

The Swiss approach to precision medicine

Meier-Abt Peter J.^a, Lawrence Adrien K.^b, Selter Liselotte^b, Vayena Effy^c, Schwede Torsten^d

^a Swiss Personalized Health Network (SPHN) and Swiss Academy of Medical Sciences (SAMS), Bern, Switzerland

^b Management Office, Swiss Personalized Health Network (SPHN), Bern, Switzerland

^c Department of Health Sciences and Technology, ETH Zurich, Switzerland

^d SIB Swiss Institute of Bioinformatics and Biozentrum, University of Basel, Switzerland

Summary

Precision or personalised medicine/health aims to prevent, diagnose and treat diseases by taking into account individual variability of genes, environment and lifestyle for each person. In order to tap the full potential of the increasing amount of molecular, biological and clinical health data, new infrastructures are required that permit collection, storage and analysis of high quality data and adequately link biobank samples to clinical data. Many countries have started to build interconnected “precision/personalised medicine ecosystems”, but the federalist and heterogeneous healthcare system has so far prevented nationwide coordinated activities in Switzerland. Therefore, the Swiss Personalized Health Network (SPHN) initiative has been launched. Its mission is to lay the foundations for personalised health on a national level by the development of a nationally coordinated interoperable data infrastructure to enable nationwide accessibility and exchange of health-related data. This paper describes the goals of SPHN, its current procedures and funding regulations, its organisation, its ethical and legal framework for responsible data processing, its data management infrastructure and information security and its relevant partnerships with other organisations and institutions. Although the SPHN initiative starts with the institutions of higher education such as university hospitals, universities and the ETH domain, other hospitals, public health institutions and medical practitioners, as well as private institutions such as industry and health insurers, will be included into the initiative at a later time point. Ultimately, the SPHN initiative shall lead to the development of an effective Swiss personalised health ecosystem, which is required to advance effective individual prevention, diagnosis and treatment of disease states and to push Switzerland to the international forefront of personalised health-related research and health care.

Key words: *precision medicine, personalised health, Swiss Personalized Health Network (SPHN) initiative, Swiss interoperable health data infrastructure, ethical and legal framework for responsible health data processing, health data management infrastructure and information security*

Correspondence:

Peter J. Meier-Abt, MD,
Swiss Personalized Health
Network (SPHN) and Swiss
Academy of Medical Sci-
ences (SAMS), Laupen-
strasse 7, CH-3001 Bern,
Switzerland, Peter.Meier-
Abt[at]unibas.ch

Introduction

Precision medicine is “an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person”. This definition by the US National Institutes of Health (NIH) is similar to and closely overlapping with the definition of personalised medicine that “seeks to improve stratification and timing of health care by utilising biological information and biomarkers on the level of molecular disease pathways, genetics, proteomics as well as metabolomics” [1]. Still other terms are used for the same concept such as “individualised (systems) medicine”, “stratified medicine” and “P4 (predictive, preventive, personalised and participatory) medicine”. Although this variety of terms is unfortunate and continues to create confusion about their real meanings, it is important to realise that basically they all stand for similar goals and expectations. It is true that the practice of medicine always has been tailored to the individual characteristics of each patient. Also, genetic polymorphisms, i.e., multiple variants of single genes between individuals, have been taken into account for individualisation of drug treatments for decades [2, 3]. Thus, the basic concept of precision/personalised medicine is not new. However, what is new is the enormous potential and promise for new discoveries based on the advances of “-omics” and information technologies since the sequencing of the human genome in 2004 [4]. Here we use the terms “precision medicine” and “personalised medicine” interchangeably. Furthermore, to extend the concept of precision/personalised medicine to public health and the prevention rather than treatment of diseases, the term personalised health is preferentially used in this article. More than ever before we can today collect and analyse large amounts of health-related data from molecular constituents of cells (genes, epigenetics, proteins, metabolites, etc.) to clinical phenotypes of diseases (imaging, electrophysiology, etc.) and to personal lifestyle and environment (lifestyle tracking, “quantified self”). Increasingly, wearable or embedded devices connected via a network allow interaction with patients in real time, enabling new approaches in diagnostics and individualised therapies. These data have an enormous potential for biomedical research and individual health care in the future, provided they are accessible and used effectively for meaningful correlation and association studies. “Big health data” will increasing-

ly drive biomedical research and probably reverse the traditional paradigm “from experimental animals to humans” [5, 6] into “from first in humans to validation in animals” as, for example, is already being done in investigations of the role of epigenome-based alterations for human cancer [7]. To tap the full potential of health data for the benefit of individuals, close links between basic molecular genetic research, imaging facilities, medical laboratories, clinicians and clinical information systems are required. The development of such a “precision/personalised medicine ecosystem” requires new infrastructures that permit collection, storage and analysis of high quality data and adequately link biobank samples to clinical data [8]. Furthermore, patients and citizens have to be included, not only for consent to release their data or samples for use in research, but also as active partners supporting research and helping to advance medical knowledge [8]. These issues raise unprecedented ethical and legal (e.g., data protection) questions that must be considered even more within an extended personalised health ecosystem.

