Think Tank

ROUNDTABLE: **Scandinavia**

Improving healthcare with existing biobank and quality registries

Proceedings and results from the EIT Health Roundtable Meeting

13 August 2018 at Campus Solna, Karolinska Institutet, Stockholm, Sweden

Introduction

Using Big Data for healthcare in Scandinavia

This report contains the proceedings and conclusions of an EIT Health Think Tank Roundtable Discussion about Improving healthcare with existing biobank and quality registries in Scandinavia. Leading experts presented best practices and engaged in discussions that have generated many actionable recommendations.

The 13 August 2018 Roundtable in Stockholm, Sweden was one of several such meetings organised around Europe by the EIT Health Think Tank to obtain regional perspectives that further a discussion on pressing healthcare issues. Conclusions and recommendations stemming from these discussions are used to ensure that EIT Health's strategy and activities focus on what matters most. The Think Tank also guides EIT Health Public Affairs efforts aimed at contributing to health policy and healthcare system improvements across Europe.

The EIT Health Think Tank is a forum of experts and thought leaders cooperating to shape the future of healthcare in Europe. The Think Tank brings together EIT Health Partners with other leading healthcare stakeholders to agree on means for ensuring that innovation reaches the citizens and patients who need it most. Through central and local exchanges, Think Tank members seek to identify healthcare needs and potential solutions to those needs.

By identifying key pressure points and catalysing discussion, the Think Tank drives need-focused innovation within the EIT Health community and beyond, to better meet the needs of European citizens.

The following are proceedings of the EIT Health Think Tank Scandinavian Roundtable Discussion, held 13 August 2018 at **Karolinska Institutet**, Stockholm, Sweden. The document contains summaries of the two main sessions held on that day. The first session featured presentations of work being done in Scandinavia. The second session consisted of roundrable discussions on improving healthcare in Scandinavia using existing biobanks, quality registries and Big Data. The recommondations based on these discussions are summarised in tables at the end of this document.

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Participants

Chairman	
Paul Timmers	Independent Consultant and Visiting Research Fellow in Cybersecurity Policy and Digital Transformation, Oxford University, UK
Presenters	
Jan P. Andersson	Stockholm County Council, SLL, Innovation Director, Sweden
Søren Brunak	Professor, Novo Nordisk Foundation Centre for Protein Research, University of Copenhagen, Denmark
Sonja Eaker Fält	Chair, Preparatory Group of Biobank Sweden
Lili Milani	Research Professor, Estonian National Biobank, University of Tartu, Estonia
Andreas Scheutz	Research and Innovation Director, Uppsala Region, Sweden
Discussion Group Chairs	
Jan-Olov Höög	Professor, KI EIT Health Lead, Karolinska Institutet, Sweden
Eva Tiensuu Janson	Professor of Medicine & Dean of the Faculty of Medicine, Uppsala University, Sweden
Per Matsson	CTO, Thermo Fisher; Chair, EIT Health Scandinavian CLC
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Lisa Bandholtz	Swedish Pharmaceutical Society, Sweden
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Søren Brunak	Professor & Research Director, Novo Nordisk Foundation Center for Protein Research, University of Copenhagen, Denmark
Lena Brynne	Stockholm Medical Biobank, Sweden
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Tonu Esko	Vice Director and Head, Estonian Genome Center, Institute of Genomics, University of Tartu, Estonia
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Johan Liwing	Executive Director RWE External Partnerships, Janssen, Sweden
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Tobias Sjöblom	Professor, Director of the Research Infrastructure of Biobank Sweden/BBMRI.se, Uppsala University, Sweden
Nicolai Slotte	Strategist, Advisor, International Affairs, City of Uppsala, Sweden
Erik Steinfelder	Director General, BBMRI-ERIC, Austria

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Christina Wass	Project Leader, Innovation Akademiska, Uppsala University Hospital (Akademiska sjukhuset), Sweden
Ulla Wewer	Dean of the Faculty of Health and Medical Sciences & Professor in Experimental Pathology at the University of Copenhagen, Denmark
Trine Winterø	Vice Dean Innovation, Faculty of Health and Medical Science, University of Copenhagen Denmark
Observors	
Jan-Philipp Beck	Chief Executive Officer, EIT Health
Mayra Marin	Executive Officer, EIT Health
Merike Leego	Innovation Manager, EIT Health Scandinavia
Caroline Ekstrand	Communication Officer, EIT Health Scandinavia
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Menno Kok	CLC Director, EIT Health Be–Ne
Karen Wolstencroft (Rapporteur)	Medical Writer and Communications Consultant to EIT Health

Agenda

Roundtable Meeting Chairman: Paul Timmer

10:00-12:00	**OPEN SESSION**	
10:00-10:20	**Welcome and introductions**	
	Welcome on behalf of EIT Health Focus of today's agenda Welcome on behalf of EIT Health Scandinavia and importance of the topic for EIT Health Scandinavia	Jan-Philipp Beck Paul Timmers Per Matsson
10:20-12:00	**Presentations**	
	Needs, benefits and positive cases of how biobanks, data registries and Big Data can be used to improve healthcare (4D project)	Jan P. Andersson
	Needs, benefits and positive cases of how biobanks, data registries and Big Data can be used to improve healthcare (SymBIOs)	Andreas Scheutz
	The new Danish National Genome Centre and its health data context	Søren Brunak
	Swedish national collaboration to build a national biobank infrastructure aimed at facilitating medical research and development and benefiting patients	Sonja Eaker Fält
	Biobank and Big Data available for developments (incl. for industry) in Estonia: opportunities and challenges	Lili Milani
15:00–15:30	Lunch	All

13:00-17:00	**ROUND TABLE SESSIONS**	
13:00–15:00	Three parallel Discussion Groups on How to improve healthcare in Scandinavia by using existing biobanks, quality registries and Big Data – barriers and actionable recommendations	
Group 1: Industry	From the perspective of industry including developers from pharma and SMEs	Chair: Per Matsson
Group 2: Healthcare	From the perspective of healthcare providers, health care payers, policy makers and citizens	Chair: Eva Tiensuu Janson
Group 3: Science	From the perspective of science community, including biobanks, data producers and data interpreters	Chair: Jan-Olov Höög
15:00–15:30	Coffee break	All
15:30–16:30	From ideas to actions	
	Conclusions from the discussion groups	Discussion Group Chairs
16:30–17:00	Wrap up and closure	
	Summary of meeting and take-home messages	

Introductory Session

Background to the EIT Think Tank on Big Data in Healthcare

PRESENTER:

Jan-Philipp Beck, CEO of EIT Health

Jan-Philipp Beck, CEO of EIT Health, gave the following overview of EIT Health and its goals, as well as the objectives underlying the Think Tank on Big Data in Healthcare and the desired outcomes of the day's Round Table (RT) Meeting:

About EIT Health

EIT Health's slogan is "Together for healthy lives in Europe". The organisation's goal is to identify unmet clinical and economic needs within the complex healthcare systems around Europe. Based on these identified needs, EIT Health then initiates and facilitates innovation by bringing together leaders in education, business, and research.

