Precision Health

The next generation healthcare

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Foreword

Our vision

Ulf Nehrbass

Dear reader,

When thinking about research, you may picture a scientist with a test tube, looking through a microscope. Now imagine what happens when this traditional picture meets the universe of new digital technologies, such as Artificial Intelligence, Machine-learning and not terabytes - but petabytes-worth of real-life data. A revolution !

Indeed, we are moving away from the original 'scientist in the lab' stereotype towards a 'scientist as a pillar of modern healthcare', using innovative and cutting-edge technologies as the new 'building blocks'. The COVID-19 pandemic has further shown us the crucial role of science and research in addressing both current and forthcoming medical challenges, especially considering that the increasing number of patients in the future will put our healthcare systems under greater stress. For all these reasons, next-generation biomedical research needs to become more efficient and 'precise', focusing on disease prevention, smart and early diagnosis, digital health and personalised medicine - the identification of the best treatment for the right patient, at the right time.

At the Luxembourg Institute of Health (LIH), we use recent technology advancements to have a direct and meaningful impact on people's health. That is why we put the patient at the heart of everything we do. Our scientists investigate how the immune system lies at the crossroads of health and disease, being the common mechanism between numerous conditions, from cancer and immune-related disorders to neurodegenerative diseases. To do so, we collaborate closely with patients, doctors and hospitals in a tightly interconnected cycle - the so-called 'bed-to-bench-to-bed' approach. Data and samples derived directly from patients allow us to develop new therapies and diagnostic solutions, which will in turn be brought back to our patients to address their currently unmet medical needs. This is the core of our 'translational' and 'precision' health vision.

You will now embark on a journey in the ever-evolving field of biomedical research. We hope to motivate you to pursue a career in this exciting domain and to encourage you to innovate and redefine the boundaries of traditional professions, thereby contributing to shaping the future of 'precision health'.
Wishing you a stimulating read !

Ulf Nehrbass,
LIH CEO

LUXEMBOURG INSTITUTE OF HEALTH

Who we are: Luxembourg Institute of Health & IBBL

Frank Glod, Chief of Scientific Operations

The Luxembourg Institute of Health (LIH) was created in 2015 from the merger of the former Centre de Recherche Publique de la Santé (CRP - Santé) and the Integrated Biobank of Luxembourg (IBBL), and is made up of three research departments: the Department of Cancer Research (DoCR), the Department of Infection and Immunity (DII) and the Department of Precision Health (DoPH). The IBBL is now part of our Translational Medicine Operations Hub (TMOH), which provides significant support for the projects of our research departments. Since its foundation, LIH has established itself as one of the leading institutes for precision medicine with the aim of using the results of cutting-edge research for patients in a meaningful way and preventing diseases in the long term.

At the heart of LIH's excellence lie its 425 employees, 326 of whom are scientists and technical staff with complementary expertise in cell and molecular biology, bioinformatics, statistics, clinical research and epidemiology. Their outstanding work has put LIH among the top research institutes in Europe and in the world, reinforcing the attractiveness of research at the LIH for both young and more established researchers.

Specifically, DoPH is working to ensure that novel digital technologies become routine in modern healthcare, with the goal of contributing to the improvement in population health, while DoCR and DII are investigating how dysfunctions in the immune system are responsible for the onset of complex diseases, from cancer to immune-related disorders. They are supported by a unique infrastructure, enabling them to work closely with patients and doctors to explore the mechanisms underlying many common diseases, thereby advancing the development of new therapies. Indeed, the dedicated "translational" teams of LIH and its unique biobank facilitate the translation of research findings from the lab to the patient, and support the setup of research projects with a true clinical dimension - from patient recruitment and biological sample collection, to the testing of new therapies directly on patients during clinical trials. Central to this approach are the medical doctors and nurses currently affiliated with LIH, the numerous collaborations with national and international hospitals, as well as IBBL's expertise, which ensures the collection, analysis and storage of high-quality patient-derived samples and data. By the end of 2020, 2.1 million biological samples such as blood, urine and stool were collected at IBBL to support clinical studies !

Ultimately, the goal of LIH researchers is to tangibly improve the health of Luxembourgish and European patients.

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Chapter 1

Precision Health & Precision Medicine

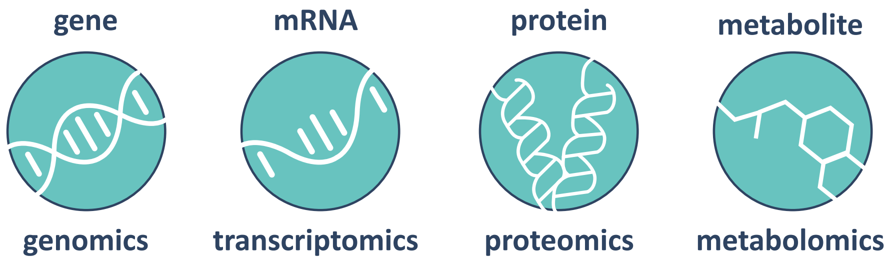
1.1 Precision medicine, precision prevention, precision health. What does it all mean ?

Guy Fagherazzi

From one-size-fits-all approaches to more tailored, personalised treatments and care, we are on our way to revolutionise how we see health and medicine. The term precision medicine is born from the promise that, with a large volume of data, we will one day be able to administer the best treatment, tailored exactly to the person, at the right time, instead of treating each person the same based on their disease alone. In other words, given your profile (i.e. all your individual, contextual, biological, clinical characteristics, etc.), healthcare professionals will not implement a standard treatment but will be able to select what is the best option for you at that time.

Precision health is a bit broader: it encompasses all the dimensions of health, and not only medicine but also prevention and public health. Within it, researchers and healthcare professionals aim to find the best solution to prevent or delay the occurrence of diseases, and best improve the day-to-day lives of those living with an illness.

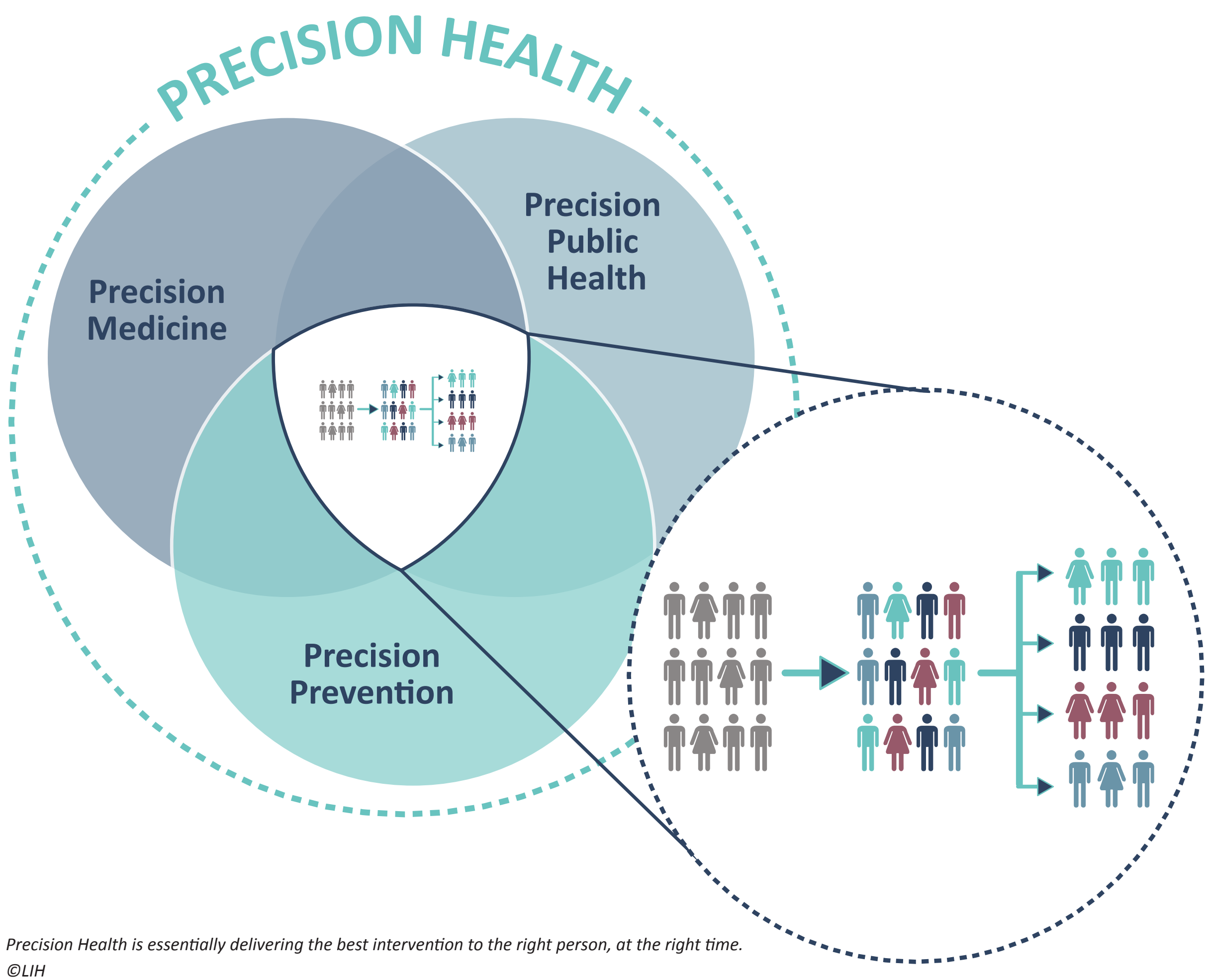
The inclusion of the concept of precision health into our everyday lives makes this one of the most exciting times to live in, and it is all thanks to the recent leaps forward in our way of thinking. Instead of viewing each scientific discipline as independent, scientists are bringing them all together in a new way of working that is referred to as the 'multi-omics' approach. Indeed, disciplines like the study of our genes (genomics), or how our cells read these genes (transcriptomics), or of the proteins that they produce (proteomics), our metabolism (metabolomics), all once perceived as loosely related, are now being 'combined' to bring us a new understanding of our health as a whole. Increasing use of digital technologies, huge advances in artificial intelligence, and developments in computational power and capacities have been essential in this, as they allow the analysis of huge amounts of data on patients and populations. With a view of our health from every possible angle, inside and out, we can gain a better understanding of diseases and how to prevent or treat them in a way that improves the quality of life of those living with them.



The 'omics' approach looks at a disease from every angle by combining different scientific disciplines.
Figure inspired from : https://www.ebi.ac.uk/training/online/courses/metabolomics-introduction/what-is/

Use of biomarkers, or biological markers, have also been game-changers in precision health. Unlike medical symptoms, biomarkers are not limited to those indications of health or disease that are reported by the patients to their doctor, but are instead objective measures of the well-being or illness of a person. A biomarker can be something we measure in your blood, but it can also be a characteristic of your voice or even just your pulse and blood pressure. Thanks to novel artificial intelligence methods, measuring and monitoring biomarkers is becoming easier every day, with biomarkers increasingly used to predict, measure, monitor, diagnose and treat diseases. Alone, they may not provide more information than your current heartrate or your sleeping pattern, but combining them in different ways can generate huge amounts of useful health information for diagnostics, treatment and research not just for you, but for the population as a whole.

The following chapters will take you on a journey into the future of medicine and healthcare. We will explore what precision health means in the context of different healthcare specialties, in the increasingly prominent context of data collection, and then give you a taste of what a career in healthcare or health-related research could look like for you.