The international scene

In view of its potential and the high expectations and promises for global health [9], it is not surprising that worldwide numerous [national initiatives](#) have been launched over the past decades to foster the development of personalised health. For example, as early as 1999 the Estonian government decided to create a population-based biobank that has the right “to collect, store and use biological samples and phenotype information for genetic research and is further expected to use the results to improve public health” [10]. Since this innovative and future-oriented decision, Estonia has reached further milestones towards personalised medicine, including the development of a nationwide technical infrastructure allowing secure electronic exchange of medical information, as well as accessibility of medical data from hospitals, primary care physicians and pharmacies in a strictly regulated manner [10]. Meanwhile other countries with universal health care and comprehensive medical registers have developed similar precision medicine programmes on a national scale, including Denmark, France, the Netherlands, Sweden [11] and the United Kingdom. The UK government mandated the Department of Health to initiate the [100 000 Genomes Project](#), the goal of which is to sequence 100 000 genomes from National Health Service (NHS) patients by the end of 2017, and thereby “to create an ethical and transparent programme based on consent, to bring benefit to patients and set up a genomic medicine service for the NHS, to enable new scientific discovery and medical insights”. On the European level the International Consortium for Personalized Medicine ([ICPerMed](#)) was established following the [PerMed project](#) funded by the European Union's 7th Framework Programme (FP7). The consortium is composed of over 30 European and international partners representing ministries, the European Commission, and funding agencies. ICPerMed aims at positioning Europe as global leader in personalised medicine research by providing a platform where members can exchange and coordinate research and funding activities at the European level and later at the global level [12]. Outside Europe a Precision Medicine Initiative (PMI – renamed “[All-of-Us](#)”) was

launched in the USA in 2015 [13]. As part of its objectives, the initiative aims to create a voluntary national research cohort of 1 million participants, to provide better treatments for cancer via the identification of genomic drivers, to modernise the regulatory landscape, and to partner with relevant private and public actors. This initiative has highlighted the importance of public participation in research and has reinforced the idea of partnership with research participants as a driver of the initiative [14]. And even more impressive, China announced the launch of the “[China Precision Medicine Initiative](#)” in March 2017 with an estimated budget of US\$9.2 billion over 15 years, indicating that China is about to take the global lead in precision/personalised medicine [15]. And finally we would like to mention the Global Alliance for Genomics and Health ([GA4GH](#)), which includes over 400 institutions that are active across multiple industries such as health care, research, disease advocacy, life science, and information technology. The mission of GA4GH is “to accelerate progress in human health by helping to establish a common framework of harmonised approaches to enable effective and responsible sharing of genomic and clinical data, and by catalysing data sharing projects that drive and demonstrate the value of data sharing” [16]. This enumeration of precision/personalised medicine initiatives is not exhaustive. Many other countries have also launched programmes to advance personalised health. These worldwide activities underline the importance of this scientific development and reflect realistic optimism for significant improvements in health care provided the required cultural change in medical practice will be achieved and the necessary personalised health ecosystem can be developed.

What about Switzerland?

Switzerland does not yet have a strong international presence in precision/personalised medicine and/or health. Undoubtedly, Switzerland has an excellent, albeit expensive, healthcare system. Also, the Swiss institutions of higher education (e.g. universities, [ETHZurich](#), [EPFLausanne](#) [www.swissuniversities.ch]) have excellent reputations in science and education. Although the public Swiss healthcare system is universal, healthcare is provided by a combination of public, subsidised private and totally private systems, and is organised largely on the level of individual cantons. This federalist principle, which also applies to the Swiss education system, until now to a large extent prevented a nationwide coordination and/or harmonisation of biobanks, electronic clinical information systems and clinical data management infrastructures. This heterogeneity of health data infrastructures has retarded the development of a nationwide personalised health ecosystem as compared to countries with more homogenous national health systems (see above). However, the deficiencies have been realised and appropriate initiatives have been undertaken on local and regional levels. In 2013, “Health 2030”, a multicentre and multidisciplinary initiative was started by several institutions in the Lake Geneva region to promote research, training and services in the field of digital and personalised health in western Switzerland (<http://health-2030.ch/>). The Universities and University Hospitals of Geneva, Lausanne and Bern, as well as [EPFLausanne](#), have decided to team up to create the first

genome centre in Switzerland. This centre will further develop genome expertise in Switzerland and make gene sequencing (DNA decoding and analysis) more accessible, thus contributing to the development of personalised health care. In the eastern part of Switzerland, the University of Zurich and the ETH Zurich founded in 2014 a [competence centre for personalised medicine](#), which drives the development, complementary to the Lake Geneva centre, special expertise in proteomics and metabolomics. This centre has recently been extended to the Zurich-Basel Health Alliance [17]. These initiatives demonstrate that Swiss scientists and clinicians have realised the necessity to team up to be able to perform personalised health-related research on an internationally competitive level. Moreover, a [Swiss Biobanking Platform](#) (SBP) has been created “to help Switzerland consolidate its position at the forefront of biomedical research by facilitating access and optimal usage of its existing and future biobanked specimens” [18]. What is needed further are close links between biobank samples and clinical disease phenotype data. Furthermore, the local/regional initiatives have to be expanded to the whole of Switzerland and complemented with a nationwide effort for making health data (e.g., clinical, molecular, laboratory, and imaging data) findable, accessible, interoperable and usable for research (FAIR) on a national scale. For this purpose, the Swiss Personalized Health Network (SPHN) initiative was launched in 2017. It will help to push Switzerland to the international forefront of personalised health-related research and health care.

