Description of Vanguard Initiative pilot “Smart Health”

The development of personalised medicine (PM), stratified or precision medicine is an evolution that cannot be stopped anymore. PM is strongly technological driven and will induce a transformation of how health and wellbeing are approached, and medicine is being implemented. The convergence of knowledge on what determines health and disease or how the process of ageing is determined, with digital technologies and access to data opens a huge potential to develop new applications to improve general health, wellbeing, and will make preventive medicine reality.

The sensitivity of new diagnostics, access to omics data and the acknowledgement that early detection is often crucial, is blurring the boundaries between health and disease. Chronic diseases, often linked to changes in general lifestyles and increasing of the average age of the population are putting the healthcare systems under increasing pressure. The development of PM will not only support the increase of healthy life years, it will also secure the sustainability of our healthcare systems.

The Vanguard Initiative Smart Health pilot was established to realise the potential of personalised medicine. This pilot will bring the agenda to implement personalised medicine to the next level.

The partner regions already have solid ecosystems combining biomedical, technological and data driven expertise. By bringing these ecosystems together, a higher added value will be reached and boost the implementation of personalised medicine; it will realise an innovative approach for health and care in Europe. Many different strategies and initiatives with PM as common denominator are currently running across Europe. These initiatives often have different focal areas or target only part of the value chain. A better integration and coordination can enforce the impact of the actions.

A thorough mapping of developing trends and relevant industry and technology actors in the different parts of the value chain, infrastructures, end users etc. in the participating regions will allow to identify strengths, barriers and needs. The pilot will align complementary assets and infrastructure and work to integrate value chains across different technology sectors to create added value and innovative applications. A roadmap will be developed to transfer new solutions for health, wellbeing and care faster to society and will contribute to the sustainability of healthcare systems

Introduction

The development of PM is an evolution that cannot be stopped. PM was defined by the Horizon 2020 Advisory Group as

"***a medical model using characterisation of individuals' phenotypes and genotypes (e.g. molecular profiling, medical imaging, lifestyle data) for tailoring the right therapeutic strategy for the right person at the right time, and/or to determine the predisposition to disease and/or to deliver timely and targeted prevention***".

This definition was also used in the Council conclusions on personalised medicine for patients, published on 7 December 2015. From this definition, it is clear that PM is strongly technology-driven and in addition, will enable preventive medicine.

PM is expected to bring transformative change of how health is perceived and how medicine is implemented. The accuracy and sensitivity of novel diagnostics and the acknowledgement that early detection is crucial in many cases, are blurring the boundaries between health and disease. The concept of a health-disease continuum is advanced in this context. Biomarkers for early diagnosis may be indicative for early therapeutic intervention or for adapting lifestyle or – given more recent insight - even facilitate personalised nutritional interventions. In this reasoning, also the boundaries between food and drugs become blurred and the food-drug continuum becomes reality. Hence, PM also includes preventative medicine and personalised nutrition. Groups of diseases that have been the focus for developments in personalised medicine are depicted in the table below. The Smart Health pilot is nevertheless open to all disease areas.

Groups of diseases where PM made progress and that are the focus of more research and development:

- Chronic diseases, including metabolic syndromes such as diabetes
- Neurological disorders
- Rare (genetic) disorders
- Cancer

To induce the transformative change of next generation healthcare and cure, PM should be defined broadly comprising the development and uptake of novel diagnostics and monitoring systems for preventive health and support of innovative therapies and healthcare applications. The ongoing evolution of a connected world sensor technologies and mobile health applications should move from gadgets to real individual health supporting systems to bring better health and wellbeing. This implies the need for a citizen-centric approach on both data management and data-driven health innovations and applications. PM developments are impacting virtually all domains of modern medicine. Approaches building on the latest insights on the biological functioning of single cells are currently among the most promising areas. One of the key factors for successful implementation of PM is the availability to standardised, accessible, processed data, which also enables the re-use of publicly available data for exploring multidisciplinary research goals. Next to access to and gathering of data, the availability of a highly qualified biomedical and healthcare workforce to generate, analyse and process PM data to translate data into new products and applications is an essential requirement.

The Vanguard Initiative is meant to develop more effective innovation policies and encourage interregional cooperation in value chains across borders. This should help increasing competitiveness and resilience while better aligning investment pipelines across borders to create new opportunities.

Pillars supporting PM

The figure below is structuring the ideas of how the Vanguard Initiative Smart Health pilot is being developed. The pillars were updated in 2021 and highlight the broad topics of interest for the Smart Health pilot. The boxes below indicate more concrete ideas for demo case projects. The demo case ideas are more flexible and might vary throughout the pilot.

The first pillar – data and digital technologies – is largely about observation, measurement, data collection, data capture, analysis and most importantly synthesis leading towards decisions. These decisions have to be precise and effective.
The second pillar – convergence of technologies – is about adding and combining state-of-the-art technologies, using them to create more insights as well as new therapies or diagnostics.
The third pillar – preventive health – is stemming from the understanding that it's better to keep people healthy than to restore health. Health is not solely an aspect of the body, but also of the mind. All of these factors need to converge in order to maintain health. The patient needs to be empowered, aware of the importance of prevention, have easy access to primary care, and have tools that will support his own desire to stay healthy, which leads to the fourth pillar – sustainability of health.