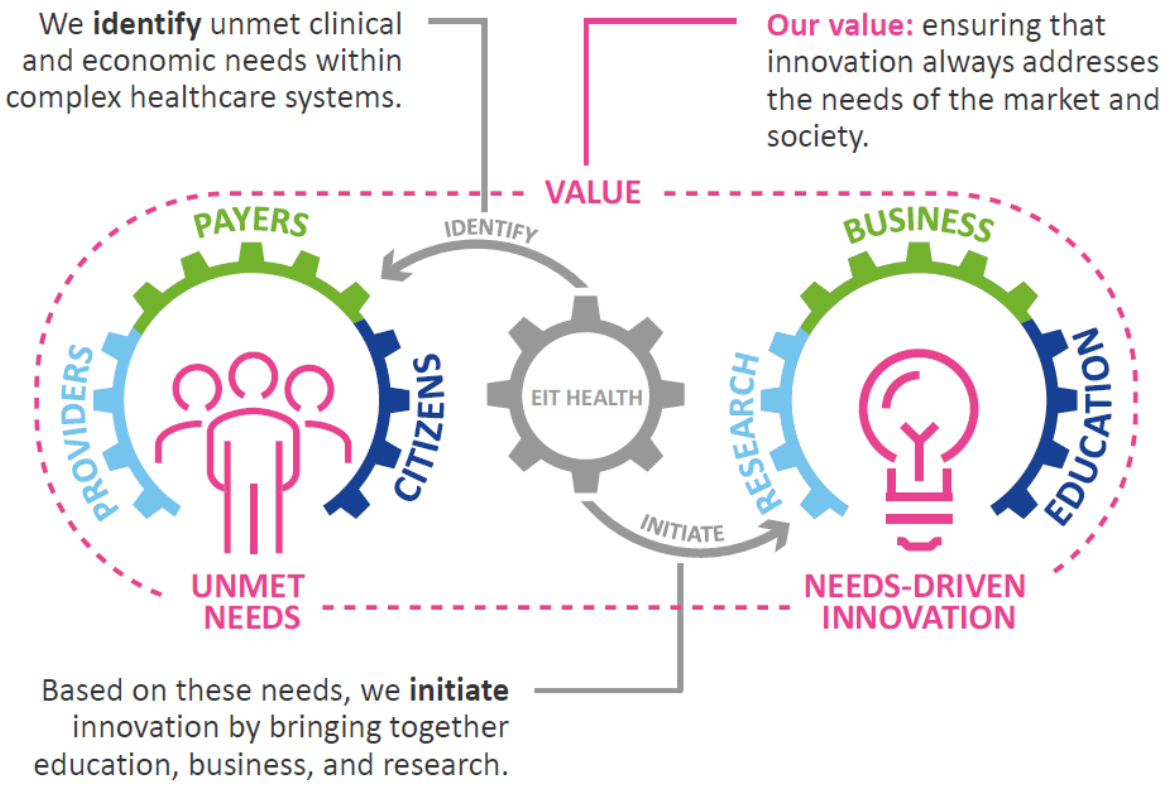
EIT Health is Headquartered in Munich, Germany, and the network comprises six regional offices (Co-Location Centres) in UK–Ireland, Scandinavia, Spain, France, Germany–Switzerland and Belgium–Netherlands – as well as seven further developing innovative regions, the EIT Health InnoStars. The strength of EIT Health lies in the expertise and resources of its unique, diverse and growing network of partners, which currently comprises 140+ leading organisations across all key areas of healthcare (the pharmaceutical industry, medical technology, payers, public and private research institutions, and universities).

EIT Health believes that to bring innovation into the healthcare domain, all these different actors need to be connected, so they bring together world-class thought leaders from partner organisations who can contribute their visions and share their organisations' assets to accelerate innovation.

The value EIT Health brings is in ensuring that this innovation always addresses the needs of the market and of society, to ultimately benefit citizens and patients while supporting economic development in European regions. This focus on "needs-driven innovation" was critical for the day's RT discussions for the UK-Ireland region.

About EIT Health Think Tank

The EIT Health Think Tank is a forum of experts and thought leaders cooperating to shape the future of healthcare in Europe around key topics of relevance and importance in this field. Big Data is one key topic. The Think Tank brings together EIT Health Partners with other leading healthcare stakeholders to agree on means for ensuring that innovation reaches the citizens and patients who need it most. Think Tank members seek to identify healthcare needs and potential solutions to those needs. Think Tank dialogue feeds back into EIT Health activities to ensure resources and innovation are optimised to address healthcare's most pressing issues. It enables a two-way exchange between those who demand health innovation and innovators in the EIT Health partnership who supply it.



The aim is to bridge the gap between the reality facing healthcare providers with ambitious goals at a European level, recognising that while many innovations are currently being developed and tested around Europe, a large proportion are not implemented and never reach citizens. For each key topic, the objective is to reach a consensus on the challenges faced, to understand the barriers at opportunities, and to agree on needs.

The Think Tank spans both European and regional levels: focusing on topics of European relevance, barriers and opportunities are defined at a regional level (via the RTs), and these findings are then consolidated to derive recommendations for initiatives or policy changes.

Expected outcomes of the Round Table meeting

By the end of the day's RT meeting it was hoped that the following would be achieved:

- Actionable ideas for projects (quick wins) that could be implemented regionally and have measurable impact
- Actionable ideas for projects that can feed into the EIT Health Innovation Platform and inform programming
- Input to the policy-making process at regional and/or European level

Three key messages to help ensure these objectives are achieved are:

1. Let's not only report but also build
2. Do we understand where we have disagreements?
3. Identify actionable outcomes

Focus of today's agenda

PRESENTER:

Paul Timmers, Roundtable Chairman, Independent Consultant and Visiting Research Fellow in Cybersecurity Policy and Digital Transformation, Oxford University, UK

The morning session would comprise a series of presentations illustrating different perspectives on the successes, opportunities and challenges relating to biobanks, data registries, and Big Data in the Scandinavian region.

Armed with this insight, in the afternoon, participants would be split into three focus groups to discuss issues and, most importantly, identify **actionable outcomes** that could be recommended to EIT Health for how to improve healthcare in Scandinavia using data from three key perspectives:

1. Industry, including developers from pharma and SMEs
2. Healthcare providers, healthcare payers, policy makers and citizens
3. The science community, including biobanks, data producers and data interpreters

Welcome on behalf of EIT Health Scandinavia

PRESENTER: **Per Matsson**, CTO, Thermo Fisher; Chair, EIT Health Scandinavian CLC

Per Matsson considered that the elevator pitch for EIT Health was 'the implementation of health innovation for the benefit of citizens' health and healthy aging'.

On the topic of biobanks and registries, Per Matsson said that in his experience over the years, access to data and healthcare information has always been a stumbling block to progress. It was not the lack of science or innovative ideas, but rather having the tools to implement these ideas quickly. A key focus of the EIT Health Scandinavian co-location centre (CLC) is to engage healthcare providers in this process. Within the region, there are healthcare providers who both deliver healthcare and also reimburse healthcare. There is also a good ecosystem within the Scandinavian group of countries in which to test new innovations in data sharing and access, across borders.