The Swiss Personalized Health Network (SPHN) initiative

Mission

The mission of the [SPHN](#) initiative is to promote the development of personalised medicine and personalised health on a national scale in Switzerland [19]. SPHN will lay the foundations that are needed to facilitate research projects in this area, such as the development of a nationally coordinated interoperable data infrastructure to enable nationwide accessibility and exchange of health-related data. Rather than creating a centralised database, SPHN will build a dynamic network of existing data sources and fund the efforts that are needed in order to make data nationwide interoperable and sharable for research. The ultimate goal is to promote personalised health and wellbeing, by being able to prevent, diagnose and treat unfavourable individual health conditions more precisely. This will allow the risk of developing such conditions to be reduced and permit more effective treatments of disease states with fewer adverse events. Ultimately, the SPHN initiative shall lead to the development of a personalised health ecosystem on a national level [8, 19], which is required to advance effective individual prevention and treatment of disease states.

SPHN organisation

At the beginning of 2016, the Swiss Academy of Medical Sciences ([SAMS](#)) was mandated by the State Secretariat for Education, Research, and Innovation ([SERI](#)) and the Federal Office for Public Health ([FOPH](#)) on behalf of the Swiss Confederation to implement the SPHN initiative. The SPHN project organisation involves partners at the na-

tional level, at the technical level, and at the institutional level. SAMS is the overarching body of the project.

The National Steering Board (NSB) is the highest governing body of SPHN and is responsible for the overall strategy, for maintaining regular contacts to the superordinate political authorities and for external communications in coordination with SAMS. It includes representatives from key institutions in Switzerland (e.g., university hospitals, universities, ETH-Domain, swissuniversities, SNSF, SIB Swiss Institute of Bioinformatics, a patient organisation). The members of the NSB are appointed by SAMS on behalf of the Swiss government. The integration of representatives from additional institutions (e.g., cantonal and private hospitals, health insurers, industry) is foreseen in the future.

The Executive Board (EB) is the operative body of the SPHN and is responsible for the scientific strategic planning and the operative tasks of the initiative. It comprises experts from a variety of disciplines such as clinical sciences, medical/clinical bioinformatics, epidemiology, etc. The EB suggests projects, themes, and the content of calls for proposals to the NSB that the SPHN initiative could support. In addition, the EB defines the scope and requirements for coordination of data infrastructures and data semantics in collaboration with the Data Expert Group (DEG).

The DEG is an advisory group of the Data Coordination Centre (DCC) at the [SIB](#) Swiss Institute of Bioinformatics. It is responsible for defining standards for data semantics, formats, and exchange mechanisms in order to reach nationwide interoperability of molecular and clinical patient data.

The ELSI advisory group (ELSIag) addresses the ethical, legal and social challenges that SPHN will face. It is composed of experts from various relevant fields such as bioethics, life sciences, law and social sciences. It also includes representatives of SAMS, swissethics, and patient advocacy groups. The group will advise the NSB on the development of guidelines for data sharing or processing and managing questions of intellectual property, authorship and attribution according to national and international standards.

The International Advisory Board (IAB) is composed of international experts. It provides advice, expertise, and peer-review of project proposals and of the initiative as a whole.

Finally, the Management Office (MO) is operated by SAMS and is in charge of the administrative and daily operation of the initiative such as preparation of the meetings of the various boards, controlling, budgeting and reporting.

Current procedures and funding regulations

SAMS acts as the legal entity and bears the organisational, legal and financial responsibility for SPHN, in compliance with the service contract signed between SAMS and the Swiss Confederation for the period 2017–2020. On this basis, the Swiss government has allocated a total of CHF 68 million to the initiative; thereof, CHF 18 Mio are dedicated to the BioMedIT project which is under the responsibility of SIB Swiss Institute of Bioinformatics (see section below). The matching-funds principle applies to all financial contributions: the participating institutions must pro-

vide own contributions (in cash and/or in kind) to match the funds provided by SPHN.

In the first period 2017-2020, funding priority is given to the development of nationally coordinated data infrastructures in order to achieve interoperability of local and regional information systems. This will optimise the use of health-related data from both patients and healthy citizens for research. SPHN is not creating or funding the development of a central database; however, SPHN will fund the additional effort/capacity (e.g., software, personnel) necessary to make clinical phenotype data interoperable and usable for research and to link them with other types of human data (e.g., -omics data, imaging data, laboratory data, etc.).

SPHN has defined three instruments to implement its strategy which are summarised in [table 1](#).

Owing to the sensitive nature of health-related data, the ELSIag has developed an “Ethical Framework for Responsible Data Processing” within SPHN. Adherence to this framework is required for participation in the SPHN funding schemes and activities.

