

# **Genomics England: 100 000 Genomes Project**

## **Potential Participant Literature: Research report**

November 2014

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# Executive Summary

## Background

In order to develop the patient information literature for the 100,000 Genomes Project, Genomics England commissioned Randall Fox to conduct a series of qualitative research interviews with potential patients and with Healthcare Professionals.

At Stage One the research focused on the Patient Information Leaflet (PIL) and the Consent Form. The longer Patient Information Booklet (PIB) was also included in the research as a secondary focus. This stage of research also explored literature aimed at children 6-10 years old and young people 11-15 years. In addition, all research participants commented on an Infographic giving an overview of the 100,000 Genomes Project.

In the light of findings from the initial wave of 39 research interviews (Stage One), the literature was redeveloped. Stage 2 then revisited some of the respondents from Stage One and asked them to look at an updated PIL and Consent Form. The Children's and Young People's literature was also revised and was discussed by a group of young people who had not previously seen the literature.

## Research approach

Stage One included a total of 33 potential participants (with a sample representative of those who would be eligible to participate in the Project) and 9 HCPs, who had been involved in the pilot. All interviews were depths or paired depths conducted in person or by telephone/Skype.

In addition we looked at the Children's and Young People's literature in two YPAG group sessions and in 5 of the patient interviews, where we spoke to a parent of a proband child aged 6-15 years, and, where appropriate, the child themselves.

At Stage Two we revisited 17 respondents from Stage 1 via phone or email, and one further session was conducted with a Young People's Advisory Group.

## Stage 1: Main findings

### Context

1. The research identified some key issues that are likely to affect how patients with cancer vs. those with genetic conditions may respond to the consent process. These offer a useful background when thinking about development of the patient information literature:

- Potential participants forming the cancer cohort are likely to be recruited at a very challenging time, when they are already assimilating a large amount of information about their possible diagnosis, prognosis and treatment plans. They may find it difficult to engage with longer documentation, and the consent process would probably need to be conducted within a tight timeframe. They may also find decisions around feedback about other conditions/information relevant to their children very challenging at this time;
- Potential participants forming the genetic disease cohort are likely to be more engaged and involved in genetics generally. Within our sample, many were very positive about the possibility of research into their condition, as they were conscious of the lack of understanding/funding with regard to their condition. It seems likely that many from this cohort will have more established relationships with their clinical team, and others experiencing similar issues;
- As such, within our research, genetic participants seemed to have a more immediate sense of excitement, and of the potential of the project for them/people like them. Indications were that these patients would be more likely to stay engaged with the Project's development over time. While many cancer patients were also enthusiastic about the Project, there were certainly some in our sample who were less engaged in what the 100,000 Genomes Project might mean and the potential impact for them/people like them.

### **Patient Information Leaflet (PIL)**

2. It was clear from the research that potential participants struggled to read and fully understand the PIL. The language was felt to be dense, technical and hard to take in, with a complex sentence structure and a dry, 'legalistic' tone. Many patients spoke of having to read the same passage, or the entire leaflet, repeatedly. Participants with English as a second language, or poor literacy skills, found it especially challenging, and generally needed the literature to be filtered or translated by a family member or friend.
3. The structure of the leaflet meant it was difficult to navigate, as sections did not follow an intuitive order. There appeared to be a great deal of repetition (e.g. around security), which meant many were unsure if they were reading the same, or a subtly different point, leaving them unconfident about their understanding as a whole.
4. Many HCPs expressed concern that patients would not be able to appreciate the full implications of the Project from reading the PIL and that it was a document aimed more at 'covering the Project', rather than truly informing patients. They anticipated that it would be a challenge to talk patients through the project and its implications using the PIL. However, some felt that the literature was similar to other patient information literature they encountered, and could be more accepting.

5. Even after repeated reading, most potential participants struggled to get a clear sense of the Project's remit, their commitments, and the feedback they would receive. Particular passages/topics were particularly challenging for patients or fell short of giving an adequate explanation:
- **Genome/genomic medicine:** both patients and HCPs called for a short explanation, early in the literature, of what these terms mean and of the implications for them/for healthcare;
  - **Understanding the overall concept and aims of the project:** the leaflet frequently failed to communicate a clear overview of the Project goals/aims/commitment. For example, patients were left unsure of how the project would operate (i.e. as a large database/lending library); that the Project is run on behalf of the government/ NHS; the overall goals of the project; the inclusion of both genomic and personal record data;
  - **Feedback:** there was a high degree of confusion around what feedback would be available. The distinction between the different types of feedback, and whether each was optional or a core element of the Project, was extremely unclear;
  - **Involvement of family members:** there was no clear explanation of the commitment required from family members of patients with genetic conditions, the reasons for their involvement, or of what feedback they would receive and how;
  - **Insurance:** the wording around insurance in the PIL suggested to many that insurers could access information after 2017, which created serious concern.
6. In addition, certain areas were pulled out as concerns only by HCPs:
- **Data protection:** HCPs expected this to be a significant worry for patients, especially in the light of the Care.data programme. They wanted to see this information clearly pulled together towards the beginning of the leaflet for reassurance;
  - **Feedback timings** were a concern. HCPs were worried that the PIL appeared to be making unrealistic commitments to patients about the turnaround ('within a couple of weeks') and regularity ('these results may periodically be updated and returned') of feedback;
  - **Tonally**, whilst the language in the PIL was generally felt to be less promotional than some other literature encountered, HCPs were concerned to ensure that all language used is neutral (e.g. use of 'groundbreaking' to describe the Project was questioned).

### Infographic: explaining 100,000 Genomes process

7. This was a strong element in the overall communications and, for the majority of respondents (including BME/those with lower literacy skills), the Infographic offered a much clearer introduction/overview of the Project's remit and goals, and their commitment, compared to the PIL.

The visual approach and positive, benefit-oriented tone were generally well received. Young people aged 11-15 years old were also very positive about the content and presentation of the Infographic, although this was only explored briefly with these groups.

8. Many HCPs imagined the Infographic would be a useful tool in introducing the Project to potential participants by providing a quick overview of the Project set up/remit, and the potential benefits, although it was felt to lack detail around what was personally required of individual patients. HCPs raised some concerns that the language (especially in the introduction), and the final references to personal benefits for participants, verge on inappropriate/coercive.

### **Consent form**

9. Potential participants were broadly accepting of the use of legalised, dense language in the consent form, as it tended to fit with their expectations. However, HCPs were often highly critical of its length and the complexity of its language, especially those aware of moves to improve the clarity and accessibility of language used in consent forms in their own setting. Many wanted to see a much simpler form, with repetition stripped out, in order to help patients understand what they were consenting to. Both HCPs and potential participants also wanted easier cross-referencing between the two documents.
10. The issue of feedback (points 16, 17 and 18) was particularly confusing in the consent form, and criticised widely by both potential participants and HCPs, especially as the language in the Consent Form vs. PIL was not always consistent.

### **Patient Information Booklet (PIB)**

11. Participants found the PIB (especially the cancer version) substantially easier to navigate and assimilate in comparison to the PIL. Participants looking at this version as their first introduction seemed to get a broader grasp of key elements of the project, and were more confident about their understanding. Those reading sections of the PIB as an alternative to the PIL wording nearly always found them clearer and easier to assimilate (including those with English as a second language).
12. In comparison to the PIL, the language was generally felt to be clearer and more straightforward and accessible. Participants thought that the tone was warm, engaging, even appreciative (rather than legalese) and the structure was substantially easier to navigate, due to clear sections, Q&A format, even the use of coloured text for questions.
13. However, the length of the document raised strong concerns among both HCPs and potential participants, especially if this document is positioned as the main source for informed consent. The length and structure meant there was a real danger of participants missing key elements of the Project, and/or disengaging, due to feeling overwhelmed. Certain elements of the PIB – such as the

upfront table, and the 'contents' page (in the genetics version) directing different participants to relevant sections – were less effective.