Precision Health is essentially delivering the best intervention to the right person, at the right time.
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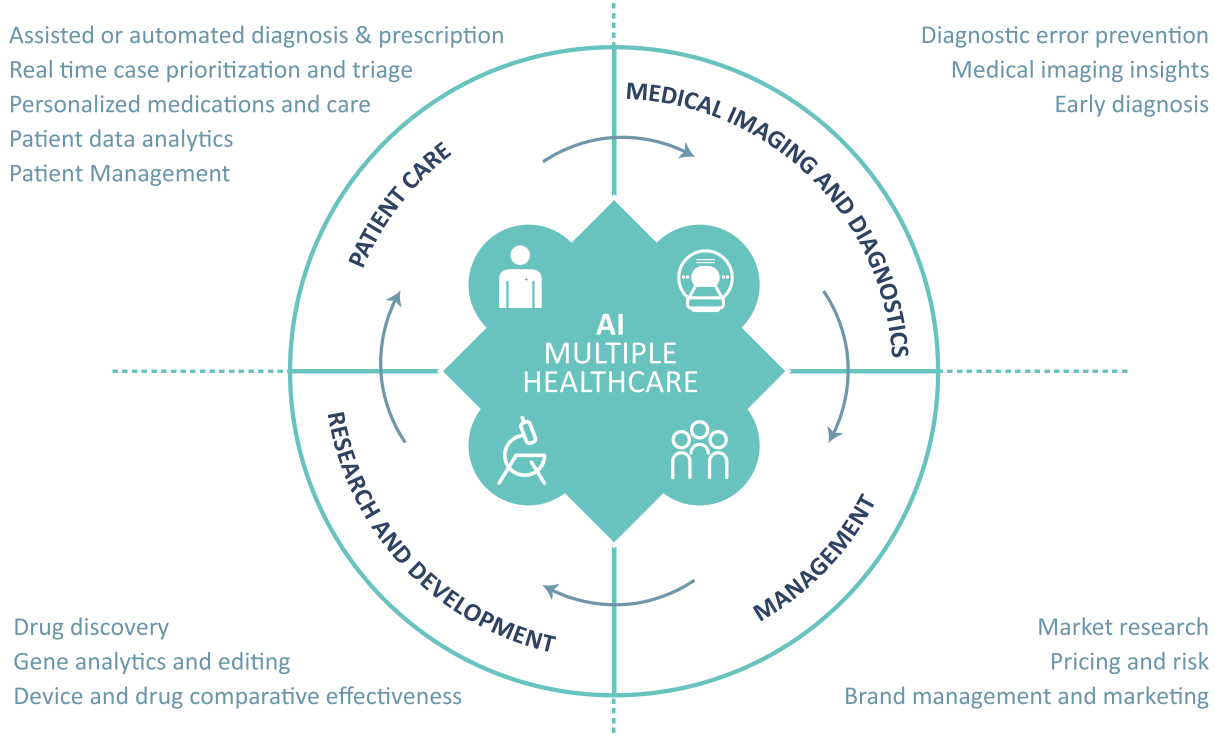
1.2 Artifical Intelligence - your doctor's right hand

Guy Fagherazzi

Artificial Intelligence, or AI, could enhance and simplify the healthcare system by transferring tasks from the human to the machine, or even by performing tasks that are impossible for humans. Today, in the world of health, AI is everywhere. You can find it in the hospital, where it can be used to automatically detect tumours in a scan ; you can find it in your home, where, for people living with diabetes, it can accurately predict the dose of insulin that needs to be administered at a given time.

However, AI also comes with many challenges. AI relies on algorithms, a set of instructions written in 'computer-language' that can tell a machine how to accomplish a task. In the world of healthcare, to train AI algorithms we usually need a large set of health data, often referred to as Big Data, from which the machine learns. However, we have to make sure that the data we are using is of good quality and diverse enough to encompass all the potential situations algorithms will face in clinical practice. Despite how complicated it sounds, training an AI algorithm is the easy part of the process ; the biggest challenge is to collect enough high-quality data to enable the machine to correctly learn how to solve a problem. Otherwise, the algorithms will not work properly in certain situations, produce systematic errors or generate distorted results.

In healthcare, most datasets have been collected from white males, and algorithms usually tend to work fine in this group of people. Instead, for females or other ethnicities, we sometimes observe biases, simply because there is not enough data to properly train the algorithm. As part of their tasks, AI researchers have to carefully validate and test their AI algorithms in different population groups to ensure safe usage of their solution for all. This way, no one will risk receiving a wrong diagnosis or treatment because they have different characteristics than the population whose data were used to train the algorithm !



Today, artificial intelligence has many applications in healthcare. Its use will only expand in the future.
Figure inspired from: https://research.aimultiple.com/healthcare-ai/

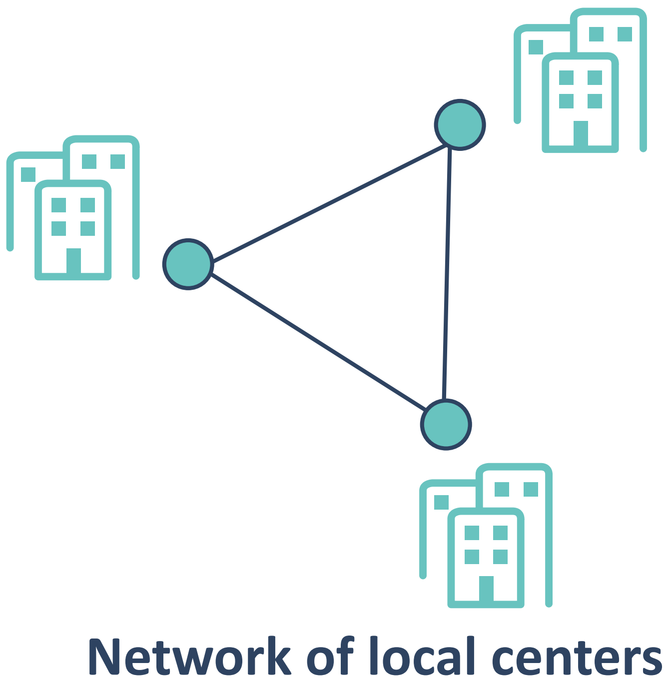
1.3 Clinnova - the potential of health data

Jasmin Schulz

We learned how collecting the right data makes the difference between a functional and a biased artificial intelligence algorithm, and so a correct or incorrect clinical result. But where do these data even come from ?

As you grow and age, you will change addresses, doctors, even country. Your health data, records of vaccinations or even history of disease, will remain stored in snippets at that doctor's practice or in that dusty drawer 'somewhere in your desk'. But what if this was not the case ? What if all of your medical information was stored digitally and we could decide to make these data available to doctors or research ? Could these data be used to improve healthcare ?

The answer is yes. However, with an increase in complex chronic diseases and an ageing population, the health sector is lagging behind in digitalisation, lacking a comprehensive, long-term overview of a patient's medical history. To support this, Luxembourg started the Clinnova programme. Clinnova is a precision medicine programme that will use clinical, biomedical and patient-generated data from prospective patient groups to support treatment choices. In collaboration with Baden-Württemberg and Saarland, Germany as well as the Grand Est, France and Basel, Switzerland, Clinnova will establish a network of partner centres. It will mainly focus on three immune-related disorders (inflammatory bowel disease, rheumatoid diseases and multiple sclerosis). Clinnova is built around the needs of specific diseases, using cases as well as the feedback from physicians and patients involved. With a strong emphasis on data quality and standardization to train effective AI algorithms, Clinnova aims to support personalised treatment solutions for patients.



In Clinnova patient data are stored in local Data Integration Centres and will be interpreted by federated analysis.
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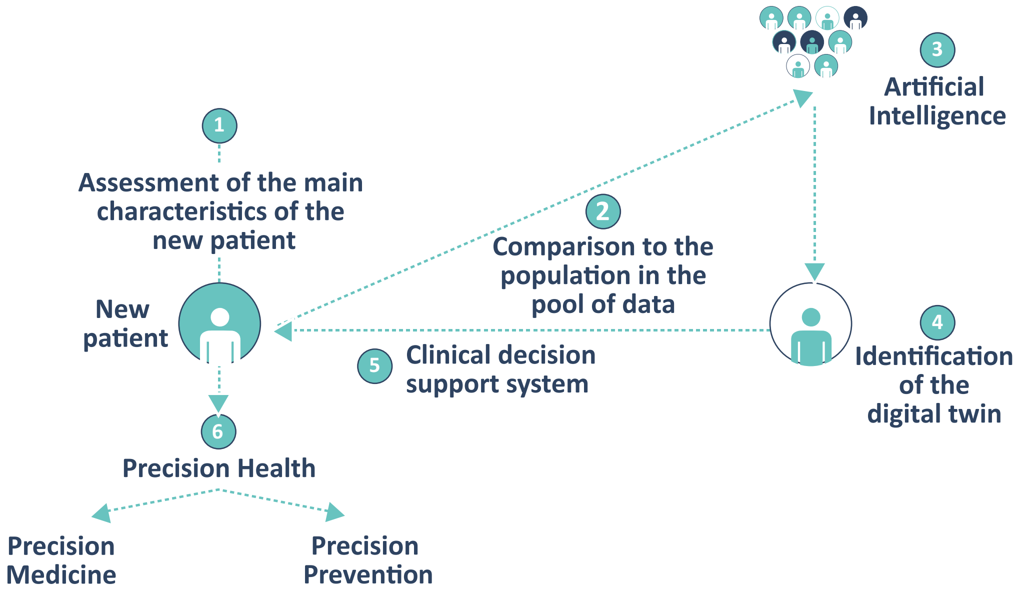
1.4 Digital Twin - a 'you' made of everyone else

Guy Fagherazzi

Each one of us is unique, both as a person and as a patient. So why do we all get the same treatment based on our symptoms alone ? If we managed to make precision health a reality, we could soon personalise treatment using a patient's 'digital twin'. The digital twin is a very new concept in health research and comes from the industrial world, where a digital avatar of a physical entity (e.g. plane or a car engine) is virtually recreated, with similar elements and dynamics, to predict how it will perform in real life. Digital twins could be used in the medical field to analyse health and individual characteristics of a patient and how their health will change over time. The principle is then simple: a new person falls ill and goes to a doctor that doesn't know anything about them. The doctor will visit the patient and then search for, in a large data bank of many people with the same disease, an average individual who will have similar or identical health characteristics as the new patient. This 'digital twin' will have data showing how their health changed over time. The doctor could use these data to make clinical decisions and to anticipate how the disease will progress in the new patient. They could then advise the new patient and suggest a change in therapy or a personalised prevention programme adapted to the patient's profile. This enables physicians to no longer rely solely on the experience they have acquired over the years, but also on detailed records from thousands of patient files.



Lots of data are collected on a large group of patients to then identify subgroups that could benefit from a specific treatment to improve their health.
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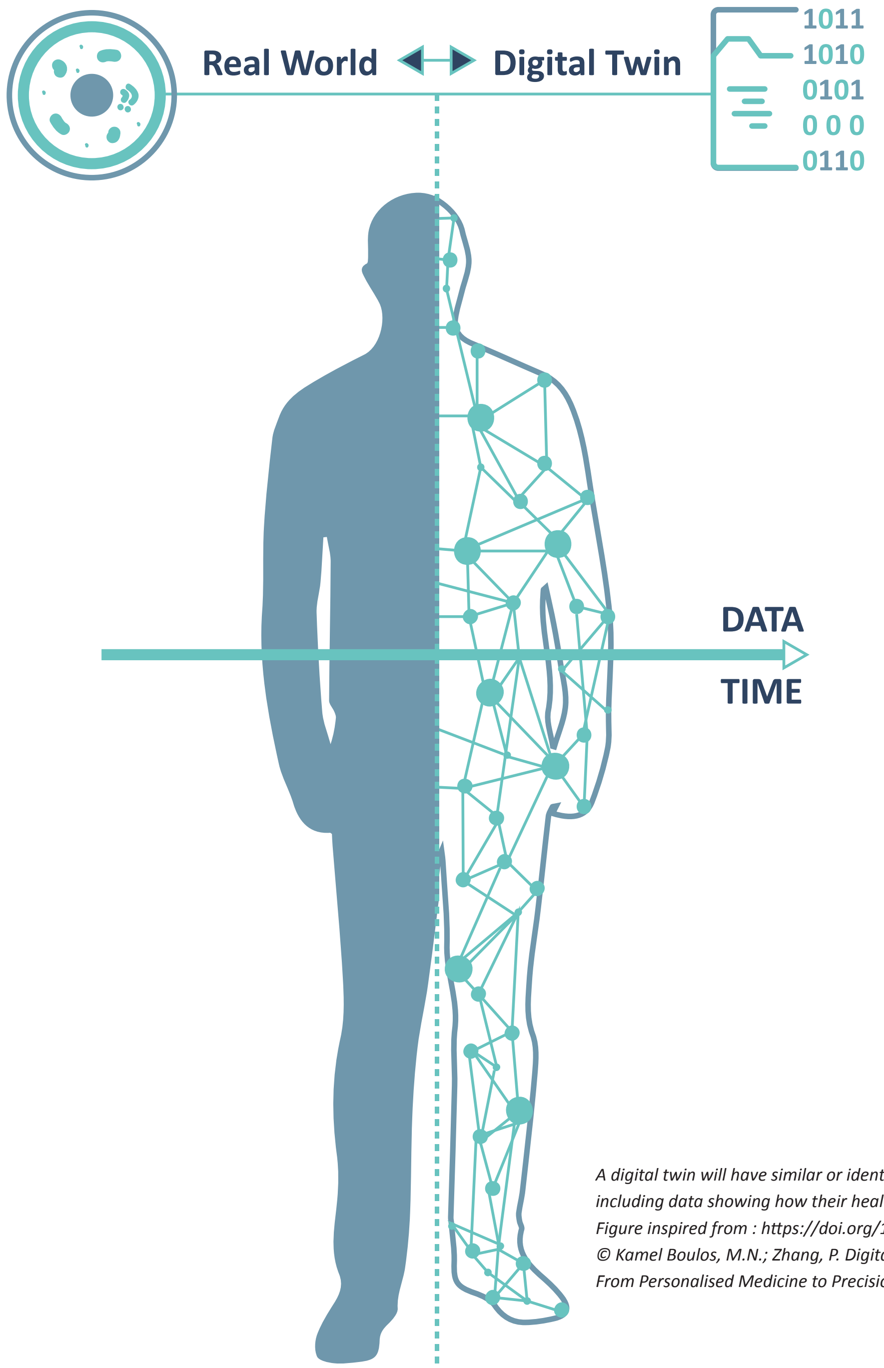