He considered that risk management was a fundamental part of the process of driving innovation – innovation being synonymous with risk for all stakeholders – and was also the biggest perceived barrier. Why should healthcare providers trust industry? What is the risk for patient safety? It is a 'Catch-22' situation with compliance regulations also adding a layer of complication, limiting the direct access of industry personnel to healthcare professionals when formal contracts are not in place. The framework of the EIT Health consortium can help overcome these barriers and facilitate inter-disciplinary communication to drive innovation.

An example of how EIT Health can help translate ideas into tangible products and services is the RABBIT (Registers And BioBanks In Transition) programme, an initiative of the EIT Health Scandinavian CLC. EIT Health has already allocated €300,000 as 'seed money' for the programme in 2019. The aim is to accelerate the implementation of innovations by enabling better use of existing biobanks and registries by industry, academia and healthcare within the region, as well as learning from this pioneering work to enable scaling-up to a European level.

He hoped that participants would leave the meeting today as ambassadors of EIT Health, understanding the benefits and opportunities the organisation can provide for innovations in health and healthcare, as well as contributing their own insight and expertise to the day's discussions.

Summary of discussions: Open Session

KEY POINTS AND RECOMMENDED ACTIONS:

Key points and recommended actions that may be of potential interest to EIT Health for future initiatives are highlighted in bold blue letters. These points inform our Summary of Recommendations.

PRESENTATION:

Needs, benefits and positive cases of how biobanks, data registries and Big Data can be used to improve healthcare (4D project)

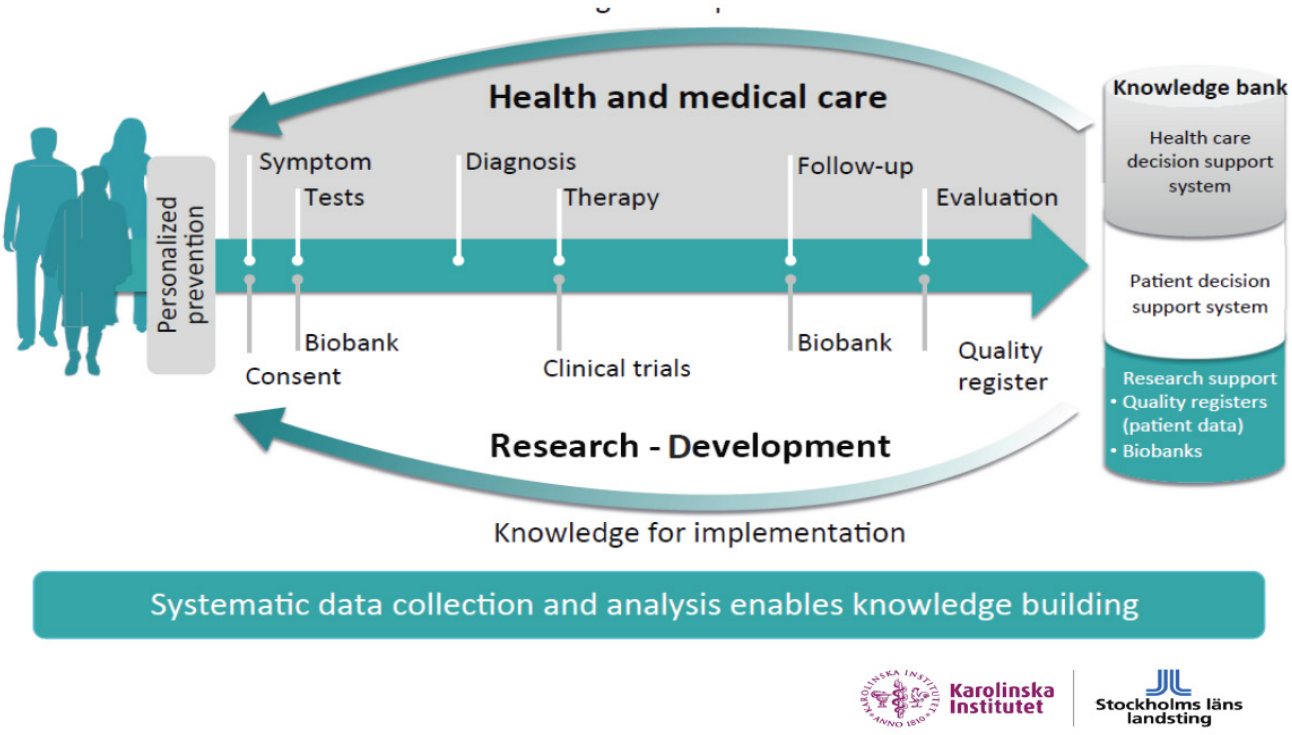
Jan P. Andersson, Stockholm County Council, SLL, Innovation Director, Sweden

Jan Andersson gave an overview of the 4D Project ('D' standing for 'diagnosis'), a collaboration between Karolinska Institutet and Stockholm County Council (SCC): https://ki.se/en/staff/programme-4d. The overall aim of Programme 4D is to improve the health of citizens, and increase the participation of individual citizens in four key areas that have a high prevalence and health impact:

- Rheumatoid arthritis (RA)
- Breast cancer
- Type 2 diabetes
- Heart failure

The programme has created generic models for these prevalent diseases making the patient, or individual citizen, a central partner in information exchange and knowledge building. It aims to use new technology to bridge the gap between what patients need and what healthcare can offer.

Previously, there were a multitude of healthcare providers and pathways that patients could choose when diagnosed with one of these conditions. The intention of 4D was to streamline the process. There is an opt-in procedure of informed consent for patients to share all their healthcare data – about 91% of people have said yes. Tests are then undertaken, biobank samples take, and, based on the diagnosis, patients are offered treatment or entry to clinical trials with subsequent follow-up and evaluation. This systematic data collection and analysis along the care pathway enables knowledge building, which bridges the gap between healthcare and research.



The programme generates information on three levels: for patients, for the healthcare system, and for the research/scientific community. It has now been in place for five years and is realising tangible benefits in these therapy areas.

In heart failure, the care process is now more structured, there is an increased awareness amongst patients, and this has been reflected in a significant reduction (15%) in hospital readmissions.

Similar success has been seen in a study aiming to prevent progression to Type 2 diabetes. Those with prediabetes were screened and processed at four primary care centres. All care episodes were handled with the digital smartphone app DiaCert work tool creating a consensus for a programme of physical activity in combination with a healthy diet. As a result, 30% of prediabetes patients normalised their HbA1c level and 50% of patients with prediabetes improved their HbA1c levels over 20 weeks (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5761151/).

