the valuable clinical visit time. Currently doctors can’t see patient’s previous diagnosis at a glance but rather need to browse through the patient’s different case summaries (epicrisis). Sometimes a clinical specialist has to switch between multiple EPR applications as the data across various systems is not properly synchronised. Clinical specialists working in more than one care providing institution, find the differences in user interfaces as well as functionalities of the different hospital information systems rather confusing. Already the display of existing structured data, which is properly gathered in a single medical specialist desktop application in a manner that fits the clinician’s logic is seen as a needed functionality of faster decision making. The usability of different electronic patient records and clinical information systems play a key role in the quality of entering and reusing the gathered medical and health data. Furthermore, currently the medical information systems often lack predefined processes and functionalities for the clinicians to enter the medical data in a structured manner resulting in unstructured poorly usable EPR data. Usability analysis and development of usability guidelines would help to set quality standards for implementing user interfaces in new clinical information systems.

Problems to tackle with digital decision supports

Helping clinicians to manage in the growing information load was seen as the key reason why DDSS applications are needed in oncology. Today, genetic counselling is already part of the breast and ovarian cancer treatment in Estonia. Rapid developments in genetic science are diversifying and growing the amount of information clinicians need to consider in decision making process. In the future decision support systems will become vital in genetic counselling and oncologist workflows to effectively interpret the genetic risk factors in disease prevention and treatment planning. They could make the preventive screening programs more effective...
through finding the right groups of patients as well as consider more factors in assigning proper treatment schemes.

Regarding the Cardiovascular diseases, decision support was seen more in the context of making better use of medical data and increasing patient engagement in his or her health management. It was seen as a primary healthcare support tool for health promotion and disease prevention through better patient engagement. There are already quite a few genetic markers for assessing the risk for cardiovascular diseases and diabetes type II, but the connection with evidence based clinical processes is not yet clear nor applied. The genetic info is not used in current clinical process and its extensive use is not predicted in coming years. Nevertheless, patient health management tools increasing patient awareness and engagement could provide immense value in the prevention of widely spread CVD and diabetes as well as provide better quality for chronic patient monitoring.

The need for creating new processes for prevention and monitoring

The clinical expert interviews emphasised the need for better patient engagement, more focused prevention and guidance provided to risk group patients at early stages. Clinical process and potential decision support mapping proposed new processes in primary healthcare. For example, an automatically generated risk index in GP's registry, based on family health history, patient's health data and self-filled lifestyle questionnaire in patient portal. These potential new workflows should be further discussed with GPs, nurses and other clinical specialists.

8.1.3. Goals and stakeholders of decision support

In order to provide medical doctors, other healthcare stakeholders, and patients with adequate decision support, we first need to obtain a holistic understanding of the problem domain of personalised healthcare as a whole. For obtaining this kind of understanding, a DDSS has to be treated as a socio-technical system. Socio-technical system is defined as a software intensive system that has defined operational processes followed by human operators and which operates within an organization. A socio-technical system can be viewed as a system that contains both a social aspect, which may be a subsystem, and a technical aspect. For holistic modelling of socio-technical systems we rely on agent-oriented modelling, which is a methodology for designing socio-technical systems that has been successfully used in designing such systems in the healthcare domain.
Agent-oriented modelling described in\textsuperscript{47} is a holistic methodology for analysing and designing socio-technical systems consisting of humans and technical components, both of which are subsumed under the concept of \textit{agent}. In AOM we start analysing the problem domain of the socio-technical system by using a goal model. A goal model is a container of three components: goals, quality goals, emotional goals, and roles\textsuperscript{48}. A goal is a representation of a functional requirement of the socio-technical system. A quality goal, as its name implies, is a non-functional or quality requirement of the system. An emotional goal is a goal that aims to affect people’s emotional state or wellbeing\textsuperscript{49}. Goals, quality goals, and emotional goals can be further decomposed into smaller related sub-goals, sub-quality goals, and sub-emotional goals. The resulting hierarchical structure is used to show that the subcomponent is an aspect of the top-level component. Goal models also determine roles that are capacities or positions that agents playing the roles need to contribute to achieving the goals. An important objective of goal models is to serve as communication media that facilitate discussions between technical- and non-technical stakeholders for generating understandable domain knowledge.

Figure 16 represents the overall goal model for decision support in healthcare. In the goal model of Figure 16, we first present the uppermost goal – “Support decisions” – with the attached quality goal “Individualised”. The roles relevant for achieving the highest-level goal are GP, GP Nurse, Specialist, and Advisor. In the course of the workshop on agent-oriented modelling of DDSS conducted in the project, other more loosely related stakeholder roles were proposed, such as (the Estonian) Health Insurance Fund, Hospital, patient’s Relative, patient’s Representative, non-governmental-organisation (NGO) representing patients with a certain condition, and the related Governmental Organisation, such as, for example, the Estonian Road

\textsuperscript{46} Original contribution by the authors.
Administration. All of these roles are represented in Figure 16. At the stage of goal modelling it is of no importance who or what is going to perform the roles. For example, the role Advisor can be played by some “intelligent” piece of software or alternatively by a human. The main goal – “Support decisions” – has been divided into the sub-goals “Stay healthy”, “Diagnose”, and “Cure”, each of which represents an important aspect of achieving the highest-level goal. The functional goal “Stay healthy” is characterized by the emotional goal “Motivating”, meaning that staying healthy has to be emotionally attractive for a patient. The quality goals attached to the functional goals “Diagnose” and “Cure” respectively mean that diagnosing has to be precise and cure must be efficient. Achievement of these quality goals can be measured by the corresponding Key Performance Indicators, but this is of no relevance at the initial stage of the problem domain analysis overviewed in this report.

Figure 17: Goal model elaborating the “Stay healthy” sub-goal

In the discussions among the project team it was emphasized that most of the possible savings in healthcare can be obtained through offering decision support to meet the sub-goal “Stay healthy”. Prompted by this, we have further elaborated the “Stay healthy” sub-goal in Figure 17. As Figure 7 reflects, in order to stay healthy, emotionally motivating drivers should be set for individuals. Also, in order to meet this goal, different kinds of information has to be obtained by gathering data originating in sensors, querying the Estonian Health Information System and the Estonian Gene Bank, as well as by interviewing would-be patients in an informative way. Other aspects of staying healthy are informing patients in a discrete fashion about possible problems due to, for example, genetic background, personal advising of patients, identifying risky patients by considering probabilities for one or another condition or disease, and automated and digital screening of risky patients. Also, visits of risky patients to GPs and GP Nurses (specialists are not required at this stage) should be prioritized according to the risk level of each individual patient. Finally, risky patients should be monitored in domestic conditions in the manner that would be emotionally motivating for them. An important sub-aspect of monitoring risky patients is collecting and analysing data.

General requirements for the DDSS and the functional prototype are given in Annex 8.

50 Original contribution by the authors.
8.2. The Exemplary DDSS Prototype
8.2.1. Usage of DDSS in Two Clinical Scenarios

After mapping the existing processes of the three selected clinical fields, the design group created two clinical scenarios for displaying the usage of possible decision support systems. Two potential scenarios are described in Service Blueprints (Annex 1.1 and 1.2):

- Scenario B: Chronic Patient: Monitoring and Personalised Treatment (Cardiovascular Diseases, Diabetes Type II).

