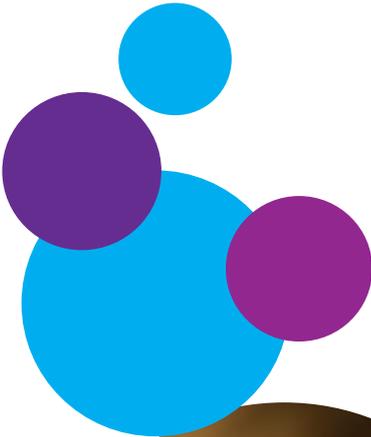




**Genetic Alliance UK**  
Supporting. Campaigning. Uniting.



**Genome Sequencing: what do cancer patients think?**

**Patient Charter**

## Genetic Alliance UK

Genetic Alliance UK is the national charity working to improve the lives of patients and families affected by all types of genetic conditions. We are an alliance of over 180 patient organisations. Our aim is to ensure that high quality services, information and support are provided to all who need them. We actively support research and innovation across the field of genetic medicine.

Genetic Alliance UK undertakes various projects and programmes that add evidence and knowledge to improve health service provision, research and support for families. These initiatives include:

- Rare Disease UK, a stakeholder coalition brought together to work with Government to develop the UK Strategy for Rare Diseases.  
[www.raredisease.org.uk](http://www.raredisease.org.uk)
- SWAN UK (syndromes without a name), a UK-wide network providing information and support to families of children without a diagnosis.  
[www.undiagnosed.org.uk](http://www.undiagnosed.org.uk)

Download a copy of this report here:

[www.geneticalliance.org.uk/genomesequencingpatientcharter.htm](http://www.geneticalliance.org.uk/genomesequencingpatientcharter.htm)

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We would also like to thank Gillian Crawford and Professor Anneke Lucassen, who joined our Live Chats to provide expert input into our discussions with participants.

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The Genetic Alliance UK team

## Executive summary

This Patient Charter makes 9 recommendations for consideration before genome sequencing becomes widely incorporated into NHS services as part of clinical cancer care. Recommendations are grouped under three broad themes, based on what is important to patients, as told to us by our project participants.

**It is important that patients understand the genetic nature of cancer and the relationship between cancer and genomics.**

- The power and limitations of whole genome sequencing should be clearly communicated to patients, as should the difference in the uses of genomic changes present only in cancer cells (somatic mutations) and those present in all cells (inherited mutations).
- Patient expectations should be managed during recruitment to genomic studies, and considered in communications to patients about how such studies could impact on patients, their families, and/or future cancer patients.
- Engagement of cancer charities and patient networks is integral in raising the knowledge of genomic sequencing and to ensuring patients understand the scope of genetic studies.

**A streamlined pathway should be established to ensure patients receive the necessary dedicated care required based on all findings from genome sequencing.**

- A streamlined patient pathway should be developed that supports healthcare professionals in the NHS and the independent sector fulfilment of their respective roles in considering treatment of cancer based on genetic tests and in dealing with identified additional findings through genome sequencing.
- Further work and research is necessary to better understand the appropriate timing for sharing information about additional findings obtained through genome sequencing to cancer patients and their families already facing the significant challenge that cancer poses.
- Dynamic consent to receive additional findings should be the standard model of consent when genome sequencing is used in clinical cancer practice.

**Research studies can benefit from the willingness of patients to contribute to research through sharing their genetic data.**

- Patients are in the main supportive of research, and welcome opportunities for their genetic data to be used in genetics and genomics studies in relation to their treatment.
- Communicating to patients the aims of research and how results will be used, could lead to greater involvement of patients in research using genetic data, with greater confidence from patients in the work being undertaken.
- Genomics research studies should take better advantage of the NHS, medical research charities, and patient groups as a source of recruitment.

## Introduction

Whole genome sequencing is a technology that offers great utility and with a wide range of possible uses, including the diagnosis and development of future treatment of many conditions. This, coupled with the fact that the speed and cost of sequencing have dropped dramatically, means that for the first time, large-scale, routine genomic medicine could become a reality for NHS healthcare.

The UK has been a pioneer in many aspects of research and medical genetics, over the last two decades<sup>i</sup>. Gene testing for both inherited and cancer cell specific mutations has been a mainstay of cancer treatment and prevention for many years, and will continue to have a very valuable role for several years. This current cancer genetic testing is not the subject of this report, which addresses whole genome sequencing.

In 2012, the Prime Minister committed to sequencing 100,000 genomes before the end of 2017, with the overall aim of the UK becoming the first country in the world to use genome sequencing in mainstream clinical practice.<sup>ii</sup>

### What is whole genome sequencing?

Whole genome sequencing describes the process of reading an individual's genetic code. A sample (usually a blood sample) is taken from the individual, and for cancer patients, a sample is also taken from their tumour via biopsy.

Sequencing can be used to read a single gene, all of the genes (known as the 'exome') or the complete DNA sequence of a person (known as whole genome sequencing).

Throughout this document, we are only addressing whole genome sequencing.

As this initiative starts to take root within the NHS, healthcare policy and decision-makers will need to draw on the informed views of the patients and families who will be the end-beneficiaries of whole genome sequencing technologies in order to make effective decisions around its use.

In 2015 Genetic Alliance UK published our first charter examining patient views of whole genome sequencing. This had a focus on the rare disease patient perspective. Rare disease is an important area of potential research and patient benefit for whole genome sequencing and one of the three strands on the 100,000 Genomes Project, alongside infection. Other of the strand of the 100,000 Genomes Project and another important area of potential benefit is in cancer, which is the focus of this, our second charter. The 100,000 Genomes Project aims to sequence the genome of 25,000 cancer patients, and the genome of their tumours.

Cancers arise because of changes to the DNA in one or more cells that lead to uncontrolled growth of cells resulting in a tumour. These harmful changes can arise spontaneously, can be inherited, or can be caused by exposure to certain chemicals in the environment. This means that a tumour cell will have slightly different DNA to a healthy cell of the cancer patient. By comparing the DNA of a tumour cell and a non-tumour cell, geneticists can sometimes identify genes in which the cancer causing mutations have occurred. This information could be used to inform treatment, with some cancers responding better to certain drugs because of their genetic basis. This is called personalised medicine.

We hope that this Patient Charter will be used by policy and decision-makers to encourage more in-depth and creative public and patient involvement in health care decision-making.

## Our approach

My Cancer, My DNA is a project aimed at understanding from cancer patients, and their families, their needs and expectations of whole genome sequencing in clinical cancer care and research.

The project took place over six weeks, in January and February of 2016. We used online engagement events to share information about genome sequencing with participants, and to hear their experiences and views.

The engagement events took patients through several aspects of whole genome sequencing in cancer. The first event involved watching a YouTube video on genetics and reading an infographic containing information about cancer genomics, before completing a quiz to assess basic understanding of these two topics. The second and third events asked patients to listen to a seven minute podcast which told in two parts the fictional story of Sara, who was learning about how whole genome sequencing could be used to find a personalised treatment for her myeloma. At the end of each part of the story, participants completed a questionnaire to share their opinion on different, ethically contentious issues drawn out in the podcast. In-between the podcast sessions, we held two Live Chats via Google Hangouts. In each Live Chat seven participants joined Genetic Alliance UK and an expert to talk via video call about a topic related to the project. The first chat covered the difficulty of receiving additional findings and informing family members, while the second chat covered the use of genetic data in research. For one hour, participants could share their thoughts and experiences, and question the experts. A final quiz at the end of the project asked patients for their view on the value of genome sequencing in cancer care.

The project was reviewed by Genetic Alliance UK's internal ethics committee, to ensure that the project was carried out safely, with considered consent and respect to autonomy and privacy of the subjects and in accordance with ethical principles.