In RA, a digital app 'Pain in the joints' allows for rapid screening of key symptoms, such as swollen joints, pain, fatigue, stiffness, with the resulting information being sent to the primary healthcare provider. The aim is to shorten the time between diagnosis and treatment. Based on the information received, the healthcare provider can recall the patient, assess, and refer as needed. From 2011 to 2016 the number of patients diagnosed with RA within 20 weeks from onset of disease has increased from 50% to 70%.

These simple digital innovations allow better interaction between citizens and the healthcare system and greater involvement in their own health and care.

Can EIT Health help facilitate collaboration between healthcare and smaller companies/ businesses? European laws are currently a hurdle and difficult to interpret, and the responsibility of risk means that in many cases such connections are avoided, resulting in smaller companies being unable to test their products.

PRESENTATION:

Needs, benefits, and positive cases of how biobanks, data registries and Big Data can be used to improve healthcare (SymBIOs)

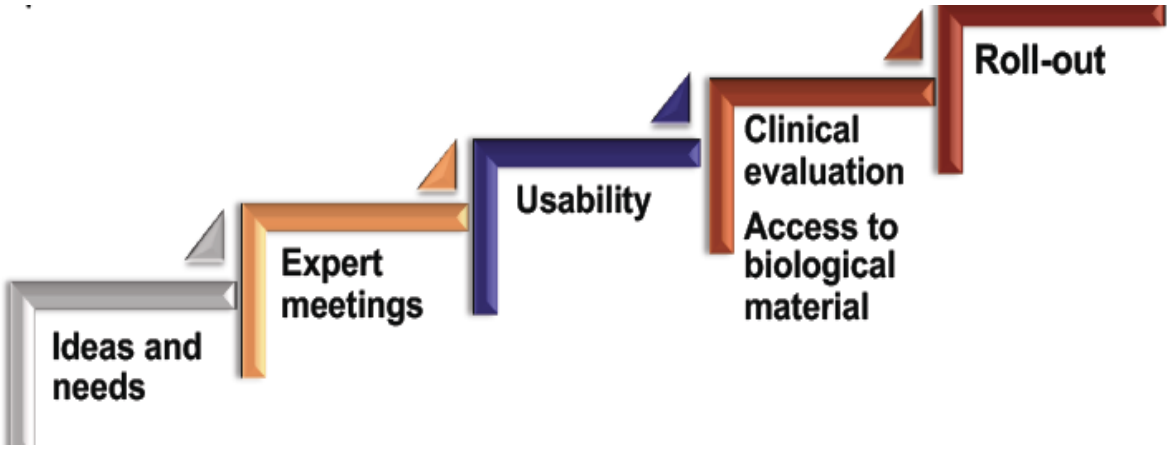
Andreas Scheutz, Research and Innovation Director, Uppsala Region, Sweden

Andreas Scheutz discussed healthcare challenges in the Uppsala region of Sweden and their plans for investments in registers and biobanks to be translated to better value for citizens and patients. Sweden in divided into six healthcare regions and Uppsala forms part of the Uppsala–Örebro healthcare region, comprising seven counties and 2 million inhabitants. Region Uppsala is the county council of the region and provides a range of public services, including healthcare. Uppsala comprises eight municipalities and around 370,000 inhabitants, and is one of the fastest growing regions in Sweden, both economically and in terms of population.

Region Uppsala is also responsible for implementing the regional development strategy for Uppsala, based on sustainable development goals and executed in collaboration with other actors including companies and universities. In the healthcare sector, Region Uppsala supports 26 primary healthcare centres and two hospitals, one of which is Uppsala University Hospital, one of the largest in Sweden. Uppsala University Hospital has multiple roles – it is a county hospital, a specialist centre, a training hospital, and a research centre. Uppsala University Hospital receives € 217 million annually for care of patients from other counties, around 25% of its total revenue.

The healthcare challenge in the Uppsala region, as well as in other regions of Sweden and around Europe, is that the proportion of elderly people in the population is increasing, partly due to advances in the healthcare system. This is likely to continue and is associated with an increase in the prevalence of chronic diseases. Alongside this, the working population is not increasing, so increased healthcare provision will need to be made with a restricted budget.

It is therefore important to develop smarter solutions to health and healthcare, and innovation is part of this. Since 2017, an Innovation Strategy for healthcare has been in place within Region Uppsala. It was recognised that healthcare providers could not make the transformation alone, and collaboration with industry and academia was necessary. An innovation office – Innovation Akademiska – was developed to support internal innovation and acts as a gateway for companies that need access to resources within the healthcare sector thereby enabling early, structured collaborations between healthcare and industry. The aim is to shorten the time from an idea to a tangible product/service by giving companies access to the healthcare environment and resources, guiding them through the process, and ensuring collaborations are undertaken within a proper legal framework. Innovation Akademiska also ensures that healthcare providers are aware of the new solutions created and can make use of them for their patients.



As part of this, the goal is to make better use of investments in registers and biobanks and to convert these investments into real patient value. Several examples of how this is already working in practice were reviewed:

Uppsala Biobank: This project has streamlined the work of the biobanks in Uppsala by amalgamating the multitude of biobanks that used to exist; now all 160 sample collections are housed in one single biobank – Uppsala Biobank – which is jointly owned and managed by Region Uppsala and Uppsala University. Uppsala Biobank was first to introduce healthcare-integrated biobanking, whereby samples for research can be collected through the hospital's routine procedure for sample collection whenever a patient interacts with the hospital. The project is continuing to develop infrastructure to support research using their biobank data.

SymBIOs: SymBIOs is a process to facilitate industry's access to biological samples. Many companies need access to such samples, for example blood, urine, amniotic fluid, to validate their products. In some cases, this needs to be from specific patient categories, for example, patients at different stages of certain types of cancer. Innovation Akademiska is developing a model (SymBIOs) to help companies access samples – ensuring that legal, ethical, logistical, and cost perspectives are considered. It guides the companies and coordinates the different actors involved including Uppsala Biobank, the Ethical Vetting Board, and the hospital laboratory to ensure the process runs smoothly.

Uppsala Clinical Research Centre (UCR): UCR was formed in 2001 as a non-profit organisation by Uppsala University and Uppsala University Hospital. It is now Sweden's largest clinical research centre combining academic excellence with clinical expertise in an innovative research infrastructure. UCR's services include all aspects of clinical studies, biobanks, laboratory analyses, and quality monitoring in health and healthcare. Studies undertaken at UCR using the wide range of available Swedish national registry data have led to improvements in patient health and care and have led to cost savings when procedures have been identified as being redundant. UCR is also a world leader in registry-based randomised clinical trials and has had several studies published in the New England Journal of Medicine over the past six months (http://www.ucr.uu.se/en/).

However, these successful regional projects are not enough, and it is important to think more broadly – nationally or at an EU/international level.

Biobank Sweden is a very good example of this. All county councils and universities with medical faculties are collaborating at a national level in Biobank Sweden. Industry and patient organisations are also engaged with the aim of developing a common, improved and sustainable biobank infrastructure for healthcare, academia, and industry.