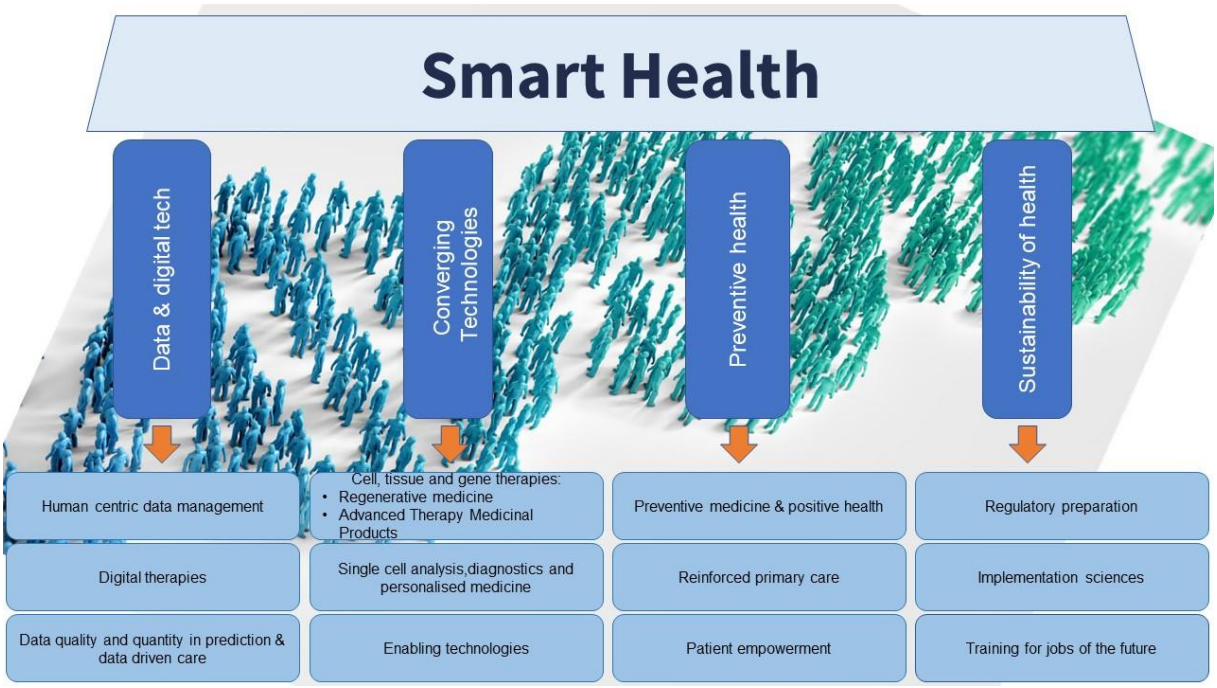

Figure 1. Smart Health pillars and potential underlying demo cases.

1. Data & digital technologies

One of the prerequisites to make PM reality is the stratification of the population, which strongly relies on the collection and analyses of large datasets. Data includes genome data linked to health records and lifestyle information of people. Additional omics information will further help finer stratification of populations through identification of specific biomarkers linked to certain

health conditions or correlated to the onset of or predisposition for diseases. Further relevant data are generated through advanced imaging technologies.

The Commission announced in the Communication on the European Strategy for Data its intention to deliver concrete results in the area of health data and to tap into the potential created by developments in digital technologies. The collection, access, storage, use and re-use of data in healthcare poses specific challenges that need to be addressed within a regulatory framework that best serves SMEs and individuals' interests and rights, in particular as regards the processing of sensitive personal data relating to their health. As a follow up, the Commission adopted its Data Governance Act proposal (2020) laying down conditions around access to certain categories of data, and containing provisions to foster trust in voluntary data sharing.

The European Health Data Space (EHDS) is another Commission priority that aims at making the most of the potential of digital health to provide high-quality healthcare, reduce inequalities and promote access to health data for research and innovation on new preventive strategies, diagnosis and treatment. At the same time, it should ensure that individuals have control over their own personal data.

The EU will boost the development of trustworthy data-sharing systems to promote data driven innovation which is also important in the PM development. EU Data governance act and action to build EU Health data Space are initiatives which are affecting the PM thematic area. Close collaboration and joint innovation actions between several stakeholders and member states in health data sharing and experimentation should be addressed in the Vanguard pilot cases. New pilot cases can be taken forward also via the Gaia-X collaboration framework and trusted technology deployment with the goal of scale through federation. Gaia-X is an initiative to develop an open software layer of control, governance, and the implementation of a common set of policies and rules to be applied to any existing cloud/ edge technology stack to obtain transparency, sovereignty and interoperability across data and services.

- *Human centric data management*

Integrating personal data across multiple scales of biological functioning, will improve diagnostics and enable better stratification. Such stratification will be a basis for understanding differences in health risks and response to treatments. Longitudinal studies of healthy and diseased populations (cohorts) provide a wealth of data that needs to be translated into knowledge for PM applications. The current opportunities created by new technologies of data gathering through consumer wearables, sensors, apps and other decentralised diagnostics, generate new combined sets of clinical and lifestyle data. Already many initiatives around Europe and globally are collecting such data.

However, standardisation of the data and ethical issues on ownership of data are not properly addressed. Indeed, not only the development of biomarkers, new diagnostics and wearables are key, the development of standardised data acquisition and processing methods, safe / fast data transfer and storage as well as an active role in it for patients and citizens are equally important aspects. New developments like artificial intelligence and virtual reality can get more information out of datasets. Linking those technologies with the cohort data sets will be important in the development of PM.