### Who we worked with

171 people registered their interest in the project, with a final total of 87 cancer patients, family members of cancer patients, or those living with an increased risk of developing cancer (e.g. BRCA1 or 2 mutation carriers) completing a consent form. Of those registered, most were female (86%), with 71% of registered patients falling between the ages of 35 and 64. A range of cancers were represented, including but not limited to: Prostate Cancer, Testicular Cancer, Ovarian Cancer, Breast Cancer, Endometrial Cancer, Lymphoma, Leukaemia, Bowel Cancer, Lung Cancer, Liver Cancer, Melanoma, Kidney Cancer, Tongue Cancer, Ehlers-Danlos syndrome, Multiple Endocrine Neoplasia and Von Hippel-Lindau Disease.

70% of registered participants had a cancer diagnosis, while 28% had been diagnosed with a predisposition to cancer. 90% of participants identified as white British/Scottish/Welsh/Northern Irish/English. 2% were from the Republic of Ireland, and 1.5 % identifying as white and black African. 9 participants listed their ethnicity as 'other'.

75 participants took part in our first session, 71 in our second, 63 in our third and 50 in our last session. We were joined by seven participants in each of our live chats.

Participants were recruited from Genetic Alliance UK's relevant membership. We have also collaborated and recruited via Bloodwise, Breast Cancer Now, Cancer Research UK and Cancer52 memberships to ensure that participants in this project represented a range of cancer types. Additionally, we have promoted the project to 150 cancer charities across the UK to increase representation from all devolved nations. Patient recruitment took place over two months via charities' communication channels, namely newsletters, websites and social media.



Rare Disease UK (RDUK) is the national alliance for people with rare diseases and all who support them. Membership is open to all and includes patients and family members living with a rare disease, patient organisations, clinicians, researchers, academics and industry. RDUK provides a unified voice for the rare disease community, capturing the experiences of patients and families and raising the profile of rare diseases across the UK.

RDUK was established in November 2008, by Genetic Alliance UK, following the European Commission's Communication on Rare Diseases: Europe's Challenges. RDUK successfully campaigned for its adoption in June 2009. Since then, RDUK has worked to ensure that the UK's health departments acted on their obligation to develop a UK Strategy for Rare Diseases, and worked to engage with the rare disease community to shape its content. Since the publication of the UK Strategy for Rare Disease by the Department of Health in November 2013, RDUK has focused on ensuring that the implementation of the UK Strategy is effective and accountable.

[www.raredisease.org.uk](http://www.raredisease.org.uk)



SWAN UK (syndromes without a name) is an initiative run by Genetic Alliance UK offering support and information to families of children with undiagnosed genetic conditions.

Not having a diagnosis can be very isolating for families and SWAN UK aims to combat this by providing online peer-to-peer support, as well as providing and signposting to useful information. SWAN UK is also raising public and professional awareness of undiagnosed genetic conditions and the unique challenges faced by affected families.

SWAN UK launched in May 2011 thanks to a five-year grant from the National Lottery through the Big Lottery Fund, and in 2014 it received a second grant from the National Lottery through the Big Lottery Fund to establish the first local SWAN UK support networks in England. Since launching, SWAN UK has been approached by over 1000 families and was shortlisted in the 2013 National Lottery Awards in the 'best health project' category.

[www.undiagnosed.org.uk](http://www.undiagnosed.org.uk)

## Case studies

### Gill Crawford, Clinical Research Fellow, Principal Genetic Counsellor

*I was involved in a 'My Cancer, My DNA' live web chat that focused on the issue of "additional findings" - in this context results that predict disease or conditions that are unexpected for the person being tested - during genome sequencing. I was keen to take part as I believe it is essential to gather patient perspectives about both the potential and the limitations of new health technologies, particularly since these are already being implemented in routine clinical services. Genomics is a complex area, so hearing and engaging with patient stories is crucial to help shape my own future practice and to understand some of the ethical and practical issues associated with genome sequencing. I found the web chat very interesting; the participants were open and honest in sharing their experiences and were able to articulate the complex issues that were important to them. This sort of insight is crucial in helping to design responsible genomic services.*



### Chloe Judd, cancer patient



*My boyfriend found a lump in my right breast when I was 28. The doctor said it was probably nothing, but referred me a consultant breast surgeon who ordered an ultrasound. After the ultrasound and a biopsy, my diagnosis was confirmed as breast cancer. I was totally okay with it but everyone else around me was falling apart.*

*I am type 1 diabetic, so reacted really badly to the steroids of the chemotherapy. I was put in the High Dependency Unit for five days after my first treatment. After that, I was kept in every time to keep an eye on me. I was allergic to two of the chemo drugs and had some serious complications. I had a single mastectomy, full lymph node removal and radiotherapy soon after. Being part of the study was amazing and I am so excited to see what genome testing and tailored cancer treatments can do for patients like me in the future. I believe it's so important for any potential risks and information to be available to the rest of my family given how effective early detection can be in saving lives.*

### Natalie Percival, Macmillan Advanced Nurse Practitioner

*As new initiatives are developed, it is often appropriate for advanced nurses to become involved with service development to help meet patient needs, and address patient demands, with the overall aim of improving patient outcomes. My role is ever expanding but I see each element important to support the patients I care for. BRCA testing has been a defined extension of my role for over a year now and I am a Key Healthcare professional who is able to provided women with the information they need to be able to make an informed decision about BRCA testing. This role is a key component of my wider nursing role and often women will ask me about how to access this service and the implications it may have for themselves and their family. Becoming involved in such an initiative has again highlighted the importance of advanced nurses gaining a rapport with patients which place them in a distinct position to be able to discuss wider aspects of their care.*



## Andrew Anderson, cancer patient



*Having been misdiagnosed three times, and in desperation paying privately for the necessary ultrasound, I was finally diagnosed with advanced testicular cancer in May 2000. At the time of diagnosis, the best prognosis was that I had less than six weeks to live. The cancer had spread to my abdomen, my lungs, and I had a satsuma-sized lump on the side of my neck. Surgery followed the next day and I started chemotherapy two weeks later. Complications from the abdominal tumour caused serious internal bleeding. Over one hundred blood transfusions enabled me*

*to escape surgery and, the rest of the four cycles of BEP chemotherapy, while not easy, went reasonably smoothly.*

*If I've learned anything, I've learned that 'knowledge is power' – the more knowledge available to the oncologists the better the patient's chance of recovery. As with most cancers, the earlier the disease is diagnosed and treated, the easier the whole experience is for the patient, and the cheaper for the NHS. To this end the project seemed to be a complete no-brainer. It was a pleasure to assist the study – my survival is not my achievement, it's the achievement of hundreds, maybe thousands, of people and if I can 'pay it forward' to help future patients it is absolutely my privilege to do so.*

# 1

## It is important that patients understand the genetic nature of cancer and the relationship between cancer and genomics

### Background to cancer genomics

Changes (known as mutations) in DNA are a hallmark of cancer. DNA mutations can lead to uncontrolled cell growth and the development of a solid mass and/or abnormal cells circulating in the blood. Cancer predisposing mutations can sometimes be present in every cell of the body because they have been inherited, or they may only be present in the cancer. Mutations that are only present in the cancer itself are known as somatic mutations, and can arise by chance or through exposure to certain environmental carcinogens.

Current knowledge suggests that approximately 3 in every 100 cancers arise from inherited mutations, though this varies by cancer, and may change as we learn more about the genetics of different cancer types<sup>iii</sup>. Inheriting a cancer predisposition gene mutation increases an individual's risk of developing cancer above the general population, and often increases their risk of developing cancer earlier in life. However, it doesn't guarantee an individual will develop cancer, because additional somatic mutations must also typically happen for a cancer to occur. For some cancers, increased surveillance, or risk-reducing interventions can be used to reduce the increased risk.

Somatic mutations are important to the development of most cancers. By looking at the DNA in a cancer cell and comparing it to the DNA from a patient's healthy cells, sometimes a mutations critical to a cancer's growth could be identified, and used as a target for treatment to stop or slow that growth. Using information about mutations in cancer cells to decide which treatments to use is sometimes called personalised, or precision, medicine. Clinical trials of personalised treatments are underway, and global research studies should uncover more information about the genetic mutations underlying different cancer types, over the next few years. DNA sequencing will therefore have an increasingly important role in improving diagnosis and treatment options for cancer patients.