14. A number of HCPs spontaneously suggested that this document might be more effective in a secondary role, providing supplementary information, for patients to read either prior to, or after, agreeing to participate in the Project. Alternatively, potential participants (who didn't see both the PIL and PIB) suggested that a stripped out version of the PIB, with a clear, upfront, summary of the Project (possibly along the lines of the Infographic) and the requirements for them, followed by further detail for those who want to know more, would work well as the core information literature.
15. Some HCPs also expressed concern about the 'promotional' tone and language used in the PIB, in comparison to the more neutral PIL; language such as 'groundbreaking', 'real opportunity', and the reference to your doctor 'suggesting' you take part, for example, were felt to be inappropriate.

### Children's literature

16. Young people developed a clear list of their priorities for literature content and the issues that need to be covered, as well as their preferred tone and approach (direct, non-patronising, non-didactic). They also identified their optimal format (interactive and engaging, e.g. animated version of the Infographic).
17. Some parents and young people suggested that a parental guide to accompany the Children's/ Young People's Literature would be valuable, to give advice to parents about how to talk through the issues with their children, and how best to support their children in making a decision about participation.
18. The version for 6-10 year olds was generally regarded as appropriate, with the language level and visual approach hitting the right note, although there was some desire to make the overall literature more compressed and physically accessible. It is worth noting that, due to sampling challenges, relatively few children in the 9-10 age bracket were involved in the research, and there were some indications from slightly older children/parents that the literature might be too simplistic for this age group.
19. The research indicated that the version for 11-15 year olds required further development. The language and general approach/content were felt to be over-simplified; the tone was frequently regarded as patronising; the structure and flow were not optimal; and some areas that young people felt were important to cover were missing (including more detail about the nature and goals of the Project and the commitment required of young people). Whilst visuals explored were only very draft, in general young people were keen for a more stripped-out, focused visual approach (rather than a visual per page).

### Further issues

20. A number of further issues emerged during the course of Stage One:

- **100,000 Genomes:** some, with low literacy/English as second language struggled to know how to read the figure. Further more, the number itself mystified many: no reason is given in the literature for this number and without help (given in PIB) potential participants didn't have a sense of the value of this sample size;
- **Genomic Pioneers:** although this didn't appeal to everyone, for a substantial group, this was a motivating and engaging idea. They were attracted to being part of something special/that will make a difference. Being kept in the loop and getting info back also appealed and strengthened perceptions of openness/transparency around the Project, particularly if this information is to be presented in an accessible/layman's format. Ideally, online and paper versions were requested;
- As participants are likely to Google the Project it is, of course, vital that the website supports the information literature. Some in our sample, who had watched the video currently on the home page, could assume diabetes and particular forms of cancer mentioned in this film were the focus of the Project.

## Stage 2: Main Findings

### Responses to new PIL (Version 0.10)

1. Most felt that the new PIL represented a real improvement, especially in terms of its overall clarity and the ease of understanding – generated by clearer language, structure and flow. Potential participants were especially positive about the use of bullet points, 'key point' boxes, and cross-referencing across documents (i.e. with the Consent Form). Tonally, the document was also felt to be straightforward, even reassuring, with an appropriate level of detail. Whilst the new PIL was still felt to be longer than ideal, many acknowledged that this length may be unavoidable for consent to be fully informed.

NB Whilst participants were certainly benefiting from reading the document for a second time, these improvements also seemed to be very directly driven by changes made to the document.

2. However, some key areas were identified, where the new PIL – whilst often a substantial improvement on the first stage PIL – would benefit from further optimisation to ensure full clarity:
  - **Family involvement for genetic participants:** clearer explanation is required of the involvement of family members, what form their involvement would take, and what feedback they would get and how;



- **Different types/levels of findings:** whilst the coverage of these issues in this version was an improvement, a visual aid clearly setting out the different feedback types and what each covers is likely to be helpful. Potential participants sought greater clarity around the kind of results that Additional Findings and Incidental Findings would cover. Carrier Status threw up a number of issues and being more explicit about who this would be offered to should help.
  - **(Future) health records:** accessing health records was much clearer and more explicit. However, slight rewordings could help to clarify that records will continue to be updated in the future.
  - **Confidentiality/anonymity:** strengthening communication around the 'barcode' approach would help lessen confusion around how information can be simultaneously anonymous, yet fed back to clinical teams.
  - **Commercial/for profit organisations:** ideally, when commercial/for profit organisations are first mentioned it would be helpful to either provide a brief explanation, or reference a later section. Reassuring patients that access will be 'for scientific and medical research purposes' has also worked well previously.
3. Whilst not looked at directly in this Stage, it is worth mentioning that some potential participants were disappointed that the Infographic appeared to be 'missing'. This visual element was extremely popular within the first stage of research and worked well both to give an overview of the project/commitment required, and to help potential participants feel excited and engaged about the goals, and potential of the Project.

### Responses to Consent Form

4. Most felt the Consent Form, whilst still long, was reasonably clear and that the language was more accessible than in the previous version.
5. However, point 20 (informing family members) was particularly challenging, in part because it hadn't been covered in the PIL, so was encountered for the first time within the consent form. It prompted concerns around issues of confidentiality and lack of control. A clearer explanation, in the literature, of how this element will work, why it is included and what will be done to protect the confidentiality of the participating patient seems important.
6. It is worth mentioning that the issue of what happens to findings beyond your lifetime/the 'legacy' of passing access to your information to future generations came to the forefront for some of those we spoke to at Stage Two, who had been reflecting on this issue since we initially spoke to them at Stage One, and point 20 can further highlight this issue.

## Responses to concept of longer booklet

7. Whilst a minority felt that the PIL offered sufficient information, the majority were positive about the idea of a longer booklet or FAQ document to be held by the participant– available in hard copy and via the website. Most felt there was a role for providing more detailed information on specific issues, for giving a more extensive and explanatory overview of the Project, and/or as a keepsake for participants.
8. While not explicitly discussed with respondents, the research indicated that, if the patient information literature is presented only in an electronic format during the consent process, then offering participants a hard copy to take away, or access to the document via the website, would be sensible. A number of those we spoke to said they would to review and remind themselves of what they had agreed to, in their own time.

## Children's and Young Person's Literature

9. Both documents were positively received at Stage Two. The Children's Literature had not changed significantly from the Stage One version (when it had been generally well regarded). But the Young People's version had been significantly re-worked and the Stage Two version was considered to be a strong step forward. The content, level of detail, tone and language of both were felt to be strong. The major improvements in the Young People's document were: the inclusion of a glossary, the increased complexity of content, the use of key points pulled out in boxes, and the overall tone of the visuals used.
10. A small number of suggestions/ideas came forward from young people for optimisation of the communications :
  - Suggestion of a separate booklet for siblings, who might have different concerns/might need more support thinking through the implications of findings;
  - In both YP and Children's information, tying 16 years to adulthood was felt to be over-simplistic, and focusing simply on this being an age at which you consent directly was preferred;
  - There were also suggestions to tier/update the information as children get older, to ensure that they are in a position at 16 to make an informed decision;
  - There was concern that Additional Findings would be a challenging area for any child, so young people suggested that a parental document encouraging parental support/discussion of this issue might be the most useful approach.

# 1. Background

This report presents the findings of qualitative research studies around the patient information literature for the 100,000 Genomes Project.

From January 2015 Genomics England will begin the process of sequencing 100,000 genomes, involving around 35,000-40,000 people.

In addition to a consent form, Genomics England will produce literature explaining to patients the background and purpose of the 100,000 Genomes Project, what participation entails, and what they are consenting to. As well as literature for adults, literature and an assent form appropriate for children and young people aged 6-15 years will also be required. An infographic explaining the Project has also been developed by Information Is Beautiful.

In order to optimise the consent process, a programme of qualitative research was required to understand the how well the literature developed meets the needs of those who could potentially be eligible to participate in the 100,000 Genomes Project, and the perspective of Healthcare Professionals involved in the Project pilot. The research was intended to provide guidance to ensure that the information supplied to patients is as clear and informative as possible, and in particular that potential participants are able to make informed consent when agreeing to participate in the process. The research was tasked with exploring responses to the consent/assent forms, the information leaflets and booklets, and the Information is Beautiful infographic.

