The use of genome information in health care: ethical, legal and societal issues

Report of the Issue framing workshop

Brussels, 23 February 2018

King Baudouin Foundation
Working together for a better society

sciensano

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COLOPHON

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CONTENTS

1. INTRODUCTION AND CONTEXT

WHEN DO I HAVE MY DNA CHECKED?

In recent years, genomics has become an important field in medicine. The technologies used to sequence our DNA have evolved significantly to the point where it is now possible to read and analyse a person's DNA with great accuracy at a reasonable price.

Many are convinced that the use of genome information in healthcare will save costs and enhance quality of care by improving diagnosis, identifying targeted treatments and opening up opportunities for screening and personalized prevention. They emphasize the opportunities that advances in genomic technology can deliver for clinical practice and public health: the dream of genomic medicine.

Today 'next generation sequencing' is already being increasingly used to identify disease-causing mutations in thousands of patients with rare or undiagnosed diseases and to guide the use of precision medication in cancer patients. There is a growing expectation that genome-sequencing technologies will be applied to a much wider range of clinical situations, bringing many more clinical improvements, from better prediction of personal disease risk (also in healthy individuals), avoidance of adverse effects of treatments, to improved treatment response. Eventually the use of genomic medicine could open doors to applications such as gene therapy, genome editing, or still other applications as yet unknown to us.

Others argue that there are many questions surrounding genomic medicine: not only technical and medical scientific questions, but also ethical, legal and societal issues. These could have a profound impact on health and healthcare. People need to be confident that genomic medicine works for their common benefit, with no exploitation, and with sufficient guarantees for the protection of their privacy.

Our healthcare system is founded on a set of values and principles that bind together patients, citizens, care providers, hospital staff, policymakers and many others. It is a kind of 'social contract', ensuring that the provision of (health) care is effective and equitable. This results in rights, but also obligations and responsibilities for all those involved. We need to understand how those rights and responsibilities work in an era of genomic medicine.

Genomics has the potential to revolutionize many areas of medicine, but it can also increase discrimination, inequality, the cost of healthcare or even change the concepts of sickness and disease. Moreover, in order for genomics to be useful, the DNA of as many people as possible needs to be examined and these results need to be shared within the scientific community. It is important now, at the beginning of this revolution, to consider how we want genomics to affect our healthcare and whether we need to review this social contract.

Genomic medicine is also one of the emerging technologies that could have a potentially disruptive impact on society. These technologies are increasingly being governed beyond the parameters of the nation-state. Moreover, only a small minority in the population understands the scope of the applications of genomic medicine and their impact on the individual and society. Therefore, genomic medicine also raises the question of what it means to be a citizen, both now and in future, in an increasingly globalized, technology-driven society.

These questions matter to all of us: policymakers, care providers, but certainly also patients and citizens. So, the first question is: When do I have my DNA checked? When do I find it useful? What do I want to know? What don't I want to know? Am I willing to share my DNA information? If so, under what conditions? Do I feel obliged to participate in genomic research, because one day, I might benefit from the results of this research? Is there such a thing as genomic citizenship?

So far, the perspectives of citizens on these topics have hardly been explored at all, either in Belgium or anywhere else in the world.

A CITIZENS' CONSULTATION IN BELGIUM

The Belgian Minister of Public Health asked the Sciensano Cancer Centre and the King Baudouin Foundation (KBS-FRB) to discuss these issues with citizens. Sciensano and KBS-FRB are therefore organizing the citizens' forum 'When do I have my DNA checked?'.

Thirty-two citizens, selected to form the most diverse possible group based on gender, age, and socioeconomic and professional background, will deliberate together over during three weekends (in September to December 2018). They will be well informed, since there will be targeted exchanges with experts, policymakers and other stakeholders.

A citizens' forum is a tried and tested method that has been proven to create and formulate balanced views and perspectives on 'wicked' societal challenges. It is based on well-informed, open discussion, reflection and deliberation rather than opinion polling. The goal is not to reach a consensus, but to explore the different perspectives that remain in society after well-informed deliberation.

The citizens will begin their deliberations by looking at real-life practical case studies. These case studies are just the starting point for candid learning and discussion: they inspire a critical attitude and trigger important questions and discussions. The case studies will be presented to the citizens in a booklet as an introduction to the citizens' forum.

After three weekends of hard work, the citizens will address their perspectives and recommendations to the relevant policymakers and stakeholders. As such, this initiative aims to generate relevant inputs into policymaking and the wider public debate.

THE BIGGER PICTURE

The citizens' forum 'When do I have my DNA checked?' is part of the broader Sciensano/KBS-FRB collaborative initiative 'Genome, health and citizens'. Recently KBS-FRB completed a similar project on reimbursements in health care: 'An agenda for change' (*www.citizensandhealthcare.be*).

The citizens' perspectives will be captured in a report that will be presented to various stakeholders at a workshop in early 2019. The results from this workshop, extensive analysis of the discussions during the weekends and an additional normative analysis will lead to a final report by the end of 2019. This report is meant to serve as a guide for policymakers in the area of genomics.

ISSUE FRAMING WORKSHOP

The project officially began in Brussels on 23 February 2018 with the issue framing workshop 'The use of genome information in health care: identifying and discussing the ethical, legal and societal issues (ELSI)'.

Over fifty Belgian experts, policymakers and stakeholders listened to experiences and examples put forward by experts from Belgium and other countries. In an interactive setting, they set the scene for discussion points, interesting case studies and problems to be addressed during the citizens' forum. Everyone had the opportunity to pinpoint the most imminent issues relating to genomic medicine in their everyday practice and to specify which questions absolutely should be deliberated on by citizens. The results from the issue framing workshop, which are reported in this document, then serve as an input for the citizens' forum.

2. GENOMIC MEDICINE – WHY, WHEN AND A NORMATIVE ELSI FRAMEWORK

This chapter integrates the presentations of Prof. Martina Cornel, Prof. Guido de Wert, Prof. Heidi Carmen Howard and Dr. Philippa Brice with contributions by Prof. Marc Abramowicz, Prof. Pascal Borry and Dr. Nancy Thiry.

FROM THE HUMAN GENOME PROJECT TO THE $1.000 GENOME

Around the year 2000, the first draft of the sequence of the human genome was published. It was framed as 'decoding the book of life – a milestone for humanity'. It was also expected that it would revolutionize the diagnosis, prevention, and treatment of most, if not all, human diseases. In 2007 an important technological step was taken with the introduction of next-generation sequencing to replace classical Sanger sequencing.

The price of sequencing plummeted: while the cost for sequencing the first human genome was $100 million or more, the threshold of $1,000 per genome is now within range, at least for the sequencing part. The analysis and interpretation part is still more expensive, and the counselling phase is not included in this price. Some authors therefore make a distinction between whole genome sequencing (WGS) and whole genome sequencing and analysis (WGSA).

GENOMIC MEDICINE IN THE PHASES OF LIFE

The aims of genome sequencing and analysis are directly related to research because there are still many gaps in our knowledge of the contributions of the genome to health and disease. In addition, the current aim of genomic medicine is certainly also to 'improve' pre- and postnatal diagnosis and screening.

This diagnosis and screening involves (routinely) offering a particular test, battery of tests or even whole-genome sequencing and analysis when there is no indication in the medical or familial background of the candidate. For the future, genome sequencing and analysis holds out the promise of personalised or tailored medicine, which may or may not include informed reproductive decision-making and offering of reproductive choices.

Patient diagnosis and patient care

Genomic medicine in patient care represents the simplest case. This type of genome testing is done in the presence of a specific indication. The most important situations are the ones where the patient is confronted with an unexplained disorder or with cancer. Ethical problems in this context are linked with incidental findings, informed consent and re-contacting the patient.

Incidental findings

Genome analysis will reveal numerous unexpected findings: these might have positive but also negative consequences for patients. This discussion is not new. It already existed for genetic tests and in other areas of medicine, but with genome analysis it happens on a much larger scale. There are many different types of incidental findings: some are 'actionable', meaning that the findings are helpful for prevention or treatment of the tested individual, while other incidental findings can be helpful for reproductive purposes and others might have an unclear or unknown impact.