Another good example is the **Swedish Cohort Consortium** (www.cohorts.se), a national technical and collaborative infrastructure, aiming to facilitate greater use of Swedish cohorts for research. Many projects are underpowered by using only one cohort at a time, leading to uncertain results with little benefit for patients and citizens. Rare diseases, for example, are impossible to study in individual cohorts due to lack of statistical power, so combining multiple cohorts permits better-powered solutions and more valuable results.

PRESENTATION:

The new Danish National Genome Centre and its health data context

Søren Brunak, Professor, Novo Nordisk Foundation Centre for Protein Research, University of Copenhagen, Denmark

Søren Brunak gave an overview of the development of the new Danish National Genome Centre. Initially, the main barrier to collecting and using genomic data was the general public's suspicion and lack of trust. A public debate was held on the legal bill regarding establishment of the National Genome Centre which resulted in many scaremongering newspaper headlines such as 'the state will take your DNA'. Despite these challenges, the law was eventually approved in parliament.

This allowed for the creation of a single National Genome Centre for precision medicine, operating as an agency under the Danish Health Ministry. Once fully developed, there will be a national infrastructure for whole genome sequencing using this single national database for storage. All data generated by the healthcare system will be required to be stored in the database. Written consent will be required from patients and they will have a right to self-determination (opt-out) in the case of personal genetic data. The centre will also receive data generated by citizens – from wearable devices, for example. The collected data will be available to the healthcare system and for research. The bill passed into law on 29 May 2018 and since that time the technological infrastructure has been put in place; the funding model is now being finalised, and it is anticipated that operations will commence in 2019.

This project forms part of the overall National Strategy for Personalised Medicine in Denmark which is based on the following six key principles and focuses on the dual application of collected healthcare data: for treatment and for research.

1. The Danish efforts within Personalised Medicine are to focus on the patients. Genome sequencing is to be used for treatment purposes and in research projects.
2. Confidentiality, the individual's right to self-determination, protection of information and research ethics approval are paramount.
3. The use of Personalised Medicine as a standard offer in the healthcare system must be evidence-based and economically sustainable.
4. Genome sequencing and data processing must be based in the public sector.
5. The national infrastructure and adopted standards must be used, and data must be shared securely for the benefit of future research and treatment.
6. The distribution of research funds as part of the strategy must take place in competition – and research projects should in principle be nationwide.

These principles are also underpinned by the principles of health data reform in Denmark, namely:

- Data security
- Confidentiality
- Patient safety
- Patient involvement
- Development and quality
- Modern legislation
- Transparency

These developments in the use of healthcare data in Denmark have been well received by both politicians and industry.

The Genome Denmark project (http://www.genomedenmark.dk/english/) has now provided a regional reference genome that is expected to improve the power of future association mapping studies and ultimately precision medicine initiatives (Maretty et al, 2017: https://www.ncbi.nlm.nih.gov/pubmed/28746312). In future, genome-based biomarkers could prove valuable for a range of diseases in one go.

Progress is also being made with several other successful genotyping projects. The Danish Blood Donor Study, for example, has already genotyped 110,000 samples.

This detailed genetic information allows us to look more closely at multimorbidities (Hu et al, 2016: https://www.ncbi.nlm.nih.gov/pubmed/27498692), their disease pathway, and how best to manage them. Importantly, it can give us insight into the critical transition between health and disease. However, to do this it is essential that data is collected during the 'healthy' period so that parameters in both periods can be compared and the disease trajectory can be computed. Multimorbidity has been shown to influence disease outcomes: a study found that diagnosis trajectories of prior multi-morbidities were able to predict mortality from sepsis (Beck et al, 2016: https://www.ncbi.nlm.nih.gov/pubmed/27812043). Collection of 'healthy' data should therefore be a key priority for the Scandinavian countries.

Although there is now a huge amount of healthcare data available in Scandinavia, it has not changed format for several decades. We now need better systems that are able to effectively and rapidly interrogate the data so we can produce meaningful results and make effective use of the information quickly – this should be another key priority across the Scandinavian countries.

From work on genomics we have learned that the genome is full of compensatory mechanisms that protect people from getting certain diseases. Large datasets are needed to investigate these mechanisms further and understand their relevance to patients' health.

Engagement with patients and citizens, and communication of the positive benefits of the collection, and use of their data is key to greater acceptance. They need to understand that the use of data is not a threat: Data Saves Lives. Distrust arises when there is commercial gain. EIT Health may have a role in bridging this gap.

PRESENTATION:

Swedish national collaboration to build a national biobank infrastructure aimed at facilitating medical research and development and benefiting patients

Sonja Eaker Fält, Chair, Preparatory Group of Biobank Sweden

Sonja Eaker Fält gave an overview of Biobank Sweden and the challenges that have been encountered during its development. There is currently a good climate for biobank research in Sweden coupled with strong public trust in data collection and research. Sweden has a well-characterised population involving a personal number system, national health registries, population-based registers, and quality registers. The benefits of biobanks are that they are disease oriented, use large population-based cohorts, and have a long-term research impact.

The Swedish biobank landscape comprises 450 biobanks. A total of 250 biobanks are managed by the county councils/regions and universities and include approximately 160 million samples. Around 90% of all stored samples are managed within the county councils/regions, and data is mainly used for healthcare and research.

There are another 200 biobanks in the private sector, either laboratories (4%) or private clinics, companies, or clinical research organisations (96%). Data is mainly used for single studies.

There are two main types of sample collections in these biobanks:

Existing sample collections:

- Samples collected earlier and stored for healthcare purposes (about 95% of all stored samples): Several hundred thousand samples are taken within the healthcare system each day. Some of these samples are stored in biobanks within the healthcare system, mainly tissue samples for diagnostics, treatment, and follow-up. Information about samples and diagnostics are stored in the Laboratory Information System (LIS) which is linked to the patient medical record (PDL). Access to samples for research is given after an approved biobank application, approved ethical vetting, and consent from the donor in accordance with approval from an Ethics Review Board.
- Samples collected earlier and stored for research (about 5% of all stored samples). These may be from:
    1. Specific academic trials: access for others limited. Samples are stored during the study.
    2. Larger prospective collections/cohorts (samples, data): these are national prospective cohorts with millions of samples for research with high scientific impact. The data may be available for others, subject to an approved biobank application, approved ethical vetting, consent, and permission from the group or committee granting access to the specific collection.
    3. Clinical trials – not usually stored within the county councils/regional biobanks. Access for others limited.

Newly collected samples: *For a specific research study (academic, pharmaceutical, medical technical).*

Biobanks have huge potential and are an invaluable asset for research. While they are already used extensively, there are several challenges that need to be overcome. There are over 250 biobanks in 21 counties/regions

and seven universities, which represents a significant organisation challenge. Within the healthcare system there is often a lack of resources to expedite requests for access. In addition, there is a lack of standardisation amongst biobanks, as well as technical issues and a complex ethical and legal landscape.