SPHN’s Ethical Framework for Responsible Data Processing

From data generation, to storage, use and re-use, health data such as the data of relevance for the SPHN present several legal and ethical challenges. In Switzerland there is a dense legal grid on which health data activities are based. The Human Research Act, the Data Protection Act and the Human Genetic Act are the closest related to the activities at stake; however, several other laws apply depending on the specific activity. All SPHN activities will be developed in compliance with the requirements of the law. However, beyond the strictly legal compliance, an initiative such as the SPHN requires a clear ethical vision that will guide its trajectory and essentially will determine its impact. The broader aim of interoperable and harmonised data systems that will help advance biomedical science and ultimately will contribute towards improving the health of people is a shared interest. We all are stakeholders in better science and better health. This is at the core of the ethical vision of the SPHN.

The first mandate of the ELSIag was to offer precision to this ethical vision by explicitly articulating the ethical principles that shape the vision. The result of this mandate was the development of an ethical framework for responsible data processing that will serve as the basis on which SPHN will handle all data-related matters. Therefore, the framework should be understood as an instrument of the SPHN’s ethical vision that aims to support SPHN partners in contributing to this vision. In particular, it aims to ensure that the scientific activities in relation to personal data that are conducted in the context of the SPHN meet adequate

standards of ethical sustainability, promote the rights, interests and well-being of research participants, promote the efficient production of valuable scientific knowledge, and generate public trust around the activities of the network. In that respect, the framework is not a directive, but rather a common code that serves our common interest as a society.

Given the sensitive nature of personal data and of health-related information that can be extracted from it, there is universal consensus that such data should be handled with special caution. As a consequence, a number of institutions and governments have issued principles and recommendations regarding data handling in the context of scientific research. (The exact definition of the terms “principles” and “recommendations” as they are employed in this document is provided in the “Work plan and methodology” section of the document.) Most of these documents also contain guidance relative to the issue of data access in human biomedical research. Although there is no consensus on a clearly identifiable set of principles and recommendations in this specific area, some of them are more recurrent than others. The development of the SPHN’s framework was based on systematic review and assessment of such principles and guidelines. The ELSIag identified the most frequently invoked principles and recommendations, and considered them to be the normative standard in the field. On the basis of this review, analysis and further deliberation the ELSIag identified four basic principles that constitute the normative backbone of responsible data processing ([fig. 1](#)). These key principles are:

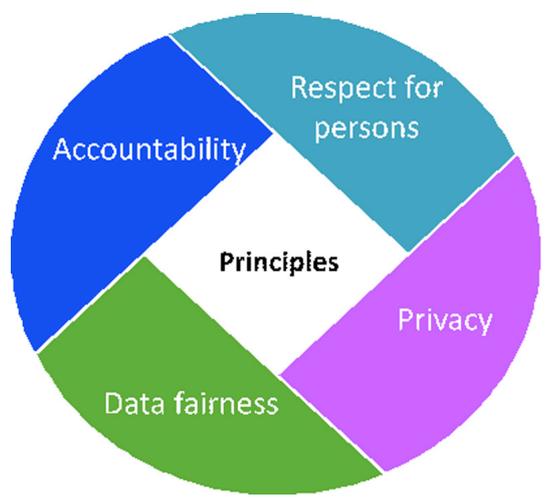
1. **Respect for persons**
This principle requires that the rights and dignity of individuals, families and communities contributing health data in the context of research and clinical care, as well as other types of data that can be useful for biomedical research, are respected, protected and promoted. A central demand deriving from this principle is that of consent for data uses. This includes the responsibilities of data users when consent is revoked- a particularly challenging issue in the world of big data and constant interconnectedness. Furthermore, this principle has implications for the communication of clinically actionable findings to individuals as well as for the return of research results to participants.
2. **Privacy**
This principle requires that the privacy and confidentiality of health data is protected. Privacy protections can be achieved through a number of technical and governance measures. The ensuing guidelines in the ethical framework reiterate the importance of data security and anonymisation standards along with additional controls and oversight of data uses.
3. **Accountability**

Table 1: SPHN funding instruments.

Instrument	Description	Funding scheme
Infrastructure implementation projects	Projects that are devoted to building a progressive shareable data system enabling nationwide interoperability of molecular and clinical patient data.	Collaboration agreement (Leistungsvereinbarung)
Infrastructure development projects	Projects to develop and test new technologies, methods and infrastructures for personalised health related research.	Call for proposals
Driver projects	These projects are based in a concrete research field (e.g., cancer research/oncology) and will push the implementation of a nationwide “personalised health ecosystem” by testing and challenging interoperability between clinical data management systems at university hospitals and other platforms within the whole network.	Call for proposals

This principle requires an accountability mechanism to ensure fair, lawful and transparent data processing. Accountability requires that those processing personal data for research purposes can be held responsible for the consequences their activities may have on both research participants and society as a whole. Procedures and mechanisms adopted to govern their data processing activities should be open to scrutiny. In particular, research participants have a right to access information regarding how an organisation processes their data, including the conditions under which it grants access to