The study was conducted by RandallFox in September and October 2014 on behalf of Vivienne Parry, Head of Engagement at Genomics England. Findings from the research were used to inform changes made to the literature, as well as the Genomics England presentation to the Research Ethics Committee on October 23<sup>rd</sup> 2014.

## 1.1 Objectives

RandallFox were commissioned to explore responses to the literature amongst potential participants, including children and young people, and amongst Healthcare Professionals who had been involved in the pilot study. Most interviews were in-depth interviews, either conducted on the phone/skype or face to face, supplemented with a small number of groups conducted with children and young people.

Specific objectives were to:

- Provide feedback on the clarity/ease of understanding of each of the key pieces of consent literature;

- Provide detailed developmental feedback on areas of improvement, in terms of clarity and engagement;
- Explore in detail the expression of certain key areas of focus, which the team anticipated might be challenging for potential participants:
  - The involvement of commercial organisations;
  - Data privacy and security;
  - Future contact with the 100,000 Genomes Project;
  - Feedback on findings;
  - Withdrawal process.

The focus for this element of research was firmly on the literature itself, exploring the best way to express defined policies, and as such was not intended to explore reactions to those consent policies and how they might affect potential participants' responses to involvement in the 100,000 Genomes Project. Specifically, the following were defined as beyond the remit of this research:

- Exploring levels of interest in participation in the scheme, and reasons for this;
- Assessing responses to the logistics of taking part (beyond any issues raised in the literature);
- Developing consent policies themselves, including any consent issues between family members (e.g. estranged partners; different priorities between patients and family members).

However, where such responses emerged spontaneously, they are recorded within this report.

## 1.2 Methodology

Research was conducted in two waves. Stage One explored the Patient Information Leaflet (PIL), Patient Information Booklet (PIB) and Consent Form, as well as initial versions of the Children's and Young People's Literatures and Assent Form. Following updates to the literature based on feedback from Stage One, Stage Two explored an updated Patient Information Leaflet and Consent Form, as well as an updated version of the Children's and Young People's Literatures. The children's Assent Form remained unchanged. In Stage One, the PIL and PIB were initially explored as alternative information sources, but by Stage Two the intention was for the PIB to operate as a secondary piece of reference material rather than a core information source.

Full copies of all the literature discussed by respondents, together with annotated notes detailing feedback on specific issues and phrases, can be found in the appendices to this report, as follows:

**Stage One:**

PIL, Stage One: Appendix 1

PIB, Stage One: Appendix 2

Consent Form, Stage One: Appendix 3

Infographic: Appendix 4

Children's literature, Stage One: Appendix 5

Young Peoples' literature, Stage One: Appendix 6

**Stages One and Two:**

Children's and Young Peoples' Assent Form, Stage One and Two: Appendix 7

**Stage Two:**

PIL, Stage Two: Appendix 8

Consent form, Stage Two: Appendix 9

Children's literature, Stage Two: Appendix 10

Young Peoples' literature, Stage One: Appendix 11

Note 1: Some documents have been reformatted to allow sufficient space for annotation.

Note 2: as Children's and Young People's literature at Stage two was explored in one group only, all detail is contained within the full report, so appendices are for reference only.

Fieldwork for Stage One of research was conducted between 5<sup>th</sup> and 23<sup>rd</sup> September 2014. Fieldwork for Stage Two was conducted between 6<sup>th</sup> and 8<sup>th</sup> October 2014. All fieldwork and analysis for both stages of research was conducted by Sam Neill, Ali Percy and Anumita Sharma. As is customary with market research, potential participants were offered a small financial incentive as a thank you for participating, but HCPs were not offered an incentive

**A. Detailed methodology: Stage One**

Stage 1 included: a total of 33 potential participants; two groups of young people, conducted via the Young People's Advisory Group (YPAG) in Liverpool and Nottingham; and 9 HCPs. Potential participant interviews included a small number of interviews with parents of proband children 6-15, and when

deemed appropriate by the parents, the proband child/children also viewed the literature and took part in the interview;

This was a robust qualitative sample.

### Potential participant interviews

The potential participant interviews were structured to take into account the following variables:

- Existing condition: A split between potential participants with cancer diagnosis, and potential participants with genetic conditions. All potential participants with cancer were post-diagnosis; with a spread of stages of treatment and recent recovery (all had been treated within the last two years). Potential participants with genetic conditions had all been given a definite or tentative diagnosis of a genetic disease, but had not had this confirmed by genetic, or molecular testing (diseases/ conditions represented included myocardiopathy, Alstrom Syndrome, Ehlers-Danlos Syndrome, Polycystic Kidney Disease, Primary Ciliary Dyskinesia, deafness);
- Geographical location: Interviews were spread across England;
- Gender and Age: A mix of men/women and a spread of ages;
- Socio-Economic Background: Potential participants were drawn from across the range of socio-economic groups (SEG);
- Inclusion of those who might find written literature especially challenging, including a small number of interviews conducted with those with low literacy/reading levels, and those with English as a second language (drawn from the Pakistani, Bangladeshi and Indian communities);
- A small number of interviews with ‘family pairs’ comprising a proband adult and close blood relation;
- Representation of a range of ethnic backgrounds, including Bangladeshi, Pakistani, Bengali, African-Caribbean, and Indian as well as white British.

The interview structure with potential participants was split as follows:

Number of interviews	Cancer	Genetic Conditions	Number of individual participants
English as a second language	2	2	4
Low literacy	2		2
Family pairs		3	6
Parent (with children where appropriate) – with English as		1	1

<b>a second language</b>			
<b>Parent (with children where appropriate)</b>		5	<b>5 (plus 4 proband children/young people)</b>
<b>No recruitment restrictions</b>	10	5	<b>15</b>
<b>Number of individual participants</b>	<b>14</b>	<b>19, plus 4 young people/ children</b>	<b>Total number of participants: 33 plus 4 children/young people</b>

The research for the potential participants comprised a mix of face to face and telephone/Skype interviews. The majority of respondents viewed some of the literature prior to the interview, and were asked to record their comments either via an online portal or on paper. About a quarter of the sample encountered the literature for the first time in the interview itself.

Of the adult interviews, 16 were asked to review the PIL, but were shown extracts from the PIB to explore alternative wordings, with 8 interviews focused on the PIB. In addition, all potential participants looked at the Consent Form and at the Infographic explaining the 100,000 Genomes Project.

In the parent (and child) interviews, and YPAG, the sessions looked at the (relevant) Children’s or Young People’s Literature and the Assent Form. Some also looked briefly at the Infographic. Parents also reviewed the PIL and Consent Form.

#### **Young People’s Advisory Groups (YPAG)**

The sessions with YPAG – for both Stage One & Stage Two were convened as part of the YPAG regular meetings. The Young Person’s Advisory Group was set up in 2006 with the support of the National Children’s Bureau. The aim of the group is to increase the input and influence of children and their families/carers into the development of clinical research. More information about the YPAG can be found here: <http://www.crn.nihr.ac.uk/children/pcpie/young-persons-advisory-group/>.

Each session lasted 2 hours, comprised a mix of young people aged between 10 and 19 years, and each group included between 8-11 young people.

During these sessions, young people initially explored their ideals, in terms of feedback format, and having been introduced to an overview of the Project, also discussed which areas they felt needed to be included within the literature for Young People. The group then worked through the literature in pairs, before pulling together their thoughts and suggestions for optimisation.

#### **HCP interviews**

For the 9 HCP interviews, HCPs were sent in advance copies of the PIL, Consent form, and PIB including Infographic. They viewed these, and then a follow-up phone call was conducted to discuss their opinions. These interviews lasted between 20 minutes-1 hour.

The HCPs had all been involved with the pilot, came from a mix of institutions, and included the following roles:

- Genetic counsellor
- Clinical consultant (both cancer and genetics conditions)
- Nurse consultant (cancer)
- Biobank technician

Of the 9 interviews, 4 were from an oncology background, and 5 from a rare disease background.