An important ethical question relating to incidental findings is **the right to know**, but also **the right not-to-know**. The **autonomy** of the tested person needs to be respected in thi s context. The right not-to-know is enshrined in many European jurisdictions, but it is a so-called 'prima facie' right, meaning that it is an important right, but it is not absolute. There might be a conflict of duties towards the interests of third parties (i.e. children or other relatives).

What is the role of the medical professionals in this? Do they need to look further than the clinical question that was raised? What do patients want in this regard?

Informed consent

Informed consent is considered to be a prerequisite for any type of genetic testing. In practice, however, it becomes quite complex for broad testing in a genome analysis context. Many people in the field even doubt whether it is possible to obtain a truly valid informed consent, given the complexity of the information that is obtained as a result of a genome analysis.

We need to think about alternative models for informed consent, maybe more towards a generic consent or a flexible consent. This could mean that at first, people receive more basic, generic information and more detailed information is only then provided if they are a carrier of a particular genetic variant.

Re-contacting

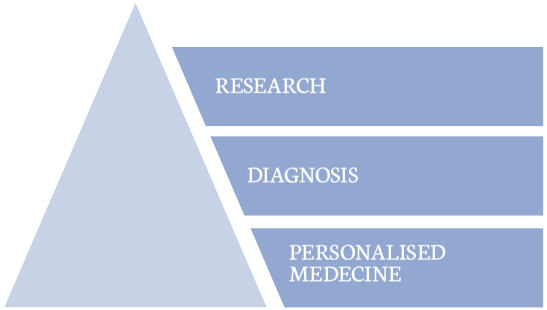
Re-contacting is another important ethical point. If people have a genetic variation whose meaning is unknown, and later on, after more research, it becomes clear what this variant might mean, does the physician/geneticist/laboratory have an obligation to re-contact the patient? The European Society of Human Genetics is preparing a document on this issue. In the Netherlands, the Dutch Health Council reached the provisional conclusion that re-contacting may be ethically sound if this information is necessary to solve the patient's clinical question and if it is **proportional** (if the benefits clearly outweigh the possible disadvantages).

Screening for non-reproductive purposes

In most Western countries, the criteria for screening are similar. They include that the screening should address an important health problem, the test should be of good quality, there should be pre-test and post-test counselling and respect for autonomy, the advantages should clearly outweigh the possible drawbacks of screening (proportionality), and the screening should fit within a **just distribution** of the scarce resources available for healthcare.

GENOMIC MEDECINE

AIMS



MEDICAL CONTEXTS

- PATIENT CARE (test on indication)
- NEWBORN SCREENING (heelprick)
- CASCADE SCREENING
- OPPORTUNISTIC SCREENING
- PRENATAL SCREENING
- PRECONCEPTION CARRIER SCREENING
- HEALTH RISK SCREENING (not on indication)

PROBLEM AREAS

- Storage of data and sampels and access
- Incidental finding (actionable, with reproductive impact, unknown meaning)
- Recontacting patients (obligation or not?)
- Informed consent (closed, open, dynamic, for non-competent persons, opting-out)
- Child's right - open future
- Obligation of proband to inform/activate participation among family members
- Blurring between testing and screening
- Reproductive choices and counselling
- Termination pergnancy
- Uncertainty predictive factors for late onset diseases
- Experimental treatments on fetusses
- Consensus on screened disorders
- Criteria for reproductive genetic screening
- Eugenic dream
- Genomic citizenship (for better future healthcare)
- Misuse of data by third parties (employer, insurance, advertising)
- Clinical relevance
- Quality of tests
- Proper counselling
- Uneven distribution of knowledge and use of genomics among patients
- Patient considered as a person (not the expression of his genes - biological reductionism)
- (National/regional) economic strategies
- Global technology
- Technology driven society

ELS ISSUES

- Autonomy (informed decision, the right to know, the right not to know, self-determination, open future)
- Proportionality (advantages outweigh disadvantages)
- Medical need/ just distribution of scarce sources
- Responsibility
- Consenting for others (minors, ...)
- Autonomy model (informed consent + non directive counseling)
- Informed decision making
- Unsubstantiated, high-risk clinical research
- Public trust in medicine and science
- Ownership
- Privacy
- Confidentiality
- Solidarity
- Commercialisation

Newborn screening

Newborn screening is probably the simplest case. So far, newborn screening (Guthrie test, heel prick) focuses on a range of treatable childhood conditions. Its use is accepted in most countries in the world. The aim of newborn screening is to achieve early diagnosis of treatable or manageable conditions to avoid irreparable damage to health.

The number of conditions tested is increasing all over the world because the number of treatable diseases is increasing, but each country decides for itself. Discussion and decision-making on a policy level also takes time. The Belgian regions and the Netherlands are screening for 10 to 20 conditions. The USA recommended uniform screening panel now consists of >50 conditions. In the direct-to-consumer market, tests can be bought that cover several hundred conditions.

A more complex problem is formed by conditions that occur later in life, but are already detectable in neonates. Examples are DNA variations that cause breast cancer at a young age or inherited variants increasing the risk of colon cancer (HNPCC – Lynch syndrome). In principle, medical interventions are available to mitigate these risks.

According to some ethicists, however, there are real ethical arguments against genome analysis in the context of newborn screening because it undermines the child's **right not-to-know (autonomy***)*. It prevents **self-determination** and an '**open future**', namely the possibility for the child, later on in life, to make up his/her own mind. Secondly it is unclear whether the possible benefits really do outweigh the harms (proportionality).

Cascade screening

If there is one person in a family with a genetic disease that has been confirmed (by genetic or genome testing), it is useful to also check other family members who are at risk. This is the principle of cascade screening. In the Netherlands, a long-term study on cascade screening for familial hypercholesterolemia has been running for many years. Cascade screening is usually carried out for treatable or preventable conditions. In general, there is a lot of support for cascade screening because it is proportional. Obviously, informed consent remains a prerequisite.

Nevertheless, one important element that needs to be addressed is family communication. It is important that relevant information should be disclosed within families in order to be able to consider the options. In a context of non-disclosure, very difficult situations already arise today. There are situations where medical professionals are bound by confidentiality, effectively tying their hands. In Australia, there is legislation that allows professionals to break **medical confidentiality**, in Belgium there is none.

Do individuals have a duty to tell to other family members about their risks? Should probands be penalised if they do not inform their relatives about relevant medical conditions for which they are at risk? France said yes. This is a far-reaching issue. How do you define this duty? Is it limited to first or second degree family members? Australia has said third degree. These are concrete topics that are important to reflect upon.

In the Netherlands, there is a tendency among ethicists, geneticists and policymakers to believe that under those circumstances (especially for preventable diseases) the proband (the patient who was first tested positively) not only has a **responsibility**, but even an **obligation** to participate actively in contacting his or her relatives in order to enable them to engage in preventive actions.

Opportunistic genomic screening

Opportunistic genomic screening means that laboratories performing clinical sequencing deliberately search for and report on a pre-determined list of incidental findings in addition to the results directly relevant to the initial reason for testing. The predetermined list of incidental findings includes conditions with onset in either childhood or adulthood, but for which the link between genetic variation and the increased risk of disease is scientifically and clinically sound and relevant.

The American College of Medical Genetics and Genomics is strongly in favour of opportunistic screening and advocates the screening of some 60 actionable variants as a 'package deal' (take it or leave it).

The question remains as to whether opportunistic screening is proportional. It blurs diagnosis and screening and the **coercive offer** is at odds with respect for autonomy. Should people at least have the choice to '**opt out**'?

Screening for reproductive purposes

Preconception carrier screening

Why wait until a child is born? Preconception carrier screening allows couples to know beforehand whether they carry functional mutations for the same genetic disease, increasing the risk of giving birth to a child with a recessive disorder.

Preconception carrier screening may be justified if it meets the criteria for reproductive genetic screening, particularly if respect for autonomy and proportionality are guaranteed. There are clear advantages of preconception carrier screening as compared to prenatal screening: for carrier couples, there is more time for reflection and informed decision making; additionally, there are more options, including prenatal diagnosis and termination if the fetus is affected. But they can also accept the risk and optimise the treatment, or they can choose for pre-implantation genetic diagnosis with embryo selection, the use of non-carrier sperm and/or oocytes, refrain from pregnancy, adopt a child or change partners.