Hypertension and cardiovascular diseases (CVD) were combined with diabetes type II because of the similarities of occurrence, prevention and chronic patient monitoring in these two clinical fields. Breast and ovarian cancer scenario was framed to focus on the prevention using personalised approach through gene based risk assessment. The two service blueprints display how application of the DDSS can make the clinical decision making process more effective as well as raise patient engagement in treatment process resulting in increased quality of the whole clinical process.

8.2.2. The Exemplary DDSS Prototype

The exemplary scenarios and the prototype is based on EBMeDS scripts as well as established risk factors for diabetes type II (in case of CVD and diabetes II chronic patient monitoring) and established risk factors for breast cancer (in case of breast and ovarian cancer). The exemplary prototype focuses on providing contextual notifications and suggestions for patient and clinical specialists alike based on patient genotype and phenotype data.

Views of decision support notifications for clinical specialist users are drafted to be displayed in health professionals’ electronic patient record (EPR). Decision support notifications for patients are drafted to be displayed in their patient portal (PP) personal health record (PHR). The first level of digitally supported decision making is improved data usage and visualisation of already existing health information. In parallel to developing DDSS, improvements in the existing health information systems are needed to improve the quality of data entered and facilitate clinical decision making in general.


Scenario A displays the process for personalised breast cancer prevention based on established risk factors (genotype and phenotype). It focuses on prevention of breast cancer and displays how the potential DDSS can help genetic counsellor and other medical specialists better interpret the risk factors derived from genetic sequencing results. Furthermore, it displays how the risk factors and preventive steps might be presented for the patient. For detailed scenario description, please see Annex 1.1.

Genetic Risk Analysis Summary for Patient\(^{51}\)

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\(^{51}\) Original contribution by the authors.
8.2.4. Scenario B: Chronic Patient: Monitoring and Personalised Treatment (Cardiovascular Diseases, Diabetes Type II)

Scenario B, focusing on chronic patient monitoring (CVD and diabetes type II) presents various DDSS application possibilities helping both the medical doctor to better grasp and analyse the vast amount of data as well as simplify health management for the chronic patient through contextual notifications, diagnosing supports, better patient steering guidelines and clinical process management. The exemplary chronic patient monitoring DDSS-s notifications are based on EBMcIDS scripts developed by Duodecim.

52 Original contribution by the authors.
Medical Publications. The six exemplary EBMDS scripts include: notifications for patients needing preventive medical attention and suggestions for prescribing medications based on patient diagnoses. Please see Annex 1.2 for exemplary EBMDS scripts used.

Prototype view B1: Patient Portal PHR Notifications
Patient steering DDSS – care plan and it's notifications. DDSS health analytics for patient – feedback based on his /her data (weight and physical activity).53

Prototype view B2: Professional EPR Patient List and Notifications
DDSS for Health counsellor: group and plan based chronic patient management.

Prototype view B3: Professional EPR Diagnosing and Treatment Suggestions

53 Original contribution by the authors.
Diagnosis and Treatment suggestions based on EBMcDS scripts.

- **ANTS KASK, 60**
  - **CURRENT MEDICATIONS:**
    - Micardis 80mg 1 tablet morning
  - **GENERAL DATA:**
    - 06.03.1960
    - 31.6 BMI (182cm/105kg)
    - 135/80 mmHg BP
    - B blood type

- **PROBLEMS**
  - Hypertension: 2008
  - Obesity: 2010
  - Pre-diabetes: 2011
  - Dyslipidaemia: 2011

- **DECISION SUPPORT**
  - **Diagnosis:** Prediabetes (R73.0) based on: HbA1c 6.2%; Dyslipidemia (E78.2); [see blood test results >>]
  - **Treatment suggestions:** Diet therapy, physical activity plan; assign plans >>
  - **Medications:** Initial dose of Rosuvastatin 10 mg (1x at night for dyslipidemia)

- **RISKS**
  - **High Type II Diabetes Risk**
    - Risk score 15-20 points. Among this risk group, it is estimated 1 in 3 will develop the disease.
  - **High risk of Myocardial Infarction**
    - 1.8 times higher general risk of myocardial infarction.
Prototype view B4: Professional EPR Medications and Patient Steering Suggestions
Treatment suggestions based on EBMeds scripts, patient steering support.\textsuperscript{54}

\textsuperscript{54} Original contribution by the authors.
9. Description of the trends in IT environment, options analysis

Healthcare is starting to adopt new treatments, medications and protocols but is lagging far behind when it comes to the overall model of healthcare. We basically deliver healthcare the same way it was done a hundred years ago. However, due to the exponentially growing possibilities the technology is currently introducing, we can now start bringing healthcare back into the homes of people.

9.1. Overview of trends in IT environment for healthcare

In this section we will describe seven trends in IT environment for future healthcare, based on the source.

Trend 1. Empowered Patients

Healthcare cannot advance without physicians letting their patients help themselves and be a full partner in making the decisions that affect them. This is increasingly facilitated by the technology these days and is actually the purpose of personalised healthcare.

Trend 2. Augmented Reality and Virtual Reality

Augmented reality (AR) is a real-time view of a real-world environment that is enhanced by computer-generated sound, video, graphics, GPS data, or inputs we may not have thought about yet. For example, imagine wearing an AR device while you are walking, and receiving promotional offers from shops you pass. Simultaneously you see the real and online worlds superimposed. A company called Metaio, for instance, provides an AR application for technicians to service and repair the Volkswagen XLI cars without any prior training. Instructions are projected on top of what they are looking at in the auto shop. In a similar way, getting information via digital contact lenses could greatly augment the practice of healthcare.

As another example, Google Glass, a wearable computer with an optical head-mounted display, was made available to testers and developers in 2013. As of July, 2014, it is not yet commercially available, although Google did sell it publicly for one day in April, 2014. Google Glass has a touchpad on the temple piece, a camera, and an optical display. It works like a smartphone by letting users take photos and videos, browse the web, take notes, and make calls. Wearers access the Internet via natural language voice commands such as “OK, Glass, do a search for diabetes”.

Trend 3. Telemedicine and Remote Care

Going back in history, Hugo Gernsback was a pioneer in both radio and publishing. He designed the first home radio set and published dozens of magazines in the early 1900s. He wrote an article about the future of radio telecommunication in the February of 1925 issue of “Science and Invention”. In the article he envisioned the device termed “teledactyl” (“tele” means far, “dactyl” means finger in Greek) that was meant to allow doctors to see and touch their patients through a viewscreen with robotic arms that were kilometres away. He predicted that the practice of medicine would look much different already by the 1970s. From their offices doctors would diagnose and treat patients in their homes via machines and devices that worked through radio waves. The predicted in 1925 change is only now about to take place.

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Trend 4. Body Sensors Inside and Out
What do we do when we need to measure different health parameters? We go to a lab and provide blood sample; or to the hospital where they measure blood pressure, ECG, and perform other diagnostic tests. After that we wait and bring the results to the doctor to discuss the next step. If we need a radiology imaging or a laboratory test, it might take a lot of time due to waiting lists worldwide. This is changing now due to the increasing use of different internal and external body sensors.