Figure 1: The SPHN Framework for Responsible Data Sharing – key principles. **Respect for persons:** This principle requires that the rights and dignity of individuals, families and communities contributing health data in the context of research and clinical care, as well as other types of data that can be useful for biomedical research, are respected, protected and promoted. A central demand deriving from this principle is that of consent for data uses. This includes the responsibilities of data users when consent is revoked- a particularly challenging issue in the world of big data and constant interconnectedness. Furthermore, this principle has implications for the communication of clinically actionable findings to individuals as well as for the return of research results to participants. **Privacy:** This principle requires that the privacy and confidentiality of health data is protected. Privacy protections can be achieved through a number of technical and governance measures. The ensuing guidelines in the ethical framework reiterate the importance of data security and anonymisation standards along with additional controls and oversight of data uses. **Accountability:** This principle requires an accountability mechanism to ensure fair, lawful and transparent data processing. Accountability requires that those processing personal data for research purposes can be held responsible for the consequences their activities may have on both research participants and society as a whole. Procedures and mechanisms adopted to govern their data processing activities should be open to scrutiny. In particular, research participants have a right to access information regarding how an organisation processes their data, including the conditions under which it grants access to other data users. These basic principles of transparency are constitutive elements of accountability. **Data fairness:** This principle requires that data that can be used for research purposes and research results should be made available for further research use to advance the common good of scientific knowledge. Health data is an invaluable resource that can be used to improved health knowledge and the delivery of health care. This potential generates an obligation to make such data available for ethical research. Data fairness requires that data access is timely and that data are not locked into exclusive access agreements that will hinder researchers from using them. On the basis of this principle and specifically for the purposes of the SPHN, data accessibility should be made possible without financial profit. Figure reproduced with permission from [27].



other data users. These basic principles of transparency are constitutive elements of accountability.

4. Data fairness

This principle requires that data that can be used for research purposes and research results should be made available for further research use to advance the common good of scientific knowledge. Health data is an invaluable resource that can be used to improved health knowledge and the delivery of health care. This potential generates an obligation to make such data available for ethical research. Data fairness requires that data access is timely and that data are not locked into exclusive access agreements that will hinder researchers from using them. On the basis of this principle and specifically for the purposes of the SPHN, data accessibility should be made possible without financial profit.

The idea of the framework is that the demands all four principles must be met simultaneously. It is their synergy, and not pursuit of any of these in isolation, that can ensure the best outcome. On the basis of these principles specific guidelines aiming at facilitating their translation in action were derived. It is worth noting that this framework will continue benefiting from further consultation with all stakeholders and it will be supplemented with additional elements as the networks' needs evolve.

Data management infrastructure and information security

“Real-world” health data and outcomes are considered key to the fulfilment of the personalised health research promise. In a small country like Switzerland, we can only achieve sufficiently large datasets by working together and combining our efforts across the country. However, with few exceptions, the information within the Swiss healthcare system today is fragmented into a plethora of isolated environments, seriously hampering the efficient use of the data for research purposes [20, 21]. Challenges include: data being organised in domain-specific silos using incompatible information management systems; different procedures applied for data collection, quality assessment, metadata annotation and semantic encoding; and divergent local approaches to handling legal processes. As a result, combining biomedical and health information from different hospitals, research institutions, and other sources in order to perform cross-sectional analyses in a meaningful and efficient way is hardly possible today.

The role of the Data Coordination Centre (DCC) at the SIB Swiss Institute of Bioinformatics is to establish a dynamic network of technically and semantically interoperable resources of personal health information, i.e., making clinical information in Switzerland “FAIR”: findable, accessible, interoperable and reusable. During the year 2016, working groups of the DEG on clinical research data warehouses, semantics, interoperability and data quality, infrastructure and security, and bioinformatics and data analysis have developed an initial roadmap for achieving Swiss-wide interoperability of health data for research. One priority will be to ensure that SPHN data standards and interoperability policies are as much as possible aligned with relevant international efforts to facilitate research collaboration and the exchange of analysis tools. As new data

types become available (e.g., novel analytical techniques), new international data standards arise, or new scientific priorities are established, the DCC will regularly revisit and adjust its standardisation and interoperability policies. Collecting large volumes of “big data” alone is, however, not sufficient; a series of other important factors will determine if big data ultimately also becomes meaningful data for research projects: data quality assurance, annotation of data context (metadata), standardisation of experimental protocols, harmonisation of data semantics, availability of «unstructured» and uninterpreted raw data, access to physical samples in biobanks, etc. In the first phase of SPHN, the clinical data management systems at the university hospitals will form the cornerstones of the data integration activities. Significant efforts will be required for generating a patient-centred view of the data and making the complete set of data of a patient with the corresponding informed consent information sharable for research projects.