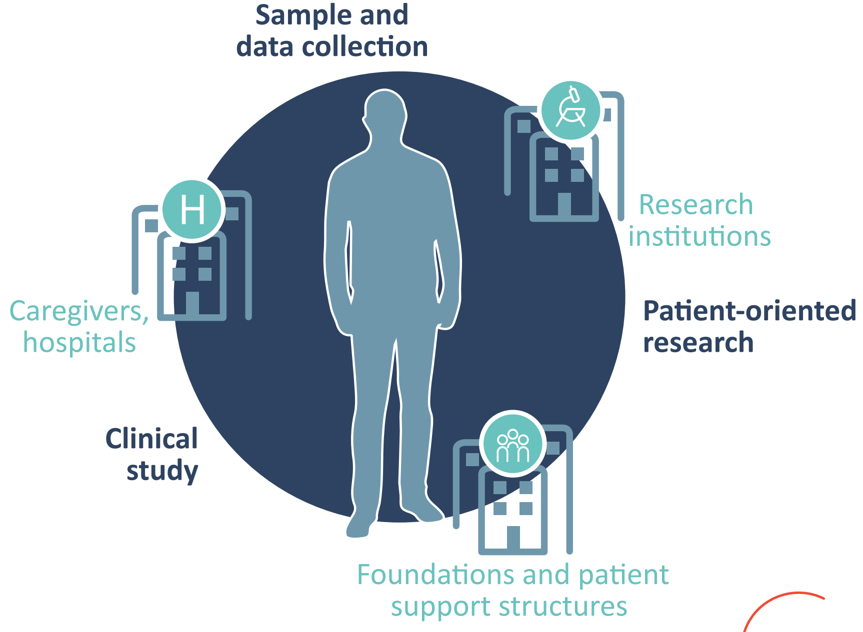
A digital twin will have similar or identical health characteristics as the patient, including data showing how their health will change over time.
Figure inspired from : https://doi.org/10.3390/jpm11080745
© Kamel Boulos, M.N.; Zhang, P. Digital Twins :
From Personalised Medicine to Precision Public Health. J. Pers. Med. 2021, 11, 745.

1.5 'Together' to personalise cancer treatment

Simone Niclou / Lars Geffers / Yong-Jun Kwon / Barbara Klink / Guy Berchem

Cancer remains a huge psychological, clinical and financial burden within society, and it is projected to increase over the next few decades, in line with an ageing population. The LIH is dedicated to patient-centred cancer research and to foster a fast 'translation' of basic research findings - research aimed at 'translating' results from basic research into results that have a direct benefit to patients. To do this, the LIH has decided to exploit its research expertise in cancer, to initiate a National Centre of Translational Cancer Research (NCTCR) programme in Luxembourg.

The NCTCR aims to bring together patients, caregivers, hospitals, research institutions, foundations and patient support structures under the same 'roof'. The objective is to improve patient care by providing access to innovative individually tailored (personalised) cancer care and treatments. It will include: translational research for precision oncology, particularly to understand individual tumours at the cellular level ; cancer 'models' created from tumours extracted from patients, to test drugs or study the biology of cancer ; and innovative therapies using immune cells to combat cancers. Novel digital tools (apps) for patient monitoring and communication will be an integral part of the programme. Ultimately, the NCTCR aims to have clinical studies examining the efficacy of new treatment and prevention approaches.



Starting with the individual cancer patient, the NCTCR will operate on the levels of sample and data collection, patient-oriented research, and clinical studies.
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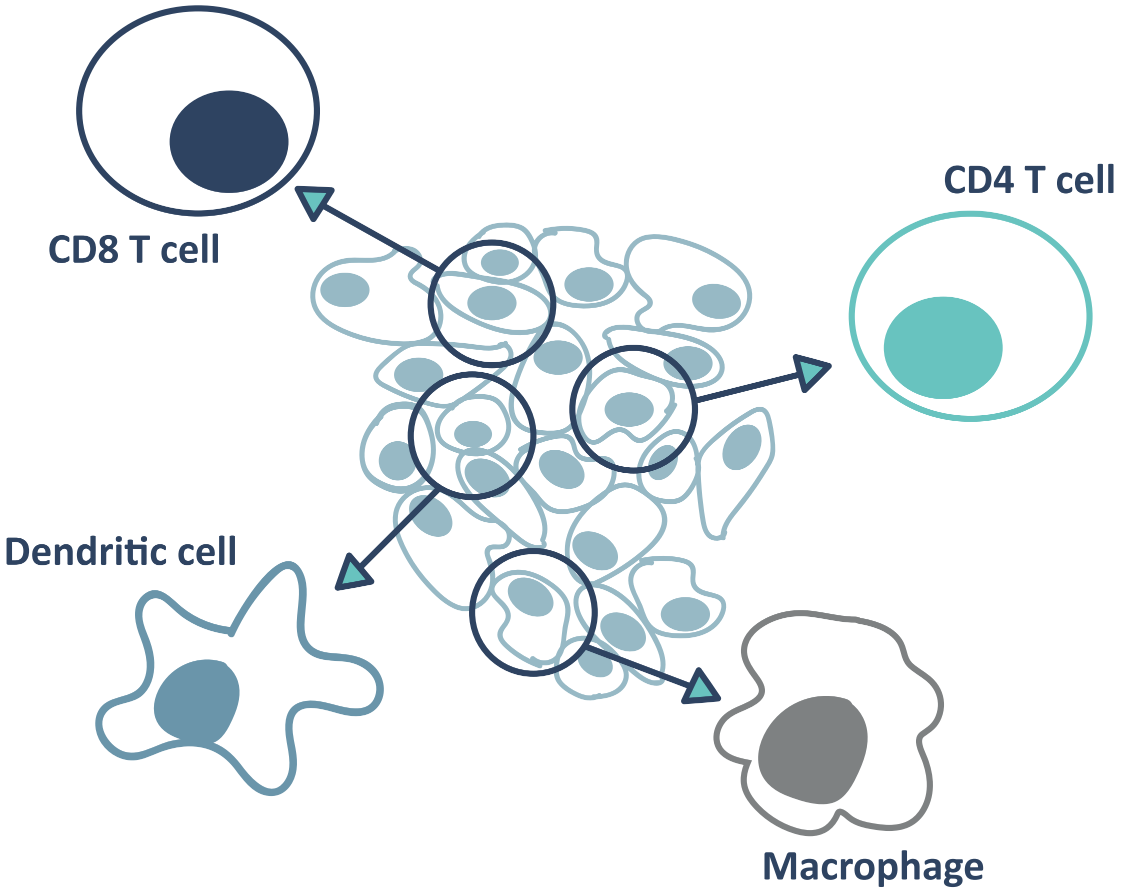
1.6 Deep Immuno-phenotyping - every one of your cells as unique as you

Markus Ollert / Feng He

When our body is attacked by foreign invaders (e.g. bacteria, viruses or fungi) or is under other harmful disease conditions (e.g. cancer), the immune system will fight against the foreign attackers or the diseased cells or tissues. Like an army, the immune system is composed of many types of cells, each with a different role. Any type of dysregulation, in any type of the involved immune cells, might cause disease.

More and more evidence shows that immune dysregulation is heavily involved not only in infectious diseases, but also in cancer, autoimmune, neurodegenerative and many, if not all, other types of disease. Indeed, human disease could originate from a reduced capacity of the regulatory arm of the immune system to prevent unnecessary attacks against normal cells in the body. It is in this context that it becomes important to have a deep immunophenotyping strategy.

Deep immunophenotyping is used to reveal the precise immunological status of each individual patient. Using markers present on the surface of cells, it can identify each cell that plays a part in a disease. It can help us to better understand the complexity of the origin and the development of infectious diseases, but also cancer, neurodegenerative diseases (e.g. Alzheimer's or Parkinson's disease) and even autoimmune diseases (e.g. rheumatoid arthritis). Not only that: deep immunophenotyping can predict which patient will have worse symptoms, or take longer to recover. In the context of precision medicine, this is also particularly relevant as every person's immune system is unique. In order to make medicine truly personalised, both the diagnosis and the treatment options for various diseases should be chosen based on information that can only be revealed by personalised deep immunophenotyping.



Deep immunophenotyping can identify each cell that plays a part in a disease.
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Chapter 2

Data is the New Gold

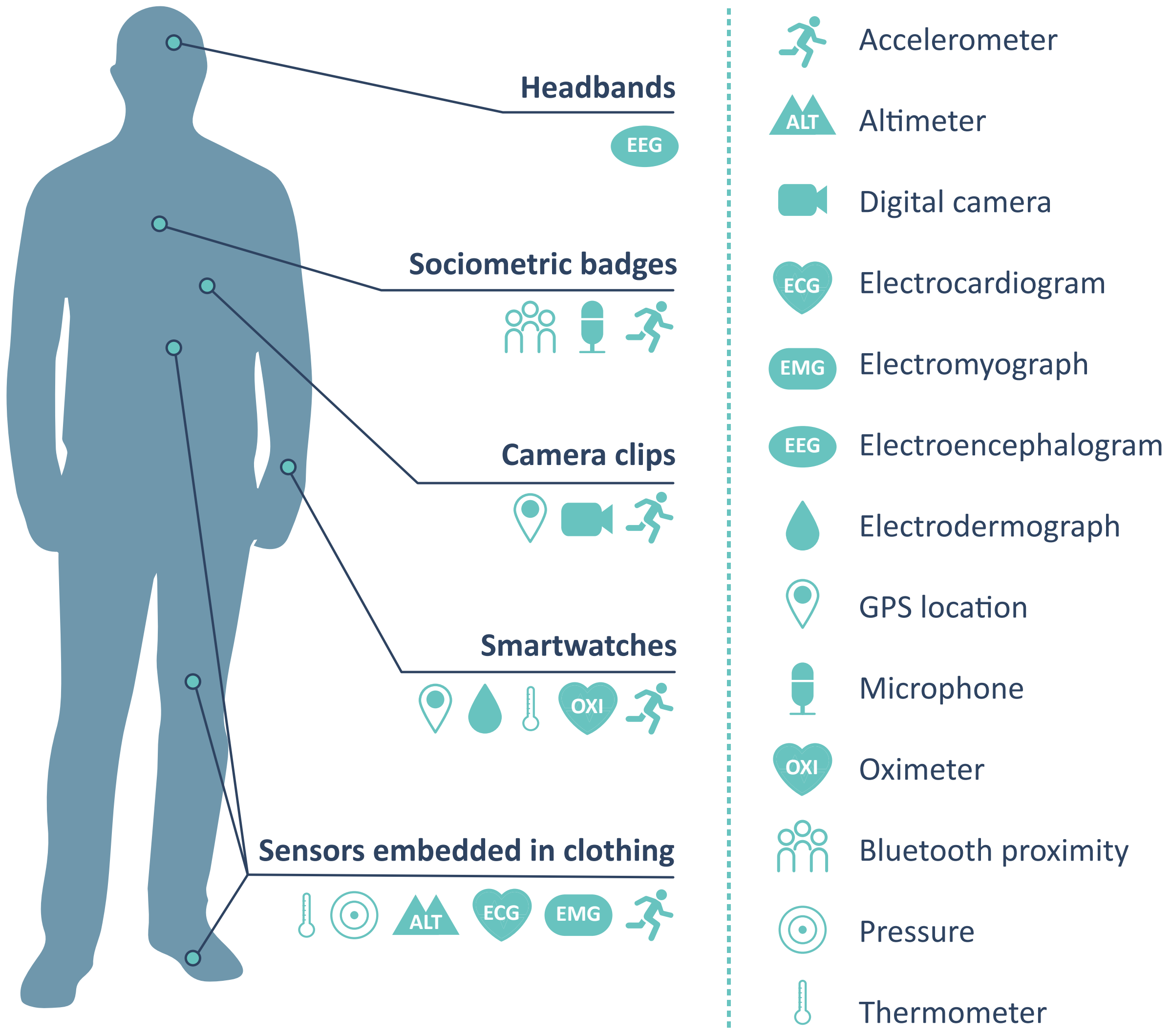
2.1 Connected health - the data surrounding you

Laurent Malisoux

If you have a smart-watch, or even just use your smartphone to count your steps in a day, you are not alone. In 2019, about 86% of the European adult population used smartphones. The smartwatch market reached almost 7 million shipments in 2020. The sensors embedded in the wearables continuously collect large amounts of digital data, things like your lifestyle (sleep, physical activity) or physiology (heart rate, sweat). But did you ever stop to think about what could be done with all these data?