Trend 5. The 3D Printing Revolution
To start with an example, a 14-month-old baby in the US had so many heart defects that it made the upcoming operation difficult. To better prepare in detail, hospital officials at Kosair Children’s Hospital in Louisville, Kentucky contacted the J.B. Speed School of Engineering, where a polymer model of the baby’s heart was created with a 3D printer. This provided vital insight ahead of surgery. Once the cardiothoracic surgeon had a model he knew exactly what he needed to do. The model allowed him to reduce the number of exploratory incisions and the overall operating time. This is just one example of how 3D printers could assist medical professionals.

Trend 6. The End of Human Experimentation
Today, new pharmaceuticals are approved by a process that culminates in human clinical trials. A clinical trial is a rigorous process from development of the active molecule to animal trials before the human ones, costing billions of dollars and requiring many years. Patients participating in the trial are exposed to side effects, not all of which will have been predicted by animal testing. If the drug is successful in trial, it may receive approval, but the time and expense are present regardless of the trial outcome. But what if there were another, safer, faster, and less expensive route to approval? Instead of requiring years of “ex vivo” and animal studies before human testing, what if it were possible to test thousands of new molecules on billions of virtual patients in just a few minutes? This would require building an adequate virtual model of the human body, which is now closer than ever.

Trend 7. Medical Decisions via Artificial Intelligence
In 2011, people witnessed an interesting and at the same time weird competition on the television quiz show Jeopardy. It featured the two best players in the history of the show, Ken Jennings, who had the longest unbeaten run of 74 winning appearances, and Brad Rutter, who had earned the biggest prize of $3.25 million. Their opponent was a huge computer with over 750 servers and a cooling system stored at a different location so as not to disturb the players. The room-sized machine was made by IBM and named after the company’s founder, Thomas J. Watson. It did not smile or show emotion, but it kept on giving good answers. At the end, Watson won the game with $77,147 leaving Rutter and Jennings with $21,600 and $24,000 respectively.

9.2. **How to create flexible solutions in DDSS for healthcare?**
Today’s dynamic world requires changes in our information systems’ development and maintenance methods. A traditional method, in which the manual programming is the main form of development, does not give the necessary flexibility to respond to changes in environments. Our challenge now is to increase the participation of domain experts in solutions’ development and maintenance. Meeting this challenge is crucial in developing DDSS for healthcare because, as can be concluded from this study, the new opportunities given in healthcare by the technology are growing very fast. One promising direction for developing adaptive and evolutionary DDSS for healthcare is the *model-driven approach.*
Model-driven engineering (MDE)\textsuperscript{57} is a general software development approach that focuses on creating and exploiting abstract representations of the knowledge and activities that govern a particular application domain instead of putting all the emphasis on the computing (or algorithmic) concepts.

According to the particular model-driven approach, the goal model, decision model, process model, data model, user interface model, and integration model define the solution, and the user can only after a short while begin to test the application. All solutions are usable on mobile devices.

Processes\textsuperscript{58} are executed to achieve some predefined outcomes. These results are consistent with some organizational objectives. We term the desired result of the process as a \textit{process goal}. A process goal is formed using state variables and must have exact measures. It is notably important to have on-place target values for process goals, which allows a self-adaption of the system\textsuperscript{59} \textsuperscript{60}. However, we should start goal modelling by representing goals as generic and abstract.

Throughout the development, a central role is performed by a decision model. Decision models are created according to the decision theory\textsuperscript{61}, which is concerned with identifying the values, uncertainties and other relevant issues in a given decision with its rationality and the resulting optimal decision. Within a process, different options for sub-processes enable one to make directed decisions.

A decision model consists of rule formulae, which in turn consist of Condition and Action parts. A rule formula allows one to perform a wide range of calculations. The rule formula offers the basic mathematical operations (addition, subtraction, multiplication, division), more advanced operations (such as exponentiation or binary AND), comparisons (greater than, less than, etc.), and a wide variety of formula functions for different purposes and data types (date and time calculation, string handling and manipulation, conversion functions, system functions, etc.). Conditions and actions are the key elements of the approach and they allow simple programming interface and expandability of the solution. \textit{Because of the simplicity of the user interface, end users such as medical doctors, other healthcare professionals, and patients themselves should be capable of inserting and editing the rules.}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure18.png}
\caption{User interface of a rule-based decision model\textsuperscript{62}}
\end{figure}

\textsuperscript{61} M. Peterson, An Introduction to Decision Theory (Cambridge Introductions to Philosophy), 1 edition ed., Cambridge University Press, 2009, p. 325.
\textsuperscript{62} Yoga Systems, 2015.
9.3. Internet of things (IoT) for smart environments

In this section we point out some more technologies and approaches that could be used in model driven engineering\textsuperscript{64} \textsuperscript{65} of the DDSS and other smart solutions in healthcare. A huge amount of scientific literature is published on the IoT, and it does not make sense to address the entire matter here because the corresponding surveys are available, such as, for example\textsuperscript{66}. Therefore we focus on the information that we obtain from the sensors for decisions that are to be made based on them, as namely this aspect is relevant for DDSS in healthcare. The IoT for smart environments is defined as follows\textsuperscript{67}: “Interconnection of sensing and actuating devices providing the ability to share information across platforms through a unified framework, developing a common operating picture for enabling innovative applications. This is achieved by seamless ubiquitous sensing, data analytics and information representation with Cloud computing as the unifying framework”.

To create the DDSS and other smart IoT solutions, the main focus should be put on data storage and analytics. For real-time processing and storing data, the NoSQL databases should be used\textsuperscript{68}. Data analytics includes artificial intelligence algorithms for temporal machine-learning and for supporting decision-making processes\textsuperscript{69}.

\textsuperscript{63} Yoga Systems, 2015.
\textsuperscript{64} J. Arlow and I. Neustadt, Enterprise Patterns and MDA: Building Better Software with Archetype Patterns and UML, Addison-Wesley Professional, 2004, p. 528.
\textsuperscript{65} A. Hesselund, "Domain-Specific Multimodeling," 2009.
10. Analysis of the current situation of Digital Decision Support systems in personalised medicine, barriers to implementation and supportive arguments

The aim of Digital Decision Support in Personalised Medicine is to assist decision makers to understand and make informed decisions in an environment of continuously increasing amount of health and medical data and to automate actions based on the collected evidence. The decision makers could be healthcare professionals, patients, healthy individuals, scientists or any other third party. Currently DDSS applications are used very occasionally in Estonia. One can argue that e-prescription and processing of health insurance claims fall into the DDSS category but in any case the algorithms applied with these services represent most simplistic functional classes like feedback and data organization. Based on the site visits to Finland and the USA and on the desktop research, we did not find any large scale DDSS applied in other countries either. There are different commercially available clinical DDSS-s used in Finland, USA and other countries but they run almost exclusively on the database of the particular healthcare organisation. The applicability of DDSS is strongly dependent on the general ICT maturity of the healthcare system. The DDSS-s rely on standardized and structured data, information mobility and accessibility, as well as on the agility of organisations and providers to change their processes. Development of these aspects in an e-health ecosystem can be followed in 4 steps.