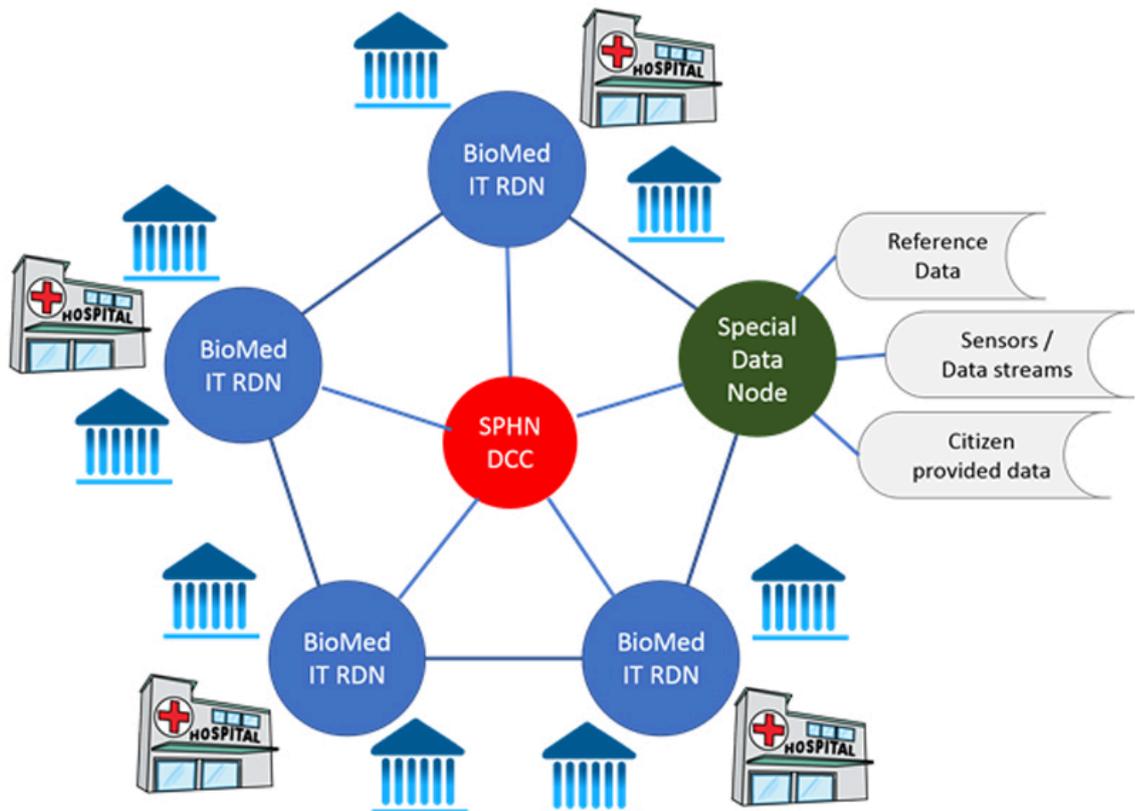
Research on human health data has to fulfil stringent requirements with respect to data protection, IT security and access control in accordance with legal rules and institutional policies. Whereas structured clinical information is relatively small in volume, biomedical data generated by modern analytical techniques, such as next generation sequencing or imaging technologies, is growing at breathtaking speed. Storing, managing, and analysing these data poses significant challenges with respect to IT resources. Rather than establishing an independent IT infrastructure,

SPHN will operate by partnering with established IT competence centres at Swiss universities. The Swiss Research Infrastructure Roadmap Project “BioMedIT” at the SIB Swiss Institute of Bioinformatics will establish a network of secure distributed high-performance IT infrastructures, which are operating under the same standards for data protection and information security, and deploy interoperable compute resources. This network of interoperable data and computing resources has to be dynamic and scalable in order to adapt to new partners and data sources (e.g., other hospitals and care provider, claims data, environmental parameters) joining in the future, and to accommodate new paradigms for data sharing and processing such as citizen-managed data (<https://www.healthbank.coop/>, <https://mi-data.coop/>), or privacy-aware data processing approaches (<https://www.dtls.nl/fair-data/personal-health-train/>) [22, 23]. This will enable the Swiss research community to address the massive data sharing, analysis and integration challenges posed by personalised health research and process data efficiently in compliance with the legal regulations and the SPHN ethical framework for responsible data processing (fig. 2).

SPHN Partners

The integration of all relevant actors is key to the success of the SPHN initiative, in particular in a small country like Switzerland. SPHN will therefore coordinate its activities

Figure 2: Distributed ecosystem of interoperable and sharable data and compute resources. Identifiable patient information will remain at hospitals. Encoded (de-identified) research data with patient consent will be processed on a project basis at regional data nodes (RDN) after appropriate ethical and institutional review. Depending on the specific project requirements, data can be analysed in a distributed manner (computation moves to data), or a defined subset of data can be combined at one of the regional nodes for the duration of a specific project (data moves to computation). The network of interoperable nodes will be progressively extended as needs arise, for instance, by additional data nodes bringing in new types of information or specialised computational services.



with the relevant institutions in personalised health-related research in Switzerland [24].