Whole genome sequencing looks at 3 billion letters of DNA code and generates vast amounts data, compared to tests that look at the genes (which comprise only 2% of the genome). It is therefore challenging and time-consuming to analyse and correctly interpret whole genome sequencing data. Projects such as the 100,000 genomes project will be vital in improving our ability to use the data to improve clinical care

**Recommendation:** The power and limitations of whole genome sequencing should be clearly communicated to patients, as should the difference in the uses of genomic mutations present only in cancer cells (somatic mutations) and those present in all cells (inherited mutations).

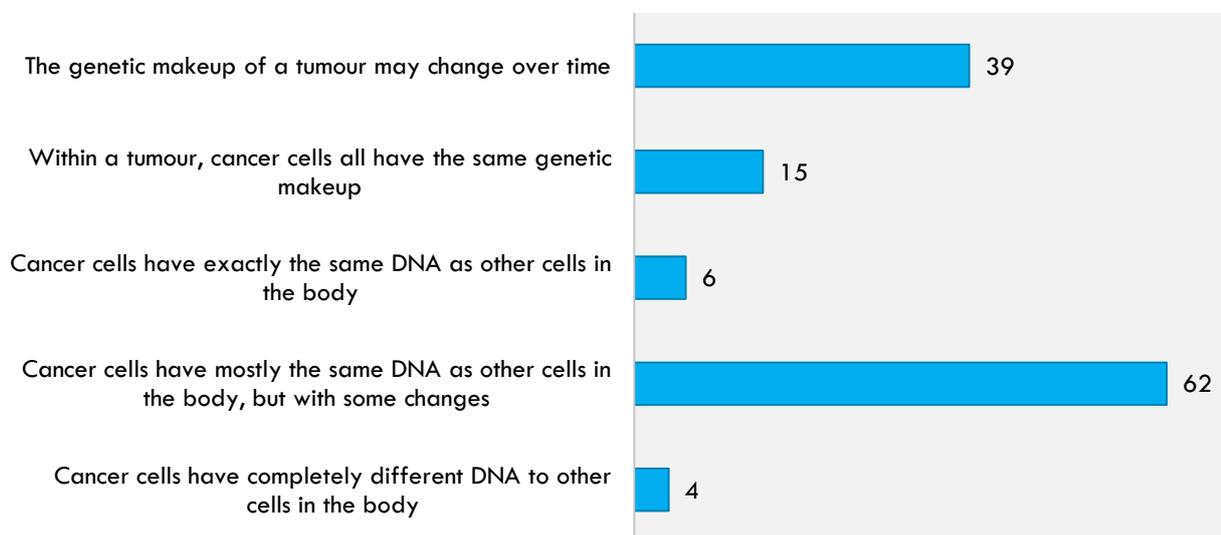
**Action by:** a collaboration between patient and research charities, clinicians and research groups.

The participants in our project had a strong understanding of basic genetics. It should be noted, however, that the participants were a self-selecting group, which likely reflects a pre-existing interest

in cancer and genetics. Additionally, our recruitment method, which involved reaching out to patients through our working group and our own patient group networks, meant that we were recruiting many patients who were already engaged with charities or patient organisations suggesting a possible interest in cancer and cancer research beyond their individual experience. The level of knowledge shown, therefore, may not be representative of the general population.

We were impressed by the awareness of the participants in respect of cancer specific genetics. Most participants, for example, correctly answered that cancer cells have mostly the same DNA as somatic cells but with small changes, but participants were less sure when it came to differences between cells in a tumour. Most participants were not aware that DNA makeup could change between tumour cells, and only around half of patients knew that genetic makeup of tumour cells could change over time.

Participants also had good understanding of what an inherited cancer gene mutation meant for their likelihood of developing cancer. Most participants correctly identified that an inherited cancer predisposing gene mutation means a person is more likely to develop a cancer, and could pass that increased risk on to their children. They were also aware that the risk of cancer could potentially be reduced or prevented by undergoing risk reducing interventions, and that regular check-ups might be helpful.



| Tick all that apply. If a person inherits a faulty gene that is associated with cancer:  |           |
|--|-----------|
| Answer Options   | Responses |
| That person will definitely develop cancer   | 3         |
| Healthy living will have no effect on their risk of developing cancer  | 6         |
| That person is more likely to develop cancer   | 67        |
| That person can avoid developing cancer by living more healthily   | 16        |
| That person might be able to reduce the risk of developing cancer by undergoing medical treatment, such as taking drugs or removal of an at risk part of the body, e.g. a mastectomy | 67        |
| That person might avoid developing cancer by undergoing medical treatment, such as taking drugs or removal of an at risk part of the body, e.g. a mastectomy                         | 33        |
| That person could pass the risk onto their children  | 69        |
| That person should have regular checkups with specialists to check for signs of cancer   | 63        |
| <b>Total respondents</b>   | <b>74</b> |

Ensuring better understanding of role of genomics in cancer could help patients clearly understand the value of whole genome sequencing.

We believe a collaborative approach between charities, researchers and healthcare professionals will be necessary in order to produce appropriate materials to improve understanding of the relationship between genomics and cancer.

**Recommendation: Engagement of cancer charities and networks are integral to ensuring patients understand the scope of genetic studies.**

Participants agreed that it is important to clearly communicate the aims of a study to patients, as well as how the results of that study will be shared, and what individual results might be made available to participants.

Our working group of cancer charities also highlighted the importance of informing patients of both the extent of the likely impact of any study findings for them individually, and the benefit to future patients. This should help participants decide how engaged they would like to be in the project on an ongoing basis.

Many participants, while keen to share their genetic data for research, were not concerned about being informed of the research results if they did not offer any new information about their individual health.

Where new information about their health did come to light through a research study, most participants would want to be informed, although a third felt that this follow-up should only be offered if the process did not substantially increase the cost of the research.

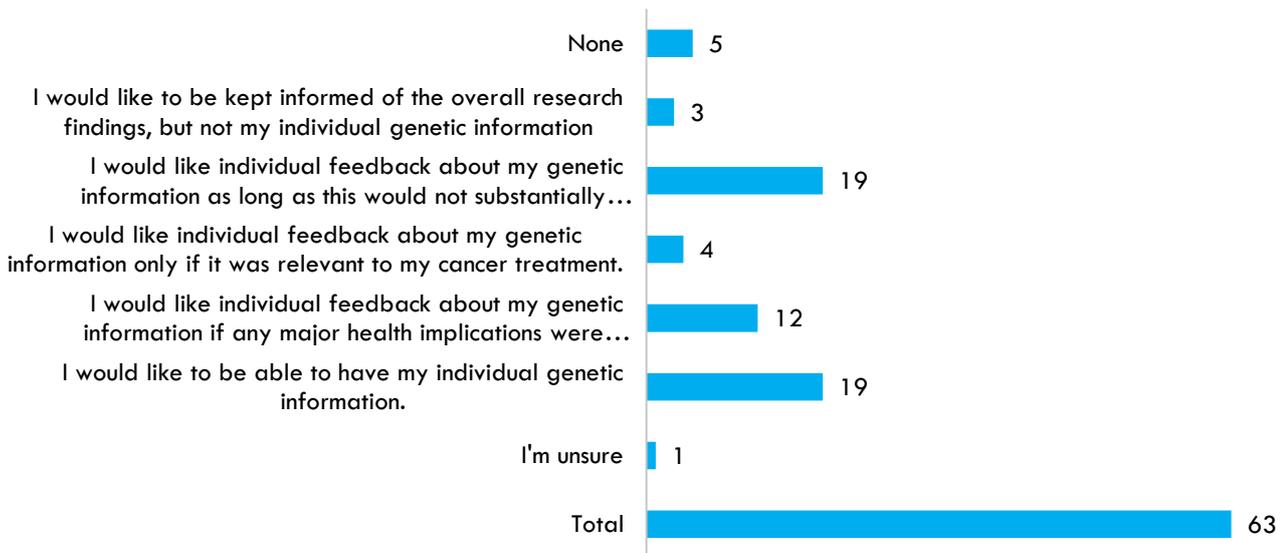
If a study is likely to produce information about a participant's health, the scope of this information and the method of its communication should be made clear.