Digital efficiency in healthcare

Level 0
- Data on paper
- Event based information documentation for storage and communication
- No data structuring guidelines
- Institution-centered healthcare service
- Information stored and accessible at the healthcare provider, data moving with people

Level 1
- Digitized data, document and event based architecture
- Systems for healthcare institutions for paperless communication cost reporting to insurance provider
- Data not valued per se, created and stored as a side product
- Variety of data standards, local taxonomies
- Different user interfaces for data input, low information usability
- Key information is structured (e.g. the name of diagnosis)
- Institution focused healthcare service, no major adjustments in healthcare processes

Level 2
- Patient-centered architecture
- Systems for better information and work management for healthcare workers
- Data seen as valuable. Back-looking analytics of population groups and key indicators (institutions measuring the effectiveness of current practices)
- Structured data, international taxonomies and classifications used
- Interface designed for data entry and display (e.g. usability guidelines to align interface design of different information systems)
- Patient as an observer, patient can see information
- Key processes redesigned to benefit from digital efficiency (bookings, prescriptions)
- Services designed to large population groups (pregnant women, chronic patients, middle age women, etc.)
Level 3
- Person-centered architecture (involving non-medical service providers and information)
- Intelligent systems, decision and behavioural support for patients and medical workers
- Value retrieved from data, projective big data analytics to guide care and policies
- Patient as participant, patient creates, shares, monitors data
- New processes and financing models, data analytics is informing management
- Goal driven service architecture, networked service providers
- Processes redesigned and new job roles (e.g. genetic counsellor, health coordinator)
- Goal driven service design, personalised service bundles

Currently, different aspects position Estonian healthcare either to Level 1 or Level 2 on the digital efficiency scale. Usage of standardized data classifiers, structured data entry, new processes and organisational changes are a prerequisite to implement decision support systems. Intelligent systems that provide decision and behavioural support are on the third maturity step, Level 3. To implement DDSS-s, key prerequisites need to be established before intelligent systems can function in regular clinical practice.

The medical data structure varies substantially in Estonia. Data needed for already developed scripts can often be found only in free text. This research also revealed that the same health related or medical data coincides in several databases (EHIF, EHIS, EGCUT, healthcare providers, etc.). This in turn leads to the question about choosing the right source for DDSS scripts development. No audits of nation-wide databases have been carried out to validate data quality. The same concerns healthcare providers’ databases, with the exception of EHIF audit of healthcare providers diagnosis quality. The above-mentioned facts feed the criticism against the exploitation of digital tools and electronic environments among the healthcare professionals. The promised benefits of the secondary use of digital health and/or medical data in the somewhat uncertain time in the future is not outpacing the instant difficulties and inconveniences of the implementation of cumbersome and not user-friendly electronic patient records, and other software applications. The vague design of health and medical information systems’ user-interfaces seems to be one of the main barriers in a wider and more sophisticated use of e-health applications, including DDSS. The findings of this study revealed that inconvenient user interfaces are not a problem in Estonia only but almost in all researched countries. On the other hand, we found that healthcare organisations which have put substantial efforts in implementing information systems (dedicated also for secondary use of health and medical data in a user friendly and accessible mode) have achieved great success in care quality and in client and user satisfaction. Kaiser Permanente’s Health Connect and Intermountain Healthcare precision medicine software Syapse are good examples to confirm this finding. Concerning Kaiser Permanente, it is important to outline that their share of information and communication technology budget is around 6% of the total health plan budget. In Estonia it is substantially lower (less than 3%) and needs to be increased for achieving the necessary computing and analytic capacity needed for personalised medicine.

DDSS has been introduced in Estonia already almost 10 years ago. Despite of that, the idea to use it in the context of general practitioners or hospitals information system has not gained strong support from the healthcare professionals. Similarly there have been several organisational and personal obstacles in developing the idea to embed DDSS into EHIS. It seems that the physicians working in larger hospitals are not seeing the benefit of DDSS in their daily work and GP-s have much more urgent issues in their electronic patient record development. In such context it is obvious that healthy people or patients even don’t dream about the DDSS in the Patient Portal or other web environment to help them make more informed decisions about their health.
The low interest background towards the DDSS is probably also caused by the fact that there is almost no e-health education at the Medical Faculty of the University of Tartu and at Estonian healthcare colleges. The future medical doctors, nurses or other healthcare professionals do not receive any dedicated courses for secondary use of data or about the use of e-services in healthcare. Yet, it seems that recent developments in genomics, treatment methods and health information technology might change the situation. Finland and UK are exceptional examples of using DDSS in GP’s working environment for years already. The results are now more extensively published which might change the attitude also in Estonia. The benefits of the DDSS implementation are gaining more value in correlation with the achievements in pharmacogenomics, with understanding the value of data quality and with the use of personalised medicine approach in many specialties, e.g. oncology.

From the individual’s and patient’s perspective the opportunity to use and share longitudinal health and medical data transparently to make health related decisions is increasing the interest towards different e-services. In the era of continuous lack of healthcare professionals DDSS will obviously be a valuable asset for patients in the near future.

It is also important to make distinction between different treatment guidelines and DDSS scripts. Guideline is a set of recommendations for different actions in case of certain clinical condition. Guideline consists of suggestions for actions in different episodes alongside the clinical process. Digital decision support algorithm is based on the evidence based guidelines but has meaning only in one particular episode described in the guideline. Therefore one clinical guideline is often a source of several DDSS scripts.

Healthcare systems and public health in general are pursuing for a longer life expectancy and higher life quality of human being. The aim of large scale implementation of the concept of personalised medicine with the help of DDSS is to improve individual health management and care quality as well as to decrease care caps. Above mentioned goals could be achieved only with the help of high quality and computerized data analytics. The cornerstone of applicable analytical results is well structured and semantically unambiguous data. DDSS is not directly related to the data quality but acts as a mediator for primary and secondary use of digital data. It is a tool to control the data quality through the strict definitions of data standards, structure and taxonomy used in the scripts. Use of different DDSS applications has potential to improve the quality of data and user interfaces of different e-health applications. Successful integration of different databases proves the interoperability capacity of particular application. DDSS can also clearly bring out the benefits of secondary use of collected genome, health and medical data and promote the use of analytical tools in all health and care spheres. As stated previously, already the display of existing structured data, which is properly gathered in a single medical specialist desktop application in a manner that fits the clinician’s logic is seen as a needed functionality of faster decision making.
11. Implementation strategy for the digital decision support, including risks management and implementation plan

11.1 Context

When considering the possible development of the DDSS for the Estonian healthcare, an important question arises. Namely, should the existing information systems, such as EHIS, EHIF or EGCUT, just be complemented by additional functionalities for the DDSS or should an entirely new information system – the so-called Decision Support Information Systems (DSIS) be developed for that purpose? The answer to this question is crucial in making up mind about the architectural solution for the DDSS. This question has been prompted by the following issues and questions that were raised during the current project, the objective of which was analysing the feasibility of the DDSS for personalised healthcare in Estonia:

1. For DDSS, there appeared to be a need for data transformations from one format to another, so that the resulting data, such as, for example, the anamneses with separated fields, would be stored somewhere. Into which databases or registers should this data be stored?

2. Will implementing of DDSS bring along the need for the creation of new data such as, for example, some kind of metadata about the usage of DDSS rules? If the answer is positive then where should that data be stored? Who should store it and who can access the data? How could this kind of data be used in the future?