## **B. Detailed Methodology: Stage 2**

At Stage 2, 18 respondents from Stage One, were recontacted, to review the changes made and explore whether these were sufficient. 9 x 30 minute telephone depths were conducted (including one paired depth with a proband adult and family member) and the responses of a further 8 respondents were gathered by email.

Across these respondents, there was a mix of:

- Those who had looked at the PIL and those who had looked at the PIB at Stage One;
- Potential participants with cancer diagnosis, and those with a rare genetic condition;
- Mix of gender, age and ethnic backgrounds represented;
- Due to tight timeframe, participants with English as a second language and those with low literacy levels were not included.

For this stage all respondents were sent the new PIL and Consent Form in advance, along with a short set of questions to consider and respond to.

In addition, one further group was conducted with the Young People's Advisory Groups in Birmingham.

### **1.3 A note on confidentiality and quotation attribution**

All views and quotations coming forward from the sessions have been anonymised, as is customary in qualitative research. For HCP quotations, job role is recorded.

### **1.4 Acknowledgements**

We would like to thank all those who participated in the research for giving up their time to put forward their opinions. We would especially like to thank the following organisations who helped us to gain access to their members as potential participants:



- Alstrom Syndrome UK (<http://www.alstrom.org.uk/>)
- BME Cancer Group (<http://www.bmecancer.com/index.php> )
- The Cardiomyopathy Association (<http://www.cardiomyopathy.org/>)
- Contact A Family (<http://www.cafamily.org.uk/>)
- Ehlers Danlos Support UK ( <http://www.ehlers-danlos.org/>)
- Muscular Dystrophy Campaign (<http://www.muscular-dystrophy.org/>)
- Primary Ciliary Dyskinesia Family Support Group (<http://www.pcdsupport.org.uk/>)
- Polycystic Kidney Disease Charity (<http://pkdcharity.org.uk/>)
- Young People’s Advisory Groups in Liverpool, Birmingham and Nottingham (<http://www.crn.nihr.ac.uk/children/pcpie/young-persons-advisory-group/>)

We would also like to thank the following individuals for their support during the project: the team at YPAG, especially Jennifer Preston, Kirsty Widdowson, Carly Tibbins, Claire Callens and most especially the young people themselves; Professor Bobbie Farsides and Kate Harvey at the Nuffield Council on Bioethics for their input into the formation of the Children’s and Young People’s research element; and Dr Nadeem Qureshi and Rose Thompson at the BME Cancer Communities for their input into the formation of the BME research element.

## 2. Context: attitudes and emotional state and levels of awareness

We begin this report with an overview of differences in evidence between the cancer cohort, and those with/parents of children with rare genetic diseases. Although the research was not specifically tasked with exploring any difference in attitudes to the Project, or genomic medicine in general, some themes emerged which may have implications for the information literature. We will then go on to outline some general variations in response to the Project, and look at how needs for information and reassurance differed across our sample.

### 2.1: Differences between cancer and rare genetic condition cohort

NB We spoke to cancer patients post-diagnosis/in treatment, so the following reflects their recollections of their experiences/mental state at the time of diagnosis.

A number of differences emerged – in terms of general attitudes to, and awareness of genomic medicine and genomics - but also in terms of the emotional state of participants around recruitment stage.

#### A. Context for cancer cohort

Both HCPs and potential participants felt that patients forming the cancer cohort are likely to be recruited at a very challenging time, when they are already assimilating a large amount of information about their possible diagnosis, prognosis and treatment plans. Many stressed the speed with which their treatment had progressed – moving from first GP visit to operative treatment in a few weeks. Potential participants recalling this time felt this was a very intense period emotionally, and both HCPs and patients felt that the quantity of information already being absorbed, and the emotional changes being managed at this stage, could be overwhelming:

*There are so many tests, and biopsies ... the doctor said they tried not to overburden me with information... your brain does go into freeze (Cancer participant, female)*

*They may not read it at all. Their priority after all is to be diagnosed and to start treatment (Cancer consultant)*

In addition, for cancer patients, the idea of looking at genetic issues around their cancer can be especially frightening; many we spoke to said that a key issue at their diagnosis stage was the fear that their cancer might be hereditary, and therefore impact on their children or grandchildren:

*The first thing I asked my consultant was 'is this going to affect my children?' (Cancer participant, female)*

Cancer participants were often not knowledgeable about genomic treatment around cancer, with the exception of those who had experienced tailored treatments for breast cancer:

*I had no idea, but since I've been being treated, talking to other women, all our treatments are slightly different – it's amazing. (Breast cancer participant, female)*

This was felt to have a number of implications.

Firstly, some potential cancer participants felt that they might not have been keen to engage with a project such as 100,000 Genomes at this stage, as they were already overloaded with information, and their emotional and mental 'headspace' was at a premium:

*I was struggling to come to terms with the fact I might die. There is no way on earth I could have read through all of this stuff, when fighting to live, and coping with my emotions, and those of my family. Making rational decisions would have been impossible (Cancer participant, female)*

Even those who were very supportive of the project felt they would have struggled to engage with lengthy or complex documentation, especially as the consent process would probably need to be conducted within a tight timeframe. Some also mentioned the difficulty of taking in complex information whilst experiencing the side effects of treatment:

*I couldn't read this yesterday – I had chemo-brain. It knocks you out (Cancer Participant, female)*

Secondly, some – especially those with family experiences of genetic issues, or who feared their cancer diagnosis itself may have a genetic component – felt they would find decisions around feedback about other conditions/information relevant to their children especially challenging at this time. This perspective was also echoed by HCPs working within oncology.

It is worth mentioning that a small number of the participants that we re-contacted at Stage 2 stressed that they had continued to reflect on this issue, following the first interview. They wanted to make the point that consenting within the short time frame prior to operations could add stress, and that this process therefore needs to be handled very carefully to avoid alienating, or over-burdening potential participants:

*They would have to be sensitive to the utter turmoil of diagnosis – you can barely make a decision about your treatment, never mind what is going to happen to your genome (Cancer participant, female)*

Treating the recruitment process with sensitivity was expected; beyond this, being able to revisit the commitment after treatment (e.g. by looking through a longer booklet/asking more questions), or even offering staged consent, (to allow patients to reconsider their involvement after treatment/having come to terms with diagnosis), were suggested, to help potential participants make informed consent in an emotionally relaxed state.

However, it is worth noting that a contrasting viewpoint was also expressed, with the potential cancer participant cohort expressing a very strong interest in participating in trials/additional monitoring during their treatment/diagnosis process. This interest was driven both from an altruistic point of view, and also due to an assumption that their own treatment would be monitored more actively:

*If they offer you a trial of anything, I think you take it – anyone with cancer would. You think you'll be tested more thoroughly. I wasn't eligible for any trials, but I was desperate for one! (Cancer participant, female)*

*All trials are good, I think – they might help you, or help someone else in the future (Cancer participant, female)*

*When they say you're a great candidate for a test – you feel you're doing something, and that they are on top of you, of what's happening to you (Cancer participant, female)*

## **B. Context for genetic cohort**

In comparison, not surprisingly, potential participants forming the genetic disease cohort were often reasonably well informed about their condition, and they also displayed higher levels of knowledge in general around the role of genetics in healthcare, and genomic medicine:

*I then ended up finding out about the genome project, because then I was doing my own research and I was just going through websites and you guys were cropping up (Genetic participant, female)*

Having had time to accept and research their diagnosis they were often in a more stable emotional position and better able to engage with the idea of taking part in the Project.