There is a wealth of information in different regions, regional hospitals and databases in different jurisdictions. Access to this information however, is not optimised to generate knowledge from the information. Broad access to population data is necessary for genomic stratification of the (healthy) population and should be linked to diseases or certain health outcomes and will be essential in the development of preventive medicine. The number of examples of regional stratified populations in Europe is growing as more population studies

are ongoing and also regional different diets have been shown to influence health. Closer collaboration among different regions and cross-border access to population cohorts will accelerate the development of innovative applications based on knowledge extracted from such databases. One could consider also one step further down the process and implement cross-border sample sharing (biobanks) next to data sharing.

Access to existing population data, cohorts, databases and biobanks as well as capturing new types of, often user-generated, data are major tools to develop PM further. Substantial efforts are ongoing to provide access to such infrastructure with the ESFRI agenda that addresses complementary infrastructures. At regional level, however, often very relevant infrastructures exist, which have not been identified by supranational initiatives. In this respect, issues related to standardisation of data and procedures, privacy and ethical issues are better prescribed in large supranational initiatives but often remain a major challenge at regional level. Addressing these issues is essential to maximise the potential of the information available and to realise cross-border collaborations.

The data challenge thus has different angles to be addressed. There are the technological aspects related to data acquisition, storage, access and (re)-use, but also the developments building on data offer enormous opportunities. The importance of High Performance Computing (HPC), Artificial Intelligence (AI), Virtual and Augmented Reality (VR and AR) are just some of these technologies that will drive PM to unbiased impact. Finally there is also the ethical and legal aspects, in which Europe is taking actions that will leverage the trust and the acceptation of PM. The aim is to study how a data driven society could facilitate seamless, effective and smoothly functioning service paths consisting of services of several service providers. And build people's trust to utilize data driven, AI enabled services in a timely and ethically sustainable manner.

- *Data quality and quantity in prediction & data driven care*

Lifestyle, including exercise, nutrition or smoking habits, can strongly influence the risk of developing certain diseases. Collecting and monitoring personal lifestyle data (novel data sets from molecular omics, big data and tailored biosensors) can give insight into these risk factors and can help mediate them before the onset of disease. This topic is also interlinked with pillar three, preventive health.

Predictive analytics is used to find patterns in next generation data sets to identify risks and predictions about future outcomes. Data driven care is renewed with statistical modelling, data mining techniques and machine learning or artificial intelligence (AI) approaches. Also demo cases about digital twins and synthetic data can be listed under this topic.

New coordination and support actions are needed, for example, to create a framework and criteria for contextual data collection, consolidation mechanisms and means in sharing personal data in multi-stakeholder RD projects. The focus is on creating the framework for the data driven society and care. And to investigate the operating models in data sharing and knowledge transfer between higher education, research, and businesses and build competencies in the start-up and SME ecosystem to use data analytics and AI tools in the data driven economy linked to health and care. The aim is to clarify the contextual significance of data sharing, processing as well as secondary use of data. The purpose of data sharing needs to be clear in the shift from treatment to prediction, and also when generating, AI driven decision making in people's life-events (education, employment, retirement, etc).

- *Digital therapies*

Innovative solutions that make use of health data and digital technologies, among others digital health solutions based on data analytics and artificial intelligence (AI), can contribute to the

transformation and sustainability of healthcare systems, while improving people's health and enabling personalised medicine. The development of these technologies requires access by researchers and innovators to substantial amounts of (health) data

Digital therapies are evidence-based therapeutic interventions driven by software programmes. They can either be used to prevent, manage or treat a disease. Examples include apps, websites or wearables that help to change behaviour or can monitor symptoms.

Smart devices such as wearables now link patients to doctors, transmitting critical medical data in real time from hospital beds and private homes as well as mobile equipment used at emergency sites and in transport vehicles. Wireless devices implanted in the body permit patients to be continuously monitored to alert healthcare providers of changes that may require necessary action.

2. Convergence of technologies

PM is strongly driven by the convergence of technologies and expertise in biomedicine, ICT, nanotechnologies and engineering. PM relies on diagnostics and clinically validated biomarkers. Access to innovative technologies bring preventative medicine as part of a PM approach within reach and hence it is expected to contribute to the sustainability of healthcare systems. The availability of PM solutions has the inherent objective to bring expensive therapeutics only to those patients that are likely to respond to the treatment. It will also increase the impact of prevention and reduce the cost of unwanted side-effects of non-effective treatments.

Within the Vanguard Initiative Smart Health pilot "Convergence of Technologies" pillar we focus on the following areas, notwithstanding the understanding of the broader aspects of convergence:

- *Cell, tissue and gene therapies*

Cell-based therapy can be defined as therapy, which is based on the injection of cellular material in the patient. This can be starting from cellular material of the patient (autologous) or from a donor (allogenic). Cell therapy can involve the adjustment of stem cells (E.g. hematopoietic, neural, mesenchymal) resulting in cells that can repair damaged tissues and hence embraces regenerative medicine, which ultimately may lead to the development of new biosynthetic organs and body parts, such as joints. Regenerative medicine includes stem cell therapies, biodegradable biomaterials or new drugs that help to repair damage.
Smart implants for example allows for the creation of new kinds of geometries, such as trabecular lattices to encourage bone in-growth on a given implant. The technology offers not only the capability to create and test these geometries, but to prototype them using the intended manufacturing process and to do so quickly.