Although technically feasible, people very seldom ask for carrier screening for recessive disorders unless a child with such a condition has already born. People are most often willing to become pregnant and give birth without too much medical intervention. 'Why would I want to know all my risks?', is their reasoning.

A relevant question is for which disorders preconception carrier screening should be made available, whether this should be limited to recessive disorders and/or to childhood disorders, and whether genetic variations for late onset diseases should also

be included (e.g. cancer genes, early-onset Alzheimer genes, the Huntington gene etc.). Other questions include who decides on the list of disorders and on the basis of which criteria.

Some ethnic groups have already been using preconception genetic screening for decades. A well-known example is Dor Yeshorim, an organisation based in New York offering genetic testing to help eliminate the possibility that two Jewish Ashkenazi carriers of the same genetic disease will start a relationship, leading to a risk of bearing a child with a fatal or debilitating genetic disorder.

Also in the area of testing, there are companies offering direct-to-consumer tests.

Prenatal testing and screening

Prenatal diagnostic testing must be distinguished from prenatal screening. Testing is done if a previous child or relative is affected. As a result, testing is usually more targeted: geneticists will search for a specific genetic variation in an unborn child who is at increased risk of having a disorder. Prenatal screening, on the other hand, applies to all pregnant women and may, in future, cover many conditions.

A debate in genome analysis for prenatal screening is currently focussing on the non-invasive prenatal (NIP) test used for detecting Down's syndrome (trisomy 21). The screening is not only contested from a 'pro-life' perspective, but also from the perspective of certain patient organisations. Nevertheless, there is a strong consensus in many countries that prenatal screening for Down's syndrome is justified, if – and this is crucial - it meets the criteria linked to the **autonomy model**, meaning that informed consent is important and that **non-directive counselling** is provided.

Concerning the NIP test and the use of genome analysis on a 'genome-wide scale' to screen for more genetic variants other than Down's syndrome or other gross chromosomal anomalies, the ESHG advocated against implementing genome analysis in this context. They argued that it would be totally impossible to inform pregnant women about the implications of this complex testing method. Additionally, the test would result in a huge number of predictive risk factors for late-onset diseases. It would undermine **informed decision-making**, rather than facilitate it.

There is a second angle on the NIP test. It provides an opportunity for (fetal) personalised medicine. NIP tests may identify risk factors for a whole range of pregnancy complications and fetal conditions that may be prevented or treated in utero, including premature delivery, pre-eclampsia or maybe even Down's syndrome. However, fetal research remains highly experimental and it may lead to therapeutic misconception. Lay people may wrongly assume that experimental interventions have a proven medical value. That may be the case later, but at present it is not.

We need an ethics on fetal research that balances the interests of both future children and pregnant women, and takes into account the possible risks of well-intended in utero interventions for pregnant women.

Susceptibility screening

The 'current' role of genomic medicine is basically limited to the previous chapters, in the opinion of many (European) genetic ethicists and geneticists. In current genomic medicine, the focus is on so-called highly penetrant genetic changes. Most often these changes cause a rare disease. In the past it was often hard to diagnose rare diseases, simply because of the rareness of the disease. It was some time before the patient encountered a competent specialist who recognised the symptoms and ordered the correct tests to confirm the diagnosis.

With the new technologies of next generation sequencing, which allows whole exome or even whole genome sequencing and analysis, this diagnostic problem can be solved for many people, and there is ample evidence in the scientific literature that we are gaining years of health and saving public money by doing genome analysis as a first step in people with diseases of this kind.

What is 'not current' is finding genetic susceptibility genes for common disorders in individuals. Diseases such as heart disease, diabetes, psychiatric disorders etc. are caused by a combination of genetic factors and the environment. For these diseases we have no evidence today that genome analysis can support diagnosis at the individual level. As soon as knowledge of the human genome and its impact on diseases increases, however, there is a chance – and the opinion among experts differs – that we will be able to use genome information for diagnostic, predictive and prognostic purposes for more common diseases. People will realise that they can get information from their genome to know more about their risks of having these diseases. Unlike with rare diseases, however, the relationship between their genetic constitution and the disease is much more complex, and people need to understand the complex nature of genomic information in order to integrate it correctly in their health choices.

There is a responsibility for governments to provide genomic tests of high quality in the contexts where the benefits of these tests outweigh the downsides. The question is whether governments should, at the same time, make sure that genomic and clinical data of patients are protected.

In the future, everybody will have access to his or her genome. It will be cheaper, it will be offered, and we will see apps on smartphones that give 'some kind of interpretation' – hopefully scientifically correct and with clinical useful interpretations - of a person's genome data. Some people will have rapid access to these applications and will use it, but other people will not. We need to anticipate what the era of genomics and other forms of big data will bring us, and how these data will be used. Also, citizens who are not accessing these technologies should be included in the healthcare system on an equal basis and should not become **second-class citizens**.

In conclusion, genomic analysis and especially whole-genome-sequencing-and-analysis seems to be at odds with the accepted criteria for screening. This applies in all types of screening and it is, at least for the time being, disproportional. It is premature. But whole-genome-sequencing combined with targeted analysis may have added value in many types of testing and even screening. The criteria for targeting require ethical and societal scrutiny, taking different contexts into account.

Lay public opinions and views in genomics:
'Your DNA, your say' and the SIENNA Project

Prof. Heidi Howard from the Centre for Research Ethics & Bioethics at Uppsala University shared insights from two projects aiming to obtain lay publics' views on genomics.

'You DNA, Your Say' *is an online survey consisting of 25 questions geared towards capturing the public's attitudes on sharing medical and genetic information. Nine films accompany each section of the survey to explain what everything means (e.g. 'biobank', 'medical information', 'data sharing', etc.). The survey and the films will be translated into 15 languages. Everyone can fill out the online survey, but in several countries, active recruitment strategies were employed to find 1000-1500 participants per region.*

www.surveys.genomethics.org

Although data gathering and analysis are still in progress, Prof. Howard already shared some interesting data: among the general public in the UK, 42% of people are prepared to donate their DNA and medical data for use by medical doctors, 38% for use by non-profit research centres, and 18% for use by for-profit organizations.

SIENNA *is a project, funded by the European Commission, which aims to examine the ELSI of genomics, AI/robotics and human enhancement. The methods are the same for each subject and the issues will be studied in parallel. 11,000 people from 11 countries will be questioned over the phone about the awareness and societal acceptance of these technologies. Additionally, one-day citizen panels will be organized in five countries with each time 40 participants about their views on the ethical issues.*

http://www.sienna-project.eu

Prof. Howard went on to focus on the methodological aspects of involving lay publics' perspectives in genomics. She stressed the importance of reflexivity in a process like a citizens' forum, since it is easy to miss some bias creeping into their views. For example, the mere act of inviting citizens to discuss these issues for three whole weekends implies that these are important issues. It is important to counter established bias and leave space for different ways of thinking: diversity and nuance are core concepts, both during the citizens' forums and during the analysis.

Genomics, health and policy in the UK

Dr. Philippa Brice from the Public Health Genomics (PHG) Foundation in the UK talked about policymaking in the area of genomics. The UK is making considerable efforts to transform the national health care system to incorporate personalized medicine. In 2012, the 100,000 genomes project was launched (www.genomicsengland.co.uk). This project aims to combine genome analysis with longitudinal health records and phenotypic information. The public is being involved in the ELSI aspects of the project, but Dr. Brice indicated that these efforts might be construed as an effort to convince the public of the benefits of genomics, rather than a genuine interest in their perspectives.

Dr. Brice focused on genomics as a rapidly changing field. Today's truths may be overruled tomorrow. This has a profound impact on the issues that patients, families, doctors and society face. We need fluent policy making – tools and policies capable of dealing with these rapid changes - in areas like data management, data sharing, confidentiality and informed consent.

On the subject of genomic citizenship, Dr. Brice focused on the questions for individuals: Will individuals accept genomic data sharing for direct medical benefit of family members; for direct medical benefit of others; for medical research (public/private sector); for the wider public good?