#### Managing expectations in the 100,000 Genomes Project

The 100,000 Genomes Project communicates to participants about what they can expect through their website. On the site, potential participants can read about the aims of the study, and an infographic gives an overview of what participants will experience as they move through different stages of the study. Information is also provided on how genetic data will be stored and used. The website also communicates the limits of the study for the individual's healthcare:

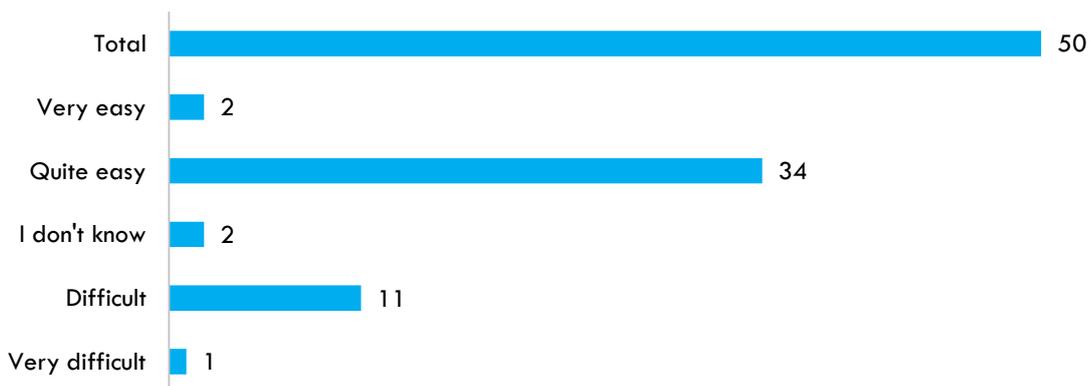
"In many cases we won't find anything, or we won't find anything in time to help the participant. But people who take part in the Project will be helping others in the future with the same condition."

**If you did consent to your genetic information being used for research, what feedback on the research findings would you like?**



Those conducting studies should be encouraged by our finding that most participants felt that whole genome sequencing is easy to explain, although 24% of participants felt it was difficult, or very difficult, to explain. This suggests, perhaps, that participants are confident that the complexities of whole genome sequencing are not beyond the average patient, but further work with patients could help establish what types of information delivery (video, leaflets, meeting with a healthcare professional) would be most useful and valued. Communicating the scope of studies should, therefore, not be a difficult barrier to overcome for studies.

**How easy do you think it is to explain whole genome sequencing to people in a way that enables them to make an informed decision about whether to have their whole genome sequenced or not**



**Recommendation:** Patient expectations should be managed during recruitment to genomic studies, and considered in communications to patients about how such studies could impact on patients and/or future cancer patients.

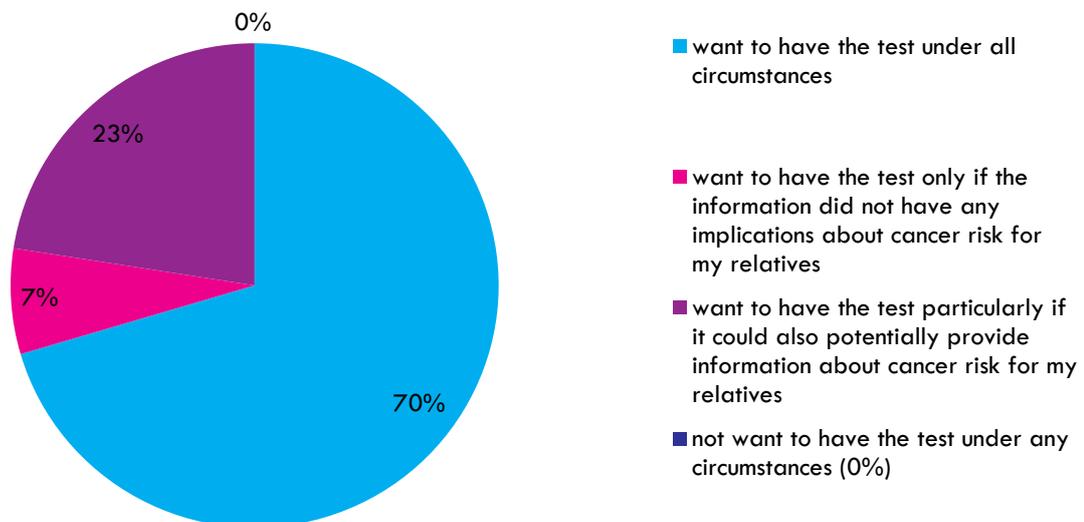
## 2

### A streamlined pathway should be established to ensure patients receive the necessary dedicated care required based on all findings from genome sequencing

Participants valued information about the genetics of their cancer, and about findings with implications for their future or their family, should any be uncovered during genome sequencing.

The majority of participants would have their genome sequenced for the purpose of tailoring cancer treatment under any circumstance, but 7% felt they would not agree to genome sequencing for this purpose if the findings could contain predictive information about the future health of family members. Conversely, 23% of participants would be more likely to have their genome sequenced if it would reveal this kind of information about family members. There were no participants who would choose not to be tested.

**Imagine yourself in the following situation: A genetic test is available that could provide information to allow your cancer treatment to be better tailored to you. Please select the response that best describes how you would feel. "I would..."**



Participants were split on how they would prefer to access genome sequencing. 40% of participants, when asked, felt they would prefer to access genetic testing through an appointment at a cancer clinic, while just over a third, 34%, would prefer to access genetic testing through referral to a specialised genetic clinic. When able to elaborate on this response in an open text question, participants commented that they already had to attend many appointments at their hospital, so adding to these would be unwelcome, however, they wanted to hear about any findings from genetic testing from an expert in that field.

*“A lot depends on the training of the oncologist or surgeon in genetics and understanding the science.”*

*“I feel it could be more stressful to have to attend an additional appointment at another centre to have the genetic testing done when ultimately the test will be carried out the same way.”*

*“In my experience my cancer clinicians did not give me confidence in their knowledge of BRCA faults, and the geneticist did not give me confidence in their knowledge of cancer treatment. One stop expert ‘shop’ would be preferred.”*

Currently, cancer patients undergoing cancer predisposition gene testing are often referred to a specialist genetics clinic for testing. However, patients undergoing tumour testing usually have this arranged at one of their oncology appointments. Tumour testing can sometimes reveal cancer predisposing gene mutations that are not restricted to the cancer cells and may have been inherited. Currently, these are often not included in the tumour testing report. The responses of our participants suggest these pathways might benefit from revision and integration to improve cancer care, meet patient needs and provide more patient choice.

It is important that patients are confident in the expertise of the health professionals they encounter, while also reducing the number of visits to different departments. A streamlined pathway that ensures the patient is seen by the most appropriate specialist for more detailed discussion when required (for example if a mutation is identified) would help achieve these aims. Wherever the genetic testing takes place, there should also be provided improved training to ensure clinicians have the appropriate knowledge to provide information and confidence to.

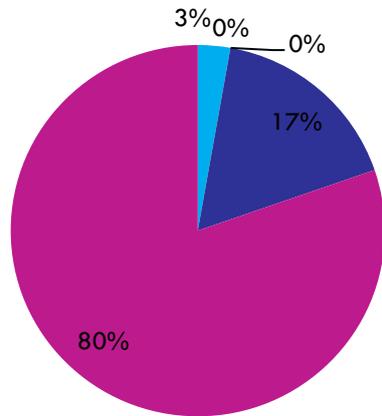
Currently, most genetic tests look at select genes that are relevant to cancer. The test may be used to see whether an individual has a genetic predisposition to cancer, or a specific mutation that has arisen and caused the cancer. In these circumstances, the genetic test often provides a simple ‘yes’ or ‘no’ answer, and is very unlikely to yield health information unrelated to cancer.