Cell therapy also includes Advanced Therapy Medicinal Products (ATMP). The European Medicine Agency defines ATMPs as medicines for human use that are based on genes, tissues or cells. They can be classified in three domains: (1) gene therapy medicines, (2) somatic-cell therapy medicines and (3) tissue-engineered medicines. A lot of progress has been made in this field with regards to genetic diseases. It also includes cancer treatment that can be used for the specific secretion of chemokines, cytokines or growth factors that influence the activities of other cells in the body. As this type of therapy is often in clinical developmental phases, there are important challenges to address during scale-up and commercial phase. This includes administer routes, industrial processes, distribution channels and so on. This is to be

addressed in an international, cross-border set-up given the economic potential of international implementation of cell-based therapies. Producing cell-based therapies combines a multitude of different technologies and requires close monitoring of the cellular status. Single cell technologies (imaging, sorting, cell culture, omics, …) become increasingly important in this field as well.

Gene therapy is one example of ATMPs that is quickly becoming one of the most prominent new frontiers of medicine. Most vaccines used to fight COVID-19 are a part of this new paradigm. Some gene treatments have been here before the pandemic, while many new ones are now joining medicine as approved treatments for melanoma, spinal muscular atrophy, lymphoma, multiple myeloma, leukaemia and others.

Gene therapies are essentially about using genetic code to benefit the patient. It can use different delivery mechanisms (viral vectors, lipids, electroporation, and others) or gene altering tools like CRISPR-Cas. Gene therapies have a particularly close association with PM, since many diseases are only now discovered to not be parts of larger families of diseases because of their similar profiles of symptoms, but are rather rare diseases with a distinct genetic profile.

- *Single cell analysis, diagnostics and personalised medicine*

Single cell analysis is the study of gene expression profiles between individual cells. It can combine genomics, transcriptomics, metabolomics and cell-cell interactions to study the heterogeneity seen at the single cell level. It makes it possible to study mechanisms that are overlooked when investigating a bulk population of cells.

Lab-on-a-chip is one of the technologies that allow single cell characterisation and stimulation. Ultimately, organ-on-chip applications may be developed. Organ-on-chip technology aims to mimic human organs and organ systems in vitro on a microfluidic chip. As such these models will provide a better understanding of health and diseases, and can be used as first cohorts in on drug development and cell biology.

These technological developments require the combination of cell biology (e.g. biomarkers), semiconductor technology, microfluidics, imaging, data processing, … Also, a lot of challenges are to be taken to industrialise these new types of tools. New infrastructure and data processing systems are thus required to further invest in cell-based therapy.

- *Enabling technologies*

An enabling technology is innovation that drives radical change in the performance and capabilities of users. The technology can be cover several ecosystems and areas, including for example biopharmaceutical production technologies, biomaterials or drug delivery.

Another example is innovation in medical imaging. Non-invasive medical imaging technologies allows for higher resolution, specificity and sensitivity, and can create more targeted approaches. It includes more traditional radiology technologies, as well as MRI or PET for example. It also includes research in the field of image processing and artificial intelligence software. Nuclear medicine is a speciality that uses radioactive tracers or radiopharmaceuticals to diagnose or to treat diseases. Also innovation in proton therapy falls under this topic. It require profound knowledge of biology, imaging, radiology and nanotechnology as well as IT.

3. Preventive health

The health of an individual can be characterised by the following equation:

Health = Genome (human + microbiome) + Lifestyle + Environment

Health and disease status are affected by our lifestyle, while self-management is becoming more and more evident as an essential driver for our health and wellbeing.

Lifestyle = Exercise + Dietary Intake + Behaviour

In general, health promotion and prevention are intertwined activities affecting citizen's health and wellbeing. The COVID-19 pandemic has proven more than ever the need for prevention. Nevertheless, the share of health-care expenditures allocated to prevention remained limited so far - in 2018, prevention represented only 2.8% of total health expenditures in Europe countries, making it timely to address this issue[1].

- *Preventive medicine and positive health*

Being healthy is more than the absence of disease. Positive health focusses on the promotion of wellbeing and healthy lifestyles (exercise, nutrition, mental health) and can contribute to a healthier, longer life. Preventive medicine proactively focusses on preventing diseases. It may include screening for genetic predisposition and its interplay with the (social) environment and lifestyle.

Chronic non-communicable diseases (NCDs), such as heart disease, cancer, diabetes, Alzheimer or chronic lung or kidney disease, are the world's leading cause of health burden and mortality and are continuing to increase in both incidence and prevalence, hence putting increasing pressure on healthcare systems and society. According to a study of the World Economic Forum in 2011, NCDs are expected to cost USD 47 trillion by 2030 or 75% of the annual global GDP in 2010 (Bloom et al., 2011[1]).

The challenge for healthcare in the 21st century is to deal with the complexity of the so-called non-communicable diseases and the often 'silent' transition from health to disease. Very often, the late onset of symptoms is delaying treatment, while a shift towards prevention may generate more health life years at the benefit not only of the patient and his surroundings, but also of healthcare systems and economy in general as chronically ill cannot fully contribute to the economy.