PUBLIC TRUST IN GENOMIC MEDICINE

Micro-questions with macro-impact

The evolution from genetic testing to genomic medicine triggers a complete set of questions with potentially macro-level implications. It is important to realise that what seems, at first sight, to be a very small, detailed, even technical question - like the list of diseases for which tests will be offered in the contexts of prenatal or preconception carrier screening – is immediately linked to much bigger societal debates about disability, **human rights, diversity** and **eugenics**. These are inherently connected to the tension between the preventive logic in public health and individual reproductive and health choices. These logics often collide. Framing the exact issues in the specific contexts in which genomic analysis will be used, and their consequences, is therefore not easy.

Technology is never neutral. Offering a technology has societal implications that are often very difficult to anticipate. A certain test at a certain moment can easily become a **societal norm**, something that people are expected to do, so that they are consequently expected to take the logical steps if a test result turns out to be unfavourable. Are we as a society prepared to keep other options and choices open? Is there the danger of a commercial push that being screened becomes the norm? We need to ask ourselves whether this is a desirable evolution or not.

From genetics to genomic medicine

The context has changed. During the days of genetic testing, 15 years ago, many of

the questions asked were reflective, prospective and even hypothetical. Today, they have become pressing. Although many questions are similar, things change when they become a reality. For example, preconception carrier testing was already happening 15 years ago, but we were talking about one condition. Now carrier screening can encompass hundreds or even thousands of conditions, in one simultaneous test. The scope of the discussion has changed.

The issues about data sharing and privacy were already discussed during the implementation of the human genome project, but the speed with which data are generated nowadays, and also the number of individuals participating worldwide in genome testing and analysis, have exploded. The framework and context have become completely different.

The issue about family communication is in essence an old problem, but it has been limited to a minority of families. These days, and certainly in the future, communication within families about genetic risks will become an issue in the majority of families, and maybe even in every family.

Education

The public should not only be educated about genetics but also about the ethical, legal and social issues involved. The same holds true for geneticists, professionals, experts and others, who need to be educated about ELSI aspects as well. It has been described many times in the scientific literature that medical professionals are sometimes rather naïve – e.g. they have wrong premises - about what people want to know and what people can handle.

Genetic research and biobanks

The first aim of genome analysis is research. In the future, we might see the results of this research being turned into true personalised medicine in many ways, but only when genomic data and health from many thousands of patients and healthy individuals can be pooled. This means that the ethics of research and the ethics of biobanking (banking data and samples) will become crucial.

Traditionally, the ethics of biobanks was focused on autonomy issues (self-determination) and privacy issues. Now one might argue that **solidarity** could become an important value in this context with some reciprocity: if I may profit from the evolution of scientific knowledge through genome analysis, maybe I have a **responsibility** to contribute to this progress too. One might call this a form of **genomic citizenship**.

Societal repercussions: privacy and solidarity

The question concerns how to balance this vision on genomic solidarity and genomic citizenship with the privacy issues. We cannot expect people to contribute to research if they cannot **trust** that their personal data are safe, that some form of **anonymity** is guaranteed, that their **privacy** is not harmed.

For-profit organisations, like biotech and pharma companies, also wish to access the genome data of both healthy and sick individuals, together with their phenotypic data. Crossing genome data with clinical and phenotypic data may be useful for developing new drugs, new tests, but it can also be used by insurance companies or even employers to stratify risks. When it comes to genomic medicine, scientific stakes are clearly mixed with economic and industrial stakes.

To illustrate the value of these combined data, some enterprises have offered genomic analyses almost free of charge in the past, on the condition that people also fill in inquiries about their health. It is clear that these companies can easily monetise that information. Less visible, but even riskier, are the situations where genomic companies combine the genomic data of the persons who have been tested with the data that these people place on social media or with health and lifestyle data that are transferred via all kinds of health apps.

One should therefore take into account the possible misuse of genetic information by third parties, especially private insurance companies and employers. Adequate regulation is needed in order to protect the interests of all stakeholders in a balanced way. The main question is how this can be made to work in practice.

Finding balance

The issue of privacy is an important element, but if we protect data too much, research is no longer possible because the data are not useful. We need to find a balance with systems of controlled access, but also with shared information of clinical variants. Labs and research groups should have an obligation to share this information, which they are not doing today. Patients should be aware that genotype and phenotype data can be shared, for their own benefit, for the benefit of their family members, but also for the benefit of future patients. Although we need to have safeguards concerning privacy, we should not make interaction between scientists and clinicians impossible by applying regulation that is excessively strict.

There is a feeling among many researchers that ethical boards and review committees of hospitals and universities are currently no longer favouring (not-for-profit) research because of their strict interpretation of the ethical and legal frameworks. We need to reassess how strict we want to be with the ethical criteria for research in medicine. Practical research considerations need to be taken into account, and research ethics committees should not become autocatalytic, rendering research impossible.

Personalised & patient centred medicine

Is identity embedded in nature (the genome) or in nurture (education and environment)? This has been a subject of debate for many decades and some consider that there seems to be a growing tendency to emphasize the role of nature. Especially young people seem to believe that their identity is in their genes. That may also be the reason why they consider genomic information to be so important.

The whole concept of genomic medicine is very often used in a very reductionist way. What are the relationships between personalised medicine and the traditional ethical and philosophical notion of the **patient as a person**, including the concepts of shared decision-making and autonomy? Healthcare is not only about biomarkers, but first of all about people's interests and moral and legal rights.

There is also a trend to stress personal responsibility in health, particularly when this is used in a retrospective way. If patients are suffering from a disease related to their unhealthy lifestyle, there is a societal trend to declare these people guilty, as if it were their own fault or responsibility.

This vision might have serious implications for **solidarity**, one of the pillars of our healthcare system. Moreover, the assumption that people who live an unhealthy lifestyle are willingly and voluntarily choosing that lifestyle may be an unacceptable premise.

A new social contract

Our healthcare system is founded on a set of values and principles that bind together patients, citizens, care providers, hospital staff, policymakers and many others. It is a kind of a 'social contract' ensuring that the provision of (health) care is effective and equitable. This gives rise to rights, but also obligations and responsibilities for all involved. It is important that now, at the beginning of this revolution, we should consider how we want genomics to affect our healthcare and whether we need to review this social contract.

Genomic medicine also represents one of those emerging technologies with potential to have a vast impact on society and which is increasingly governed beyond the borders of the nation-state. As a new technology, genomic medicine raises the question of what it means to be a citizen both now and in future, in an increasingly globalised, technology-driven society.

3. GENOMIC MEDICINE – PERSPECTIVES FROM STAKEHOLDERS

This chapter integrates the results from the subgroup discussions, the panel discussion and the concluding plenary discussion (see also addendum 1).

GENOMICS AND ME (AND MY UNBORN CHILD)

Capturing genomic literacy and genomic value assessment

Many of the stakeholders fear that the knowledge and understanding of genomics among lay people/citizens is low, or may even be non-existent. Thus, it will be hard for citizens – certainly at the beginning of the citizens' forum - to assess the impact of genomic testing on their own health, the healthcare system and society. It was therefore suggested to capture, both at the start of the forum and also during the course of the forum, their understanding and appreciation of the role of genomics in their own lives.

How do citizens imagine living with genomics in their daily life? What place do they give genomics in their lives? Could it be important for them, now or later? Does genomics change their perspectives on life, on health, on their relationships with relatives and society?
What are their hopes and fears concerning genomic testing? What are their expectations? How does genomics compare to other health problems and health care related issues?
Which parts of genomics do they understand, and which do they not?

Information needs

There are different levels of information provision to people who have their genome screened or could potentially have it screened. The first is at the individual level of the person taking a test. In that situation the information provided should be more clinically oriented and focused on the questions/needs of the specific individual. This is all about proper counselling.

The second level of information provision is at the level of the population. This comes closer to raising awareness and public education.

Information provided to the individual patient should be adapted to his/her specific informational needs and desires. These needs can differ significantly between individuals, depending on the personal situation, capabilities and competences. Clinicians / counsellors often overestimate the health literacy of their patients and are not always aware of the influence of social/economic, ethnic/cultural and educational backgrounds on individual choices. Therefore, a much more patient-centred approach to counselling is needed.