Whole genome sequencing allows analysis of much more of our genetic information and allows broader questions to be asked. A consequence of this approach is that individuals may get answers that they weren’t expecting or answers to questions that they had not intended to ask.

This more open questioning of the genome could enable patients to receive a diagnosis for their condition when previously it may never have been possible to establish a cause. However, in looking for a diagnosis, it is possible to discover additional information about an individual’s health.

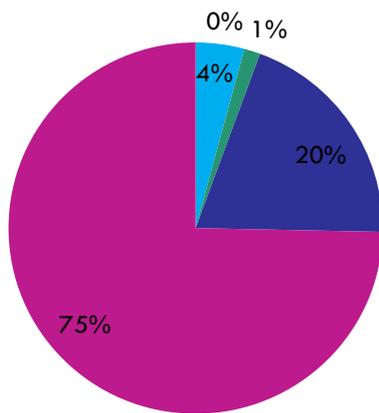
For example, an individual with cancer might discover that they have an increased risk of a non-cancer condition. Or it may be found that they have a gene mutation that might not affect them personally, but if their partner happened to have a mutation in the same gene, children that they have might be born with a genetic syndrome such as cystic fibrosis. Additional information like this could come as a shock or could be expected depending on whether the patient is aware of having a family history of that specific condition.

**"If an additional finding shows that I am at significant risk of developing a condition (not life-threatening) that could be prevented then..."**



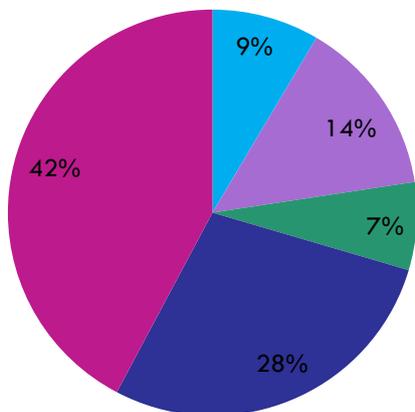
- ... I definitely would not want to know
- ... I don't think I would want to know
- ... I don't know if I would want to know
- ... I think I would want to know
- ... I definitely would want to know

**"In the unlikely event that an additional finding shows that I am at significant risk of developing a life-threatening condition that could be prevented and/or treated then..."**



- ... I definitely would not want to know
- ... I don't think I would want to know
- ... I don't know if I would want to know
- ... I think I would want to know
- ... I definitely would want to know

**"In the unlikely event that an additional finding shows that I am at significant risk of developing a life-threatening condition that could not be prevented then..."**



- ... I definitely would not want to know
- ... I don't think I would want to know
- ... I don't know if I would want to know
- ... I think I would want to know
- ... I definitely would want to know

Participants were mostly open to receiving additional findings that indicated life-threatening or life-limiting conditions, if such findings could be identified during DNA sequencing carried out as part of ongoing cancer care. As with our previous work with patients with rare diseases, participants were less likely to seek these findings if they related to an untreatable condition, compared to a treatable condition. Whilst 95% of participants felt they would like to receive additional findings that showed risk of developing a life-threatening condition that could be treated, with 75% “definitely” wanting to know, this dropped to 70% for an untreatable condition, with 42% “definitely” wanting to know.

There are two reasons why whole genome sequencing might make additional findings when examining a patient’s genome. Either the study is intentionally examining parts of the patient’s genome to find answers to a particular set of questions identified at the beginning of the study or the study has unintentionally identified a piece of information about the patient’s health in the process of carrying out the planned activity of the project. The former is vastly more likely than the latter, and the information provided to participants in the recruitment phase of the project should have covered both possibilities. In the latter case of an unintentional discovery of health information, the research project should have a process in place to decide whether to inform the patient of their finding.

In our previous examination of whole genome sequencing from a rare disease perspective, the pathway and process for dealing with these additional findings was straightforward. In the rare disease context, the correct team to inform a patient of an additional finding and begin the process of delivering appropriate care is a clinical genetics team, a principle component of any rare disease genome sequencing initiative. The engagement of a clinical genetics team in a genomics study focusing on cancer treatment is not certain and would be more peripheral in any case. It is therefore important to ensure that there is an established streamlined pathway to ensure that additional findings are dealt with appropriately.

We propose that a genetics team should be involved in any decision to feed back unintentional additional findings from any particular project, and that if more than one team is involved in decision making they should take care to ensure consistency across the project.

In this case and for those projects where findings to be fed back are identified at the beginning of the project, the notification pathway should be to the appropriate regional genetics centre and to the patient’s GP. The next step should be an invitation from the regional genetics centre to attend a clinic to be given the findings, following which the regional genetic centre’s usual pathway should be followed.

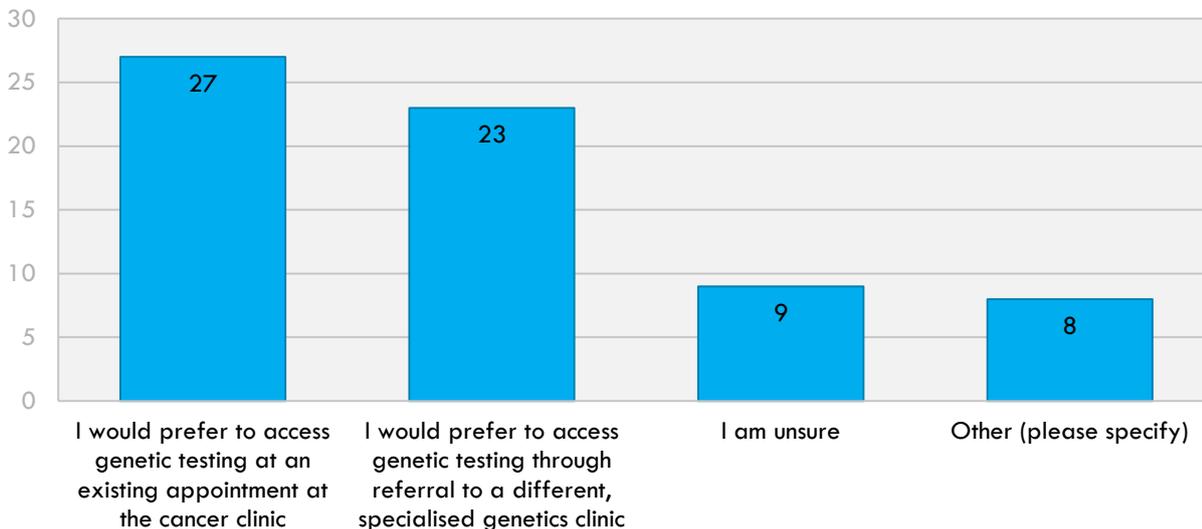
**Recommendation: A streamlined pathway should be developed that supports healthcare professionals in the fulfillment of their respective roles in treating cancer and in dealing with identified additional findings.**

During our first live chat, some contributors suggested that while they had felt able to take on new information despite already dealing with a life threatening condition, others might not feel this way, and participants suggested an assessment of a patient’s capacity to cope with such findings should be built into the consent process.

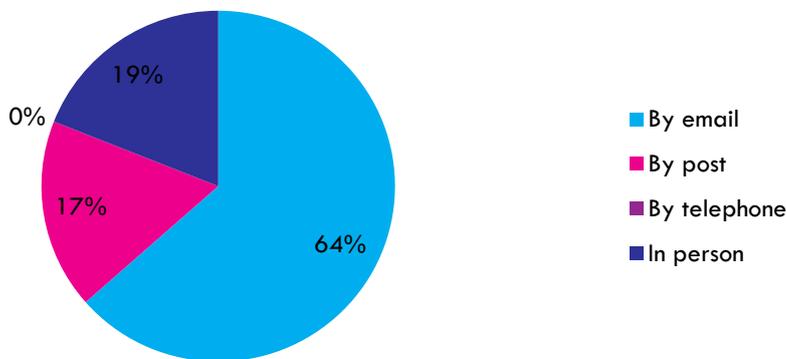
Participants were also questioned in one session on how they would prefer to receive the results of genetic testing. In each scenario appointments with the appropriate specialist in person would be scheduled if the DNA sequencing test identified anything. The majority of respondents (63.5%) would prefer to receive results by email, while 17.5% of patients would prefer results by post, and 19% in person. No respondents preferred telephone results.