3. It is quite clear that over time data attributes will change because of introducing new diagnostic and treatment procedures, development of new sensors, inserting new decision rules and modifying the existing ones, etc. How to manage these changes in an evolutionary way so that the healthcare information system(s) do not need to be reprogrammed? Is there a need for preserving modification history? If this is the case, where should the modification history be stored?

Depending on the answer to the questions listed above, we might need a new decision-support information system (DSIS), which should be developed consistently with the findings of this project as well as those of another parallel project “Information architecture and data management for country-wide personalised medicine” by the Software Technology and Applications Competence Centre. The implementation strategy of the DSIS should consider the following aspects:

1. Proper elicitation and representation of requirements for the DSIS is crucial for the successful design and implementation of the DSIS.

2. The process of the DSIS development alone is not sufficient and will inevitably bring about a serious need for improvement of several medical information systems. The reason is that the data acquisition logic of other medical information systems may be different from that of the DSIS for historical reasons. For example, the quality of the data stored in medical information systems may not be of sufficient quality for decision support or the DSIS may need data that is not yet available in medical information systems.

3. The architectural solution for the DSIS should consider the following factors:
   a) As was emphasized in previous sections, currently ICT is developing very fast and exponentially, which means that new and different methods, protocols, sensors, microchips and other technologies come out every year. The architecture of the DSIS should be flexible enough to keep pace with these developments;
   b) The architecture must allow for high-level describing of rules and offer an easy way for editing them, so that medical doctors, other healthcare professionals, and even patients themselves would be able to edit the rules;
   c) The issues of responsibility. After some years a patient will be able to use the decision support by him- or herself. This may also mean that the responsibility for health-related implications of using decision support will move to the previous level: from medical specialist to GP, from GP to family nurse, from family nurse...
to patient, etc. What are the possible implications of these kinds of responsibility shifts?

d) As the data stored in the DSIS will probably replace the distributed data currently held in several databases and registers, there is a need for efficient modern architectural solution.

The development of DSIS is a very serious endeavour that needs cooperation of all parties and development teams of medical information systems and registers and databases containing medical data. As developing a new DSIS as a whole can be complicated endeavour at the moment, we recommend dividing the development of the DSIS into stages, to determine goals for each development stage, and to create an organisation capable of coordinating and managing the development of the DSIS. It is crucial to determine goals and requirements for the DSIS as a whole, using the methodology described in previous sections, which caters for obtaining holistic understanding of decision support in healthcare. When doing that, it has to be considered that most of the possible savings in healthcare lie in prevention, as has been pointed out in this study. Therefore a crucial aspect of personalised healthcare is changing the health behaviours and habits of people through analysing genome data, collecting data about health behaviours and offering decision support based on the analysis of the collected evidence. Currently data of this kind is collected and analysed only sporadically.

11.2 Implementation strategy

Below is presented the implementation strategy for DDSS-s in personalised medicine in Estonia. As stated in previous subchapter, the implementation plan should be divided into stages and phases.

1. The prerequisite for the implementation of DDSS for personalised medicine in large nationwide scale is integration of genome, health and medical data throughout the whole life span of the person. The success and usefulness of DDSS implementation depends on the size of the samples in EGCUT, linking of the data stored in different medical databases and inclusion of data of as many residents as possible of Estonia into the data pool.

   ACTION: Establishment of organisational and information technology framework for linking persons’ genome, health and medical data for the processing with different DDSS-s over the whole life span depending on the user or quality goal.

   RISKS: Vaguely defined structure of the framework. Poor government of established organisation(s). Low engagement of stakeholders, especially healthcare professionals, patients’ representatives and policy decision makers.

2. External independent audit of data collected in nation-wide and institutional health related and medical databases (EHIS, EGCUT, healthcare providers, etc.). Cross-analysing of medical databases using data mining methods among others. Implementation of existing decision support scripts or developing new ones needs structuring of currently collected data and auditing of collected information as a prerequisite for any further step.

   ACTION: Audit and analysis of existing nation-wide and institutional (e.g. healthcare providers) medical and public health databases to agree about the sources of different data necessary for DDSS algorithms.
RISKS: Low willingness for cooperation among the database owners. Lack of resources to make an audit.

3. Decision about the scope, scale and schedule of the development and implementation of DDSS applications. Prototyping of DDSS and analysing of its implementation feasibility during this study with clinical specialists in context of Estonian e-health environment and using different scenarios revealed that different medical specialties are using in large extent the same health related and clinical data for decision making. DDSS applications should be mainly user and/or function rather than disease specific. Only gathering and usage of machine readable structured data can lead to integration of different databases along the life span of the person and integrating phenotype (health, medical, environmental, etc. data) and genotype data.

This research proposes classification of DDSS into 6 subgroups:
1. Improved data usage and visualisation
2. Health management
3. Patient monitoring supports
4. Clinical decision supports
5. Scientific gene research
6. Public health analysis tools

It would be desirable if the implementation strategy of DDSS in Personalised Medicine pilot project will follow this classification. Estonia has no resources to deal concurrently with full scale implementation of all DDSS subgroups. There is a clear need for prioritization. It is also evident that DDSS in different subgroups are in different maturity. For instance DDSS applications in subgroup 4 are commercially available and widely in use while Scientific gene research (subgroup 5) DDSS-s are in their early development phase.

ACTIONS:
- Piloting of Finnish EBMeDS (Duodecim Medical Publications Ltd.) DDSS using data retrieved from EHIS and/or different EPR-s.
  The rationale to use EBMeDS is based on the well-established structure, excellent references and international experience of Duodecim, long cooperation traditions between Finnish and Estonian healthcare professionals and scientists, similar organisational structures in both countries, language similarities, geographic vicinity, etc.
- Development of DDSS algorithms for the use of genome data (e.g. oncology, CVD, etc.)
- Selecting and piloting of DDSS for pharmacogenomics.

RISKS: Time consuming procurement process. Risk to not include promising but not well studied applications in the pilot.
4. Establishment of an organisation responsible for the collected genome, health and medical data normalization and distribution for the open use of DDSS by different actors in health and care domain.

As mentioned above, implementation and management of DDSS-s requires the establishment of procedures for handling different DDSS subgroups, for quality control of acquired or developed scripts, for different software versions, for storing and sharing of DDSS reports, etc.

**ACTION:** Foundation of organisation responsible for Decision Support Information System (DSIS) development and maintenance.

**RISKS:** Trouble to share responsibilities with EeHF and/or healthcare providers.

5. Development and publishing of a user-friendly end-user software and applications requirements for individual and professional use, keeping in mind the DDSS functionalities and importance of secondary data use and implementation of new e-services in health and care domains.

**ACTION:** Public tender for providing software and applications prototypes for different users.

**RISKS:** Time consuming procurement process. Lack of resources to make the tender. Resistance of current EPR providers and hospitals for open competition.

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70 Starren et al., JAMA 2013;309:1237
12. Optional annex: Editors’, contributors’ and international experts’ recommendations and comments to the final report document.

12.1. The integration of decision support systems with healthcare providers’ information systems

The Information architecture and data management for country-wide personalised medicine project (reference number 160112) concentrates on the development of the information system for the Estonian Genome Center at the University of Tartu (EGCUT) and integration of the said system into the ecosystem of the current Estonian e-healthcare system which includes Estonian National Health Information System (EHIS), Estonian Health Insurance Fund (EHIF), healthcare provider information systems (HIS), etc.