*I suppose with xxxx having xxxx, she wants to know every single little bit that there is to know about it; but not only that, but she wants to help (Genetic participant, mother of proband adult)*

Within our sample, many of those with a rare genetic disease were very positive about the possibility of research into their own condition, as they were often conscious of a lack of current understanding and funding:

*With cancer you're bombarded with stuff. The condition my daughter has isn't even on the British Heart Foundation website (Genetic participant, mother of proband adult)*

*EDS is relatively late in being discovered and it's quite an important thing to us to think about future generations (Genetic participant, female)*

It also seems likely that many from this cohort will have more established relationships with their clinical team, and others experiencing similar issues (e.g. via support groups), and so may be more 'immersed' in a community with similar experiences:

*I've been quite involved with the EDS charity, so I can imagine the kind of people this might help. That makes me want to do it even more (Genetic participant, female)*

Given these factors, genetic participants seemed to have a more immediate sense of excitement, and of the potential of the project for them/people like them:

*If it's going out to sufferers, they will have a different take on it to the general population – they'll be more willing to contribute, for their children, and other people in the same situation. The genetic population don't have the same context for their experiences (Genetic participant, male)*

*It's never been done before and it could help generations to come ... We'd be one of the first to help build this (Genetic participant, female)*

Indications were that these patients would be more likely to stay engaged with the Project's development over time. In comparison, whilst many from the cancer cohort were also very positive about the potential of the project, some seemed somewhat less engaged, or had a less immediate sense of what the 100,000 Genomes Project might mean and the potential impact for them/people like them. There was evidence to suggest that some of the cancer cohort patients may wish to 'move on' and put their diagnosis behind them; this was especially the case with those from BME communities.

It is also worth noting that we spoke to a small number of genetics participants who had only recently had their condition identified. They tended to be in a similar emotional state to cancer patients, and could still be struggling to come to terms with their condition and the implications. While still interested in the potential of the 100,000 Genomes Project, they could be daunted by realising that they are now being treated as a 'patient with a rare genetic disease'.

*It's been an awakening of understanding what it means. There's lots of anxiety around it ... I'm getting my head around the fact that I'm disabled (Genetic participant, female)*

### **C. Context for genetic cohort: family members**

Whilst not a core element within this research, there were suggestions that family members of those with a genetic condition may or may not be in the same mindset as their family member who has the genetic condition. The parents we talked to within the research were very willing to be engaged with anything that might help their children, or other families in the future facing similar diagnosis.

However there was some indication – both in the YPAG and in other family interviews – that siblings (especially younger siblings) might be more wary of genetic testing. This seemed to be partly driven by a less immediate sense of altruism, and families also felt that siblings might be nervous of what might be found:

*... Where it's saying about now and the rest of your life ... That's a bit of a scary thing to read. Like if we gave this to my sister and got my sister to read it, she'd be..., 'No.' (Genetic participant, female)*

*I don't think I'd do that for my sister... (YPAG, Birmingham)*

Within the sample we encountered a small number of mothers who had not yet told their children of their condition, or whose children were not able to fully understand their condition (for example due to developmental delays) and the research indicates that both of these groups might be challenging to reach. Some reluctance was evident amongst some of these mothers to discuss issues that they weren't yet ready to raise, or to commit their children to (further) medical procedures.

*Parents don't want to be pushed to tell their children something they're not ready for ... we want to have these conversations when we're ready ... I'm not prepared to put her through the trauma, just for some*

*research ... the pros don't outweigh the cons (Genetic participant, Mother of proband children aged 4 and 7)*

It is also worth mentioning that we did not include within our sample parents of children under 6 years, but again there were some indications that such parents might be more reluctant to involve their children. Further exploration with these groups would be valuable in terms of exploring their responses to the 100,000 Genomes Project in general.

## **2.2 General interest in, and differences in response to, the 100,000 Genomes Project**

Whilst this stage of research was not explicitly looking at levels of interest, or recruitment mechanics, some issues emerged during the interview process, that are worth considering.

### **A. Overall engagement with the 100,000 Genomes Project**

There was a spread of levels of interest and engagement across the sample, but most of our sample were, in general, positive about the idea of further research into rare genetic diseases, and cancers. Most felt that their participation would predominantly be motivated by a desire to help others facing similar health issues:

*It's taking samples from me to analyse to do research ... trying to find cures ... they're picking on people that have had ... like cancer problems ... I would imagine they're trying to put some sort of database together where they can hopefully ... eradicate certain diseases (Cancer participant, male)*

*They need to find 100,000 people who will let their data be used ... with the major possibility for helping people live better, even longer lives.... It's good, it's exciting (Genetic participant, male)*

*It feel like I'm contributing to research into my disease, that my kids might get – that's a big driver for people like me. When you've got xxxxx, you become invested – so it's important, the fact that they're pushing forwards research into your specific problem (Genetic participant, male)*

*I'm sure every cancer sufferer would be absolutely delighted to know that their saliva or blood ... could rapidly advance the understanding of cancer (Cancer participant, female)*

They also understood that there was the potential of possible benefit to themselves at a secondary level:

*It may come back to you, help you, if you're still having treatment for a while, which can happen – it did for me ... It makes me think I will take the chance that it MAY benefit me... this is very clear that there probably won't be any benefit, but the fact that there might is enough to make me want to take part (Cancer participant, female)*

*It's nice to see that it might help me in some way (Genetic participant, female)*

Although some low-level concerns emerged around the idea of genetic medicine (e.g. mentions of cloning, and sci-fi scenarios) most participants were largely unconcerned. Interestingly, those with more

concerns were often those who were more knowledgeable about genetics and/or had higher levels of education, who tended to be able to envisage the potential routes that genetic medicine might go down, and could imagine areas of genetic medicine that they might be uncomfortable with, or which they felt needed ongoing ethical consideration:

*I think the benefits outweigh the risks, but there is a danger of risks to your dependents too – how might people use this information in the future. As soon as things can be kept after your death, you don't know what is going to happen (Genetic participant, male)*

*At the end I still was thinking, 'Gosh, I don't know if I would volunteer for this', because I still would be worried that that information would be used and got into the wrong hands to – I don't know, to – do things, sort of Brave New World things ... or Never Let Me Go (Cancer participant, female)*

Those from more disadvantaged backgrounds, including some BME participants seemed more likely to be accepting that medical advancements were, in general, positive:

*I'm happy to do this because I've been diagnosed with something that kills people. I'm really happy to give information if it's going to help other people in a similar position to me (Cancer participant, male)*

## **B. Key concerns around specific policy areas of 100,000 Genomes Project**

A number of key issues prompted markedly different responses across our sample, resulting in a need for differing levels/types of information from the literature.

### **B.1 Security, Anonymity and Information Storage**

Some were keen to be reassured that data would be held securely, but were unsure what would constitute data security – although UK storage, and non-cloud storage were often pulled out as motivating phrases. As such, they were seeking confident statements of security, which included a list of relevant reasons to believe that security was tight, and constantly monitored and updated, and that access to the data would be strictly controlled:

*I don't need that much, I just want to know it's kept securely (Genetic participant, female)*

For others, security was less of a concern. They were generally happy to assume that a project of this type would be properly set-up and monitored, and were comfortable with personal information being widely shared, as long as they knew this was being done for ethically approved research. These participants struggled to imagine why or how any external agency would benefit from knowing about their genetic or medical situation:

*I know it's quite stringent about being secure, and all the data is confidential and blah, blah ... but for me personally ... I wouldn't mind my data being shared (Genetic participant, mother of proband adult)*

*I mean if it's part of tissue from my tumour you've had taken away, you don't want it back, do you? So what they're going to do with it is up to them – as long as they're not going to sort of try and make a mutant out of it, that's fine. But obviously, if they're using for what they said: research, whatever they do*

*with it after I've signed my bit of paper is entirely down to them; it's not my concern. (Cancer participant, male)*

*It's not like you know what they do with it normally is it. I kind of assumed they took the tumour away and did this kind of thing on it anyway (Cancer participant, female)*

That said, all respondents were expecting to see reassurances that the data would be held anonymously and that their participation in the project would not be made public.