Available consumer technologies can be used in healthcare to deliver patient care outside of the hospital or the doctor's office following a 'connected health' concept. According to this, devices and services will be designed around the patient's needs, and health-related data will be shared in such a way that the patient can receive care in the most proactive and efficient way possible. Wearable sensors are increasingly used to monitor patient health and help predict or rapidly assist with disease diagnosis. Thus, connected health enables the support of the 'medicine of the future', which is an integral part of the future precision health model.

As an example, researchers are already using this type of technology to study fitness. Wearable devices, such as pressure sensitive insoles, can provide invaluable information of factors like fatigue and running technique. Understanding how people move helps predict and prevent risk of injury. Data can be compiled with information on sleep, physical activity or metabolic markers, such as blood sugar level, to measure and understand fitness and health.



Many wearable devices exist, each able to monitor a different health-related feature.
Figure inspired from : https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1001953 © 2016 Piwek et al.

2.2 The world around a sample

Hermann Thien

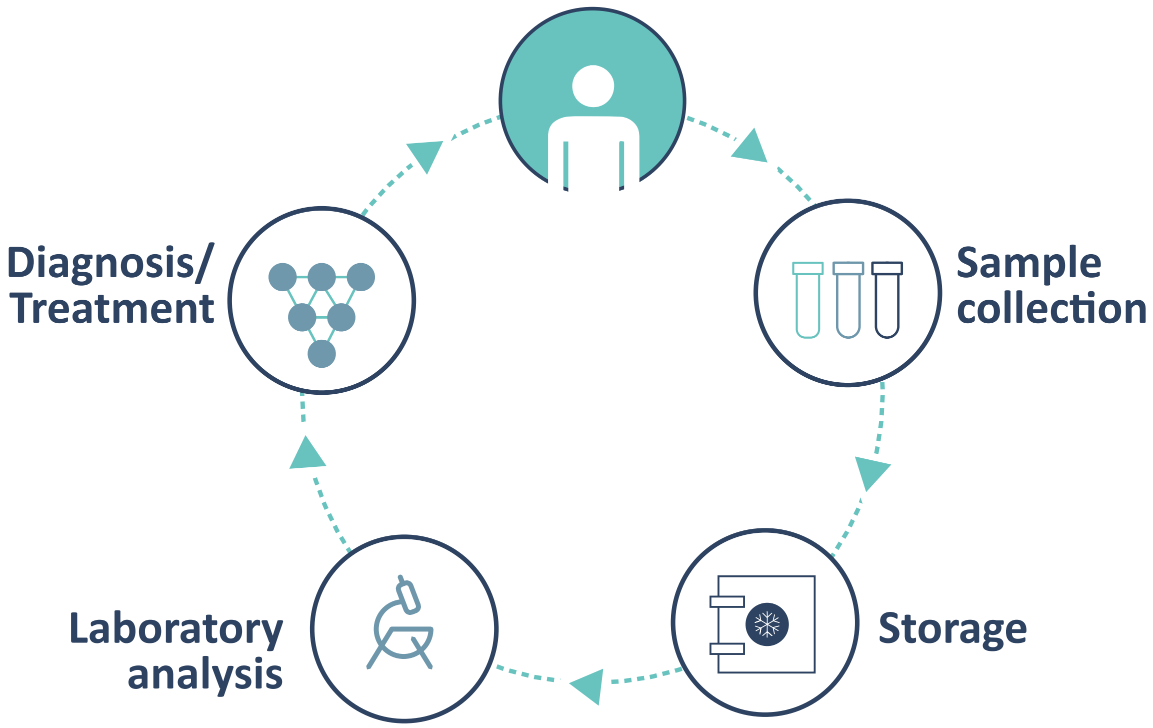
It is likely that you have come across a biological sample more than once in your life. Most of us will have given several urine samples by the time we reach maturity, and some of us will have had blood drawn for a test. Biological samples are common in research as they are used to understand how a disease affects different people and how it is responding to treatment. However, in order for biological samples to be viable, both for researchers and your doctor, it is critical that these are handled correctly so that the results represent what is actually in your sample instead of being introduced by the collection process.

At the Luxembourg Institute of Health, we have specialised teams that collect, store and distribute human biological samples, and associated data, for future use. Their work starts even before the sample is taken, where they support researchers in designing the best possible collection process to allow a smooth, efficient and standardised sample collection using 'collection kits' that contain all the materials necessary for sample collection (e.g. blood, urine, and stool).

Once collected, samples need to be catalogued and stored at an appropriate temperature. This process may seem random, but is actually extremely precise as a change in a few degrees can mean that things like proteins in a sample change shape or degrade, compromising the results. A full team is in charge of identifying if there are any improvements that can be made in transport and storage, developing processes to control these conditions and performing quality control testing before distributing the samples to researchers.

However, their work doesn't end there. Researchers continuously seek to improve existing processes and methods, trying to understand the unwanted changes that samples go through during storage, why they happen and how to stop them from affecting medical research. They even have a team that helps researchers check that the experimental method they chose will provide the results that they are looking for.

Thanks to their hard work, samples can provide crucial information that can, for example, diagnose a tumour and develop targeted therapies for it, thus providing personalised medical approaches.



From when they are taken, samples go through several steps before they can benefit the patient.
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2.3 Patient and Public Involvement - research done by you

Gloria Aguayo

Personalised healthcare puts the patient at the centre of health-related actions and research. The patient is engaged and becomes actively involved in managing their own health. However, a patient can do more than just generate data, contributing at different levels in the health and research processes.

One way that patients can be involved is via patient-reported outcomes (PROs). PROs are information about a disease, which is provided directly by the patients themselves without any external interpretation, such as that from clinicians. PROs are crucial for the 'real-world' monitoring of drugs on the market, as they enable pharmaceutical industries to detect potential side-effects and modify the drug to prevent them. They can also help define symptoms of a disease to facilitate its diagnosis.

Besides PROs, patients can also be involved in other aspects of research. Research that is done with patients or by the patients themselves is called patient and public involvement (PPI). Through it, patients become a research partner and are actively involved in the research process. PPI makes the studies more relevant and with more benefits for the patients. In addition, it makes it more likely that research results are implemented in real life and helps design research projects to have the largest benefits for patients. Often, you will find these types of studies advertised on social media.

Patient involvement in research can take many forms.
©LIH

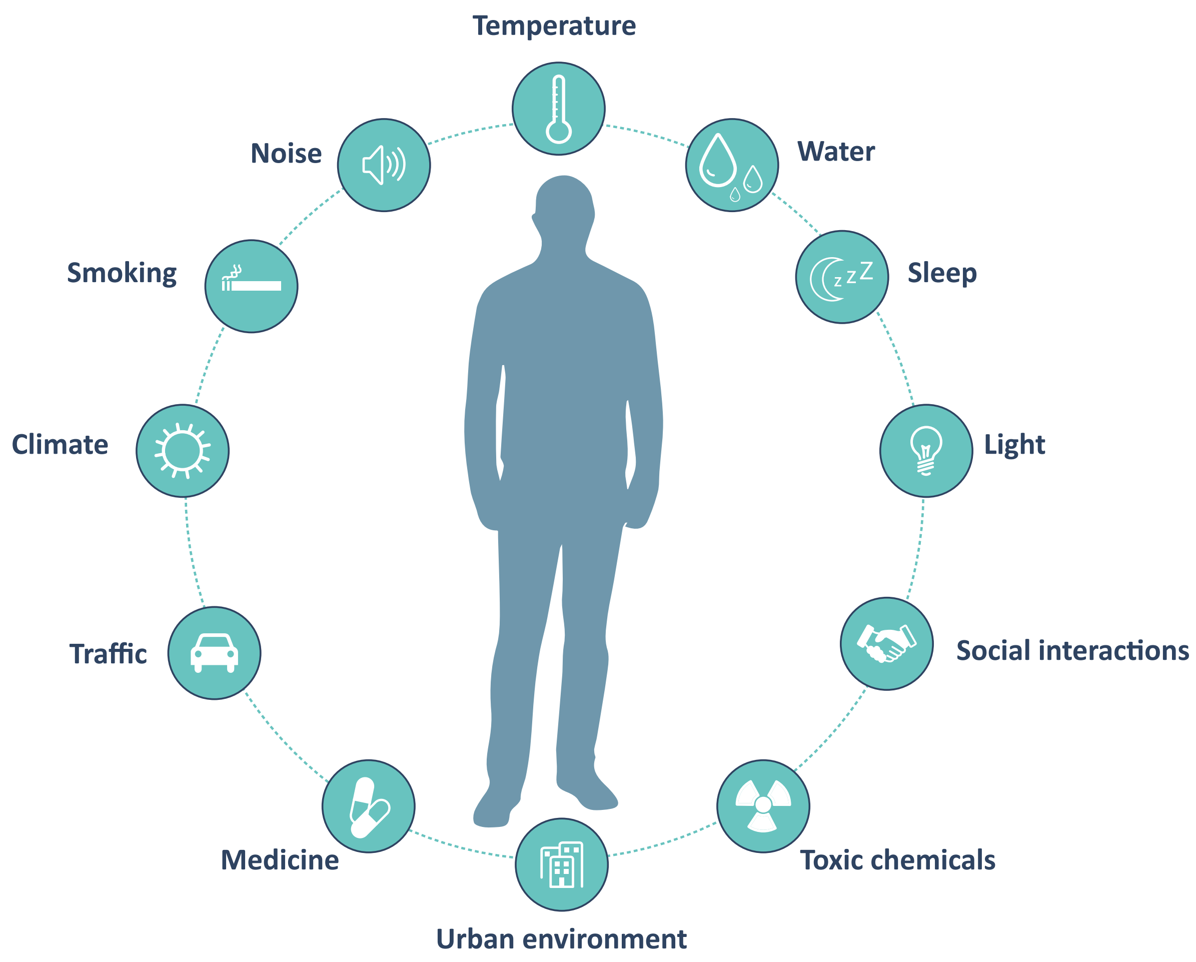
2.4 And an exposome is…?

Brice Appenzeller

Humans are continually exposed to a multitude of pollutants, with new chemicals constantly introduced to the market, in food (e.g. pesticides) but also in many other materials in direct contact with humans (flame retardants, plasticizers, antimicrobials …). It was estimated that in 2015, diseases caused by pollution were responsible for 9 million premature deaths worldwide, more than from HIV, tuberculosis, and malaria combined. Effects of exposure and disease caused by emerging pollutants (e.g. new pesticides or nano-particles) on human health are not yet known.

Each chemical may have its own toxicity or act in synergy with others, leading to more severe effects. To better understand the contribution of all these chemicals to the onset of various diseases, huge efforts have been invested in characterising human exposure to pollutants, or the so-called 'chemical exposome'. The exposome includes anything humans are exposed to from birth to death. This encompasses pollutants in the air that we breathe, chemicals on the foods that we eat, and even the minerals in the water we wash ourselves in.

To measure the exposome, biological samples (blood, urine and more recently hair) are taken, from which the pollutants are directly analysed using highly sensitive methods. Thanks to the latest advances, up to several hundreds of pollutants can be analysed to provide a much more detailed description of the 'chemical exposome' of a person. Beyond chemical compounds, anything else we come into contact with in our lifetime (e.g. noise and sun light) could play a part in our health. This new field of research brings to light a completely new dimension to a patient's history. Including chemical exposome assessment in personalised medicine will help to better identify causes of disease that are poorly understood, and improve disease prevention and patient care.



Anything we come into contact during our lifetime is part of our 'exposome'. You can see only some of the examples here.