In the spring of 2017 a new agreement was reached between county councils/regions with university hospitals and universities with a medical faculty for enhanced collaboration to support biobank infrastructure for healthcare, academia and industry. To implement the agreement, Biobank Sweden (http://biobanksverige.se/) was established (formerly the National Biobank Council and BBMRI.se). More recently, industry partners Läkemedelsindustriföreningen (LIF), Swedish Medtech, Swedish Labtech, and SwedenBIO have joined the collaboration. It also includes representatives from patient organisations and the Swedish Association of Local Authorities and Regions (SKL). The overall aim is to better utilise the strengths of these partners and to build a national biobank infrastructure for healthcare, research, industry, and for the benefit of patients. External financial support is being provided by Veteskapsrådet (VR) and Vinnova/SWElife.

The overall goals of Biobank Sweden are:

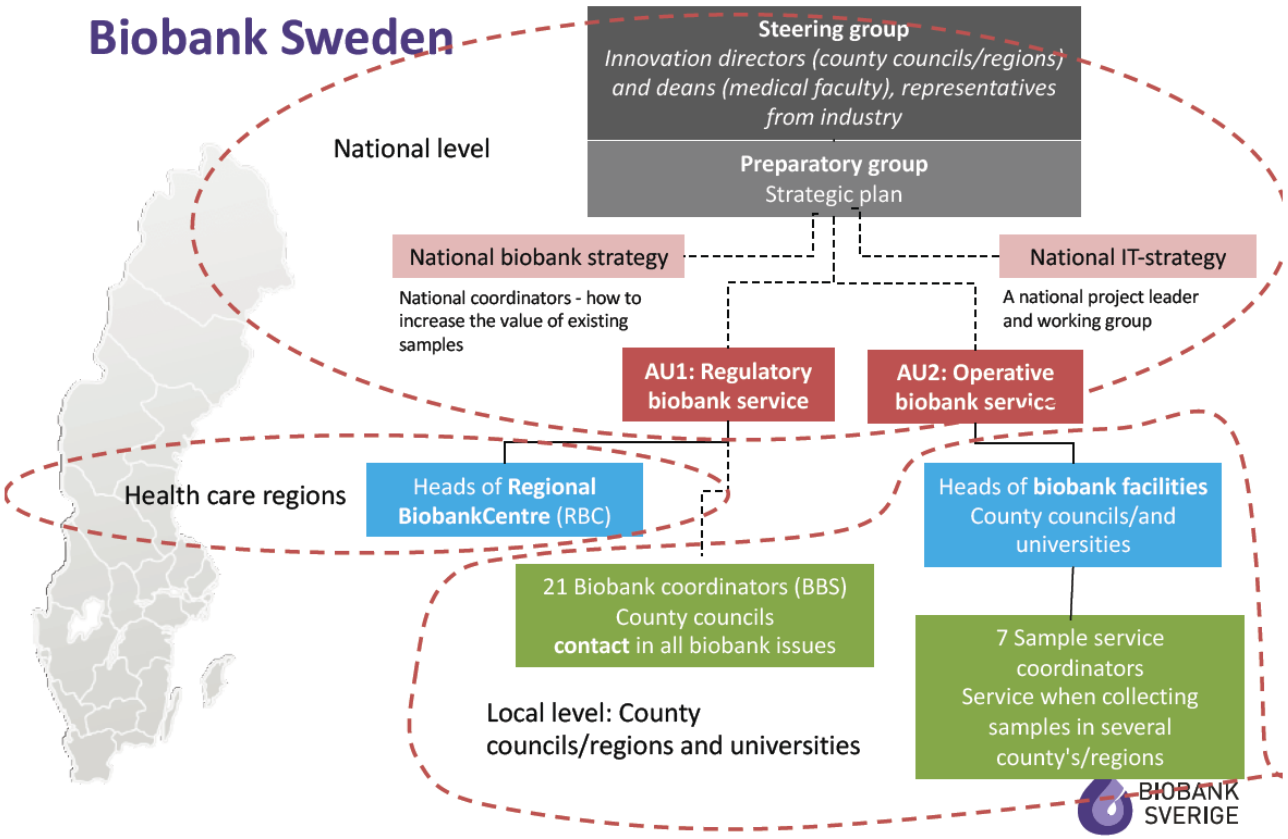
- To build a coherent, improved, and long-term sustainable national biobank infrastructure for healthcare, academia, and industry with optimal conditions for both national and international cooperation.
- The infrastructure should enable national, accessible, cost efficient, and competitive collection and biobanking which will secure the access of high-quality samples.
- This will result in a benefit for the patient and shall be conducted in a secure manner for patients and sample donors, and in accordance with their consent.

Biobank Sweden consists of a national steering committee, with representatives appointed by the county councils/regions and universities with a medical faculty, and with representation from industry organisations. It also has a strategic preparatory group, two working committees for regulatory and operative biobank services, a national network of Biobank Coordinators, and operates at a national, regional, and local level.

Biobank Sweden provides regulatory and operative advice and support for sample collection and withdrawal, as well as IT structures in order to store, locate, and apply for access to samples.

Regulatory Biobank services: Provides advice on legislation, national principals, documents, instructions and guidelines, agreements, and applications for samples, etc. Provides services on national guidelines for agreements and application for access to samples.

Operative biobank services: Guidelines for collection logistics, sample processing and storage, DNA/RNA extraction, cryopreservation of cells etc. Healthcare integrated biobanks (SIB) are now available at all university hospitals. SIB is a unique national logistics initiative for high-quality collection, handling, and biobanking of liquid-based samples for research. It includes e-referrals, a needle-to-freezer time of less than two hours, a high degree of standardisation, as well as a high focus on quality. As of April 2018, 26 hospitals have either established the SIB model or are planning to set it up.



The remaining challenges for Biobank Sweden are mainly technical:

- To progress, legal and technical prerequisites were needed for finding samples on a national basis – currently a range of IT systems keep track of different parts of the total biobank information.
- An electronic consent service that would facilitate participation and to regulate consent would be of considerable value.
- Biobank information needs to be standardised.
- National IT systems are needed for electronic applications (and national case management system) and withdrawals of samples.
- A national system is needed to link information on samples to other data sources, such as quality registers.

It was agreed that the Biobank Sweden project provided EIT Health with an excellent platform for other biobank initiatives. EIT Health could also support Biobank Sweden in developing strategies to solve some of the remaining challenges (legal, regulatory, financial etc.), and in securing national/ EU access and funding.

PRESENTATION:

Biobank and Big Data available for developments (including for industry) in Estonia: opportunities and challenges

Lili Milani, Research Professor, Estonian National Biobank, University of Tartu, Estonia

Lili Milani discussed the experience with the Estonian Biobank in terms of research, industry collaborations, and translation of this information into personalised medicine.

The Estonian Biobank was established in 2000 and is a prospective, longitudinal, volunteer-based biobank (https://www.geenivaramu.ee/en). It includes 52,000 participants and holds information on health records, diet, physical activity, collected initially by questionnaire, as well as information from DNA, plasma, and cell samples. Follow up of participants is undertaken electronically in collaboration with national registries and databases to collect information on diagnosed diseases, health insurance bills, clinical laboratory measurements, etc. There is broad informed citizen consent and clear access rules for organisations wanting to use data for research.