The analysis is based on the current reality - only 5% of adult Estonian population has donated their blood samples to the EGCUT and only approximately 2000 blood samples will be fully sequenced by the time of current research project finishes. Considering that the pilot project of personalised medicine will involve patients with very specific diagnoses and symptoms, there is a very high probability that the samples of the patients involved with the pilot project have not been fully sequenced and need to be collected during the study.

Whether the blood sample will be provided to the EGCUT by the healthcare provider or collected by the EGCUT need some further analysis and possibly additional functionality needs to be added to the HIS (ordering of the sample, taking the sample, logistics of delivering the sample to the EGCUT and coding the patient’s information). It also depends on how the project will be financed (why pays for the collection of the blood sample and the logistics). One goal of the pilot project should be developing the financing, organization and logistics of sample collection.

For research EGCUT needs patient’s health and medical information. Although the information architecture analysis suggests that healthcare service providers send the information to EGCUT phenotype database, from healthcare provider’s point of view it would be more optimal for EGCUT to query this information from EHIS (including the use of fact extraction module provided by STACC). Efforts should be made to make the information sent by HIS and collected by EHIS better structured and the delivery process more timely. This depends heavily on the chosen data formats and data exchange formats and also on healthcare provider’s ability to modify their HIS. The other goal of the pilot project should be specifying the data formats and metadata, data exchange standards. Third goal of the pilot project should be enhancing the fact extraction scripts. The fourth goal of the pilot project should be modifying the HIS and EHIS and develop EGCUT.

It is clear, that the inclusion of genetic risk score (GRS) information during the pilot project cannot take place in real time. The healthcare provider triggers the start of the GRS calculation process (the sequencing of the blood samples, analysis and calculating the GRS of patients taking part of the pilot should get high priority).

But GRS itself is not enough, to provide higher quality care healthcare providers need also access to classic decision support systems which rely on phenotype information. Since the ability of a single healthcare provider (even if it’s a regional hospital) to pay the license fees, validate decision support scripts, translate the reports, analyze the use of the system etc is close to zero, it needs to be organized by the ministry of social affairs. Decision support systems (multiple) should be centralized services with standardized online access (including data exchange between information systems and individual access via web interface).

Decision support algorithms use structured healthcare data and international data standards. While diagnoses are coded and collected using ICD-10 classificatory and surgical procedures are coded and collected using NCSP classificatory, most of the other data is non-structured, non-standardized and collected on irregular basis. Although LOINC classificatory for lab tests has
been agreed upon not all the laboratories and hospitals have migrated to the use of LOINC and at the time of writing the report the results are not sent to EHIS. All the rest of the data (weight, height, blood pressure, pulse rate, smoking habits, family history etc) needs to be seriously looked at and dealt with during the pilot. Since many healthcare episodes do not need all of the aforementioned data for the treatment, the health records of many patients do not contain this data even in free text format.

There are several options for the integration of HIS with the decision support system

a) **On demand query**: after the necessary information is collected doctor runs the query submitting all the required data to the decision support system and getting back the report. While it’s medium cost this option is certainly very unpopular among the doctors, since it requires conscious action from their side. It’s possible to consider this for the pilot project though.

b) **Automated query triggered by specific action**: possibly involving the specialized data entry form dedicated to the pilot cases (specific diagnoses), ensuring that the required data is collected. High cost and more likable for the doctors, but not sustainable in the long run. It’s possible to consider this for the pilot project though.

c) **Automated interactive query triggered by specific action**: for example after the specific diagnosis is documented an automatic query is made by the HIS and decision support system asks for additional information (for example certain type of blood pressure or smoking habits or specific lab result) in case this was not documented yet or not included with the initial query. Doctor needs to enter additional information/run additional tests and then re-trigger the query. NB! High cost.

d) **Seamless integration of decision support system**: intelligent agent monitors the documentation of the health information in HIS, runs automatic queries in the background and displays recommendations and reminders for the doctor. Very high cost but most desired by the doctors.

<table>
<thead>
<tr>
<th>Added functionality to HIS:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Modified/new informed consent forms for the patients participating in the pilot project</strong></td>
<td>Low cost</td>
</tr>
<tr>
<td><strong>Providing EGcut with the blood sample: logistics</strong></td>
<td>Medium cost (not including the cost of the sample collection and logistics)</td>
</tr>
<tr>
<td><strong>GRS trigger / query</strong></td>
<td>Medium cost</td>
</tr>
<tr>
<td><strong>Data collection based on new standards and formats</strong></td>
<td>High cost</td>
</tr>
<tr>
<td><strong>Decision support query on demand (a)</strong></td>
<td>Medium cost</td>
</tr>
<tr>
<td><strong>Decision support automated query (b)</strong></td>
<td>High cost</td>
</tr>
<tr>
<td><strong>Decision support interactive query (c)</strong></td>
<td>High cost</td>
</tr>
<tr>
<td><strong>Seamless integration of decision support</strong></td>
<td>Very high cost</td>
</tr>
</tbody>
</table>

**Contribution by:**
Kati Korm
Head of the Informatics Administration Development Department of Tartu University Hospital
Kati.Korm@klinikum.ee
12.2. Recommendations and general comments to the final report document and the planned Estonian Digital Decision Support System (DDSS) pilot from Auria Biobank (Finland)

The development of DDSS for the Estonian future healthcare and the implementing for the entire personalized medicine approach, following five facts are crucial to take into the consideration and are mostly already successfully covered in the final report:

a) The aging population and increasing life expectancy, meaning not only is demand for healthcare rising, but the entire nature of healthcare is rapidly changing. This will include the emerging need for regenerative medicine, new digital innovation, and shifting to an outcomes-based approach for patient treatments as well as medical research. Due to that, the future DDSS needs to seize those growth opportunities and to make sure that the related innovation ecosystem is strong enough. A data-analytics capability needs to build in a way that we don’t have today as well as to create partnerships with different types of people/knowledge which are essential to bring together to secure a full advantage of that part of healthcare. The fact is that digitization is going to change healthcare in many different ways, especially in level of personalized medicine.

b) Rapid advances in translational medicine have generated a massive need for clinically meaningful biomarkers, necessitating access to a large number of high-quality human samples and related data which are the quintessential resource for the discovery and assessment of such markers and ultimately for the success of personalized healthcare. Biobanking resources that have been assembled over the years primarily in the academic sector, and often with a commitment to public health could importantly support this need. In Estonia (as well as in Finland), both the biobanked samples and related clinical data is characteristically well organized and of high quality. It is widely recognized that Estonia and Finland share some particular strengths for clinical medical research, notably; established personal identification numbers to link clinical samples and the related data from the Electronic Health Records (EHR), well organized registers in health-care and on disease outcomes, and well organized clinical data, and public opinion that is generally very positive to medical research.