©LIH

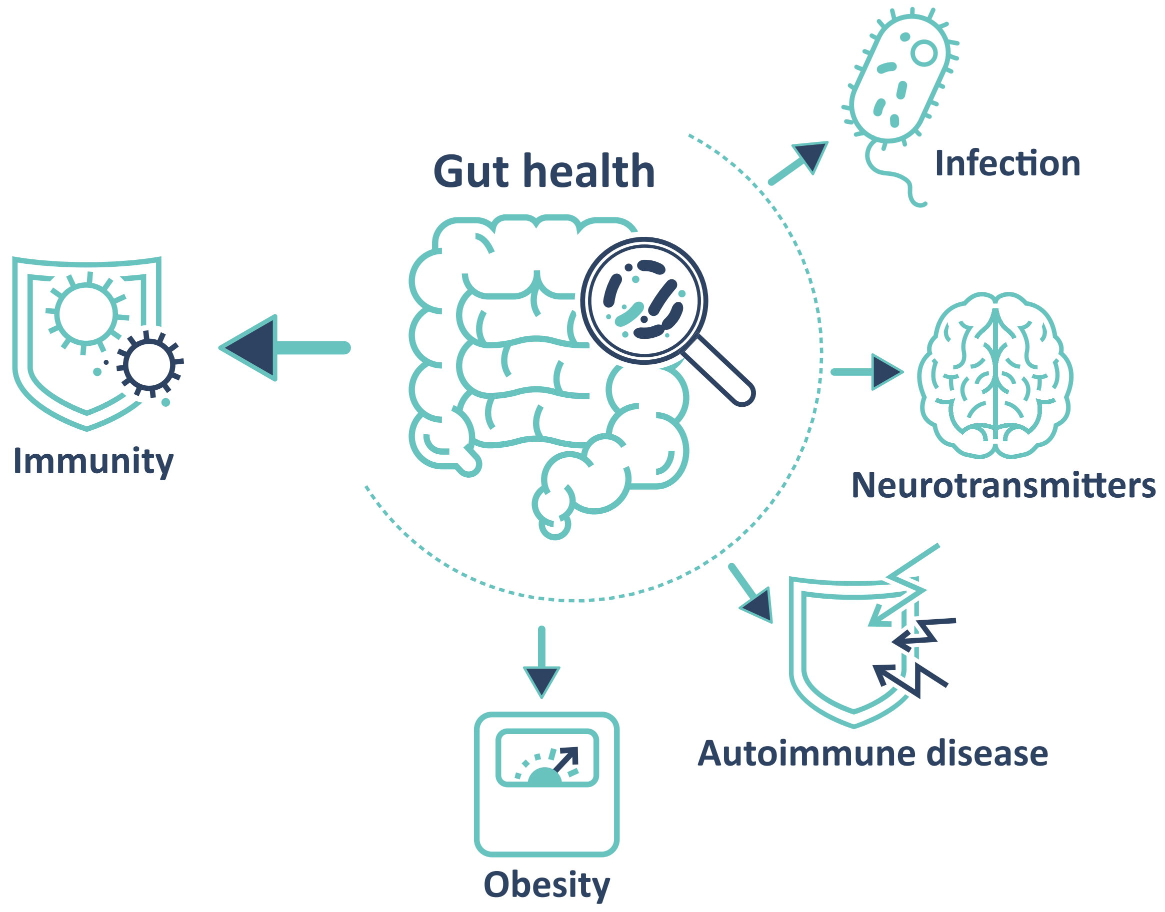
2.5 You say bacteria, we say microbiome

Mahesh Desai / Torsten Bohn

While bacteria exist all over the body (in fact, for every human cell in your body, you also are home to at least one bacterial cell), they are most present in the colon, where they survive on components of our diet that have not yet been broken down and absorbed. This undigested fraction, mostly dietary fibre, can be fermented, to some extent, by the 'gut' microbiome for energy. The resulting metabolic products can influence human health.

The term 'microbiome' encompasses all microorganisms inhabiting a particular region of the body. Often, this term only refers to the bacteria in a specific environment. The microbiome has become the focus of intense scrutiny in recent years, as until this point, we never realised just how big a part these 'healthy' bacteria played on our well-being. For example, a simple reduction in the amount of fibre we consume in our diet could result in our gut bacteria feeding on the mucous lining of our colon instead. The gaps created are doorways for infection by harmful bacteria that we ingest via our food, like salmonella or *E.coli*. However, it goes beyond just impacting the physical barriers that protect us from disease : bacteria in our microbiome can control inflammation, influence the gut-brain axis and even secrete compounds that can act like hormones.

The goal of research on the microbiome is to better understand which potential bacteria or molecules can be used to precisely control interactions between our immune system and our gut microbiomes. It is increasingly apparent that our individual responses to diet or disease treatments in the context of diverse conditions such as obesity, cancer, and autoimmune disease are linked to differences in individual microbiomes. Moving forward, prevention and/or treatment of these diseases should deliver knowledge on our individual gut microbiomes and how to best regulate them for improved health outcomes.



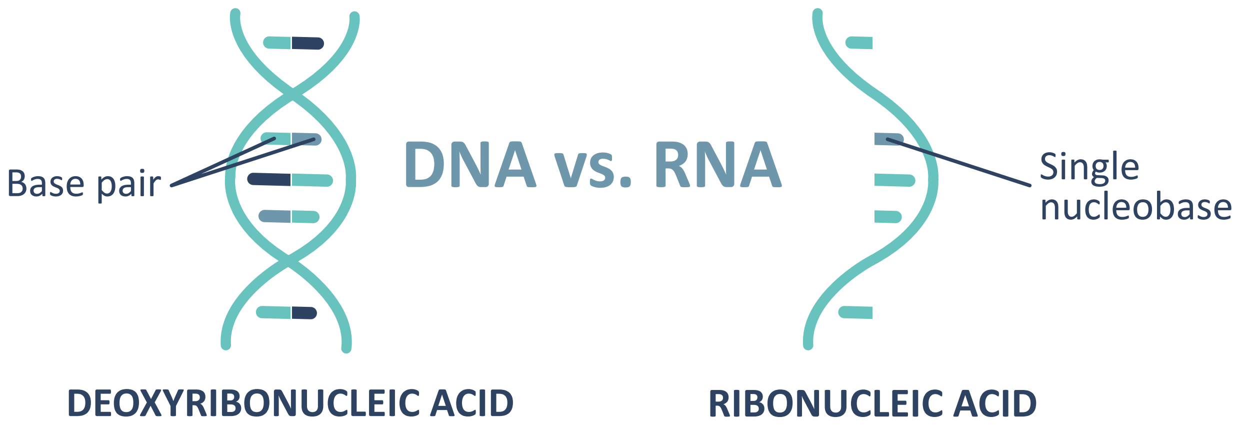
Our microbiome plays an essential role in our health, beyond our digestion.
icons © Shutterstock/doublebrain

2.6 RNA Biomarkers - how DNA talks about your health

Yvan Devaux / Amela Jusic

Encoded from DNA, RNA molecules are normally responsible for the production of proteins, the building blocks of the human body. For a long time it was believed that this was RNA's only purpose. Instead, around a decade after the genome was first fully sequenced, it was discovered that there was a very small portion of RNAs that never triggered the production of proteins. These RNAs, now known as 'non-coding RNAs', clearly had a different purpose. Research continued, and the role of RNAs expanded with it. It was found that RNAs are not only present inside the cells but can also be shuttled to release transport messages from one cell to another and that this could regulate many biological processes in humans. Most recently, RNAs were used to create the vaccines against COVID-19.

We are now entering into a new era for the use of RNAs as biomarkers and drugs for precision health. Indeed, RNAs can be used for diagnostic purposes (i.e. establishing the presence of a disease), patient stratification (the categorisation of patients into subgroups based on a clinical characteristic) and to identify patients at high risk of developing a disease or to be more severely affected by the disease. However, further research is needed to reach the stage where RNAs can be used as routine tools for precision health. Joint efforts from multiple research institutions, as well as young investigators entering the biomedical research community, are of crucial importance to speed up the discovery of biomarkers or drugs based on RNAs.



RNA molecules are created based on DNA, and only now are we beginning to understand the many roles they have in controlling our health.
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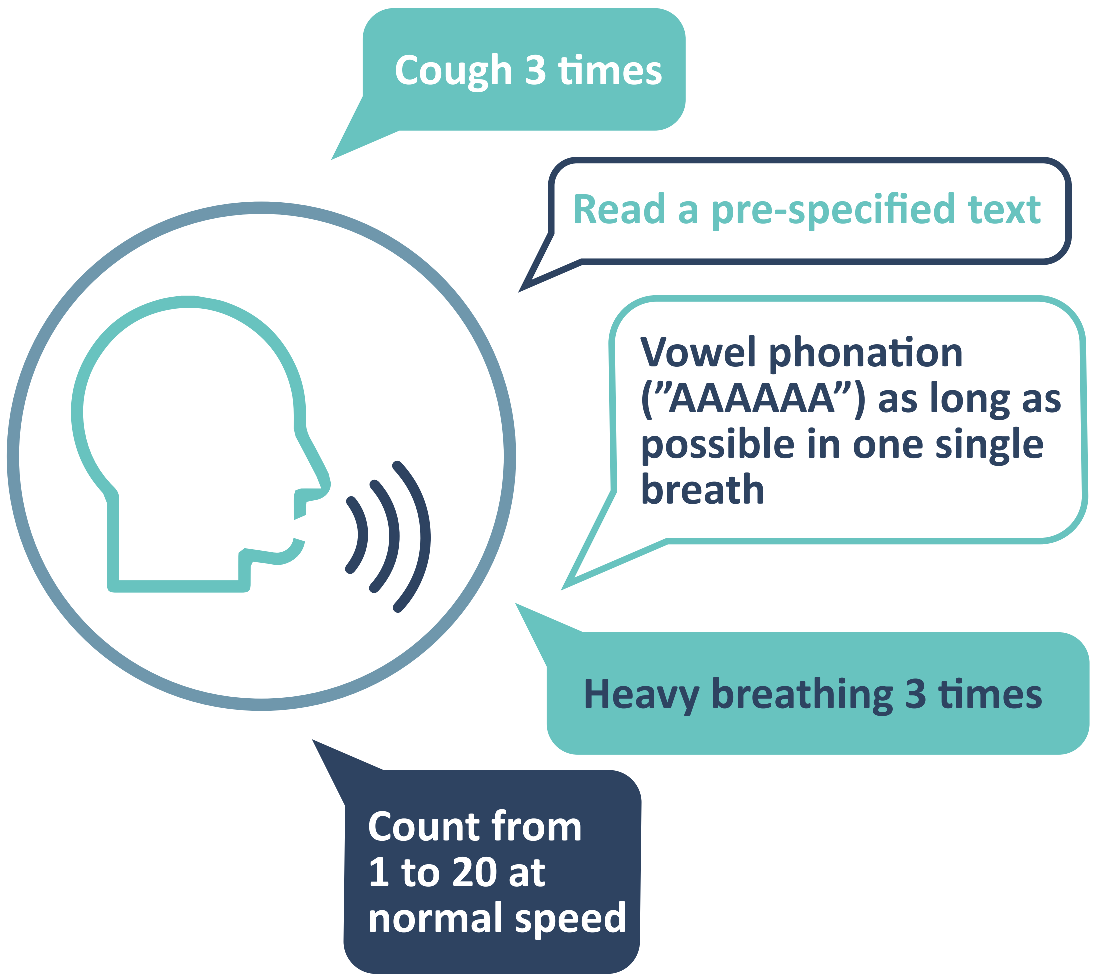
2.7 The things you say with your voice

Aurélie Fischer

Information on our health can come from all sorts of places, including our voice. By modulating the tone, speed or intensity of our voice, we don't only share insights about our emotions, but also our health. A vocal biomarker is a feature or a combination of features in the voice that has been associated with a disease or a symptom.

Vocal biomarkers are collected via voice recordings along with health information for the patient. The audios are then pre-processed to remove background noise, harmonise audio quality and to extract and select the features that will then be used in AI algorithms. Audio signals can also be converted and used as images to train Deep Learning algorithms. Following testing in the clinical setting, vocal biomarkers are finally integrated into a device such as a smartphone app, a chat-bot or a vocal assistant.

Vocal biomarkers are a key example of non-invasive tools in precision health that can be used to not only improve diagnosis and monitor the evolution of a disease, but also to provide a more personalised and timely treatment. Many voice-based applications are currently in development and may considerably improve the quality of life and care of patients.



Vocal biomarkers can be identified thanks to different recordings, each providing crucial insights on our health.
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Chapter 3

Precision Health in 2050

3.1 Augmented humans - augmented doctors

Jochen Klucken

Imagine you are a young student in the year 2050 and you have an interest in health and medicine for your future career. By then, precision health will have become part of everyday healthcare procedures. The word 'doctor' will be used as a synonym for any healthcare provider including therapists, psychologists, caregivers etc. since each will work in an interdisciplinary setting providing digitally supported healthcare to the patient.