The SIB Swiss Institute of Bioinformatics plays a key role in the SPHN initiative as it is in charge of establishing the Data Coordination Centre (DCC) and coordinating the BioMedIT project. Supported by the DEG, the DCC will elaborate and define common technical standards for data generation, meta-data and quality annotation, semantics, exchange formats and mechanisms, as well as data protection. The DCC coordinates with university and hospital IT departments, biobanks and the registries of existing and new cohorts. In essence, the DCC's role is to establish interoperability of the various types of health-related data. The BioMedIT project aims to build a coordinated network of secure IT infrastructure core facilities across Swiss universities (regional data nodes), which will enable researchers to efficiently work with confidential data. It provides expertise, software workflows, reference data sets, as well as high-performance storage and computing resources for analysis and interpretation of large volumes of personal health-related data within the SPHN, including laboratory, imaging and clinical records, -omics data and others.

The SBP is the national coordination platform for biobanks in human and non-human domains supported by the SNSF [18]. It responds to increasing requests from researchers in terms of quality, access, transparency and interconnectedness of biobanks and their associated data for research purposes. SPHN and SBP will work together on the implementation of data interoperability mechanisms between the biobanking management systems and clinical research data management platforms to ensure that sample information can be exposed together with the clinical data.

The ETH-Domain (ETHZurich, EPFLausanne) has launched a sister initiative known as Strategic Focus Area in Personalized Health and Related Technologies (PHRT). Given that SPHN and PHRT are complementary in their setting and have similar goals, the steering boards of both programmes have decided to exploit existing synergies in order to strengthen and accelerate the development of a strong personalised health landscape in Switzerland. In order to facilitate and encourage collaborations between the ETH-Domain, universities and university hospitals, SPHN and PHRT published coordinated calls for proposals in June 2017. Although the two initiatives will remain independent, the evaluation procedure will be coordinated to make the best use of available resources. In addition, the ETH-Domain has established the [Swiss Data Science Centre](#), which will be complementary to the services provided by SIB.

The Swiss National Science Foundation (SNSF) contributes to SPHN mainly through project funding through competitive calls across existing instruments, as well as through support to currently running longitudinal studies and the SBP.

Future perspectives

The current funding of the SPHN initiative is limited to the period 2017–2020. The continuation of the initiative (up to 12 years) is dependent upon the successful development of the technical requirements for nationwide data interoperability between the university hospitals and other research institutions. Also, it is of utmost importance that

once the basic infrastructures have been established, additional public and private health institutions, as well as medical practitioners, patient organisations and citizen cooperatives are included in the SPHN. The more partner institutions are participating, the larger the data pool will grow and the higher the quality of personalised health-related research will become. Gradually, the number of projects using the infrastructures developed with the support of SPHN will increase and contribute to the further development of the network. Also, the developing precision/personalised health ecosystem will accelerate cultural changes in biomedical research as well as in practical health care. Intense translational collaborations between -omics research, IT specialists, epidemiologists and clinicians will become unavoidable. And health care will become increasingly individualised and driven by data generated either by extensive molecular profiling of disease processes or by health tracking / quantified self of citizens. Patients and citizens, and not institutions, must keep absolute authority over their data, which requires the development of new dynamic consent procedures and a more systemic approach to the oversight [25, 26]. The SPHN initiative will help to build the technical requirements necessary to push Switzerland to the international forefront of personalised health related research and health care.

Disclosure statement

No financial support and no other potential conflict of interest relevant to this article was reported.

The authors have the following roles within SPHN bodies: Prof. Peter Meier-Abt is Chair of the National Steering Board; Prof. Torsten Schwedeis is Chair of the Executive Board; Prof. Effy Vayena is Chair of the ELSI advisory group.

References

- Schleidgen S, Klingler C, Bertram T, Rogowski WH, Marckmann G. What is personalized medicine: sharpening a vague term based on a systematic literature review. *BMC Med Ethics*. 2013;14(1):55. doi: <http://dx.doi.org/10.1186/1472-6939-14-55>. PubMed.
- Meyer UA. Pharmacogenetics - five decades of therapeutic lessons from genetic diversity. *Nat Rev Genet*. 2004;5(9):669–76. doi: <http://dx.doi.org/10.1038/nrg1428>. PubMed.
- Relling MV, Evans WE. Pharmacogenomics in the clinic. *Nature*. 2015;526(7573):343–50. doi: <http://dx.doi.org/10.1038/nature15817>. PubMed.
- Human Genome Sequencing Consortium I; International Human Genome Sequencing Consortium. Finishing the euchromatic sequence of the human genome. *Nature*. 2004;431(7011):931–45. doi: <http://dx.doi.org/10.1038/nature03001>. PubMed.
- Meier-Abt F, Bentires-Alj M, Rochlitz C. Breast cancer prevention: lessons to be learned from mechanisms of early pregnancy-mediated breast cancer protection. *Cancer Res*. 2015;75(5):803–7. doi: <http://dx.doi.org/10.1158/0008-5472.CAN-14-2717>. PubMed.
- Muenst S, Mechera R, Däster S, Piscuoglio S, Ng CKY, Meier-Abt F, et al. Pregnancy at early age is associated with a reduction of progesterone-responsive cells and epithelial Wnt signaling in human breast tissue. *Oncotarget*. 2017;8(14):22353–60. PubMed.
- Yan W, Herman JG, Guo M. Epigenome-based personalized medicine in human cancer. *Epigenomics*. 2016;8(1):119–33. doi: <http://dx.doi.org/10.2217/epi.15.84>. PubMed.
- Aronson SJ, Rehm HL. Building the foundation for genomics in precision medicine. *Nature*. 2015;526(7573):336–42. doi: <http://dx.doi.org/10.1038/nature15816>. PubMed.
- Flahault A, Geissbühler A, Guessous I, Guérin P, Bolon I, Salathé M, et al. Precision global health in the digital age. *Swiss Med Wkly*. 2017;147:w14423. PubMed.
- Milani L, Leitsalu L, Metspalu A. An epidemiological perspective of personalized medicine: the Estonian experience. *J Intern Med*. 2015;277(2):188–200. doi: <http://dx.doi.org/10.1111/joim.12320>. PubMed.
- Bergen SE, Sullivan PF. National-scale precision medicine for psychiatric disorders in Sweden. *Am J Med Genet B Neuropsychiatr Genet*.