On the other hand, it remains unclear what the information needs of individuals are in different genomic test contexts, but also what the needs of the general public are.

What information does an individual need in order to make a well-informed decision about having his/her genome being analysed in different contexts?
Who is best placed to counsel the person who is going to be tested/has been tested and who is able to properly interpret the results? How should such counselling be organised?
How should the public/the population be informed about tests based on genome analysis? Do we inform everybody about everything or nobody about anything? Or how can we find the happy medium?
Who should have a role in increasing genomic literacy and genomic education?

Different contexts, different questions

The questions, answers and choices, however, are different in different contexts. Citizens may discuss and decide differently on the same question in a context of preconception screening vs. prenatal screening vs. adult screening for risk factors. Also individual contextual factors might lead to divergent opinions: for people who have a relative in their family with a serious genetic disease, the questions and answers might be quite different compared to others.

Should we apply one set of criteria for the various possible screening contexts (preconception screening, prenatal screening, neonatal screening, cascade screening etc.) or should we adapt the criteria according to the context?

Preconception and prenatal testing

Several of the subgroups focussed their discussions on questions regarding information provision during preconception and prenatal testing. They emphasized that one of the problems with the NIP test is information provision and how to present this information to the expectant mother and her partner. But we also need to ask how we can take cultural differences and diversity into account.

What kind of information about genetic diseases and genomic tests would you (and your partner) want to know before you start a pregnancy?
What kind of information about genetic diseases and genomic tests would you (and your partner) want to know during a pregnancy when there is no prior indication in your family of the presence a genetic disease?
Should you just be generally informed about pregnancies or do you want to be informed about the possibilities of genomic medicine?
Who should inform you / has the obligation to inform you (your general practitioner, gynaecologist, other specialists or maternity workers) about preconception and prenatal tests? Or is more general information via brochures, a website, tutorials on Youtube, *etc. sufficient?*

Maybe unexpectedly, it was also argued that the NIP test has turned out to be an opportunity for public education and raising awareness. For many young people it is the first time they come in direct contact with genetics and genomics. Therefore, one of the biggest advantages of the NIP test is its educational and awareness-raising potential. It helps in increasing genomic literacy among the generation of young adults. Also the media attention concerning the NIP test has increased awareness about informed decision-making before and during pregnancy.

Incidental findings

Unintentionally discovered, but clinically relevant genomic variants (for previously undiagnosed conditions) are being encountered more commonly since the introduction of genome sequencing and analysis. Incidental findings have already become a reality in current genetic and prenatal testing. The NIP test, for example, has already led to unintentionally discovered findings in mother and child.

While the focus of the NIP test is to screen for the presence of certain trisomies, the possible detection of incidental findings is already included in the informed consent used by some Belgian centres offering the test (i.e. the Belgian academic centres).

The question remains, however: to what extent is it clear to lay people what an incidental finding is? And to what extent do people want to be informed about such findings?

What do citizens understand by 'incidental findings'?
What kind of information do citizens want to receive from a test? Only the specific outcomes for which the test was performed or do they also want to be informed of incidental findings? Which type of incidental findings do they want to be informed about: all, only the ones with clinical relevance or only actionable findings?
Should the clinician discuss upfront with the person being tested about how to deal with incidental findings?
Can we expect lay people / patients / persons to have a well informed opinion about this?

If people do not want to know about incidental findings, one pragmatic solution might be that they should refrain from having their genome sequenced in all contexts. As soon as a genome is sequenced, and incidental findings with clinical consequences are found, professionals might have the obligation (in some countries already legally laid down or because of moral duty) to report on those findings to the patient.
Refraining from genomic testing is at least the solution that was brought forward in a number of screening programmes that are currently running in various countries.

Dealing with uncertainty

Another issue is how people would deal with uncertainty if the results of a genomic screening were ambiguous, i.e. when the results relate to a mild or even uncertain increase or lowering of their susceptibility to specific diseases, but not to clear-cut and / or actionable findings.

People being tested might be unduly concerned about their health situation, seeking unnecessary medical follow-up and treatments. This places a needless psychological burden on patients and their families and also stresses the healthcare budget.

Is this a matter for the discretion of the professional? Should he/she decide about what results should or should not be communicated? Is it the professional who should limit him/herself, when communicating, to actionable findings or to medically relevant findings, or should he/she communicate everything? Or should professional guidelines be drawn up to deal with these issues? Or should an expert commission decide on possible criteria?

How do lay people deal with inconclusive predictive test results?
Should the clinician decide what information about incidental findings he/she will give to the person who has been tested?
Should a review commission decide on criteria for incidental findings, i.e. on which incidental findings clinicians need to report to the persons being tested?
How should we avoid genomic testing leading to over-diagnosis and consequently over-treatment and undue concern?

The question is also raised here of which professional should inform the patient about the results of his/her genomic screening? It cannot be the geneticists or the genetic counsellors, because there aren't enough of them in Belgium or even in Europe to provide counselling to everyone. Can general practitioners have a role in this, do we need new intermediate professionals, or can new communication technologies in the form of apps, websites, or maybe even online professionals be of help?

Informed consent

Many of the above issues are dealt with in the informed consent. The design and content of the informed consent process is very much linked to the type of information that a patient needs and wants. The patient needs to understand the information and the consequences of the consent he/she has given. We may have to admit that the ideal, comprehensive informed consent does not exist in the context of genomic sequencing and analysis.

In an optimal but still feasible scenario, the clinician gives the patient information adapted to his/her needs and desires. Afterwards, a counsellor should check whether the patient has in fact understood the terms of the informed consent.

Currently it seems that informed consents are becoming more and more complex. People no longer understand the terms and conditions in the informed consent and are less and less willing to agree, due to the complexity. Different forms are also used in different hospitals. This impedes the process of building trust with patients and the public.

How can an information and consent process be designed and informed consent documents be developed that can be understood by the person who is signing up for a genetic test or genome analysis?

GENOMICS AND MY FAMILY

Neonatal screening

There are currently 11 diseases for which neonatal screening is performed in Belgium. This screening is not yet based on genome sequencing and analysis, but on biochemical and metabolic tests. Only the recently added test for cystic fibrosis is DNA based.

However, there are companies already offering screening for several hundred diseases based on genome analysis. In many countries there is debate on whether the public healthcare sector should follow this tendency and extend the number of diseases for which screening is provided and/or adapt technologies and offer (full) genome screening to every newborn.

What do citizens consider a severe disease for which neonates can/should be screened?
How do we define a severe disease in the context of screening? What are the criteria?
How to decide and who decides on the criteria?
What is, according to citizens, the balance between the benefits and drawbacks of having the genome of every newborn child sequenced and analysed?

Communication with relatives

Genomics brings about shifts in the distribution of responsibilities for health at different levels: for a person's own health, but also for the health of relatives, and even for future generations. If a genomic analysis uncovers a clinically relevant genetic variation in a person, his or her family members might also carry this variant. To what extent does the person who has been tested, have a (moral) obligation to inform his/her relatives about such test results?

If the proband fails to comply with his role to inform his/her relatives, does the information responsibility shift to the clinician, the genetic practitioner or the organisation that conducted the genome analysis?

Many of these questions do not specifically relate to genomic medicine or genomic sequencing and analysis. Genetic testing already raised these questions in its early days, but with a broader roll-out of genome analysis, the problem becomes much more widespread.

How should clinically relevant results from genome sequencing and analysis be communicated between family members?
Do relatives have the 'right to be informed' when a (serious) disease can be avoided? Should this be an enforceable right?
How can the 'right not-to-know' be safeguarded for family members?
What is the amount of information that family members need to be given in this respect?
What possible shifts in the distribution of responsibilities towards health professionals does genomic medicine bring about?

GENOMICS AND SOCIETY

Reimbursement

Reimbursement for genetic testing and genome analysis is strictly regulated in Belgium. However, the number and types of reimbursed tests is increasing: recent additions include, amongst others, specific cancer tests and the NIP test. Stakeholders formulated several questions about reimbursement for genomic analysis to be put to citizens:

Should reimbursement for genomic testing be given as a priority to specific patient groups and/or specific contexts? What criteria should be used for prioritisation? Who should decide on the criteria?