Currently, within the NHS, genetic testing results cannot be delivered by email. The complexity of genetic testing, and the impact findings can have on family members, are clear challenges to making emailed results a possibility. The room for misinterpretation or mishandling of information is great. However, if NHS processes are not in line with the expectations of patients, it may be of use to re-evaluate how genetic test results are delivered to cancer patients.

**How would you prefer to access genetic testing?**



**If you had a genetic test, how would you like to receive your genetic test result?**



Further work with patients and their families could help in understanding when is the best stage in a person’s care to deliver results that indicate future development of a condition, considering priority needs for a cancer patient, and in consideration of the emotional burden of anticipated future health complications.

It will be important to involve regional genetic services in the design of cancer genomics studies to ensure that best practice in the feedback of additional findings is followed.

**Recommendation:** Further work and research is necessary to better understand the appropriate timing for delivery of additional findings to patients and families already facing the significant challenge that cancer poses.

Many participants felt that choice should drive delivery of additional findings to patients.

Within the scope of this work of examining cancer patients' attitudes to whole genome sequencing, the examination of the issue of additional findings is a challenge. Currently, the majority of findings that might be considered to be an additional finding in a whole genome study focusing on rare disease are in fact related to cancer risk. In the context of a study focusing on cancer, these findings must be considered to be pertinent, while also having implications for their future or for their family. In this report we continue to use the term "additional finding" as this is the terminology used in our previous charter, and by the 100,000 Genomes Project. Our discussion is focused on the additional implications of these findings, outside of their pertinence to immediate cancer treatment.

Regarding the type of findings received, while 31% of participants felt that everyone should receive the same set of additional findings based on standardised NHS criteria, 66% of participants believed it should be the decision of the patient which additional findings are looked for. In the current approach within the 100,000 Genomes Project, participants can decide whether additional findings' are actively looked for in their genome.

In contrast with current practice in the 100,000 Genomes Project, in our events patients called for a more flexible approach and would welcome the opportunity to be informed and decide which additional findings they would like to receive.

Open text responses revealed that many patients felt that they would only be able to make a decision on which findings to receive if they had a clear understanding of the risk conferred by the genetic mutations looked for as additional findings, i.e. the risk of developing the condition a mutation indicated predisposition to.

*"It all depends on which condition I would be at risk of developing and how quickly I would be affected and to what degree."*

*"It is unclear what constitutes 'significant risk'. Knowing in advance might help me adjust better..."*

### Models of consent: an example from the 100,000 Genomes Project

In addition to results regarding a patient's 'main condition' (the rare disease or cancer which led them to participate in the Project), participants in the 100,000 Genomes Project can ask to receive 'additional findings', fed back to them via their medical team. This is information about a specific list of 'serious but actionable' conditions, usually unrelated to the main condition.

When patients choose to receive additional findings they agree on receiving findings on the following conditions: Familial hypercholesterolaemia, Bowel Cancer, APC, Breast and Ovarian Cancer and other cancer predisposition, namely VHL, MEN1 and RET. These are conditions that can often be prevented or managed by NHS treatment. These conditions are also rare, and expected to affect 1 in 100 people who take part.

An easily downloadable opt out and opt in form to receive additional findings is available on the website, and can be submitted at any time, taking into account future findings brought to light through ongoing research.

These conditions can either be prevented or their impact reduced through interventions available on the NHS. Participants choose whether to receive results relating to the whole list, or none at all. The list will be reviewed over time, with conditions being added or removed to the list based on scientific advice. The consent given is to receive additional findings from the list, in the understanding that this list is maintained according to specific criteria. Consent is therefore not given to a fixed list of conditions. If new conditions are added to the list, they will automatically receive feedback on these too, or the opposite where existing conditions on the list are removed.

### Models of dynamic consent: an example from the Rudy Study

RUDY is a study in rare diseases of the bones, joints, and muscles, headed up by a research team at the University of Oxford. Patients in the Rudy study are all affected by a rare rheumatologic disease or are the parent of an affected child. Rudy aims to transform clinical care for participants through patient driven research. Participants in this study are participants with a voice, deeply involved in the research project. Through the website of the project, participants can choose how much they want to be involved in the study, and modify these choices as their preferences or circumstances change, have the option to search for participation opportunities and to be notified when new opportunities arise, they can decide whether their blood, their scans, and their medical histories can be shared with researchers at other labs, including elsewhere in Europe or in the United States.

Patients are able to dialogue with researchers and log on to a clinical trial webpage to learn whether one of their tissue samples has been used in research studies, including receiving research papers for which their information might have been relevant.

The feedback from patients has been extremely positive: patients feel that, within this study and given this model of dynamic consent, they can be selective and take part in sub studies within the project and increase their participation as time progresses – this is likely to increase patient participation as it implies less initial commitment.

## Storage and Reanalysis of Genomic Information

Genome sequences can be stored and interrogated at a later stage in an individual's life without needing to repeat the sequencing, to answer different questions or re-examine an individual's genome sequence in light of new scientific discoveries. This could mean that a genome re-analysed in five years time could reveal more information about an individual's current or future health than it currently does as our understanding of the genetic links to cancer and other conditions develops.

We found that patients see the benefit of their samples being reused for different research projects or at different timelines during these projects. Participants taking part in this project particularly welcomed the possibility of being informed of how their samples have been used.

A dynamic consent allows patients to be approached for different kinds of consent or to obtain their opinions as new research projects are started and new ethical questions arise. Patients discussed how important it is to have their consent revisited at a later stage, after they have had the opportunity to come to terms with the information about their diagnosis or treatment as collection of one-off consent for research tends to occur at a stressful time for the person concerned, such as before treatment or surgery.

Patients felt it was important that they be able to reconsider their decision to give consent to the use of their health information and data for research. They valued the option of opting in or out of future studies from the point of their change in decision, with an understanding that data already in use in ongoing studies would remain unaffected by any withdrawal of consent. Implementation of dynamic consent removes pressure by allowing participants to return to their decisions and review their consent preferences in their own time<sup>iv</sup>.

During our first live chat, some contributors suggested that while they had felt able to take on new information while dealing with a life threatening condition, others might not feel this way, and participants suggested that assessment of a patient's capacity to cope with such findings could be built into the consent process. Dynamic consent would ensure that patients could decide which findings they would like to receive, and when.

**Recommendation: Dynamic consent to receive additional findings should be the standard model of consent when genome sequencing is used in clinical cancer practice.**

# 3

## Research studies can benefit from the willingness of patients to contribute to research through sharing their genetic data

### Consent to receive updates

Our project found participants felt that changes in personal circumstances should be accompanied by the ability to change their decision around receiving the results of any research, particularly when receiving additional findings.

Participants made a call for choice around receiving updated results on stored genetic data. 81% of participants felt that they should be updated on any new findings available. A similar percentage, 80%, believed that individuals should also be able to change their mind about whether to receive future findings, with just under a half of the participants agreeing that they should have a say over which new findings they would like to receive.