Many of the chronic diseases can be prevented or delayed through adoption of a healthy lifestyle throughout the lifespan generating more healthy life years, free of disease. Early detection and characterisation of predisposition of certain conditions will become more important to develop preventive medicine. As the interaction between genomics, environment, and lifestyle and diet becomes better understood, the ability to predict risk and prevent chronic disease will further improve. Impact can be made for the healthcare systems, because less costs and care have to spent when health is maintained longer. Increasing the number of healthy life years, and decreasing the number of comorbidities, will also increase the wellbeing of individuals and their surroundings. This will also strongly impact the economy as people and the informal caregivers remain longer economically active, when diseases are avoided or postponed. The average life expectancy in Europe is above 80 years, however, over a fifth of that is spent in bad health[2].

[1] https://ec.europa.eu/eurostat/web/products-eurostat-news/-/ddn-20210118-1

[2] https://op.europa.eu/en/publication-detail/-/publication/96d27995-6dee-11e8-9483-01aa75ed71a1

- *Patient empowerment*

Patient and citizen empowerment allows patients, and their caregivers, to gain more control over decisions and actions affecting their health. Engaging and involving patients/citizens in the management of their own health as well as in research and innovation, may result in more relevant clinical questions and patient-centred health outcomes.

- *Reinforced primary care*

There is an ongoing trend to reduce hospital-time and procedures for patients. With the advance of tele-monitoring, care will move more towards primary and home care. This requires the reinforcement of primary care, for example by nurse-led clinics, or the organisation of community care. Innovation and projects to organise this shift fall under this topic.

4. Sustainability of health

PM is strongly technology and data driven, and technological advancement is accelerating at high pace. This results in a lag in the implementation and regulation of PM and training programmes preparing for jobs of the future. Reducing this backlog will not only support the increase of healthy life years, it will also secure the sustainability of our healthcare systems.

- *Training for jobs of the future*

The rapidly evolving technologies and developments linked to personalised medicine need training of new talent to enhance capacities and capabilities of actors involved in the development and implementation of PM. This involves not only the next generation of healthcare professionals (doctors, nurses,..), but also biomedical researchers as well as IT-specialists (digital health and care). Training for job of the future both involves the updating of curricula as well as lifelong learning courses.

Also vocational training is part of this topic. It refers to courses that focus on skills required for a particular job function. It provides hands-on, job-specific skills. It allows us to prepare the next generation of healthcare workers, and to ensure implementation of health innovation.

- *Regulatory preparation*

Innovative healthcare products or therapies such as personalised medicine, ATMPs or medical devices can have complex regulatory requirements. The novelty of many products can make it challenging to find good guidance for their regulatory needs. Demo cases under this topic can develop tools or services for researchers or start-ups that aim to bring their new products or therapies to the market.

- *Implementation sciences*

Implementation sciences involves methods and strategies that facilitate the uptake of evidence-based practice and research into regular use by practitioners and policymakers. The field of implementation science seeks to systematically close the gap between what we *know* and what we *do* by identifying and addressing the barriers that slow or halt the uptake of proven health interventions and evidence based practices.

Proposed joint action lines

Defining common application domains and vision - Enlarging the partnership

The participating regions agreed on a selected number of demo cases to work on that each cover potentially important value chains which may be developed for a further investment agenda. The demo cases to be developed under the pillars are flexible and will be regularly updated.

1. Under Pillar “Data and digital technologies”

- *A personal data management platform, We Are*

Based on the GDPR, opportunities are created for the citizen to manage and combine their own health data themself. A platform can be created to manage personal health related information, linking genomics to lifestyle information.
This, in combination with a good governance, may create a new trust and provide a competitive landscape for big & small companies and for research in academia and industry. The development of such a platform is challenging and opens significant opportunities for innovative applications.
A personal data platform would empower citizens to support research. A value chain could be created based on personal data in a cooperative model. The governance of the data platform is key to create trust. Such development may be developed at regional-interregional levels and then grow and expand. Generating trust is essential. This may also be discussed in the frame of the 1 million genomes project that is being developed. The Pan-European approach is a perfect base for in depth standardisation of data and cross-border data sharing.

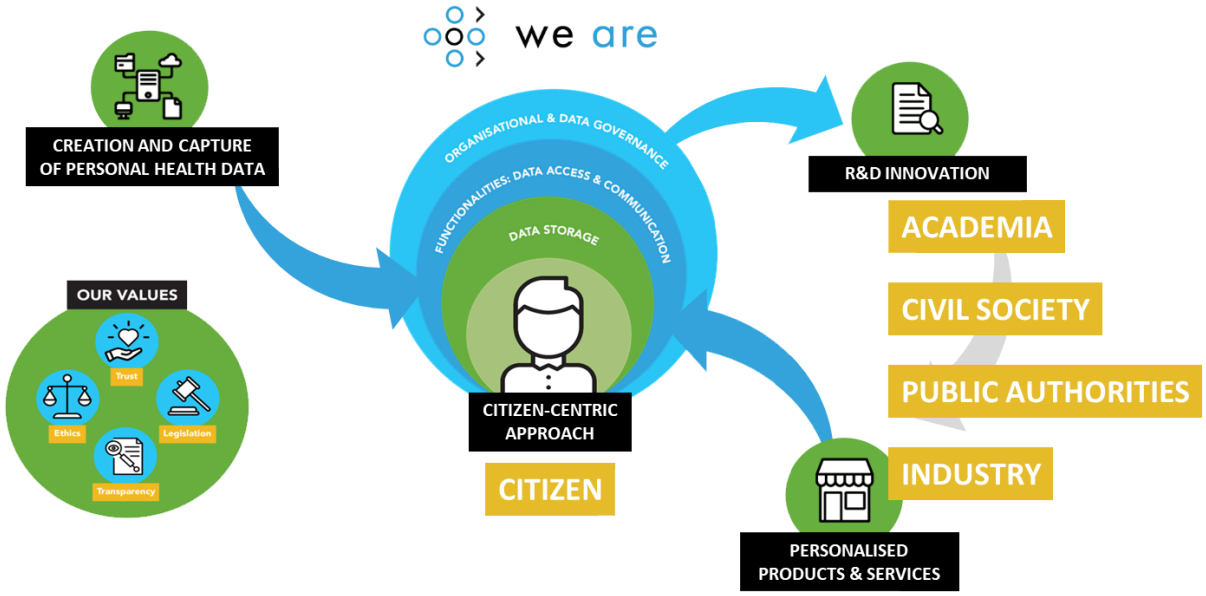

Figure 2: We Are demo case.