In principle, a genome needs to be sequenced only once. But it might be necessary to reanalyse the raw sequencing data at regular intervals as genomic research is continuously leading to new insights, which may be clinically relevant for the individual.

Is regular reanalysis of genome information desirable? Should results be communicated to the person whose genome was sequenced? If this person has died, should the information be communicated to his/her relatives? Who should organise this? Who should fund this?

Right 'not-to-know' and social pressure

When a new technology becomes available to exclude certain risks, the majority of people will use that technology and only a minority will not. As time goes by, the pressure of the majority will increase. It might be seen as 'a normal choice in life' to make use of the technology in order to mitigate the associated risk.

It remains to be seen how such societal mechanisms will operate in the case of genomic screening. In the immediate future, extended genome sequencing and analysis, not directed to specific diseases, does not limit risks. On the contrary, it will give people information about more risks. However, this will change as knowledge on the impact of the genome on health and disease increases. So in the long term, the societal pressure on an individual, a couple or a pregnant woman to make use of genome tests might increase.

However, in the current legislation on patient rights, there is the explicit formulation of the right 'not-to-know'. The question can be raised whether it is possible to escape from the coming tsunami of genomic information. People, who do not make use of the technology, might run the risk of being called irresponsible. They are even at risk of being held responsible and accountable for their choice. Therefore, some stakeholders propose to revise and reformulate the right-not-to-know in the context of genomic sequencing and analysis. The forum is an opportunity to discuss this with citizens.

Social pressure may already exist in the case of the NIP test, several participants argued. Some people regard parents who refuse the NIP test as irresponsible parents. The argument is that they might give birth to a child with a genetic disease who will make above-average use of the healthcare system.

This relates to potentially conflicting interests between public health, on the one hand, and personal choice, on the other. When the government reimburses a test, which was the case for the NIP test, it creates a public attitude that participating in the test is obvious and indisputable. Reimbursement therefore influences the choices that people make. This can reinforce the issue of public pressure on individuals.

In conclusion, safeguarding the 'right-not-to-know' and 'the right not to take a test' is not only about anchoring this right in the law and the regulation, but it is also about public perception and social pressure, which are two very powerful mechanisms.

A powerful instrument to counter such social pressure is non-directive counselling, a modern cornerstone in clinical practice and in the professional-patient/client relationship. Non-directive counselling is about listening, supporting, informing and advising the person who is taking a test, without directing that person's course of action. A prerequisite is of course that all professionals involved in genomic testing and screening are trained in non-directive counselling.

All this has to do with solidarity, one participant argues: it is about the societal acceptance of people not taking a test, acceptance of people having children with a disability, acceptance of people with a disability, and the willingness to care for them and to integrate them. These are very conceptual questions. But they go to the essence of the relationship between society and genetic-genome testing, as some philosophers and health professionals have argued in the past that people have a moral responsibility to (genetically) enhance their offspring.

To what extent does genomic medicine put the right not-to-know under pressure? Does this right need to be revised in the context of genomic medicine? If so, how should it be revised?
How can the right to know be balanced with the right not-to-know in an era of genomic medicine?
Will it be possible to escape from the obligation to be informed?
Do people have a moral responsibility to enhance their offspring?

Genomic citizenship: sharing data

Many consider genomic medicine a threat to solidarity, but could it also be a way to strengthen solidarity? The current contribution of citizens to the healthcare system is mainly financial, through the taxes, social security or insurance premiums they pay. In the era of genomic medicine one can contribute something else: data. These data, if pooled with data from other people, might be vital for health research and for building a better healthcare system. In a way, one could state that genome and health data can be 'mutualised'. It is like a new currency being added to the solidarity-based healthcare system. This view might open up new perspectives. It is a form of 'genomic citizenship' and a type of 'new social contract' in healthcare.

As in the case of financial contributions to the healthcare system, there is also a form of reciprocity associated with sharing one's genomic data: one day, the donor might profit from the advances made in research and improved care.

Do citizens find it an appealing idea to share genomic, environmental and lifestyle data in exchange for partnerships and engagement in research to further advance individual and public health?
Do citizens feel any responsibility to share their own genomic data for the wider public good?
What might 'genomic citizenship' mean to the citizen?

Genomic citizenship is all about sharing data. This raises many questions on ownership of data, protection of privacy, medical confidentiality, and regulation of access. These were major discussion topics in all subgroups and also during the debates in plenary sessions.

It is clear that these issues must also be thoroughly discussed by the citizens. But before going into the details of each of these topics, it might be interesting to capture more general ideas about genomic data sharing:

What do citizens see as advantages of sharing data for purposes beyond individual medical aspects?
What do citizens see as dangers and implications of the transfer of genomic information and health information to third parties?
What information do citizens need to be able to discuss all aspects on genome data sharing on a well-informed basis?

Ownership

Concerning the ownership of the genomic data, it was proposed that the distinction should be made between the 'raw' sequencing data and the results of the genomic analyses.

One participant could imagine two different scenarios in dealing with ownership: in the first scenario the genome is sequenced and the raw data are given (via a CD, memory stick or even an addendum to his/her medical record) to the person whose DNA was sequenced. He/she remains the owner of the raw data. One could imagine that the government decides to sequence the genome of every newborn, but that the genome information is only examined *ad hoc* in the context of a specific clinical question, or at the initiative of the owner.

In the second scenario the genome is sequenced and the data are stored in a hospital or at the institute that sequenced the genome. The genomic data are regularly 'prospectively' analysed, but it is the hospital/institute that is the owner of the data.

Another participant argues that, legally speaking, there is no real 'ownership' of the data, but there is regulation on data protection or on giving access to data. As a

consequence, in legal terms one can discuss who should protect the data (the hospital or the person who was tested), and one can legally regulate who gets access to the data. In legal terms ownership is a problematic term.

Who do citizens see as the owner of genomic data: the donor, the clinician, the researcher, the hospital, the organisation (non-profit or profit) doing the sequencing and/or analysis?
Does the owner – whether it is the donor or a third party – have the right to sell his data to others?

A public genome database

What could be the role of the government in genome sequencing and analysis, besides reimbursing specific tests or genome analyses in specific contexts? Could/should the government (or publicly funded organisations) play an active role in genomic medicine?

One participant explains that every five years Belgian public health agencies organise a large population-based survey on health and medical issues (de gezondheidsenquête – l'enquête de santé). Ten thousand Belgians are asked to give information about their health. Would it be desirable for the public administration to ask about genome information too? If that is not available, should they ask for biological material to sequence and analyse the genome of respondents?

To what extent would that approach be different from the type of information that we register today in public owned databases like the cancer registry, registries on rare diseases or health data that are kept by the mutual health insurers or the RIZIV-INAMI-NIHDI ?

Moreover, governmental agencies, like FWO, VIB and others, are already sponsoring research related databases, which include genetic and genomic information. These are databases in research institutes, in universities and hospitals etc. The data in these databases are very important for research and innovation and their value cannot be underestimated.

It should also be recognised, however, that information from these databases can be sold (and is sold) to private (research) institutes. Moreover, the industries, making use of these data are often set up and supported by public institutes or administrative offices. An example is the 100,000 genome project in the UK, but also many of the growing Belgian biotech companies originate from university or research institute spin-offs.

Another question is whether the public sector in a small country like Belgium can compete with the global industry or can counter what some stakeholders called the 'malicious influence' of certain players in that industry? Others argue that if everyone in Belgium is offered the opportunity to donate his/her DNA to a public, but regulated DNA bank, with the promise that the DNA will be sequenced once there is a medical reason for it, people would no longer be encouraged to send their DNA to private testers. These testers are often considered a 'decoy' for commercial industries to get their hands on people's DNA information (see later).