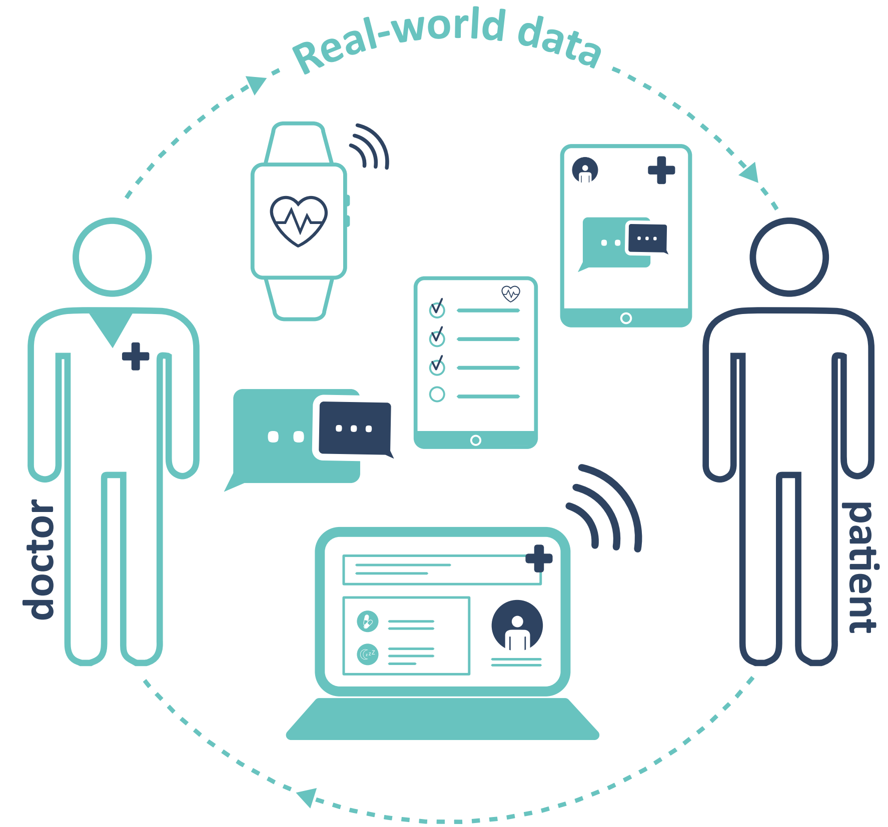
We will not distinguish between medical data that has been generated in clinical research studies that are conducted by researchers and medical data that is recorded while you see your doctor. Any medical data recorded will be stored in patient-centred electronic health records and thus, be available to anyone involved in the healthcare process (patients, healthcare provider, healthcare payer), and to researchers driving innovation in medicine.

Real-world data will now come from all kinds of sensors, smartphone-apps, location-trackers, monitoring systems and even social media. It will enable smart algorithms (also known as 'artificial intelligence') to better predict disease conditions and diagnoses, but also improve individualisation of treatment decisions and monitoring paradigms. The work of doctors will have substantially changed due to this availability of real-world data and many types of algorithm that improve transparency between doctors, patients and other involved parties.

The presence of patient-centric real-world data will also affect the way doctors and patients are involved in research and innovation. Patients will be able to participate in selecting both human and digital services. The data recorded by these services will be the basis of the innovation and development of improved services. At the same time, doctors will record their own data. They will thus both be part of research, supporting innovation and quality control in healthcare.

Medicine will have stopped being based on data and have instead become based on the value provided to the patient, where data are used for innovation, evaluation and quality control. Data access will have become one of the most important drivers and control points. Luckily, you, as a pupil who has received the right education to deal with this challenge, will know what data privacy and security means. You will understand the topic of health and medicine as an interdisciplinary concept, you will have learned about the social and ethical consequences of this new dimension, and you will have been given the ability to fight against the potential abuse of it. During your training, you will have learned about the technical and data-science requirements in addition to your clinical abilities and disease-related knowledge. You will have taken classes to enable digitally supported communication based on the patients' needs and you will have a profound understanding of privacy and identity definitions, because you are a child of the post-digital transformation age.

Being in your early 20s, you are in a very similar situation to all the 'digital immigrants' who were born some 40-50 years ago when the internet did not exist - so don't be scared, just imagine …



In the near future, technology will connect doctors with their patients, thanks to a continuous overview of their health parameters.
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3.2 Tele-Health - modern technologies improving patient care

Guy Fagherazzi

As technology has evolved, we have gradually been introduced to a world where telemedicine has become more and more the norm. Telemedicine is the use of technologies and telecommunication systems to administer healthcare to patients who are geographically separated from healthcare providers. Telehealth is a broader concept that encompasses telemedicine and can be defined as the delivering of healthcare, health education, and health information services via remote technologies. Soon, diagnoses, monitoring, and treatments will be enhanced thanks to digital technologies, to simplify the care pathway and facilitate the daily lives of patients and healthcare professionals. From prevention to disease management, telehealth solutions will allow more tailored care to integrate the specificities of the patients.

The possibilities are endless. For example, let's take Anna, a 45-year-old woman who has been treated for breast cancer in the year 2050. She is now on hormone therapy, which was specifically chosen to match her biological profile by a precision medicine-compounding pharmacist. She uses an app on her smartwatch where dozens of digital biomarkers are regularly evaluated to check her general health status. Every morning, she monitors her level of fatigue on her smart mirror through voice and image analyses. At the hospital, both the oncologist and the breast cancer nurses can view the evolution of all of her AI-based, digital biomarkers on a dashboard, in real-time. Any change in pattern leads to an alert that can get Anna scheduled for an emergency appointment with her oncologist. Thus, instead of waiting months for a routine check-up, remote digital monitoring can enable early detection of a cancer recurrence, and possibly allow Anna to prevent the development of a more advanced form of cancer.

Telemedicine uses technology to bridge the gap between patients and healthcare providers, regardless of their geographical location.
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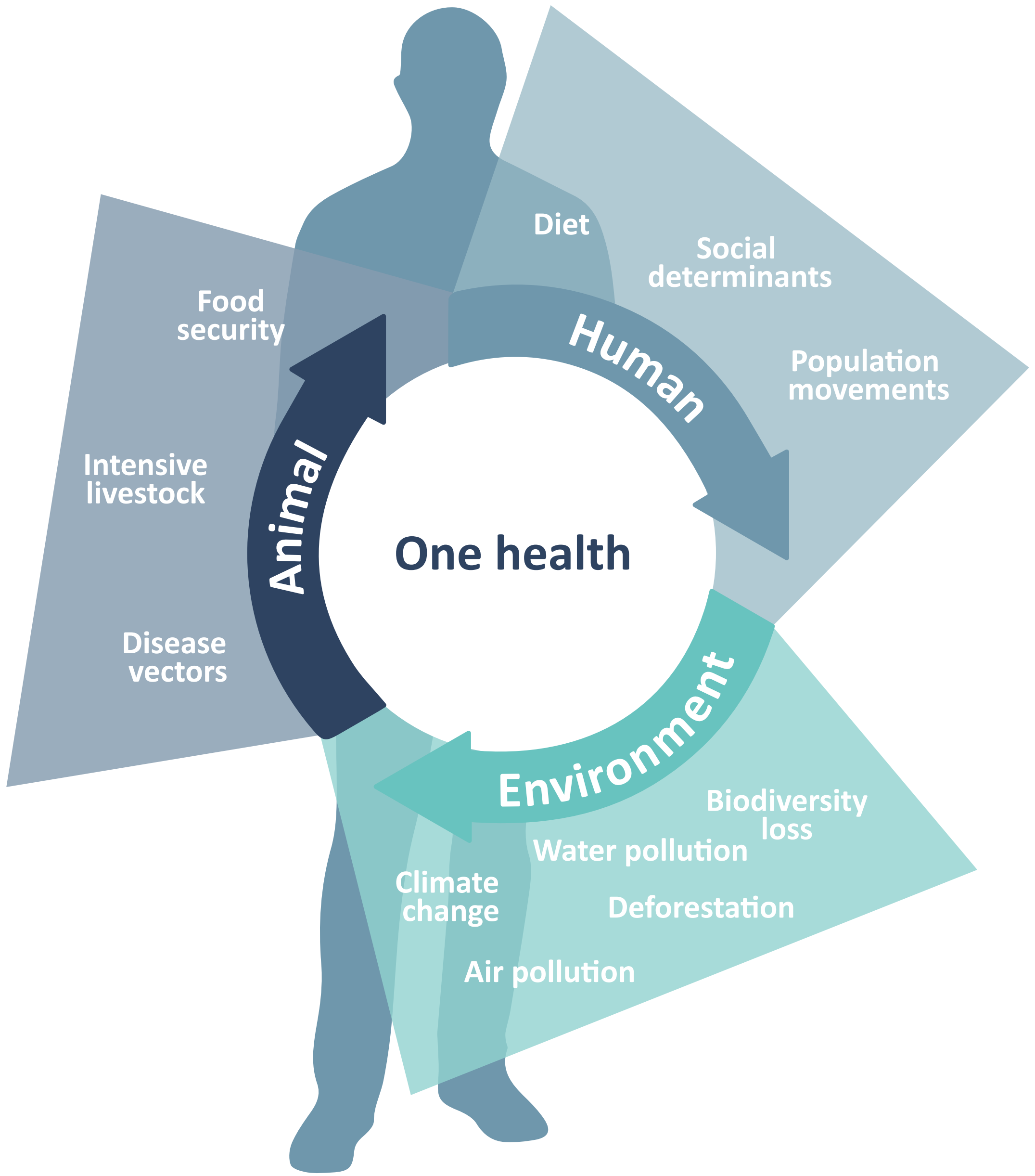
3.3 One Health Approach - everything is interconnected

Guy Fagherazzi

Everything is interconnected. This has been particularly highlighted during the COVID-19 pandemic. At least 60% of infectious diseases in humans have an animal origin. Many disease-causing viruses, such as COVID-19, Zika and Ebola viruses, avian flu, or even HIV, have animals in common. Such serious health events are expected to occur regularly, as the world's population grows, transportation intensifies, environmental degradation continues, and cities develop. Human activity plays a major role in the spread of infectious diseases: deforestation, for example, has brought wild and farmed animals into contact, facilitating the spread of new diseases to humans.

It is in this context that the One Health concept was developed to make sure that we all adopt a global vision. It encourages taking into consideration all the factors related to disease emergence. The challenge is to encourage the effective collaboration of research organisations working in human and veterinary health as well as the environment domain. The concept is promoted by international institutions such as the World Health Organisation (WHO), the World Organisation for Animal Health (OIE), and the Food and Agriculture Organisation of the United Nations (FAO).

When it comes to Precision Health, which strives to ensure the best possible health for all, independent of their lifestyle, sociodemographic background, and biological characteristics, integrating a One Health approach is now mandatory.



The 'one health' approach encourages us to look at disease emergence from all angles.
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Chapter 4

Jobs in Precision Health

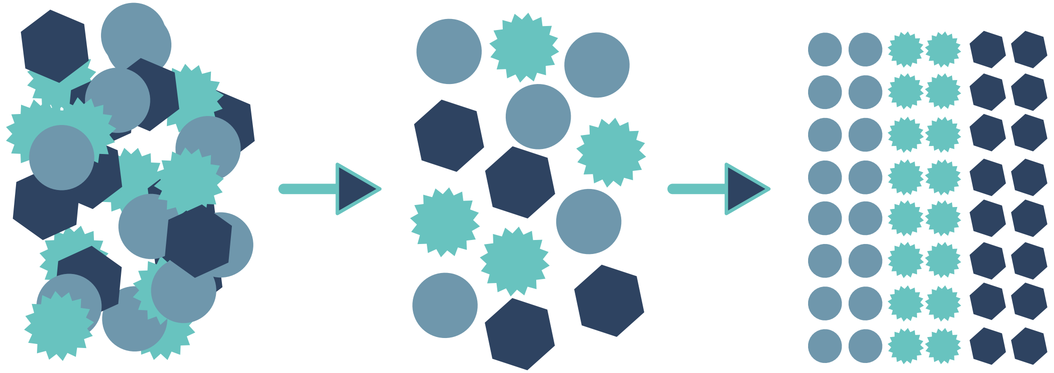
4.1 Data Manager & Data Steward

Michel Vaillant

Clinical data management has undergone a huge change over the last century, where the pharmaceutical industry has evolved from trials conducted on paper to electronic data capture (EDC) systems. A new culture of real-time data, risk assessment as well as tailored clinical monitoring strategies emerged, which in turn brought forward the expectation of faster processing of clinical trials data.

The typical clinical data manager is now becoming more of a clinical data steward or clinical data scientist dealing with new strategies and new technologies to process big volumes of data. The clinical data manager combines a background in life sciences and an education in informatics. They are able to understand the specificity of the data that need to be collected and implement the systems that store and manage them.

A data steward oversees the production of research data by the data manager and integrates the different data sources within a study. They are involved in all processes by which data are collected, managed, curated, stored and shared in the long-term, organising the collection of different data types and linking to the participant to whom they belong to. The data steward also oversees the flow of data that are generated during the study by the different stakeholders.