<u>Economic and industrial impacts potential</u>

The developments towards novel PM applications strongly rely on access to data. Data is required to be able to stratify populations and will help to develop preventive strategies or to design the right treatment for the right person.
The development of a data platform holds significant opportunities for different industries. New applications may be developed related to data storage and security, while ensuring access to metadata as a source to develop new applications. Those new applications are likely to be developed by artificial intelligence and machine learning. These developments will become increasingly important over time, the basis will be a personal data management platform.

It will provide people with access to a new way of taking care of their overall well-being and, at the same time, will promote service providers' ability to form customer-oriented and dynamic service chains in collaboration with other operators and to manage their activities based on up-to-date information. The aim is to increase trust in data sharing, promote the digital data portability and enhance real time exchange of information between service provides in the society and in the integrated care model. Research on the data analytics/DataAI will strengthen our ability for new kind of utilization of information, and model future, virtual service system with novel data flows, which did not exist before.

Societal impact potential

People have a growing awareness of the value of their personal data. They are concerned about how it's being used by public and private entities.

A personal data management platform may address these concerns and create the trust - based on ethics and safeguarding privacy - that is needed if personal data are to be used as a resource to create new insights as a basis for stratifying populations and for new applications for personalised medicine. Making personal data fully compliant with the GDPR rules should guarantee control over the use of one's own data, and hence will create confidence that the data is not misused. Creating sufficient trust for the use of personal data is an essential requirement to ensure public participation and providing access to data for research purposes and development of PM. A personal data management platform may thus deliver an important societal impact as this would address one of the major challenges of the need for data for to fully develop PM and the growing concerns on privacy and ethics related to open access to personal data.

There is a growing awareness among consumers and hence they demand more control. Organisations acknowledge the growing risks associated to safety and management of data, while authorities implement strict legislation to ensure privacy.

2. Under Pillar "Converging technologies"

- *Cell and gene hub*

Focusing on innovative cell-based approaches is very challenging. The opportunities are huge, and the results promising. There are challenges at different levels as the procedures are labour intensive and not automated, while procedures need to be performed under strict temperature control and sterile conditions according to good clinical and manufacturing practice regulation. The convergence of biomedical excellence to chip technologies will generate novel opportunities.

The development of a hub combining all expertise needed for this field to advance would generate a unique selling position, and ensure the participating regions are in leading position. The developments are expected to lead to different spin-out activities/ applications, such as lab-on-chip or organ-on-chip development.

There is a need for new talent and functionalities and the convergence of technologies is essential.

- *Cell-based immune therapy*

Setting up a cell hub that would contribute to the development of immunotherapy e.g. for cancer treatment would allow to specialise in a very challenging niche that opens opportunities at different levels, including dedicated transport, manufacturing, … while at the same time bringing this most promising treatment of cancer within reach of all in clinical routine.

- *Regenerative medicine*

Stem cell-based therapy addresses major societal challenges directly related to ageing of people and chronic health issues. Growing new bones and cartilage or growing biosynthetic organs will contribute significantly to maintaining the quality of life of an aging population.

New applications based on using stem cells are not only offering novel treatment options for chronic diseases related to ageing, spin-out applications such as organ-on-chip will be developed. In this area, the RegMed-XB programme combines the complementary expertise of the Flemish and other Dutch partners. Building on this RegMed-XB ongoing collaboration further developments may be envisioned by including complementary assets and expertise.

- *Non-invasive medical imaging*

Nuclear medicine is a promising interface area of translational research and development with the aim to improving diagnostic, therapy and implicitly disease prognosis. It can target a variety of diseases, including several types of cancer, some of them with very limited therapeutic options nowadays. An ecosystem covering the entire value chain of the radiopharmaceuticals' industry from research and development to production, by fostering coordination and breaking down existing silos would reduce the lead time and improve the efficiency. The TRACE-MED demo case will create such an ecosystem and will coordinate the research activities needed for the production of linker/carrier nanoparticles. This will help the platform to quickly bring new radiolabelled molecules onto the market. Providing the most suitable molecules for SPECT and PET technologies, to be used in theragnostic approaches will allow for more personalised therapies.

<u>Economic and industrial impacts potential</u>

The applications based on deep understanding of cell control are increasing and demonstrate the strengths of these novel applications in cancer treatments, in gene therapy or in regenerative medicine. These applications, however, are still very costly and not yet available in general clinical practice as healthcare systems are hesitant to reimburse costly treatments based on cell technologies. Costs may be reduced when procedures would be automated and standardised. So far most of the procedures need the expertise of cell technologists. Developing a cell and gene hub to develop automated procedures and standardised production of cells and tissues for the new applications would be a major breakthrough. Such and integrated technology platform would also lead to spinout activities such as cell- or organ-on-chip.