- 2017; Epub ahead of print. doi: <http://dx.doi.org/10.1002/ajmg.b.32562>. PubMed.
- 12 Nimmegser E, Benediktsson I, Norstedt I. Personalized Medicine in Europe. *Clin Transl Sci*. 2017;10(2):61–3. doi: <http://dx.doi.org/10.1111/cts.12446>. PubMed.
 - 13 Collins FS, Varmus H. A new initiative on precision medicine. *N Engl J Med*. 2015;372(9):793–5. doi: <http://dx.doi.org/10.1056/NEJMp1500523>. PubMed.
 - 14 Blaise A, Vayena E. Tailored-to-You: Public Engagement and the Political Legitimation of Precision Medicine. *Perspect Biol Med*. 2017;59(2):172–88.
 - 15 American Association for the Advancement of Science. Precision Medicine in China. Washington DC: Science/AAAS Custom Publishing Office; 2016.
 - 16 Global Alliance for Genomics and Health. A federated ecosystem for sharing genomic, clinical data. *Science*. 2016;352(6291):1278–80. doi: <http://dx.doi.org/10.1126/science.aaf6162>. PubMed.
 - 17 University of Zurich, University Hospitals Zurich, ETH Zurich, University of Basel, University Hospitals Basel. Workshop of the Zurich-Basel Personalized Health alliance. March 3, 2017. http://www.cc-pm.uzh.ch/dam/jcr:01b2d275-4aa5-4a87-a83e-ec5a9f2afa84/Program%20WS%20PH%20Alliance%20ZH-BS_2017.pdf
 - 18 Maurer F, Pradervand S, Guilleret I, Nanchen D, Maghraoui A, Chapatte L, et al. Identification and molecular characterisation of Lausanne Institutional Biobank participants with familial hypercholesterolaemia - a proof-of-concept study. *Swiss Med Wkly*. 2016;146:w14326. doi: <http://dx.doi.org/10.4414/smw.2016.14326>. PubMed.
 - 19 Lawrence A, Selter L. Swiss Personalized health Network (SPHN): Die nationale Initiative im Ueberblick. *Schweiz Arzteztg*. 2017;98(19):595–6. doi: <http://dx.doi.org/10.4414/saez.2017.05640>.
 - 20 Lovis C, Blaser J. Biomedical informatics in Switzerland: need for action. *Swiss Med Wkly*. 2015;145:w14173. doi: <http://dx.doi.org/10.4414/smw.2015.14173>. PubMed.
 - 21 Vishnyakova D, Gaudet-Blavignac C, Baumann P, Lovis C. Clinical Data Models at University Hospitals of Geneva. *Stud Health Technol Inform*. 2016;221:97–101. PubMed.
 - 22 Raisaro JL, Ayday E, Hubaux JP. Patient privacy in the genomic era. *Praxis (Bern 1994)*. 2014;103(10):579–86. doi: <http://dx.doi.org/10.1024/1661-8157/a001657>. PubMed.
 - 23 Huang Z, Ayday E, Lin H, Aiyar RS, Molyneaux A, Xu Z, et al. A privacy-preserving solution for compressed storage and selective retrieval of genomic data. *Genome Res*. 2016;26(12):1687–96. Published online October 27, 2016. doi: <http://dx.doi.org/10.1101/gr.206870.116>. PubMed.
 - 24 Newsletter Steps SPHN. #2: Getting to know the SPHN Partners. June 2017. – <https://www.sphn.ch/en/about/publications.html>
 - 25 Kaye J, Whitley EA, Lund D, Morrison M, Teare H, Melham K. Dynamic consent: a patient interface for twenty-first century research networks. *Eur J Hum Genet*. 2015;23(2):141–6. doi: <http://dx.doi.org/10.1038/ejhg.2014.71>. PubMed.
 - 26 Vayena E, Gasser U, Wood A, O'Brien D, Altman M. Elements of a New Ethical Framework for Big Data Research. *Wash Lee Law Rev*. 2016;72(3):420–41.
 - 27 Vayena E. Ein ethischer Rahmen für den Austausch von Gesundheitsdaten. *Schweiz Arzteztg*. 2017;98:36. doi: <https://saez.ch/article/doi/saez.2017.05941>. <http://dx.doi.org/10.4414/saez.2017.05640>.