Clinical data manager and data steward use new technologies to process and clean big volumes of data.
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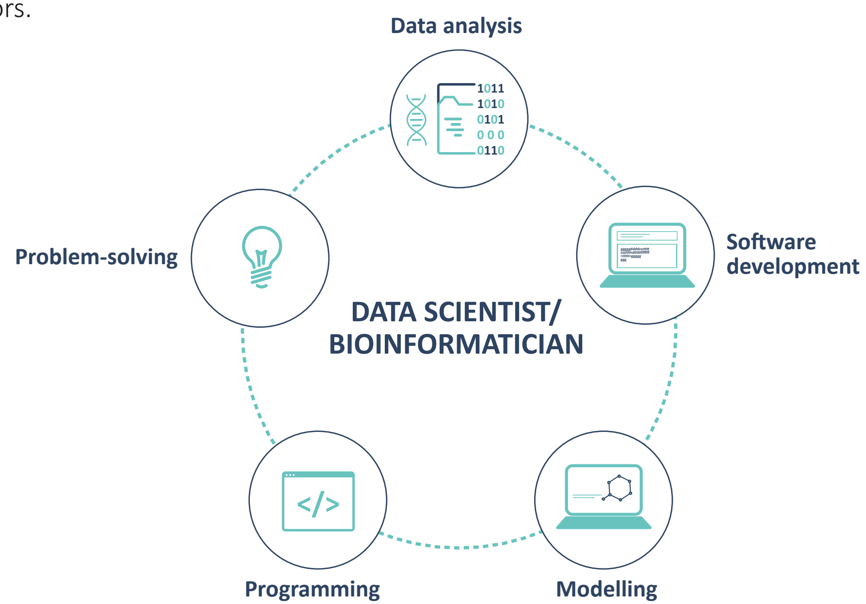
4.2 Data Scientist & Bioinformatician

Petr Nazarov

Today, data analysis has become more and more important for modern medicine and biology. Both these domains have entered the era of Big Data, where information cannot be extracted and handled without computers. The interdisciplinary field that deals with extracting and making use of the information from domains like biomedicine and data science is called Bioinformatics.

The job of a bioinformatician can be split into three main activities: data analysis (looking for the relevant facts in the data), software development (algorithms, new visualisation, etc.), and modelling. In many cases, a bioinformatician needs to combine the three activities to adapt to the research question they are trying to answer.

Can you become a bioinformatician ? Most probably - yes ! You will need to develop reasonable programming skills and understand at least basic statistics and biology. However, the most important feature you need is curiosity. You should be interested in what you are doing and excited by new discoveries. Being a bioinformatician is a rewarding position that puts you at the front and centre of many research projects. The position is constantly evolving, with top methods that are key now that will probably be outdated in five years' time. The skills developed as a bioinformatician and Data Scientist are becoming relevant to many sectors.



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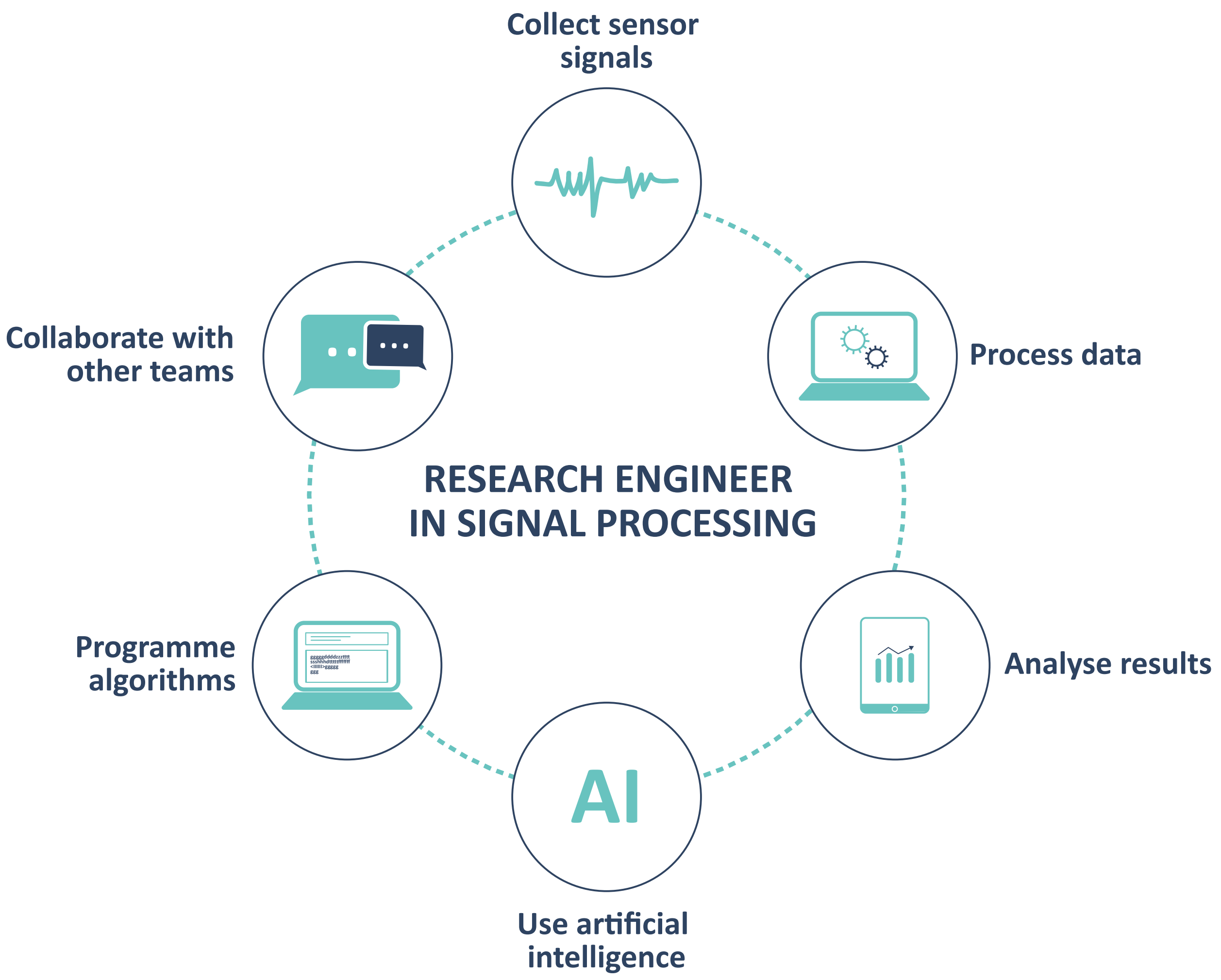
4.3 Research Engineer in Signal Processing

Bernd Grimm

During the last decade, wearable sensors have become more accurate, smaller, lighter, and cheaper. The biosignals and biometrics collected from such new technologies, combined with advances in signal processing via machine learning and artificial intelligence, have sparked a revolution in medicine, health and sports research to provide personalised treatments.

A 'Research Engineer in Signal Processing' works at the core of innovation, at the interface between engineering and medicine. The engineer knows how to use sensor technologies in the laboratory and outside in real life, as well as how to collect, process, analyse and visualise the sensor signals to derive medically meaningful data. For instance, the research engineer would configure a shoe insole with pressure and motion sensors, run experiments with the insoles to collect sensor signals and then process the data. The signal-processing engineer also applies methods of machine learning and AI to the collected data. For example, by processing large amounts of audio produced while coughing into a smartphone, the signal-processing engineer can help to identify if someone has been infected with COVID-19, reducing the cost and effort to perform such tests.

A 'Research Engineer in Signal Processing' likes to work with new technologies like sensors, enjoys exploring data and is keen to program algorithms to derive meaningful information. In this profession, one collaborates with diverse teams that include doctors, therapists and researchers from other fields such as biology, biomechanics or sports science.



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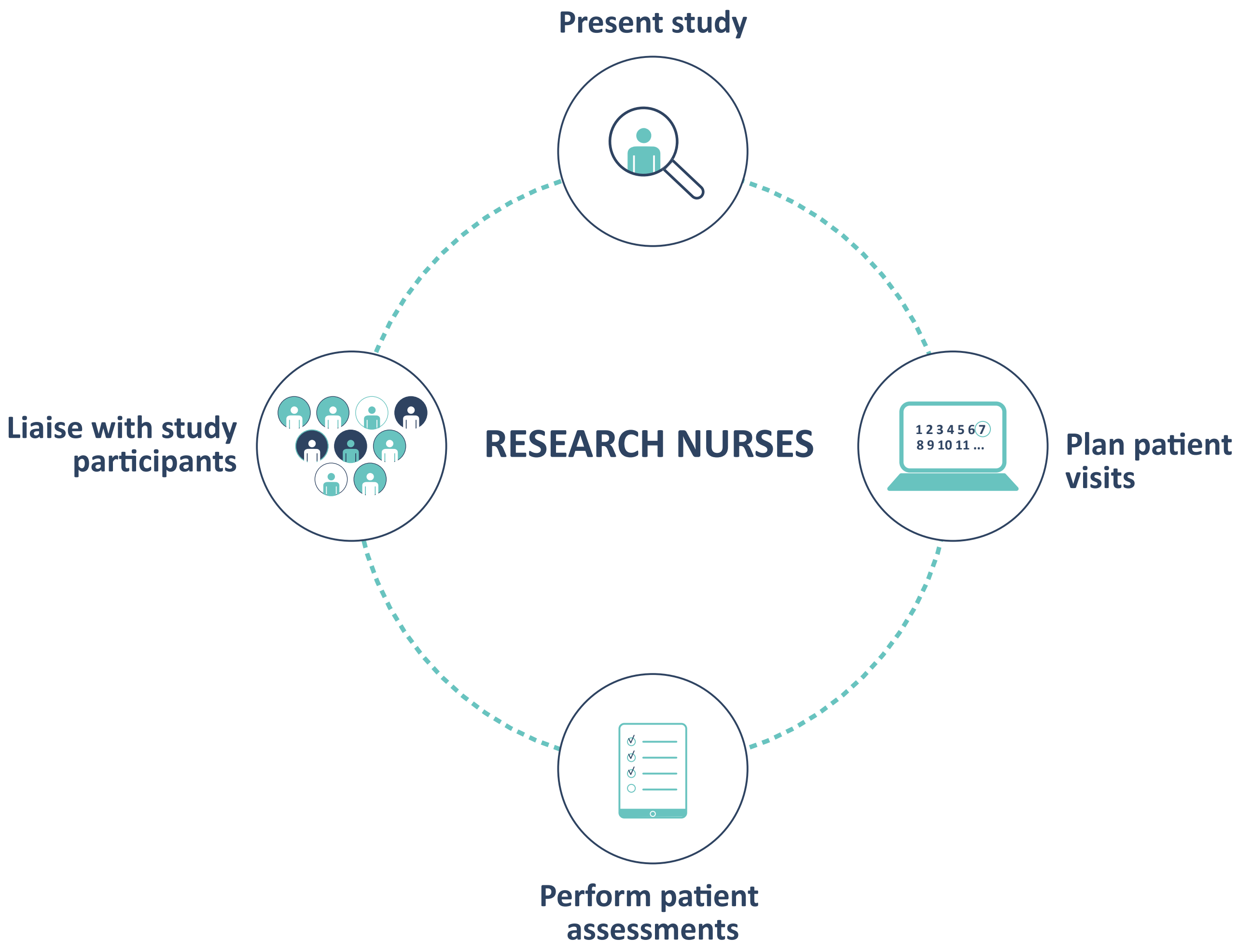
4.4 Research Nurse, Clinical Research Associate and Coordinator

Manon Gantenbein

Clinical research is an integral part of LIH activities. Its transversal and translational studies always aim to develop into clinical research projects, in order to bring tangible health benefits to patients sooner. This requires the contribution of highly qualified clinical trial specialists, such as the Clinical Research Coordinators (CRC) and Associates (CRA).

CRCs and CRAs have varied tasks on a daily basis. These can range from managing the clinical research team or the results of the study itself, to supervising authorisation procedures, finances, or administrative, regulatory and legal processes. Writing skills are frequently needed in this role, as CRAs and CRCs are tasked with submitting clinical trial proposals to the competent authorities and drafting the final reports and occasional manuscripts. They are also the main contact for industry, academia, hospitals and researchers and interact with any physician, public or private institution, interested in clinical research and developing a clinical research project.

The daily activities of the research nurses are more dedicated to the study participants and their follow-up. They include the presentation of the study to the participants, visit planning and execution of specific assessments under the guidance of the physician. Research nurses can devote more time to more precisely explain the objectives and scope of the study to the participants and have a privileged contact with the participants without however replacing the investigating physician.



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4.5 Data Protection Officer

Laurent Prévotat

By nature, precision health requires researchers, healthcare professionals and health tech companies to process a significant amount of personal data, including very sensitive information such as health and genetic data. The ability to protect the data of participants is a key factor for their enrolment in studies.

As the amount of data used in precision medicine increases, their security becomes one of the most important aspects as the impact of its misuse could have huge consequences on the data subject's life. It is therefore crucial that organisations involved in precision health activities ensure compliance with General Data Protection Legislation (GDPR) and consequently offer the necessary trust to every participant contributing to research activities.

One of the most important roles to achieve this goal belongs to the Data Protection Officer (DPO). DPOs are expected to be familiar with privacy laws and practices, IT, security, risk, as well as to have a deep understanding of the environment where they operate. The DPO should be able to work autonomously, to communicate effectively and guide other employees with a high level of independence and integrity.