Molecular diagnostics are a segment that will be important for the areas described and are based on the convergence of digital and life sciences, and represents the fastest growing segment within the in vitro diagnostics area, amongst others because of the precision, sensitivity and fast lead time, and cost efficiency. The market for molecular diagnostics was in 2015 good for over USD 6,4 billion, and the compound annual growth rate (CAGR) is expected to grow over the following 10 years until 2024 with 9%. Molecular diagnostics are used for infection diseases, oncology, genetic testing and tissue characterisation. It can be expected that the growing insight on the genetics of diseases will bring new personalised solutions and therapies for more disease domains with higher precision. The partners in the Smart Health pilot represent a significant number of large and smaller companies that are actively involved in the development and production of new molecular tests and tools.

<u>Societal impact potential</u>

Cost reduction of cell based applications would realise a major societal breakthrough and ensuring access to these novel and efficacious technologies for all, while ensuring sustainability of healthcare systems.

Cell based technologies also include guaranteeing strict temperature and sterility control throughout all procedures. Ensuring dedicated transport to bring cells and tissues from patients to lab and back to patients require special infrastructure and skills , also for not-academic trained people.

3. Under Pillar Preventive health

- *Preventive medicine*

Increasing access to technologies to monitor general health parameters and indicators of wellbeing combined with the wealth of information from -omics technologies is driving a paradigm shift in healthcare towards prevention and prediction. Medicine is becoming more personalised and but the biggest health gains to be made, will be when diseases can successfully be prevented. Given the worldwide social-economic challenges associated with NCDs, healthcare systems and society at large could benefit significantly from the uptake of personalised prevention at the core of healthcare.

An example of a preventive health programme is the Diabetes on Return programme. In Europe, there are about 60 million people with diabetes, and this number is increasing every year. In some people it develops because of an autoimmune disease (type 1 diabetes), in others it is the result of an unhealthy lifestyle (type 2 diabetes), sometimes in combination with genetic factors. Diabetes often leads to an array of physical problems: poor blood circulation, nerve damage, eye and ear complaints, kidney problems, heart disease and much more. Consequently, both morbidity and mortality among diabetes patients is high.

Given the high morbidity and mortality, and consequent high costs of the disease, it is important to ensure that the number of people with diabetes is decreasing, and that the disease impact is less severe for those who do get it. With the Diabetes on Return program, research and development is undertaken to make this possible. Scientific institutions, healthcare institutions, and technology, nutrition and care companies are collaborating to develop tools to provide tailor-made support to patients, working closely with people at-risk for diabetes or people who already have the disease.

<u>Economic and industrial impacts potential</u>

Addressing NCDs is one of the recommendations from the WHO as the burden for society are immense. NCDs are often related to lifestyle and nutritional habits. Adopting a healthy lifestyle will help to reduce NCDs and realise significant benefits for economy. Increasing the number of healthy years ensures longer economic activity and reduces pressure on healthcare systems.

The development of preventive medicine is linked to the development of diagnostics but also to sensors and wearables that monitor health and lifestyle parameters. Developments related to miniaturisation are increasingly important. This opens wide opportunities for diverse activities and sectors.

<u>Societal impact potential</u>

Preventive approaches provide clear societal benefits. However, there are also important ethical considerations to be taken into account. As diagnostics are becoming increasingly sensitive and more biomarkers are being identified, diagnosis before any symptoms are visible raises questions of what is health and what is a disease. In addition, adopting a healthy lifestyle to prevent a certain disease may not be acceptable to individuals. The issue then arises whether healthcare systems should intervene in cases of known, but not followed opportunities of disease prevention. The health-disease continuum is an area of reflection for social and humanities scientists.

Furthermore, the development of novel technologies aim to ensure that the pressure on healthcare personnel is relieved, but that patients can also check their health better and more often, allowing them a better control over their own health. Ideally, these technologies are seamlessly integrated in the patient’s own environment, in collaboration with different healthcare providers

4. Under pillar Sustainability of healthcare

- *Training for jobs of the future across the different PM topics*

The rapidly evolving technologies and developments linked to personalised medicine need training of new talent to enhance capacities and capabilities of actors involved in the development and implementation of PM. This involves not only the next generation of healthcare professionals (doctors, nurses..), but also biomedical researchers as well as IT-specialists (digital health and care).
Not only technologies are affecting the education and training landscape, there is also a shift in the traditional doctor or healthcare professional (HCP)-patient relationship. Patient-empowerment and self-management demand also a re-positioning of the healthcare system at large. Education and training programmes need to take these changing relationships into account as well. It is fair to assume that digital technologies will be instrumental in this (care-at-home, social media, tele-monitoring, video-consults etc.).

The next generation of HCPs require new skill sets to lead the implementation of personalised medicine into mainstream healthcare. Traditional curricula no longer provide a solid base with all the skills needed to optimise implementation of this revolution now underway in medicine. Add-ons (customized) to existing education programs may be the way forward to secure that the next generation of HCPs are able to acquire the skills set needed to fully reap the potential of what personalised medicine has to offer.

However, developing training or even determining which skills will be needed is hard to foresee for jobs that do not exist yet and are likely to change over the years to come. Hence, education and training systems should be capable of responding to the future needs and jobs. As PM relies on the convergence of technologies, cross-disciplinary programmes should be integrated in the education and training programmes. Social sciences and humanities may provide additional added value to address the challenges linked to education and training in the high tech based implementation of PM.