The challenge which the utilization of these resources faces is that the c) data is often maintained in a "compartmentalized" fashion within individual hospital or registry environments. It is therefore enormously difficult to understand what data are available, as well as to then access and make use of the data. In the current report, it has been a substantial effort when the individual-level metadata are identified and collected in a standardized format and listed in a high-level transparent inventory. Without proper infrastructure and protocols that link different type of health data to EHRs and makes them retrievable across a controlled vocabulary of relevant parameters, access to the information for a given project or question may not be possible, thus severely limiting the value generation from these valuable resources in applying them to discovery and assessment of DDSS and new targets for therapy as well as drug discovery. The fact that clinical outcomes contain sensitive data from human donors, sometimes vulnerable groups – the patients – makes the issue even more challenging. To protect subjects' interests, both the internal and external use of such data is subject to laws and regulations (based on the informed consent) which have proliferated into a patchwork of EU, national, institutional and data subject requirements and restrictions on the access and exchange of information that makes higher-level integration of information of the resource even more important.

d) The importance of clinical outcomes. The next big area in medicine is around the shifting from a transactional approach to an outcomes-based approach. An outcome based approach focuses on delivering a positive patient outcome. By collaborating with companies/academic investigators that could monitor patients remotely, and look for vital signs that would tell whether they should go to the hospital. This is something that should be started and implemented in DDSS as soon as possible. Shifting to an outcomes-based approach, where you just focus on what delivers the outcome, you get rid of everything else, and the physical medicine
is going to be part of that. That’s the only way to be able to deal with this aging population with constrained budgets in a part of the personalized medicine initiative. It is obvious that the Estonian personalized medicine project should place strong emphasis on the mapping of retrospective clinical samples and collection of new data from diagnostic and treatment outcomes. Based on the current fact, that only 5% of the adult population has donated DNA samples to EGCUT, the collection of one extra blood sample along with diagnostic procedure will be the way for successful implementation for the digital decision support and the personalised medicine initiative. The combination of genetic and other biomarker profiling will be the first essential step towards the implementation of specific, advanced preventive healthcare measures. Such services may otherwise be not sufficiently cost-effective to be offered to large, less precisely defined disease categories. A key issue regarding the sustainability of and the societal value generation from the project will depend on integration of data from the clinical outcomes. It is highly likely that the funding for such efforts could be much more easily obtained if clinical outcomes (natural history and/or treatment) were given substantial emphasis. However, even under the best of circumstances it is very likely that public funding will not be sufficient for optimal and sustainable development of the entire national effort. Partnering with the private sector represents an alternative and the project will explore the funding possibilities for public-private partnerships.

e) Providing access to the high quality data. A well-known vision is that the future of healthcare and medical research will increasingly shift to the provision of high quality data derived from biological samples, rather than provision of the physical biological samples. Access to data is much easier than to samples, for many reasons e.g., information can be shared, fewer legal restrictions, lower costs, etc. Importantly, data can be made accessible to a broad international scientific community and a diversity of interested parties - all of whom can create value, whereas physical samples can only be provided to a very limited number of scientists, at high cost and logistic complexity. Cutting edge research as well as further innovations in the life science industry will strongly depend on transnational access to high quality human biological data derived from daily healthcare (EHRs) and related samples, and to the associated medical information, all of which must be accessible to both academia and industry in an efficient and secure manner. Combined with the expertise of the clinicians, pathologists, bioinformaticians, molecular biologists and statisticians involved, an unprecedentedly rich resource-network representing national and Europe-wide platforms for translational medical research is envisaged to become operative and to play a major role in the development of personalized medicine and disease prevention to the benefit of citizens.

Possible future cooperation on national and institutional level
The future co-operation and/or co-competition (compete and collaborate) models between Finland and Estonia could be built on the following steps:

1. Co-operation to standardize electronic patient record (EHR) data in several clinical specialties - development of clinical digital decision support algorithms with the special attention to integrating genome data.
2. Development of software to link genome data with electronic patient record and personal health record.
3. Research and development of standards and data exchange profiles for health and behavioural data collected by the patient/citizen.
4. The establishment of mutually beneficial co-operative models that would allow clinical data and related sample resources to reach their full potential in supporting both the personalized healthcare as well as the public health agenda.
Contribution by:
Heli Johanna Salminen-Mankonen, Ph.D.
Director of Auria Biobank
hejsalm@utu.fi
12.3. **Review of Estonia’s e-health information capabilities and opportunities for cooperation with Intermountain Healthcare (USA)**

The eHealth services in Estonia were designed to leverage existing information systems capabilities in Estonia to benefit the individual health of its citizens. In reviewing these capabilities, it is clear that the unique capabilities of Estonia’s electronic information have helped to advance the direction of eHealth there, while there remain some important opportunities.

The primary e-services infrastructure of Estonia is extremely advanced. For example, almost all government services are wired, with all schools and government organizations having broadband connections. More than ¾ of residents have a computer at home, and over 80% of the population has broadband connections at home. With this high level of computer technology and internet use, it is not surprising that many standard services are primarily performed electronically, with paper-based or person-based methods being the small minority. For example, over 95% of bank transfers and income tax declarations are made online, almost two-thirds of individuals complete census forms electronically, and nearly a third of votes are cast online. This is a high level of information technology adoption. There are two primary capabilities that are leveraged to advance e-services so effectively. The first is the national identification capability that includes a national identification card and mobile ID for each individual. This allows a shared identifier to be used across multiple services, without having citizens needing to create different user IDs and authentications for each service. It also allows easy linking of information across different services. The security of the ID certification has been well-thought, and is more secure than most electronic services that do not use a national identifier and mobile ID in other countries. The second capability in Estonia is the e-state architecture, which consists of security servers that connect different public and private organization data systems to a bus architectural layer, which in turn communicates with the certification and identification service. This allows a standard approach for different organizations to be included as components in the e-state architecture, simply by setting up a security server that connects to the bus architecture.

It is interesting to note how creating such a capability has benefited Estonia, as lessons for other countries that may consider pursuing a similar path. Many countries argue for and against creating national identifiers in a way that they have done successfully, but usually it is addressing a simple problem where the arguments against a national identifier are that there are ways to share data without creating such a structure. Estonia has shown that having an identifier, and then the e-services architecture to support it, has fostered innovation and growth in many ways. Without a national identifier, data can still be shared, and even exchanged across institutions, but the task of setting up identifiers and separate data sharing arrangements and negotiations for each case becomes enough of a barrier to hamper innovation. As Estonia has demonstrated, where there is expected capability, innovations follow. They have also shown that a universal identifier does not reduce security. In fact, if done correctly, the security of such a system is higher than other approaches. Admittedly, the risks of data loss if the system is breached are higher, but it seems they have effectively addressed those issues as well.

The eHealth architecture follows a similar architecture to the government services structure, with a data exchange bus in the center of many services. In eHealth services, the biggest benefits of the e-services architecture and components have been around health information exchange, especially e-prescribing, image transfer, and transmission of health status information. Almost all prescriptions are delivered electronically, digital images are available across the country, and most discharge letters from hospitals are sent electronically. The success of how the national patient identifier and security/integration structures are implemented is a clear opportunity for Intermountain to benefit from Estonia’s experience.
Among these strengths, there remain important opportunities. These are in the areas of the patient portal, genomics, population health, and semantic interoperability. These are areas where cooperation between Estonia and Intermountain Healthcare may be most useful, either because we have successfully navigated these areas or that we are facing the issues together.