Are you in favour of a public health initiative to set up a large national genome databank for epidemiological, medical and health purposes? Would you donate DNA and medical data to such an initiative?
What political and economic choices would be behind such public genomic initiatives?
Which guarantees do you need from public instances to safeguard the 'proper' use of genomic data? What do you consider 'proper use'?
How much should society invest in genome medicine? How does this relate to other priorities in healthcare? Can the value of sequencing the genome be compared, for example, to a new cancer drug or a drug for Alzheimer's disease?
How much of your taxpayer's money are you prepared to give to the government to invest in genomic medicine?
To what extent is the public aware of the mix between public and private stakes?

Sharing with the for-profit sector

There was considerable discussion about the various for-profit players involved in genomic sequencing and analysis. However, in order to keep the discussion poised and transparent, a distinction has to be made between various types of for-profit stakeholders involved in genomic medicine.

The first stages of research usually take place in academia, public research institutes and/or academic hospitals. At a certain stage, the development is taken over by companies. Or there might be a mixture of public and commercial developers. In the case of genome sequencing and analysis there are public centres in Belgium (like the Centres for Human Genetics, but also certain university hospitals and research groups linked to universities and public research institutes) that have sequencing platforms for (usually) their own research purposes. In some cases they have developed these platforms also for diagnostic purposes or for applications in the sphere of personalised medicine.

Secondly, there are the for-profit laboratories for clinical testing (hospital and private based). These are eager to expand their field of action towards reimbursed genetic and genomic testing.

Thirdly there is the group of 'direct-to-consumer' companies. The latter group markets (pre-specified) genome analyses directly to private consumers for a fee. They are active in many different application fields, from genealogic/ancestry analysis over preconception and prenatal testing to susceptibility testing. It is unclear what these companies subsequently do with the stored DNA and genomic information from their customers. It is not inconceivable that they do more sequencing and more analyses for their own purposes, but possibly also that they sell the results to third parties.

Besides stakeholders who have an interest in sequencing and analysing genomes on a not-for-profit or for-profit basis, there are also many industries wanting to make use of genomic information. Pharmaceutical and biotech companies, for example, can use genomic information to develop new drugs and diagnostic tests. If people want better and more tailored medicines in the future, or treatments for diseases that cannot be cured today, they should agree to these companies making use of genomic information

from as many sick and healthy individuals as possible. The question is under what conditions are people prepared to give access to their information to these companies? Therefore conditions and issues like (pseudo)-anonymisation, privacy, confidentiality, governance should be discussed with citizens.

Are people also prepared to share their data with internet and social media companies? These companies might be interested in linking a person's genetic data with the data they have on behaviour, lifestyle, medical conditions etc. from that person. These data are often already (unconsciously) given to those companies via social media platforms, information on internet browsing behaviour etc. Big data approaches are used to predict purchasing preferences, steer advertising or even influence voting behaviour during elections. Genomic data could add another dimension to big data. In the past, links have been demonstrated between 'direct-to-consumer' genomic testing companies and internet companies.

A last group of stakeholders that might benefit from genomic data are private and non-private insurers, and also employers.

Should reimbursed genomic testing be confined to public organisations?
Under what conditions do citizens agree that their genome information is used by 'for-profit' organisations? Which type of organisations would they share their genomic and health information with: pharma and biotech companies for developing new tests and drugs; 'big data' companies, insurers and employers?
How should access to genomic data be regulated and who should regulate it?
How should privacy be protected when data are shared? How should medical secrecy be regulated when data are shared?
Is informed consent the ultimate instrument to deal with all the aspects of data control and data access in genomic medicine?

Geopolitical context

Even if people are prepared to share their genome information with the government, it should also be asked which government? Can that also be a foreign government? In a worldwide activity like genome sequencing and analysis, Belgian doctors and scientists send DNA samples to the US, China and other countries for NIP testing or other types of genome screening. Although we might be very aware of data protection in Belgium, we cannot guarantee similar levels of protection and confidentiality in other countries.

How should a Belgian government deal with such issues? By legislation and building all kinds of protection laws, or by organising all DNA testing itself and allowing only well-regulated public partners to sequence and analyse human DNA? These are two different levels of involvement.

So it is a matter of centralisation vs privatisation and of a regional/national approach vs a European or even a worldwide approach? In making these choices, there are aspects that go beyond the medical context; there are also elements linked to national economic strategies, geopolitical power and perhaps even military use of the data (there might be a link between biological weapon development and genetic backgrounds of populations).

These are completely new dimensions in the debate. Is this not the time to clarify those questions with citizens too?

Solidarity vs selection

Our healthcare system is based on solidarity and equity: everybody, in principle, has equal access to the care that he/she needs. However, there seems to be a tendency in society to progress towards some form of risk pre-selection in the healthcare system. For example, people with unhealthy or risky behaviour could be denied access to (some parts of) the system, or should pay more for their higher risk/usage. Genomic information might be a supplementary lever for pre-selecting people.

This applies not only to the Belgian/European system of publicly organised healthcare, but also to the private sector of health and other forms of insurance. The Belgian law prohibits Belgian insurers from making use of genetic information; Belgian residents cannot be obliged (and are in principle not even allowed) to give information about genetic tests to insurers, either genetic information with a positive or negative impact on their health or future health.

On the other hand, it is relatively easy to take out a policy with a insurer abroad. It therefore remains to be seen whether the Belgian legislation on genomic data vis-àvis insurers (and employers) will be sustainable in the long term.

Do citizens believe that genomic medicine can lead to inequality and dismantling of the current healthcare system based on solidarity and equity? Or can genomic medicine provide an opportunity to increase the quality of healthcare for all? How?
Should genomic medicine be preferentially offered to groups in the population that are currently under-served by the healthcare system?

Links with forensic science

There are several aspects in the discussion about convergence of genomic data for medical and forensic purposes. One is about the possible use of medically-oriented genetic databases for forensic applications, i.e. for the identification of perpetrators at crime scenes.

Another aspect is about drawing medical information from forensic DNA databases. One example could be the analysis of an offender's DNA for possible genetic factors for psychopathology and/or socio-pathology. Can such information be made available to the justice system, although we have to acknowledge that a lot is still unknown about genetic variations and susceptibility to unsocial and/or criminal behaviour?

Is convergence between forensic science and genomic medicine desirable, or not? Why?
Does it make sense to have separate genomic databases for forensic purposes and for medical purposes?
Would citizens allow their own data collected for medical purposes to be used for forensic purposes?

Global genomic citizenship?

It has become clear from the discussions with the stakeholders, that genomic medicine is one emerging technology with potentially a huge impact, not only on the healthcare system, but also on many other societal aspects. Like other high-impact technologies, genomic medicine is increasingly governed beyond the realm of the nation-state. How do citizens feel about these developments?

How do citizens experience their place in an increasingly globalised, technology-driven society? What is the role of their government and of other stakeholders in this evolving world?
In which direction should society develop? What is the role of technology in that future society?

4. BRIDGE TO THE CITIZENS' FORUM

Recent developments in the field of genomics have led to the transition from traditional 'monogenic genetics' towards comprehensive testing of the human genome by integrating next-generation sequencing approaches with advanced bioinformatics. This transition is being reflected in a large variety of applications in genomic medicine: from genome testing for specific indications for patients confronted with an unexplained disorder or for patients with cancer in order to improve their treatment, to expanded screening of newborn babies, non-invasive prenatal testing (NIPT), preconception carrier testing, cascade screening, health risk screening et cetera. These applications trigger a number of immediate ethical, legal, societal, organizational, governance and policy issues.

The citizen and his genome - How should we deal with autonomy in genomic medicine (self-determination, informed consent, the right to be informed/the right not-to-know, the right to an open future)? When do the benefits of genome testing outweigh the risks for the person being tested and when does the genome test become disproportionate? What do people want to know about their genome and how do they integrate this information into their when thinking about their own health?
Genomic medicine also raises many questions about privacy, data ownership, data sharing, and confidentiality. What do citizens think about sharing their data? With whom do they want to share their data and for what purposes? To what extent are they prepared to give up their privacy?

The impact of personal genome knowledge on family members - Results of genome testing do not only impact the tested individual, but can also affect his or her family members. Who is responsible for informing family members who are at risk? What about genetic testing in minors? Who decides for them?