Research using the Estonian Biobank data, in collaboration with international partners, has generated a large number of peer-reviewed publications over the last decade. In practice, it is also benefiting patients. Genetic screening for mutations that predispose to familial hypercholesterolaemia (LDLR, APOB, PCSK9) and breast cancer (BRCA1, BRCA2), was able to identify patients at risk who had not been picked up by the usual healthcare system, and who were then recalled.

The Estonian Biobank is also working on common chronic diseases and pharmacogenetics. While the effect of each single genetic variant may be small, polygenic risk scores evaluate variations in multiple genetic variants, enabling patients to be stratified according to risk.

Feedback to biobank participants is undertaken using infographics and counselling, making recommendations for how they can manage their disease, as in the example below for Type 2 diabetes. Follow-up surveys of patients and citizens show that receiving feedback on their genetic reports is very well received and associated mainly with positive emotions.

Another aspect of the Estonian Biobank's research is looking at clinical pharmacogenetics, since it is known that more than 98% of individuals carry mutations that affect response to medication.

A study was undertaken to develop and test algorithms for the translation of pre-existing genotype data from over 44,000 participants of the Estonian biobank into pharmacogenetic recommendations, with the aim of providing decision support for clinicians (https://www.biorxiv.org/content/biorxiv/early/2018/07/04/356204.full.pdf).

TARTU ÜLIKOOL

eesti geenivarami

Type 2 diabetes

Type 2 diabetes is a complex disorder characterised by a high level of blood sugar and at least partial insuli resistance. The contributing factors to type 2 diabetes include both lifestyle and genetic predisposition.

Genetic predisposition

Based on your genetic profile, you are at **average** risk of developing diabetes.

Seven out of 10 people are at lower hereditary risk than you.

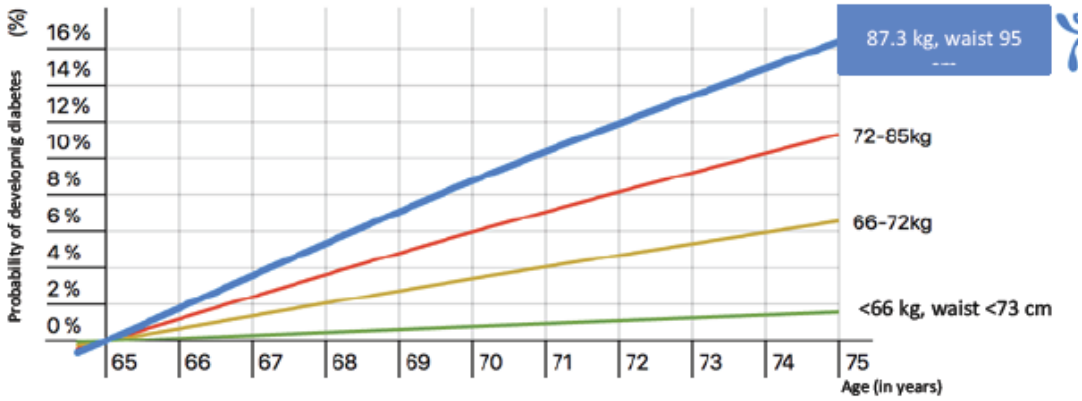
Two out of 10 people are at higher hereditary risk than you.

Effect of lifestyle and diseases on general risk of diabetes

Your lifestyle and existing conditions place you at **very high** risk of developing diabetes.

Effect of body weight on general risk of diabetes

Probability of developing diabetes considering your weight, age and genetic predisposition.



Total risk of type 2 diabetes

Your current weight places you at **very high** risk of developing type 2 diabetes. The probability of developir the disease in the next 10 years is **24%** and before the age of 70 **13,1%.**

In order to reduce the risk, it is recommended that you:

A range of public-private partnerships support the Estonian Biobank initiative including five hospitals, three universities, 32 health IT companies, 13 biotech companies, and 130 partners in the EU (hospitals, universities, health IT, pharma and biotech companies).

Summary of discussions and recommendations: Roundtable Sessions

How to improve healthcare in Scandinavia using existing biobanks, quality registries and Big Data – barriers and actionable recommendations

From the perspective of industry, including developers from pharma and SMEs

DISCUSSION CHAIRED BY:
Per Matsson, CTO, Thermo Fisher; Chair, EIT Health Scandinavian CLC

- Academia and industry collaboration: Participants agreed that collaboration significantly improves the quality of results: 1 + 1 = 3.
- Access to data: Data sharing is now possible between healthcare and industry but the speed of access to data is still an issue and creates delays. Drug development often needs fast decisions.
- Types of data: Need to define and specify different types of data: personalised, anonymised, analysed, etc; these may require different access times.
- Standardisation of data: Important and a big project to undertake, but not impossible. Using raw data versus cleaned data also creates time lags; similarly, there is an issue when combining data in different formats. It may be possible to develop AI and machine-learning technology to clean up data in the future.
- Building strength and collaboration in the Scandinavian region:
    1. Need a pilot project showing good results in Scandinavian region – it is unique and no other region in Europe has so many countries working so closely together.
    2. It has the big advantage of established mutual trust between the different independent nations.
    3. Need to develop common, smart solutions in the Scandinavian region building on good examples that are visible and scalable.
    4. It was recognised that many differences exist between individual countries and these will need to be discussed at a national level.
    5. Drive at national level, show results at Scandinavian level.
    6. **EIT Health can provide support to harmonise these collaborations, which will speed up the process, as well as facilitating the process of scaling them up to a European level.**

- Combining national data in the Scandinavian region: Need to develop systems to access/combine data while still keeping independent national databases. Also, technology is needed to allow analysis of multiple databases without combining the data. It may be possible to analyse using AI/algorithms.
- How much information do we have on the healthy state? Lots of potential, but currently limited use and would be a valuable tool and source of information for disease prevention. Example: Danish study in blood donors.
- Need access to continuous healthcare information moving forwards, especially for the elderly, comorbid population:
    1. All medical practice/treatments should be seen as clinical trials and pharmacovigilance with data collected routinely, supported by real-life follow-up.
    2. Using this approach, it could be anticipated that minimal confirmation of drug efficacy and safety would be required from costly randomised, controlled clinical trials, supported by ongoing real-life follow-up.
    3. In the future, this will be important for value-based payment.
    4. There is potential for industry partnerships, and this would reduce the overall costs of drug development.
    5. It was noted that not all samples are stored indefinitely for reanalysis or comparison.
- Trust and patient/citizen consent
    1. Need to overcome trust issues about healthcare and industry collaborations. Encourage mutual trust and sharing of data.
    2. Use of biobank data: Public trust may differ depending on its intended use – research/science has different perception (worthy) to commercial/industry use (often viewed with suspicion).
    3. **Consent for secondary use of data – needs an electronic system. EIT Health could support in developing a harmonised process. As an example, Hungary has consented the whole population.**
- Citizen and patient engagement:
    1. Need to engage citizens and patients as allies, and educate them on the importance and benefits of sharing data and use – 'Data saves lives'
    2. **Engagement of patient organisations (who see themselves as patient advocates) is key. They often have a greater openness to data sharing and use, and are also used to communicating information themselves. Get them involved in the communications using their own channels. It was noted that EIT Health was already in communication with the European Patients Forum, an umbrella organisation that works with patients' groups in public health and health advocacy across Europe.**
- Industry collaboration:
    1. **Need framework programme for industry collaborations to speed up the contractual process. EIT Health can help facilitate this.**
    2. **In particular, SMEs need support to access and use data as they do not have the same infrastructure as big pharma companies. This also needs a framework and ecosystem for collaborations; sandboxing was suggested. EIT Health can help support this process.**
- Clinical trials: Using databases to screen patients for inclusion in clinical trials would speed up the recruitment process.