The Estonian patient portal use is improving – data through 2010 shows a steady increase in the number of individuals using the portal for viewing patient records and for scheduling appointments. Currently, however, use remains low, with only about 6% of the population using the portal. At this rate, only the early adopters are using the system, and it is likely that they are the individuals where the least challenges exist with patient engagement. So it is likely not to have a significant influence on care. With such a low rate of usage, physicians are unlikely to expect individual patients to be using the portal, and it will be extremely difficult to use the portal as an engagement tool between patients and physicians. Chronic condition workflows depend on patient and physician engagement, and without strong adoption the portal won’t be an effective platform for communicating between clinicians and patients. Additionally, while the portal may be technically capable as a communication platform, it is not yet developed as a behavioral change platform. The decision support in the portal is mostly transfer of information. As a result, different technologies need to be pursued that may foster improved communication and information engagement between providers and patients, which may eventually get steered to the portal as a more advanced option. In its current state, the portal is unlikely to reach a sufficient level of adoption independently.

Current strategies for expanding health information and decision support capabilities include using genomic data as a source for decision support data, with rules to accommodate this rich data source. This leverages the national patient identifier and Estonian Biobank (EGCUT). Because the patient has the genome sequenced, authorization from the patient to run decision support against it is all that is required for the system to work. This makes the transaction with the patient simple (only collecting authorization), and removes the burden from the patient. This is a strong win for the national identifier. Estonia could be a world leader in using genetic information for decision support, especially for opportunistic decision support. The opportunity for collaboration is in defining and evaluating the decision support rules and how they affect patient care.

With all the strengths of the eHealth system in Estonia, population health seems limited. The structures that have been established using the eHealth architecture are mainly federated sources that are able to communicate with a common patient identifier. Analysis of populations is difficult using just this architecture – there also needs to be established a centralized data warehouse for analyzing the availability, concurrence and capability of data across the different sources. This will lead to an understanding of which data sources are most needed, or the information value of different sources. Such a warehouse will also allow population-level analytics, so that certain populations can be identified and analyzed retrospectively both to discover what differences in care are most pronounced in affecting outcomes, and what populations have the greatest need for proactive interventions.

Finally, semantic interoperability in Estonia remains a problem. As reported, the data format for different measures varies, such that common structured measures (for example, height and weight) are reported in text documents and therefore less accessible. As a result, other than centrally-controlled or centrally-submitted data, most observations should not be expected to be available for decision support. Diagnoses, medications, encounters, and radiology tests are centrally controlled or submitted, so they have been standardized. Specific opportunities for
collaboration exist in the following areas: a) understanding how regulation for centralized reporting (e.g., Meaningful Use) can effect structured data; b) understanding what data are most useful to structure for decision support rules; and c) how to extract data from text effectively to use in decision support (e.g., natural language processing). These are all areas where Intermountain has extensive experience and cooperation can be helpful.

Contribution by:
Adam Benjamin Wilcox
Director of Medical Informatics, Intermountain Healthcare
Adam.Wilcox@imail.org
13. Kokkuvõte

Käesolev arendusuuring on teostatud 21-liikmelise ekspertgrupi poolt Sotsiaalministeeriumi ja Tallinna Tehnikakooli vahelise riigihanke (nr. 160141) lepingu (nr. 2-2.2/6771) raames 2015. aasta esimesel poolel. Uuringu eesmärks oli analüüsida personaalmeditsiini põhimõtetest lähtuva kliinilist otsustusprotsessi toetavate digitaalsete otsustustöö rakenduste kontseptuaalseid lahendusi ning pakkuda välja strateegia nende rakendamiseks Eestis.

Töögrupp alustas häpputeetšüliis isiku jaoks kogu elukaardi vaates kolme kliinilise seisundi (südame-veresoonkonna haigused (SVH), diabeet, vähk) stenaariümite mudelite välja töötamisega. Eesmärgiks oli leida need kohad, kus digitaalne otsustustöö rakendamine on võimalik ja põhjendatud. Stenaariümist koostati nii, et need sisaldaksid realistlikke terviseandmeid ja haiguste ajalugu ning haartud olendid inimeste erinevad tervise ja tervishoiu seotud tegevused võttud aluse tegevuse tegemiseks vajavad sõltumata konkreetsetes situatsioonist või asutustest. Esitatud stenaariümid sisaldavad nii vajalikke genotüübi kui fenotüübi (sh. keskkonna ja elustiili) andmeid. Uuringu jooksul otsustati panna kokku SVH ja diabeedi stenaariüm, mille järel tekkis konkreetsest rakendamisest tuntud andmeid und otsustustöö rakendamise vajaduse saadet riikliku strateegia eest.

Kuna digitaalne otsustustöö tarkvarakasutus saab kasutada sisendina ainult struktureeritud ja standardiseeritud andmeid, paralleelsetelt stenaariümite arendamisega viidi läbi erinevad tervishoiuandmebaasides olevate andmete kaardistamine ning tõlgimine kasutatavate andmetest välja. Kliinilised eksperdid tõid välja kõik andmed, mida nad oma igapäevatöös sõltumata konkreetsetelt asetustest, kasutades olemasoleva kogemust ja võimalikuid juhtumid. Täiskogus loodi mõlemad stenaariüm sõltumata konkreetsetelt asetustest, kasutades sellist otsustustöö tarkvaralange.

Teine kõnealusele sisemiseks, mis sisaldaks kiiret ja konkreetset tervishoiuandmeid, on kliinilised stenaariümid. Uuringu jooksul otsustati panna kokku SVH ja diabeedi stenaariüm, mille järel tekkis konkreetsest rakendamiseril otsustustöö rakendamise vajaduse saadet riikliku strateegia eest. Kuna digitaalne otsustustöö tarkvarakasutus saab kasutada sisendina ainult struktureeritud ja standardiseeritud andmeid, paralleelsetelt stenaariümite arendamisega viidi läbi erinevad tervishoiuandmebaasides olevate andmete kaardistamine ning tõlgimine kasutatavate andmetest välja. Kliinilised eksperdid tõid välja kõik andmed, mida nad oma igapäevatöös sõltumata konkreetsetelt asetustest, kasutades olemasoleva kogemust ja võimalikuid juhtumid. Täiskogus loodi mõlemad stenaariüm sõltumata konkreetsetelt asetustest, kasutades sellist otsustustöö tarkvaralange.

Kulutatud analüüsi ja materjalide põhjal kirjeldati kõik erinevad stenaariümide võimalikud kasutamisvõimalused andmebaasides, kus olemasolu kogemus võimalik otsustustööks rakendada. Nii koosneb otsustustöö tarkvarald vajadus andmebaasides kasutamiseks konkreetsetest lepingutest ehk kasutusel olevat andmebaasides on võimalik digitaalne otsustustöö rakendamiseks kasutada.
geeniandmeid kasutatavate digitaalsete otsustustugede arendamine kõikide haigusseisundite puhul alles algfaasis. Personaalmeditsiini rakendamise vaatevinklist on siiski näha, et paljudes riikides käib uurimis- ja arendustoögi geeniandmete digitaalsetes otsustustugedes kasutusele võtmiseks väga aktiivselt.

Kuna selles valdkonas on areng väga kiire, siis töögruppi soovituseks on jätkata Eestis otsustustugede välja töötamist ja piloteerimist personaalmeditsiini kontekstis lähudes mõlemast (SVH/diabeet ja rinnavähk) kliinilisest stsenaariumist.


Joonis. Digitaalse otsustustoe komponendi ja nende vahelised seosed.71

71 Autorite originaaljoonis.