Data protection laws demand significant efforts from organisations to ensure a high level of protection of the data that they are dealing with. The DPO's mission would be to help their organisation ensure that personal data are processed in a fair, secure and lawful manner.

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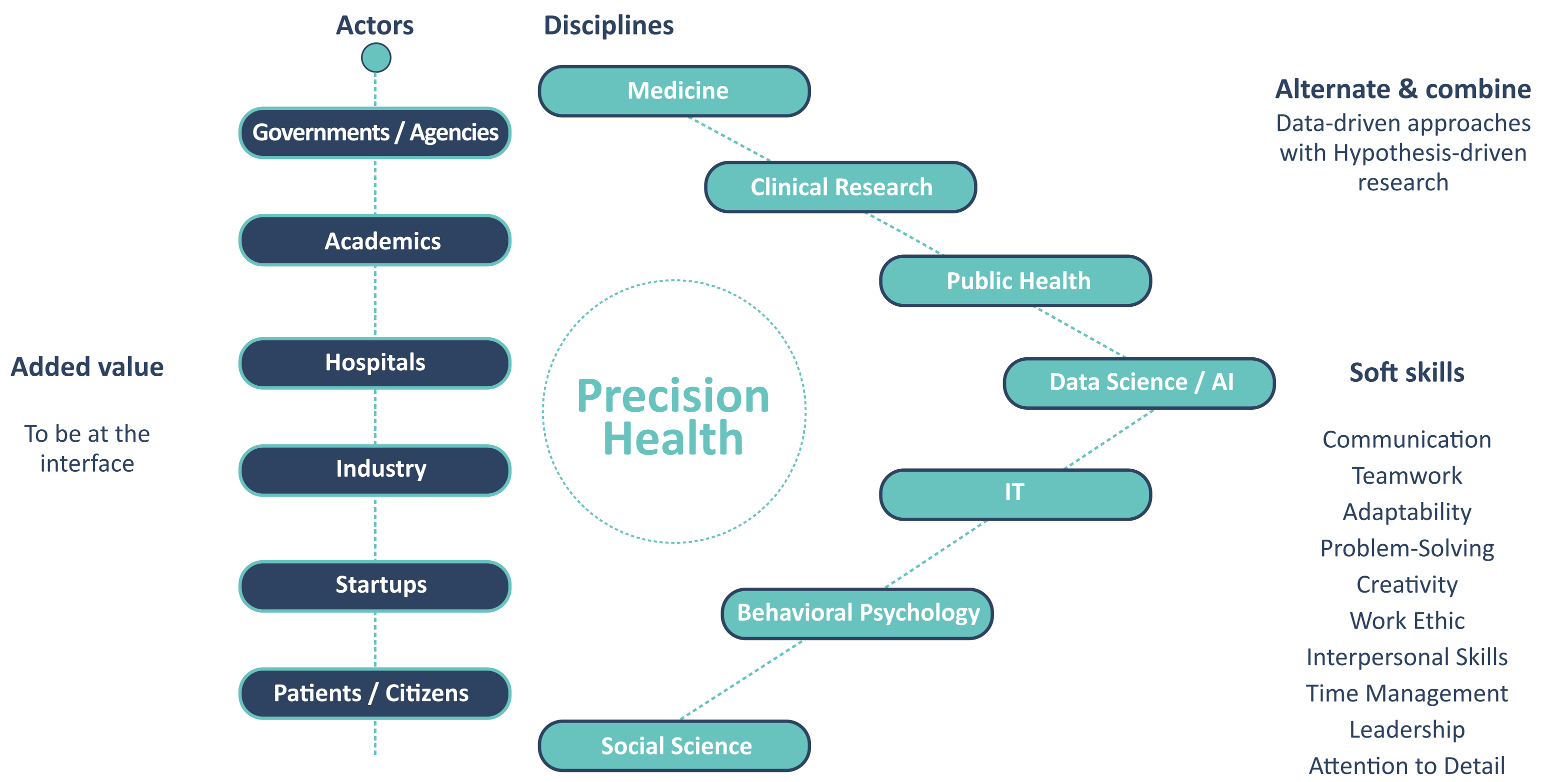
4.6 Researcher

Guy Fagherazzi

Being a researcher in the field of Precision Health starts with having an open mind. The future of healthcare is no longer only in the hands of medical doctors or healthcare professionals but will soon be based on a complex network of actors coming from different disciplines interacting with each other to offer the best possible healthcare.

Precision Health is essentially an intersection of different disciplines. So, by design, a researcher in Precision Health is a hybrid profile, who has simultaneously strong skills in one or more of the major health-related fields (such as medicine, clinical research, biology, epidemiology, public health, social science) and strong expertise in the processing and valorisation of data (such as AI, bioinformatics, data science, health IT, biostatistics...). These scientists can lead transdisciplinary research projects and are usually able to communicate easily with various stakeholders. As such, soft skills such as communication, teamwork, and creativity are probably as important as the hard skills needed for the research itself.

A researcher in Precision Health works to solve key problems to improve the health of patients or simplify their lives, with the help of large data analysis. They try to personalise their solutions to best fit with the characteristics of each patient. The use of digital data or technologies helps researchers in their tasks.



Researchers in Precision Health work at the interface of all healthcare actors and disciplines.
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4.7 The jobs we do not know yet

Guy Fagherazzi

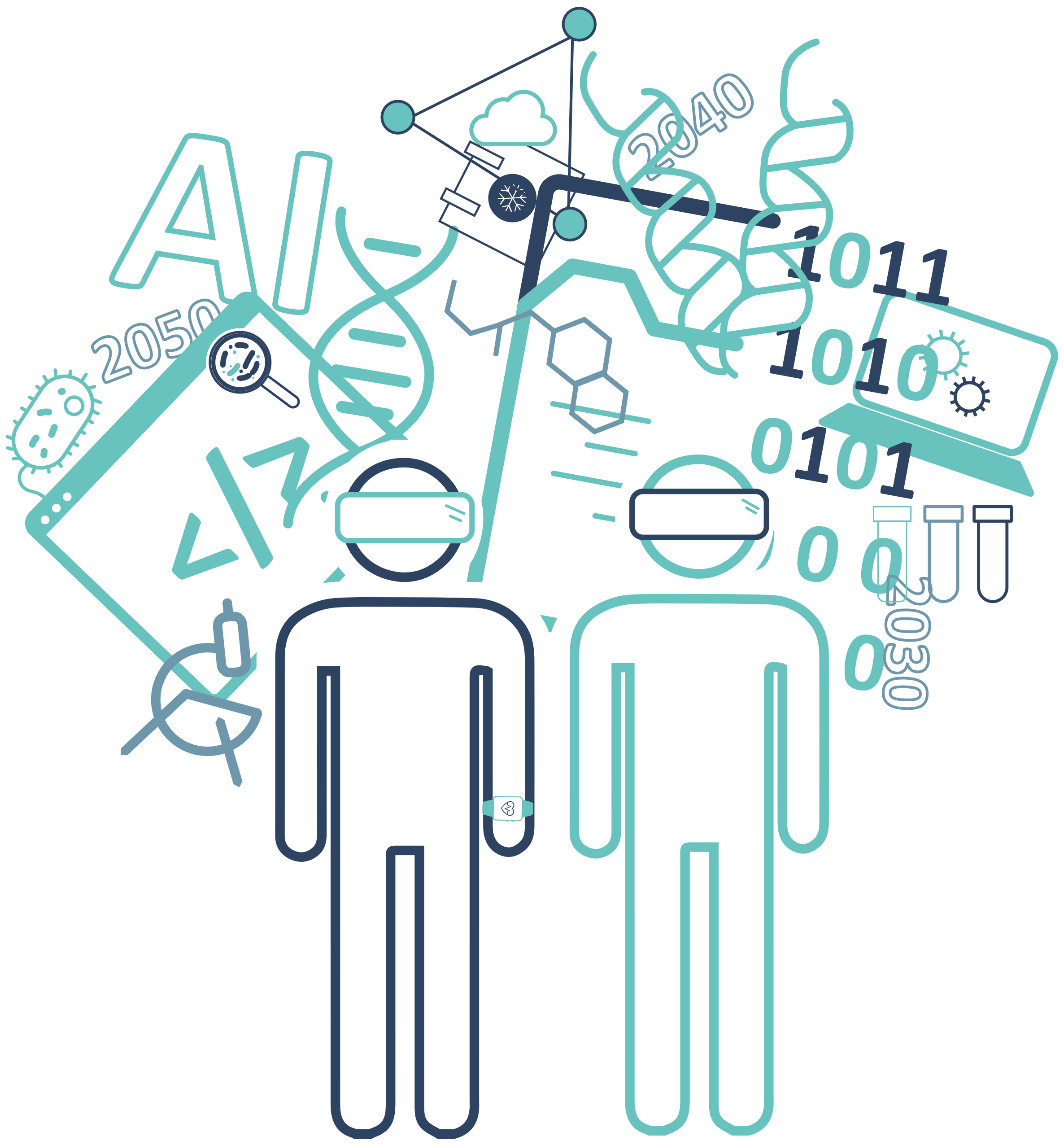
Health-related data are increasingly needed to guide care and prevention, and this tends to continuously create new types of jobs. It is often said that 85% of the jobs that there will be in 2030 are not known yet, so imagine in 2050 !

In the field of precision health, we will have augmented doctors, who will use technologies to enhance their clinical practice. We will have researchers who rely on AI and large data to discover new therapies, or biomarkers to facilitate the lives of millions of patients. Data managers, data stewards, data scientists, or data engineers will help them to manage, make available, process, analyse and use the data to improve healthcare.

We have seen in other chapters that AI algorithms can be very powerful, but also potentially dangerous if not used or validated properly. Besides, AI algorithms constantly evolve as new data arrives, so they will need to be regularly checked to make sure that they are still reliable and that they will not hurt the patients. For these tasks, experts in 'AI audit' will emerge in the coming years and will serve as independent, third-party guardians of the performances of an AI algorithm to ensure the safety of the patients.

The fields of robotics and virtual or augmented reality will also be very prominent in the future for health-related applications. These growing fields will automatically create new jobs that are just waiting to be invented.

With this book, we can only give you have a glimpse of the ways precision health will change the field of healthcare in the coming years. The rest is up to you.



The field of Precision Health is evolving rapidly, and so are its jobs. Perhaps the future holds the perfect job for you ?
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Glossary

- **Algorithm:** a set of instructions to be followed to solve a problem or calculation.
- **Artificial intelligence:** intelligence simulated by machines.
- **Autoimmune disease:** a condition where the immune system erroneously attacks healthy tissue, mistaking it as foreign.
- **Big Data:** a set of data, in this case relating to health, that is huge in volume.
- **Biological markers (biomarkers):** an objective measure of the well-being or illness of a person.
- **Biological sample:** a specimen (e.g. blood, urine, saliva, stool) collected from a person.
- **Chemical exposome:** anything humans are exposed to from birth to death, particularly relating to pollutants.
- **Deep-learning algorithm:** a type of machine learning which is inspired by our own brain’s neural network.
- **Deoxyribonucleic acid (DNA):** molecules inside the cells that contain all genetic information.
- **Digitalisation:** the conversion of data into a digital form that can be processed by a computer.
- **Digital twin:** a digital avatar of a physical entity (e.g. an organ, a person), virtually recreated, with similar elements and dynamics that enable the prediction of how it will perform in real life.
- **Genome:** all genetic information of an organism.
- **Gut-brain axis:** bidirectional communication between the central and the digestive nervous systems.
- **Infectious disease:** a disease caused by an pathogen such as a virus, bacteria, fungi or parasite.
- **Inflammation:** the body’s immune response to an irritant or pathogen.
- **Microbiome:** all microorganisms inhabiting a particular region of the body.
- **Neurodegenerative disease:** a disease that affects the central nervous system.
- **Non-coding RNAs:** an RNA molecule that is not translated into a protein.
- **Patient and public involvement (PPI):** research that is done with patients or by the patients themselves.
- **Patient-reported outcomes (PRO):** are information about a disease, which is provided directly by the patients themselves without any external interpretation, such as that from clinicians.
- **Precision health:** finding the best solution to prevent or delay the occurrence of diseases, and best improve the day-to-day lives of those living with an illness, according to each individual’s specificities.
- **Protein:** biomolecule composed of amino acids, essential for all biological functioning of cells.
- **Ribonucleic acid (RNA):** molecule essential for the regulation and expression of genes.
- **Telehealth:** the delivery of healthcare, health education, and health information services via remote technologies.
- **Telemedicine:** the use of technologies and telecommunication systems to administer healthcare to patients who are geographically separated from healthcare providers.
- **Translational research:** research aimed at ‘translating’ results from basic research into direct benefit to patients.
- **Vocal biomarker:** feature or a combination of features in the voice that has been associated with a disease or a symptom.

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This book and additional materials are available in English, German and French on a companion website: www.precisionhealth.lu