## **B.2 Ongoing usage, and especially usage after death**

Some participants were very happy for samples to continue being used, and to commit to a broad spectrum of legitimate research projects:

*They've asked for my samples, I've given my approval and signed a bit of paper to that effect – hopefully they're going to use it in the right way. Hopefully they're going to find a cure for whatever ... it's in their best interests to look after it – it's nothing to do with me (Cancer participant, male)*

Others felt very uncomfortable with the lack of clarity around the breadth of possible research areas. Whilst they could appreciate in theory why this was important, there could be concerns that governance structures might change, so that the research conducted on their samples might be in areas that they were uncomfortable with. This was especially the case when they thought about research taking place in the future:

*The issue is that it's not definitive, and in ten years, you'll still have my samples, and you could be doing anything with them...we don't know what can possibly be coming round in say ten years time (Genetic participant, female)*

In addition, and running alongside this concern, some participants were uncomfortable with the idea of samples continuing to be used after their death, at which point they would have no knowledge or control. For some this was simply the idea of thinking beyond one's own death that was challenging; others were keen for the option to automatically exit the database at their death. The idea of having to face up to one's own mortality and the research continuing after one's death unsurprisingly seemed to be especially challenging for some of our participants who were in recovery from cancer treatment.

The issue of what happens to findings beyond your lifetime/the 'legacy' of passing access to your information to future generations was mentioned in both stages, but came to the forefront in Stage Two, as the PIL and consent forms became clearer about use of samples and information after your death (and the mention of benefiting family in point 20 of consent form). Some were very keen to be able to 'pass their data on' so that future family members continue to benefit:

*It's very clear in the document that your genome will carry on being used well past your death. But it doesn't say what happens in 50 years time, when they discover something that could help your children or grandchildren (Genetics, male)*



*I know what my mum died of – I don't know what my mum's mum died of. It would be good for my son to be able to look at patterns in the family (Cancer participant, female)*

*I understand from this that my family members could access my data, so that even if I'm dead my family could find out what's going on, and my kids could find out if they've got what I've had (Cancer participant, male)*

### **B.3 Involvement of commercial companies**

The vast majority of participants were reasonably comfortable with the involvement of commercial companies within healthcare. Whilst they could voice unease about the ethical or financial stance of companies developing drugs or treatments, they ultimately appreciated that most advances would come from the private rather than the public sector, so were willing to accept that commercial companies would bring value to the Project.

*Drug companies are OK if they're going to use that research to develop more effective drugs... I know everyone thinks they're evil and dreadful, but we've all benefited... Yes they make vast amounts of money, but we all benefit ... because it gets put back into research, so I don't worry (Cancer participant, female)*

This was a view shared by HCPs, who felt that in general, their patients understand that commercial/drugs companies offer a route to better treatment and diagnosis options:

*I think people with a condition have a different perspective to the general population here (Genetic consultant)*

It is worth stating that the explanation used within the PIB around the value of the involvement of commercial companies was very valuable in cementing potential participants' viewpoints here (Section 3: Why are you letting Commercial Companies access my data). Most participants who read this were convinced of the value of commercial companies accessing the data, given the importance of commercial/pharmaceutical companies in developing new treatments and medicines, but a small minority remained uncomfortable about the possibility of a commercial, rather than a patient-centric, perspective being at work.

### **B.4 Feedback**

Throughout both stages of research, potential participants struggled with understanding what kind of feedback/results they would receive. Whilst this is a complex aspect of the Project, appreciating the different layers of feedback was made even more challenging by the fact that participants had very different expectations with regards to their ideal feedback. As such, their starting points, and their responses to alternative feedback options, could be very diverse.

- Most wanted as full a feedback as possible – and assumed that feedback would always be beneficial, in terms of allowing early detection/prevention. For these participants, optional layers of feedback and explanation could feel unnecessarily 'fussy':

*Personally, I would want to know.... You feel there's a benefit – a chance of an earlier diagnosis (Genetic participant, male)*

*It's good to find out things ... I want any feedback I can get (Cancer participant, male)*

- A substantial minority had real fears around what they might learn in this feedback, especially thinking about their children's health, and the potential for discovering carrier status that might affect their offspring. These were often participants who had already faced decisions around exploring their genetic heritage (for example one who was aware her child was a CF carrier; another whose children might inherit his genetic condition, and was weighing up when to think about screening, and/or informing them). These participants felt that decisions around genetic screening were highly complicated, and required thought, and research:

*My doctor says sometimes you're better off not finding out until you've got your life sorted out, got a mortgage sorted. Some people want to find out – some don't – there are dilemmas in families about this stuff (Genetic participant, male)*

As discussed in section 2.1, cancer patients were also aware that making this decision when in the midst of a cancer diagnosis would be very challenging:

*I would find it difficult to make this decision, when diagnosed with cancer, there is a lot of fear involved, of what's to come, and I think it would cause more anxiety knowing you might have other conditions, although deep down I know it would be best to know as prevention is crucial (Cancer participant, female)*

*If you've just been diagnosed this would be quite overwhelming. You'd be really quite worried about finding out you've got something else. It's the last thing you want to know (Cancer participant, female)*

- Finally, a minority were nervous HCPs might not pass info back - so needed reassurance that feedback would reach them, and not be filtered by HCPs:

*They [clinical team] might just never mention it and that's bothering me, that I've just participated and no one's going to sit me down and say, 'Oh, cool, thanks. Like this is what we found, this is what we didn't find' (Genetic participant, female)*

This could be particularly keenly felt by cancer patients who talked about the lack of control they experienced after their cancer diagnosis. They were aware that HCPs often know more than they tell the patient, and wanted to avoid being in this situation if they could:

*You live in a state of constantly waiting to hear back about tests, a fear of what you might find out. And you're constantly trying to read into people's faces what's going on – do they know something you don't. You don't want to add another set of tests, another set of know knowing what's happening into all of that (Cancer participant, female)*

Finally, it is worth mentioning that participants from a BME background could especially prioritise feedback, as they could be utilising treatment or consultation processes in both UK and their country of origin. A full written report was especially powerful in this situation.

## B.5 Expression of ‘rare genetic diseases’

Mixed opinions were evident amongst potential participants with rare genetic diseases on the best term to use to group these conditions, and these differences may be partially driven by the spectrum of issues encountered within the sample. As such, some participants tended to see themselves as experiencing a ‘condition’ rather than a disease – for example, this was evident amongst those with EDS:

*It’s a fault in our genetics, that’s how we are, we have it for life. Disease implies to me cancer or heart disease. A condition is something we’re born with (Genetic participant, female)*

Others participants were very comfortable with the term ‘disease’, and self-defined in this way:

*I’m comfortable with that – we’re living with a rare disease. I wouldn’t say syndrome or condition – even though it is actually a syndrome (Genetic participant, Mother of proband child)*

Taking guidance from relevant charities appears to be most appropriate here, but it seemed unlikely that a single phrase would fit all experiences.

## 2.3 Specific needs of those with low literacy/English as a second language

Whilst our sample was only small, it is worth pointing out that recruiting the cancer participants from Indian, Bangladeshi and Pakistani backgrounds was especially challenging. Those who had completed their treatment had not always publicly shared their diagnosis, and/or were not keen to revisit such a difficult time. This seemed to be exacerbated within these communities by some sense of discomfort with the cancer diagnosis, and a feeling that this might impact upon perceptions of the family as a whole. In addition – as for the non-BME sample - those who were undergoing treatment often felt they didn’t have sufficient strength of mental clarity to take part in the interview and literature review, due to the side effects of their treatment.

Not surprisingly, issues with language clarity, complexity of sentence structures, document length or unclear document structures were especially problematic for those with weaker English. The PIL and even Consent Form were both felt to be very text heavy and complicated for this audience. The PIB was not explored in its entirety with participants from BME/low literacy backgrounds, although selected paragraphs were explored, and were usually felt to be clearer in their expression.

From the sample we talked to, we would anticipate that those with lower education and lower English skills are likely to rely on others to read, translate and filter these documents:

*Anyone who does not understand English, will take someone who does to explain things (Cancer participant, female, English as a second language)*

This could either be friends/family, or NHS staff. Most of those we talked to were keen for the Project to be initially introduced to them verbally by their clinical team, and the key points and commitments explained in this way.

## 2.4: Background issues: HCPs

Four key issues emerged from speaking to HCPs, reflecting both some general concerns about the nature of the project itself, as well as their overall responses to the draft literature they read.