Societal consequences of genomic medicine - As indicated earlier in this report, such private or family-level questions are closely linked to the larger societal debates. These are primarily about the role of genomic medicine in current healthcare, but also about the type of healthcare we want in the future. Will genomic screening become the norm in our society? Are we, as a society, prepared to keep other options and choices open? Do our healthcare and social systems remain in solidarity with people who deliberately refuse to be tested? Which evolutions, in this respect, are desirable, and which not?
Other relevant questions relate to the use of (private or public) resources for genomic medicine. How does genomic medicine relate to other priorities in healthcare?
There are also logistic and organizational aspects: who can/should prescribe a genome analysis? Who can sequence and analyse the genome? Who should communicate the results to the tested person? What other support is needed to assist the tested person to understand the results and to integrate them into his/her health choices?

The genome and medical progress - Genomic medicine is still in its early days and is the focus of considerable research. The collection and pooling of genomic, health and

lifestyle data from very many individuals – both patients and healthy individuals – is therefore vital for health research and for building a better healthcare system. It was stated during this workshop that genome and health data might open up new perspectives for our 'mutualised' healthcare system. Do citizens also acknowledge these perspectives, and what is the citizens' view of the concept of 'genomic citizenship'?

Genomics outside the healthcare system - The possible impact of genomic medicine goes far beyond the contours of healthcare. There are links to forensics, but genome information can also be used in the context of employment, insurance, marketing, talent screening etc. What do citizens think about the use of genome information being decoupled from health issues?

A disruptive technology - Many of the ethical, legal and societal questions surrounding genomic medicine also apply to other imminent, data-intensive technologies that are changing our society, including ICT, the internet, social media, artificial intelligence etc. Reflecting on genomic medicine could give citizens a framework to discuss on what it means to be a citizen in a technology driven and increasingly globalizing society, today and tomorrow.

The participating citizens will be 'lay people' in relation to genomic medicine. But they are experts about their own experiences, lives and views. They will answer the questions that raise in their own language, on the basis of their own beliefs and convictions, and their own values, principles and objectives. Don't expect citizens to juggle with terms like autonomy, equity, justice, solidarity, dignity, proportionality, sustainability or the distribution of means in the same way that experts do. Nevertheless, citizens have their opinion on how these concepts are translated in their daily lives.

With the citizens' forum, the organisers will ascertain how citizens give substance to these values, principles and objectives (and how they evolve during the three weekends) in response to the ethical, legal and societal challenges raised by genomic medicine.

Concrete case studies will be used to provide a substantiating starting-point for the citizen's deliberations. These are 'taken from life' and are situated in an era of genomic medicine, now and/or in a foreseeable future. Through a process of active research, mutual discussion and deliberation, interaction with experts, exchange of opinions and arguments, the panel of citizens will work towards a substantiated and concrete set of answers and recommendations.

ADDENDUM 1. RESULTS FROM 6 GROUP DISCUSSIONS

Group 1

- Concerning data sharing: which kind of dissemination? Which data can be shared? Guidelines and balances for dissemination of data to 1) research (private and public); 2) public health; 3) relatives; 4) others?

- Approximately 20% of the public agrees to donate their data to the private sector: 1) What are their underlying fears?; 2) What would happen if private companies were somewhat 'democratized' with a partial presence of the public sector in the company?

- What do you expect from data sharing? What are your hopes?

- What legal framework should be used to give geneticists reference points when they have doubts as to whether or not to communicate this or that information to the person who has taken a test? What is the medico-legal responsibility of the professional? How far does this responsibility go?

- What are citizens' expectations in this area? What do citizens see as necessary to communicate? Or not to communicate?

- We are in a fast-moving society with far-reaching changes and evolving mentalities, practices etc. which have an influence (positive or negative) on the welcoming of people with a worrying genetic trait. 1) What kind of society do we want?; 2) What would be the impact of further genetic exploration (e.g. concerning preconception screening, how far? under which conditions?); 3) What are the underlying issues?

Group 2

- How to avoid genomic testing leading to over-diagnosis and over-treatment?

- How can people make well-informed choices - what type of information is needed (population vs individual)?

- How can proper informed consent processes be developed?

- How to evolve from a paternalistic to a patient-centred approach – roles for counsellors or a new type of health professionals who help in passing on information from the doctor to the patient?

- How can neglected populations be involved (i.e. prisoners and link to forensic research)?

- What are the rights of relatives?

- How much information do persons being tested and family members want to receive?
- What about possible shifts in the distribution of responsibilities for professionals?
- What about shifts in people's responsibility towards their own personal health, towards relatives' health and towards future generations?
- Is the public aware of the dangers and implications of genomic information going to the industry/commercial sector?
- From a public healthcare system point of view: Can we ask for your genome and do epidemiological research on it? Are people aware of the political, commercial and economic choices behind such a project? Might the government have a 'double agenda'?
- What are your fears and hopes in relation to genomics?
- Do you agree to your genome being sequenced in other countries?
- Should reimbursement for genomic testing be given as a priority to specific patient groups? Who makes the choice about these groups?

Group 3

- What should citizens be informed about so that they can 'answer':

  - the advantages of sharing data

  - understanding the impact beyond the medical aspects

  - pharmaceutical companies need data to be able to develop new medicines

- Would genomic information increase risk selection and thus unequal access to healthcare?
- Is genomics a threat to solidarity? Do we allow insurance companies to have access to genomic data?
- How could genomics strengthen solidarity? Data as the new currency. Data philanthropy.
- Involvement of the government? Not only regulation but also as public representative/initiator.
- Will it be possible to escape from the information? (Right not to know/right not to know)?

- Personal vs public responsibility (responsible citizen, responsible parents)
- Would you like to live with a list of risks?
- Which guarantees do you need from the body that stores your data?
- Under what conditions would you agree that your data is used for profit? (Pharmaceutical companies - new medicine; google amazon - big data; insurance; etc.)
- Who owns the data (property)?

Group 4

Tools, diversity

- What kind of genetic/genomic info would you want when there is no familial indication of the presence of a genetic disease? - Genomic medicine tutorial & Youtube; tv; website+online expert, or face-to-face consultation
- What is the health literacy on genomics among the public/of patients?
- What do patients need in order to improve their health literacy?

Quality of sequencing

- Do you want your data to be shared for research/diagnostics with colleagues in the field?

Societal/personal impact

- Should we aim to have genomic screening? & How should this be organized?

Use of data/risk selection by insurers

- To what extent does the government need to create a legal framework for genomics concerning 1) regulation of access to data, 2) protection of privacy (donor/testee); 3) medical confidentiality (family); 4) research aspects
- How do we avoid risk selection based on this very objective information in the public and health insurance system?

Access to data/sharing

- Safeguard trust and privacy

Tool and organisation of informed consent

- Is it better to provide more simple and accessible tools for ethical procedures in genomics?
- Are we able to facilitate and support the process of genome sequencing for every patient? (nomenclature, reviewing data when analysis is completed once?

Group 5

- Who decides on criteria/will society decide?
- How do we define a severe disease in the context of screening (carrier, prenatal, neonatal)?
- Should the clinician discuss up-front how to deal with incidental findings? -> based on relevant benchmark/expert panel?
- How much information does the citizen need to give an informed consent?
- Is informed consent an adequate tool to direct the control/use of data?
- On what basis can a citizen take a decision?
- Who will you give control over your data? (sharing, giving access, collecting, storing)
- Who owns the data?
- How is it possible to avoid individuals selling their genomic information to the highest bidder?
- Which purposes for its use can be supported (research, insurance etc.)?
- Will there be a link between forensic identification databases and medical information databases? How is it possible to deal with that?
- How much money can society invest in the genome?

Group 6

- Decision-making framework - with respect of the personal context; what is important for citizens: criteria for making decisions; policy, hospitals, ...

- Before testing - health and genome education, genome literacy, who will do what, when and where?

- Before testing - what are the options, do I want them: reproductive options vs preventive healthcare?

- After testing - what information do I need, what is informed consent, who decides? what information?

- Me and my family (and the doctor) - moral responsibility; facilitate family communication; sharing data within the family?

- Me, my data and the community - what type of information do we store? Can your info be used or re-analysed for other research? Fear of privacy/next generation; Do you have objections to the government having your data? How to enable data sharing? Data storage yes/no?

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