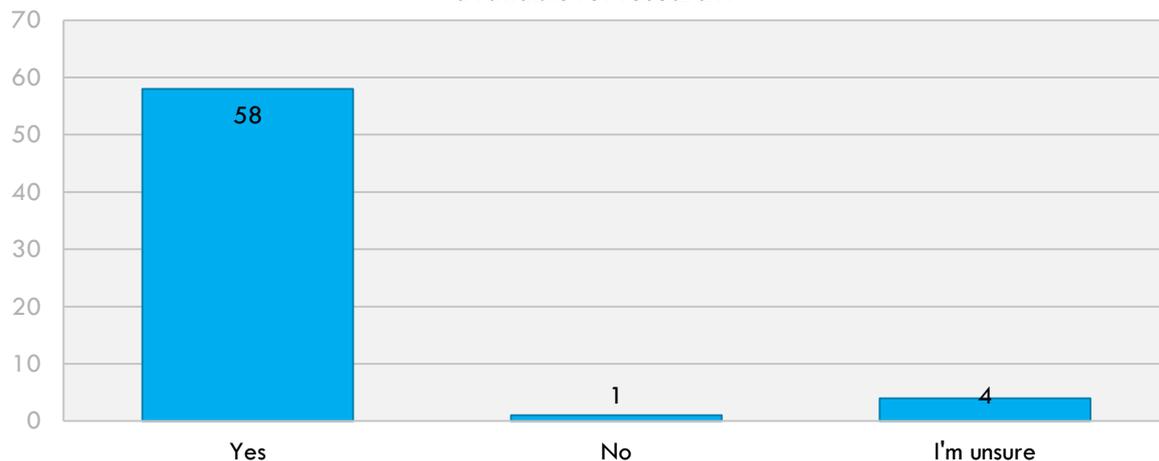
In our first Live Chat, participants strongly supported a model of dynamic consent - a framework in which, consent preferences can be modified over time, ensuring that patients can decide which findings they would like to receive and when.

In 2014 the Wellcome Trust published recommendations as to how research projects should design feedback pathways for additional findings<sup>5</sup>. As large scale genomic research projects involving cancer patients become more common, it will be valuable to examine patient experiences to assess how to balance their acute cancer care needs and the more long term issues regarding inherited risk factors, with implications for family members. At the end of research projects, it will be valuable to assess whether their additional findings feedback pathway was appropriate to the needs of those on the study. It may be that the appropriate timescale and pathway to pass on additional findings to patients will vary according to their cancer experience.

### The use of genomic data for research

Our participants strongly supported the idea of being able to take part in different research projects. This finding is unsurprising, and is supported by previous work conducted with patients by Genetic Alliance UK.

**Research on genetic data from cancer patients can help us better understand the causes of cancer. It can also help researchers develop new ways to diagnose and treatment cancer. Would you like your genetic data to be made available for research?**



In our previous genome sequencing project, My Condition, My DNA, we worked with patients living with rare conditions, and 93% of participants said that they would want their genome sequences to be used for research purposes. In this project, 92% of participants would like to make their genetic data available to research. This mirrors more broad findings that show that patients, when informed as to the potential use of their data, are usually willing to share their data for research purposes.

The participants were asked if they thought they should be able to decide to opt-out of research in future after initially consenting, which provoked a split of responses. 51% felt that either there should be no opt-out or that opt-out should only be available if it did not have any cost implications for the research. By contrast 40% felt that they should be able to withdraw their permission to use data irrespective of the impact on the research.

| <b>If you did consent to your genetic information being used for research, do you think you should be able to decide to opt-out of this in future?</b> |                         |                       |
|--|-------------------------|-----------------------|
| <b>Answer Options</b>  | <b>Response Percent</b> | <b>Response Count</b> |
| <b>No</b>  | 16%                     | 10                    |
| <b>Yes, but only if having an opt-out process does not increase the cost of the research</b>   | 35%                     | 22                    |
| <b>Yes, whatever the cost implications</b>   | 40%                     | 25                    |
| <b>I'm unsure</b>  | 9%                      | 6                     |
| <b>Total respondents</b>   |                         | <b>63</b>             |

Patients are strongly supportive of research, and welcome opportunities for their genetic data to be used in genetic and genomics studies.

In our previous project, some participants were less comfortable with certain types of organisations having access to their genetic information. In My Condition, My DNA, only 38% of respondents said that they were comfortable with private companies using their data, where the term private companies was not defined, and included pharmaceutical companies and other privately funded organisations. 31% of participants in that project said they would trust government institutions to use their data for research, compared to the 80% of participants that would be comfortable with the NHS sharing accessing their genetic data, and the 77% comfortable with universities having access.

Comparatively, participants in this project were supportive of providing their genetic data to pharmaceutical companies. 61% of participants felt pharmaceutical companies should be able to access their data. The option of private companies accessing genetic data was also provided to respondents, with no explanation of how the data would be used. Only 3 respondents approved of this access. This may suggest that patients are comfortable with private companies accessing their genetic data if the use of this data is clearly explained, and the goals and aims of the studies run by such companies are made clear. Opacity could prove to be a barrier to participation in studies.

As with our previous work, where only 31% participants said they would trust government institutions to use their data for research, patients are far less likely to approve of government accessing genetic data, with just 29% of participants approving of government access.

There are also concerns over the access of insurance companies to genetic data. No participants felt that insurance companies should have access to genetic data. Further, in our open text responses to the question “do you have any concerns about whole genome sequencing”, participants expanded on concerns over insurance companies having access to genetic data.

*"I am slightly concerned that it my information could be used by insurance companies etc which would increase premiums."*

*"I worry about social stigma and the information getting out i.e. that it could affect insurance, getting a job, mortgage etc. etc"*

*"Just about my only concern is that one doesn't want the likes of insurance companies, banks, employers etc being able to access personal genetic information. This could impact on the cost of insurance, whether finance companies would approve a loan or mortgage, employment opportunities and all sorts of other things."*

**Who do you feel should be able to use your personal genetic information for research purposes? Please select all that apply.**

| <b>Organisation type</b>   | <b>Responses</b> |
|--|------------------|
| Charities  | 31               |
| Pharmaceutical companies and medical devices companies, such as drug companies, or companies making diagnostic tests | 45               |
| Private companies working on developing faster ways to analyse large amounts of data                                 | 29               |
| Insurance companies  | 0                |
| Private companies  | 3                |
| National Cancer Registries   | 54               |
| Government   | 18               |
| NHS hospitals  | 59               |
| Universities   | 50               |
| I should be able to ask for a copy of my data  | 51               |
| I'm unsure   | 0                |
| <b>Total respondents</b>   | <b>63</b>        |

We also found that patients in our second live chat had very limited knowledge of what insurers were allowed to know about their genetic data, and were surprised that insurers did not have to be informed about predictive tests. Anxiety could be lessened by ensuring this information is made readily available to patients, and that this issue is addressed prior to sequencing taking place.

### Genetics and insurance

If you're experiencing symptoms of a genetic condition then you need to explain this to your insurer. You do not, however, have to disclose the results of predictive genetic tests (tests which will tell you how likely you are to develop a genetic condition in the future). The only exception is if you have taken the test for Huntington's disease and you are applying for a life insurance policy of over £500,000 or a critical illness policy of over £300,000. Your insurer may ask you whether you have a family history of a particular condition and if you're aware of one then you must tell them. However, if you have a family history of a genetic condition and have taken a predictive test which has shown that you will not develop the condition then you may wish to tell your insurer<sup>vi</sup>.

The breadth and complexity of this information, along with the perceived difficulty of explaining genome sequencing and its associated issues, underscore the importance of having accurate and comprehensive information available to patients. As mentioned elsewhere in this document, genetic counsellors are well positioned to provide this information to patients, answer any questions or address any concerns that patients may have.

**Recommendation: Genomics research studies should take better advantage of the NHS, medical research charities, and patient groups as a source of recruitment.**

There has been much public debate about the sharing of medical data for research in recent years, particularly around data security, privacy and access. This has included the electronic sharing of patient information collected in general practice as part of care.data, and more recently has considered the potential use and abuse of the genomic data that will be collected as part of the 100,000 Genomes Project.

In our previously project, My Condition, My DNA, some participants were less comfortable with certain types of organisations having access to their genetic information. In that study only 38% of respondents said that they were comfortable with private companies using their data (where the term private companies was not defined and may have included pharmaceutical companies and other privately funded organisations).