### A. Data protection/confidentiality

HCPs anticipated that issues around data protection would cause a lot of concern among potential participants. A number of the HCPs we spoke to mentioned Care.data as a recent issue which they felt had raised worries among patients around patient data and confidentiality. HCPs were keen to avoid the 100,000 Genomes Project running into difficulties of this nature, so they felt it was vitally important for the reassurances around security and anonymity to come early in the document and to be highlighted, in order for patients to feel reassured from the outset. In particular, HCPs felt there needed to be absolute clarity around how patient identities will be protected:

*I think we just need to be clear here who might look at information that's anonymised and who might actually see information that actually says who they are. Because that's what people get particularly worried about (Oncology consultant nurse)*

In the end the potential participants that we spoke to were considerably less concerned about confidentiality issues than many of our HCPs had expected. While still an important issue, and one which potential participants wanted clear reassurance on, none of them mentioned Care.data specifically, and there was no hint of that issue colouring perceptions of the treatment of patient data by the NHS/healthcare services.

### B. Information about genomics and genomic medicine

Across the interviews with HCPs there was a strong call for more background information in the literature about genomics and genomic medicine. This was a particular concern for HCPs working in cancer who felt it was very important for the literature to explain why cancer patients are being included in the study, and how genomic medicine should help in treating cancer. They were aware that the mention of genetics in connection with the Project could easily exacerbate the underlying fears of many cancer patients, around their cancer being hereditary, and they wanted to see a clear explanation of the fact that the study is looking at the mutations of the cancer gene, rather than hereditary genes:

*A lot of cancer patients haven't really heard that genes can be part of the issue with cancer ... So I think we're still assuming a level of knowledge that's not there across the board (Oncology consultant nurse)*

The absence of such an explanation in the PIL was a strong concern. The explanation in the introduction to the PIB was felt to be good, but would benefit from a slightly stronger emphasis on the fact that this Project is not aimed to recruit those with hereditary cancers.

### C. Ensuring consentors are fully informed

This point came through from only one HCP but it was one of her key priorities. She felt it will be crucial to ensure that all those taking consent are properly informed about the study in order to be able to talk patients through it. As with some of the points above, she was working in oncology, and she felt that the particular circumstances of participants in the cancer cohort mean this issue is even more important:

Cancer nurses are unlikely to have a good understanding of genomics (vs. the clinical teams that most genetics patients are likely to be in touch with);

Consent is likely to be taken at speed, when patients have a lot of other information to take in, and they will not have the luxury to reflect on their participation, ask questions etc.;

Unlike genetics patients, who may well have heard about the study already, because they are more likely to be in touch with patient groups etc., this may be the first that cancer patients have heard of 100,000 Genomes, and of the fact that there is a genetic basis to cancer:

*They [genetics patients] are much better informed and have much more opportunity to talk to people (Oncology consultant)*

### D. General interest in reducing length/complexity of all consent literature

Finally in this section it is worth pointing out that a number of HCPs we spoke to were very concerned about the dense and technical language of the PIL and Consent Form, and about the length of the PIB. Many felt that patients would struggle to get through any of the literature, and that more work needed to be done to make the information more patient friendly and to ensure that patients are able to give genuinely informed consent for their participation:

*We need to be clear that we're not just putting information in because we think we're covering ourselves somehow, but we're putting information in to empower them enough to make that decision (Oncology consultant nurse)*

A small number of HCPs talked about efforts made in their setting to reduce the length or complexity of patient information, with the aim of ensuring that patients fully engaged with the literature and understood what they were signing up to:

*We've done some work recently on redesigning our consent forms, because we were worried patients weren't really knowing what they were agreeing to. We are now trying to make each point understandable in one sentence (Genetic counsellor)*

## 2.5: Other issues emerging in response to the literature

In this section, we outline a small number of additional findings that have emerged from responses to various pieces of literature explored.

### A. Project name:

The explicit reference to ‘100,000 Genomes’ can confuse potential participants. As the figure is used for the title of the Project, they assume the figure is significant and important, but the literature does not ever fully explain why this number has been chosen. Potential participants do not have a context for the figure, so it is relatively meaningless

*Is 100,000 a lot in this context? I don't know (Cancer participant, male)*

The relevance of the numbers involved could emerge in response to the Project more generally, but was mentioned particularly when looking at the Infographic, which focuses on the figures, and also brings to the fore questions around how the 100,000 figure is reached by highlighting the number of participants involved.

It is also worth mentioning that 100,000 was not an easy number to read for those with low literacy or English as a second language, with a number reading this number as 10,000 or being unsure of its meaning.

### B. Genomic Pioneers

For some, there was little interest in the Project’s activities, and this idea was not relevant. However, for a substantial group, this is a very motivating and engaging idea. In particular, potential participants can respond positively to:

- The idea of being kept ‘in the loop’, so that you can see what research is being conducted, and the sense of openness, even accountability that this suggests;
- A general interest to hear about research that may benefit you, your descendents, or families facing similar health issues:

*A bit of a reward for taking part – I'd personally be interested ... I do Google search my symptoms every now and then (Genetic participant, male,)*

- The sense of taking part in something special, and seeing the impact of a unique Project:

*It's nice to help and to be part of the beginning of something (Genetic participant, female)*

- Having information provided in an accessible format, and the effort that the Project are putting into ensuring that the research is understood and shared widely;

- Some also respond positively to the idea of being pioneers, and the idea of their contribution to future genetic knowledge:

*Genetic pioneer – that’s right up my street! (Genetic participant, female)*

It is however very important that there is no sense that the information generated by the Project is being ‘ring-fenced’ – participants are very keen to ensure that all findings are shared and used widely amongst healthcare, research and patient communities.

Ideally, patients would like to choose whether to access information via the website via or post/email. Alternatives to an online log-in were especially important for the less technically minded (within our sample, this included lower SEG, BME and older participants).

### **C. Literature accessibility issues:**

Within the interviews, there were a number of calls to ensure that the literature is accessible for all:

- CD/audio version for those with low literacy levels
- Brail version for those with visual impairments
- Blue background on Infographic challenging for a few, but reported as likely to present an issue for people with dyslexia

We also talked to two parents whose children would not have been able to give informed assent due to developmental delay, and they questioned the process for such individuals.

Finally, for those with English as a second language, translated versions, with the support of a native language speaker would be ideal.

### **D. Social use of the database:**

One other suggestion emerging from one young people’s group was for the project to help participants – especially those with a rare condition – to make connections with other families for support. Whilst they recognise that this is challenging due to data protection issues, there was some discussion around whether the website could help facilitate connections between families with rare diseases:

*Sometimes you do hear from kids who want to be put in touch with someone with the same condition ... so it could work in a social way (YPAG, Birmingham)*

### 3. Stage One Findings

#### 3.1 Responses to the Patient Information Leaflet (PIL)

This section summarises key themes in response to the original Patient Information Leaflet, explored in Stage One. More detailed wording issues are covered in Appendix 1.

It was clear from the research that potential patients struggled to read and fully understand the PIL. Whilst HCPs were, in some cases, more positive about the PIL than patients (feeling that it was in line with other literature they use), a substantial number of HCPs shared potential participants' concerns that the information was challenging to read and assimilate and may not lead to properly informed consent.

##### A. Responses to language and structure: Potential Participants

The complex language and structure of the PIL posed significant challenges for potential participants, impacting on their ability to engage with, and understand, key issues including the Project's remit, participants' commitments, and the feedback they would receive:

*It was a lot to take in. I can't take in as I used to (Cancer participant, English as a Second language female)*

*I lost that [information about feedback] in the blackness of it all [the document]... (Genetic participant, female)*

*I read it all once before as you said I had to, but I don't remember anything now. Since chemo my memory is very bad. I don't remember anything (Cancer participant, female, English as a Second language)*

Many patients struggled to understand what they were reading or spoke of having to read the same passage, or the entire leaflet, repeatedly and Section 3 below details some of the specific issues that participants found especially challenging.

Participants with English as a second language, or poor literacy skills found the PIL especially challenging, and generally needed the literature to be filtered or translated by a family member, friend or even English teacher.