- *Regulatory preparation and implementation sciences*

PM develops at high pace, but sometimes its uptake can lag behind. A gap exists between the development of innovative therapies or tools and the scale up or implementation in, for example, a hospital setting. Implementation science is “the scientific study of methods to promote the systematic uptake of research findings and other evidence-based practices into routine practice, and, hence, to improve the quality and effectiveness of health services.”[3]
Implementing and sustaining innovation is a complex undertaking, that involve several components and needs to be adapted to local contexts, where multiple people interact. Implementation science thus needs trans-disciplinary research, including health services researchers, economists, sociologists, anthropologists and operational partners such as administrators, clinicians and patients. Although implementation sciences is broader than PM alone, in this pilot only demo cases linked to the implementation of PM innovation are considered.
Living labs can help in providing test beds for healthcare settings where innovation can be experienced in real live settings.

Regulatory aspects deserve special attention. The EU regulatory framework for pharmaceuticals offers tools and procedures to help high quality products to reach the market. This is complemented with the *in vitro* diagnostics and medical device legislation, the clinical trials regulation, regulation for medicinal products for rare diseases or for advanced therapy medicinal products and so on. It can be complex and innovators often struggle to identify the right legislation and good practices to comply to. Furthermore, timely and close collaboration

[3] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4573926/

with the EMA helps with collecting the evidence needed for approval of the personalised medicine products. Under this pillar, projects or services fit that assist researchers and innovators to find the relevant regulations and to collect the required evidence. Also networks or exchange platforms that bring together the needed expertise fall within the scope of this pillar.

Economic and industrial impacts potential

Personalised medicine relies on significantly increasing amounts of data monitoring one's condition. Understanding these diverse parameters is essential to make the right decisions for therapies or design of clinical trials and hence generating direct scientific impact. Training programmes for health care professionals to deal with the increasing numbers of parameters will generate major societal impact as decisions for treatments will be better informed and guarantee that all healthcare centres provide best quality treatments.
The economic impact that will be generated through these developments will be clear for the healthcare systems and for patients that receive the best dedicated treatment.

Societal impact potential

Creating awareness and training of public and of HCPs will accelerate PM implementation. Implementation sciences will further identify the most efficient way to implement PM solutions. This should ensure to provide the best treatment for the right person in the right time. Creating methods to ensure standardised interpretation may help ensure access to the best treatments for all.

Developing the value chains

Highlighting the strategic positioning of selected value chains by each partner region

Each region of the partnership is expected to provide qualitative, and if possible quantitative, background information describing key assets (e.g. existing technology clusters; numbers of actors; strategic key players; etc.) and, possibly, also describing how the cooperation through the platform is relevant.
Based on the mapping information along the different identified action lines described above, value chains supporting PM may be constructed. These value chains will be used to attract other regions with complementary assets to develop these value chains further. In addition, more value chains may be developed as the partnership is broadening. Lead and co-lead regions to develop these value chains will be agreed. These regions should commit and engage in producing relevant data and assure the participation in meetings and events.

Completing the mapping for each partner Region

The partner regions will complete the cluster/actor analysis on the agreed value chains in order to map existing competences/actors contributing to these value chains. This should help to:

- Identify additional actors and assets
- Identify common challenges/problems encountered by end-users/companies;
- Identify existing initiatives, programmes and tools, including specific allocated budgets;
- Identify the available internal resources (human and financial) to actively participate to the development of the selected value chains

Creating a pipeline of joint activities

In a preliminary exercise the following priorities (value chains) were identified:
1. Health data ownership - Personal Data (Co-lead Flanders)
2. Cell and Gene Hub (Co-lead Flanders)
3. Regenerative Medicine (Co-lead Limburg - Flanders)

4. The case for Prevention – Preventative Medicine (Co-lead East Netherlands)
5. Inter-regional platform for new radiotracers development in personalized medicine, TRACE MED (Co-lead: Nord-Est Romania)

This is by no means an exhaustive list, but it is meant to steer initial discussion with interested partner regions. We expect a growth of identified value chains in the future, when the partnership will grow over the next two years.

Framing developments under 'PM thematic areas'

This pilot will bring the agenda to implement personalised medicine to the next level while transforming the connected European industrial value chains. The pilot is active in the four phases of the Vanguard methodology. The network has been established as a learning- and co-creation community, which exchanges knowledge on a regular basis by organising tailormade workshops and connecting the different regional stakeholders in events or digital seminars. This connection is based on the quadruple helix; involving stakeholders from research & innovation, businesses and field labs, regional and local governments, hospitals and healthcare centres as well as clients and citizens. Demo-cases will be brought forth by partner regions. After an initial presentation of the demo-case proposal, complementary expertise will be assessed. A GAP- and SWOT-analysis will highlight the knowledge that needs to be added to the project and identify the pilot partners best suited to take up the role in question. The demonstration phase will entail the operation of interregional use cases based on the four pillars. The implementation in the regions will enable the last phase of commercialisation of new products and services by the private sector.

Conclusion

The Vanguard Initiative Smart Health pilot will bring the agenda to implement personalised medicine to the next level. The pilot will bring regional ecosystems together on topics related to smart health and personalised medicine. By this, a higher added value will be reached which will boost the implementation of personalised medicine. A better integration and coordination of ongoing regional activities can enforce the impact of the different actions.