In this study we asked participants about the different organisations that they would be willing to access their data and participants were open to a range of different types of organisation using their genetic data for research purposes. The organisations with which participants would be most willing to contribute data to were the NHS, universities and national cancer registries.

These findings indicate a need for better communication of the processes and collaborations within biomedical research. In practice research is a collaborative effort. Research might begin in a university or an NHS hospital or a private company and might be a collaborative effort with other stakeholders including government. In practice, government and charities are usually just funders of research, but they can take an active role too.

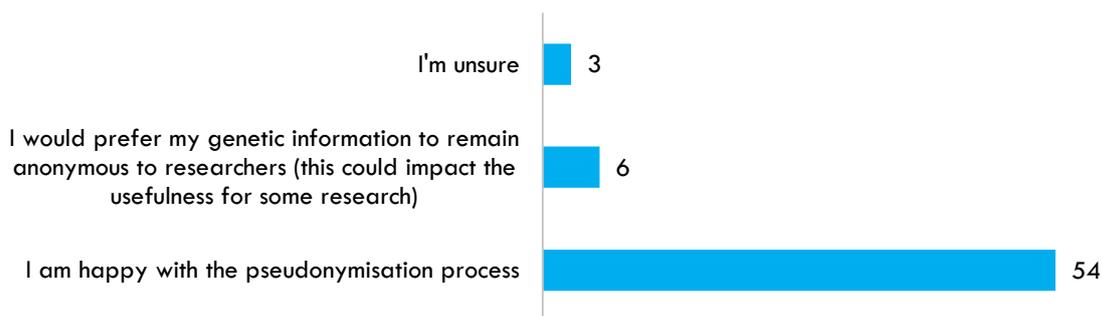
Compared to our previous project, participants in this project were more supportive of providing their genetic data to pharmaceutical companies as 61% of participants felt pharmaceutical companies should be able to access their data.

Open text responses revealed that participants were very open to having their genetic data used for research, whether that was publicly or privately funded, but that they objected to the results of that research being used to create new treatments that would be marketed at a prohibitively high price.

It is interesting to note the concern at the price of new medicines that arose from our discussions, and concerning to see that this issue could have an impact on participation in research projects. Again this is an indication of the need to better communicate how research works in practice. Findings from one research project can influence another, and most medical breakthroughs that lead to a treatment are in fact based on many research projects going back decades. It is not practically possible to limit how research findings are ultimately used.

Compared to our previous project, participants in this project were more supportive of providing their genetic data to pharmaceutical companies as 61% of participants felt pharmaceutical companies should be able to access their data.

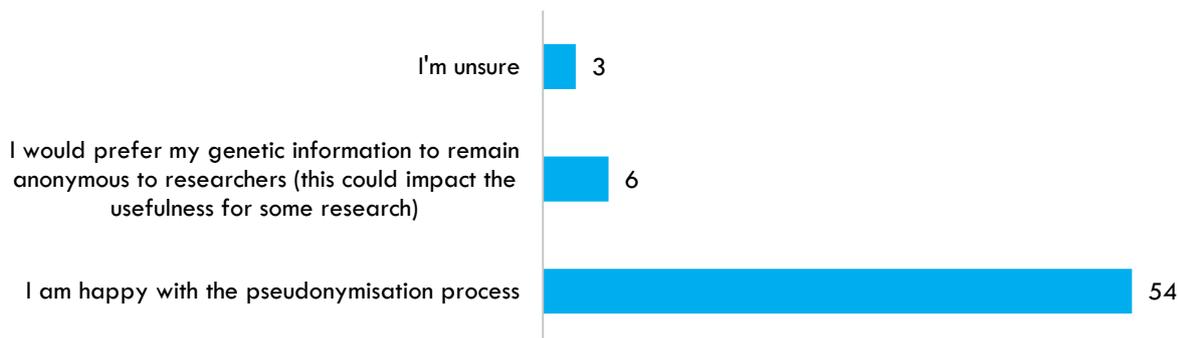
**Are you happy with researchers using pseudonymisation or would you prefer your genetic information to be completely anonymous? Pseudonymisation is a method by which researchers replace the fields that identify you with coded identifiers.**



**Data confidentiality**

Patient data can be stored safely in varying degrees of anonymity to ensure patient confidentiality. Pseudonymised records have had all identifying data removed and can only be traced back to individuals using a 'key' which can be securely stored separately from the patient data. Most participants in our project were unconcerned about sharing pseudonymised information with researchers.

**Are you happy with researchers using pseudonymisation or would you prefer your genetic information to be completely anonymous? Pseudonymisation is a method by which researchers replace the fields that identify you with coded identifiers.**



In our live chat, participants discussed pseudoanonymisation of data, and its implications. Participants in the chat commented that they would be comfortable with researchers using their genetic and health data in any way if it could potentially lead to improvements in treatment, but were wary of sharing data for studies that would be motivated by commercial gain.

*"...you can do what you want with it, if it could help down the road, I'm all for it."*

*"I am always offering my help because rare diseases are, you know, rare, and if you can find anything out, take it ... do whatever you want with it."*

*"I've said to my consultant [who also conducts research] 'please take my genes, do what you want with them, if you can help somebody.'"*

The willingness of patients to share their genetic data and associated health data opens up huge possibility for researchers and clinicians requiring health data for studies. There were, however, still concerns from participants over the safety of this data. Some expressed concern that while they were comfortable sharing healthcare data with the NHS and research organisations, they would worry about how well this data would be safeguarded.

*"[I would share my genetic data] As long as information is not passed to people like insurance companies."*

*"[I would share my genetic data] So long as the link to my actual details were never revealed to the likes of insurance companies or private companies, to my detriment."*

*"[I would share my genetic data] Providing proper safeguards are in place."*

**Recommendation: Communicating to patients the aims of research and how results will be used, could lead to greater involvement of patients in research using genetic data, with greater confidence from patients in the work being undertaken.**

## Conclusion

The results from engaging with patients within the cancer community showed that patients want to be involved in decision making about their health and about potential treatments. While patients have a good understanding of basic genetics, they may need further information and guidance when discussing cancer genetics and genomics specifically. Providing more information could help patients, and families of patients, understand the decisions made by healthcare professionals to offer or not offer tests or screening, to make informed decisions about their healthcare, and to instil the confidence to request changes to their healthcare where they feel practitioners are not meeting their needs.

Patients value information about their health, but also choice in what information to receive at any given time and how this information is delivered. Patients already living with an often life threatening diagnosis should be counselled on what other information could be made available through genome sequencing, and what this information could mean for them and their families. Patients should have a say in what findings they wish to be informed about, and at what stage in their care any additional findings should be made available to them. This choice, and the ability to register a change in mind, should be made easy to exercise.

Patients strongly support flexibility of information, and speed in delivery, as long as it means that this is provided with expertise. Access to genetic testing should be provided in a way that reduces the time and travel burden on patients already attending frequent hospital appointments as part of their cancer treatment, while also ensuring patients are attended by health professionals with appropriate specialist knowledge. A streamlined pathway that considers cancer related findings and additional findings uncovered during genome sequencing should be developed to effectively manage and prioritise cancer patient care.

In line with previous work with rare disease patients, cancer patients strongly support participation in research. Importantly, patients are prepared to take into consideration the effect that choice could have in terms of costs and timescales both for research and in a clinical setting. Patients would like to be kept informed of any findings emerging from research that could provide them with information about their individual health, but only where this would not increase the costs of a study to a point that could negatively impact that research. Research studies should take advantage of this clear willingness to share genetic data for research, but should communicate clearly to data donors how their genetic data will be used and what, if any, information might be made available to individuals that could impact on the management of their health.

Our work with cancer patients ultimately shows that this is a community of well informed patients, who value access to new information about their health, and who are keen to share this information with the wider healthcare and research community to improve diagnoses and treatments for current and future cancer patients. Engaging with cancer patients further could help elucidate further the best way to deliver findings from genome sequencing to patients, to manage a dynamic consent model for individual results and genetic data sharing, and to engage more patients in research.

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