Proposals for actionable projects – INDUSTRY perspective

1. **Building strength and collaboration in the Scandinavian region**	There is a need to harmonise collaborations with industry on Big Data initiatives. This could speed up the contractual process of data access and sharing, as well as facilitating the process of scaling up to a European level in the future. **EIT Health can provide support to harmonise collaborations with industry on Big Data initiatives in the region, leveraging the existing mutual trust between countries.** **Develop a framework and ecosystem for collaborations with SMEs – sandboxing.**
2. Trust and citizen/ patient consent	**Develop an electronic, harmonised process of citizen consent for secondary use of data.**
3. Citizen and patient engagement	**Engage with patient organisations and use their communication pathways to reach citizens so they understand the benefits to society of data sharing and use.**

From the perspective of healthcare providers, healthcare payers, policy makers and citizens

DISCUSSION CHAIRED BY: **Eva Tiensuu Janson**, Professor of Medicine & Dean of the Faculty of Medicine, Uppsala University, Sweden

- International infrastructure for health data: International efforts are needed to combine, manage, and provide access to large datasets for research – including the detection of rare variants, performing meta-analyses in large population cohorts –, for undertaking analysis on different cancer types, and for developing effective preventive care programs for complex diseases.
- Since healthcare is subject to individual country national laws, it is often seen as unacceptable to export health data outside the regional or national jurisdiction. A harmonised, EU-wide infrastructure is needed in order to facilitate patient health data movement across borders.
- A coordinated, secure and regulated environment is needed that enables the data to be accessed responsibly across national borders. This should build on and integrate existing software, IT and cloud infrastructures and involve stakeholders who are already undertaking national and international initiatives, e.g. BBMRI-ERIC, ELIXIR.
- Funding: Sustainable funding and business models are needed to support the funding of biobanks: funding for storage of samples and data, extracting the samples, and for providing access.
- Training and capacity building: This will be key to developing the skills needed for these new innovations and ways of working, and to develop the future workforce.
- Cost–benefit: More health economics analysis is needed as well as skilled specialists who can undertake this. In order to be reimbursed by healthcare payers, cost–benefit analyses of initiatives should be undertaken.

Proposals for actionable projects – HEALTHCARE perspective

1. Data access business models	**Develop data access business models, rules for access, with clear funding/ payment agreements to justify the access cost and ensure the biobank's sustainability. Needs to incorporate a legal and regulatory framework.**
2. Data cataloguing	Harmonisation of data is very expensive so an easy first step would be to develop a metadata catalogue. It is also a pre-requisite for creating machine learning tools. Possible collaboration with BBMRI-ERIC. **Develop a metadata catalogue. Not harmonised data, but an information package about what exists and where.**
3. Common data standards	Different data formats are a big problem for integration. There is a need for common understanding of the minimum requirements for data quality for use in medicine. **Develop a set of common data standards that can be the template for new datasets but can also be used for harmonisation of current data.**

4. Data integration	Several pilot projects are already ongoing in Sweden to combine biobank data and health record data; the Estonian e-Health system is already using this approach. **Develop technical solutions for integrating data and combining biobank data and health record data together**
5. Citizen and patient consent	A single electronic consent form would remove the need to collect several individual consent forms before each intervention. **Develop a single, broad-use electronic consent form with secure identification by bank ID, with safe and secure access (blockchain) to data.**
6. Communication and engagement	**Develop a communication strategy/information package for different stakeholders of positive case examples, to communicate why giving samples to biobanks is important. For healthcare payers, this could include information about how the new services make treatment more cost-effective, highlighting the clinical value of genomics.**
7. 'One-stop shop'	Develop a 'one-stop shop' for extraction of biobank samples and data. One application form for all interested biobanks. Possible collaboration with BBMRI-ERIC.
8. Skills and capacities	**Develop training programs (preferably massive open online courses) for MDs, but also for other stakeholders, to educate about these new technologies and ways of working – link with EIT Health Campus.** ▪ Genomics and bioinformatics ▪ New clinical guidelines ▪ New IT systems ▪ Cost–benefit cases, ELSI and awareness ▪ How to implement new ways of working
9. Validation of biobank data	Having central biomarker validation could enable development of risk models for complex diseases and validation of the new genetic tests based on biobank data. It would also generate evidence of whether the test has predictive power. Big cohorts are needed to confirm this. Biobanks should give quality marks to the tests. **Create a biomarker validation centre – a network of biobanks that have genomic data available which has been updated with phenotype data from health records.**
10. Automation	**Develop tools for automatic collection, analysis and reporting of health data in relation to biobank samples; automated decision support tools.**
11. Funding support	**EIT should consider developing funding schemes for new healthcare processes not just for products and services.**

From the perspective of the science community, including biobanks, data producers and data interpreters

DISCUSSION CHAIRED BY: **Jan-Olov Höög**, Professor, KI EIT Health Lead, Karolinska Institutet, Sweden

Key points and challenges were identified as:

- Ensuring improved healthcare for patients and citizens – making better use of samples and health data for tangible benefit.
- Reducing the current administrative burden: need to streamline and harmonise the processes to cut down on the paperwork.
- Improving information and communication of the value of data.
- Increasing the speed of processes, identifying bottlenecks.
- Sharing data instead of samples.
- Developing a 'one-stop shop'.
- Creating an independent organisation to handle standard contracts (single point of contact).
- Starting small and scaling-up.
- Building on trust, not fear.

Proposals for actionable projects – SCIENCE perspective

1. Communication and engagement	**EIT Health could support evidence-based communication/educational initiatives to engage citizens, patients, policy makers, and other members of society in order to build trust in data sharing and use for research.**
2. 'One-stop shop'	Collecting and cataloguing cohorts, and making them available for research, could go some way to reducing the costs of clinical trials. **EIT Health could support the development of a centralised, regulated 'one-stop shop' so researchers are aware of what data is available and where this can be accessed.**
3. Business models and framework	Harmonised data access business models would reduce administrative burden and speed up processes. An independent organisation could be established to act as a single point for handling partnership contracts. EIT Health could facilitate this. **Create harmonised data access business models and standard contracts, incorporating a legal and regulatory framework, and funding arrangements.**

EIT Health is supported by the EIT,
a body of the European Union