*I suppose if it was me, I'd have to keep reading it over and over again to get it right ... as it was I got someone to read it to me (Cancer participant with low literacy levels, male)*

The difficulties seemed to be largely due to four core reasons:

1. The **language used** was felt to be dense, technical and complicated. Tonally, patients thought it was dry and legal, and a number felt that it wasn't really written for 'people like them':

*It feels like this was written for someone who reads The Times, not for someone like me who reads The*



*Mirror (Cancer participant, female)*

2. **Sentence structures** were regarded as complicated and therefore difficult to read and assimilate:

*The sentences are very long (Genetic participant, male)*

3. The **structure of the leaflet** itself made it difficult to navigate, as sections did not appear to follow an intuitive order:

*The main thing for me was that I just couldn't work out the structure (Genetic participant, male)*

Patients also felt there was a great deal of repetition (e.g. around security), which created confusion with potential participants being unsure if they were reading the same, or a subtly different point:

*This is just too much information, you've already told me it's secure a number of times, why do they keep repeating that. It's actually making me more concerned (Genetic participant, female)*

*There's a lot of it, and by the time you've got past the one stage, getting to the next stage, then you sort of think 'oh, hang on...' and it starts to go round in circles a bit. And it's quite involved. (Cancer participant with low literacy levels, male)*

4. Finally, the **lack of Project overview** means that potential participants had to build up a picture of the Project's remit and goals, as well as their commitment, from a number of elements scattered across different sections of the PIL. As a result, they were piecing together the project as new elements were revealed or became clear. As well as being a somewhat frustrating process, this also meant they were constantly re-evaluating their previous understanding, requiring a highly active reading process. A clear, concise project overview was suggested by both potential participants and HCPs.

This difficulty in reading and assimilating had a number of implications.

A number reported reading and rereading the document to try and fully understand its contents:

*I can now explain it, but I had to read it three or four times (Cancer participant, female)*

Some participants reported that they had only read the entire document due to their commitment to the audience research process; they therefore questioned whether potential participants – especially those facing a cancer diagnosis – would have the tenacity to read the PIL thoroughly:

*I was losing the will by the bottom of the second page (Genetic participant, female)*

*I struggled [with reading this] ... reading it and then thinking 'Oh, I just can't be bothered with this', going away, reading it again. Oh, it was so heavy (Cancer participant, female)*

*One thing they need to do is perhaps condense it in some way, simplify it... (Cancer participant with low literacy levels, male)*

The language could also make potential participants feel more distanced from the Project; this literature did not ‘talk directly to them’ and as such did not help them feel on-board, engaged or enthused about the Project’s potential. A number of our participants – who were initially enthusiastic about being involved with the Project - found the lack of clarity, and the expression of ideas sufficiently off-putting that they reconsidered their interest:

*So at this stage, I would probably not take part and I would have been well up for it before (Genetic participant, female)*

Finally, the length and apparent complexity of the document can suggest that the commitment and requirement for participants will be equally high:

*One thing that was off-putting – that there is a lot to read, I’m not sure I would want to read the length of that leaflet... I’d feel like it was too much for me, like I’d have to put in lots of time and effort. Will I be re-contacted regularly, and more questions asked? There’s only so much a busy mum can give (Genetic participant, female)*

In addition to issues around the language, potential participants pointed out that the font size and typeface added to the difficulty of reading the document. A slightly larger, and very simple type face, would help the document to feel more accessible.

## **B. Responses to language and structure: HCPs**

Some HCPs felt that the literature was similar to other patient information literature they encounter, and could be more accepting than potential participants.

*It’s the kind of thing we’re used to seeing. It seems quite standard to me (Genetic counsellor)*

However, many HCPs shared potential participants’ concerns that patients would not be able to appreciate the full implications of the Project from reading the PIL due to its complex language and construction:

*It’s written from the perspective that people are really interested in the Project itself – not that they just want to know whether they’ll have extra tests, or what it means for them... this booklet will be overwhelming for people – it should be just a few pages (Oncology biobank technician)*

*I’m used to reading these and I spent several hours going through all the literature so yes, I’m a little bit worried about how it will go down with patients (Oncology consultant nurse)*

They were often aware of initiatives to make patient information within their own institutions substantially more concise and easy to understand, and felt that the PIL was in the model of ‘old-fashioned’ consent literature:

*We’ve made a real effort here to redesign all our consent literature so that it’s more accessible, because we want to make sure patients really are giving informed consent (Genetic counsellor)*

In addition, HCPs could feel that the legal approach and language used suggested that the PIL was aimed more at ‘covering the Project’, rather than truly informing patients. They anticipated that it would be a challenge to talk patients through the project and its implications using the PIL, and expected to need to do a lot of additional explanation to help potential participants fully understand:

*It feels like it's simply saying the things that have to be said ... I couldn't imagine using this one with patients because I couldn't inwardly digest it myself (Genetic counsellor)*

Some of our participants, who had a healthcare background or NHS experience, shared these concerns that the complexity of the PIL would mean it would fail to inform participants sufficiently clearly:

*My heart sank when I saw it. I understand that the information needs to be there, but I know as a practice nurse that patients wouldn't read it – it needs breaking up more (Genetic participant, female)*

Some HCPs were worried that the literature might actively discourage potential participants; they felt that the current rather dry and technical language did not do enough to convey the potential benefits of the Project:

*I think this project is going to be a hard one to sell and I really don't think this does enough to get people excited (Oncology consultant nurse)*

From a practical point of view, one HCP working in cancer, who saw mainly older patients, was keen to stress the importance of having a clear and easy to read leaflet. She felt that, in its current format, older patients might struggle to read it and that, at the very least, a large type version should be available:

*Please make everything in a larger font for my patients who are older, the majority over 65, and they invariably forget their reading glasses on the day (Oncology consultant)*

### **C. Specific issues and concerns: potential participants and HCPs**

In addition to these general concerns around language and structure of the PIL, specific passages and topics were particularly challenging for patients or left them unclear or uninformed:

#### **C.1 Genome/genomic medicine:**

Genome, and genomic medicine were rarely fully understood by potential participants, even those who were more educated around genetics. Whilst some could make a guess, the fact that this basic concept was not immediately comprehensible could mean that the entire document was either unclear, or at best, that potential participants did not feel confident of their understanding:

*I've heard about genes, rather than genomics. I guess they mean genes, but it's not clear (Cancer participant, female)*

*So far, the first thing that I'm thinking – shall I bother to read the rest of it or not – what's a genome? Why is that of interest to me? Do I care? (Cancer participant, male)*

*So is genome another word for sample? ... I was confused with that, because that's obviously what the*

*thing, the Project, is called, so why can't they use plain English? Samples is what they are talking about (Cancer participant with low literacy levels, male)*

*What is genome? Is it client data? It is relating to research? (Cancer participant, English as a second language, female)*

*I don't know what genomic medicine is (Cancer participant, English as a second language, female)*

*The first thing I did was go and Google 'genome', but it would have been nice if that explanation had been given, rather than me having to look for it myself (Genetic participant, female)*

Both patients and HCPs felt that it was vital that a short explanation was provided, early in the literature, of what these terms mean and of the implications for patients and the NHS:

*I wonder if there should be a section saying what genomic medicine is. Do enough people actually know what genomic medicine is? (Cancer participant, female)*

HCPs felt such an explanation was particularly important for the cancer cohort; this is not only because cancer patients are generally likely to be less well-informed about genetics and genetic medicine than rare disease patients, but also because there is a need to reassure potential cancer participants who may be concerned that the mention of genetics means their cancer is hereditary (i.e. the literature needs to make clear that the Project is comparing the genome of the cancer cell vs. normal cells, rather than looking for a specific 'cancer gene'):

*It needs to start off with an explanation of what genomes are and what genomic sequencing is and how this project and this kind of analysis can be useful in treating cancer (Oncology consultant nurse)*

*As soon as you mention genes in the context of cancer then people jump to hereditary and start worrying that their children will develop cancer, so the explanation needs to focus on the fact that you are looking at mutations of the cancer gene her, not hereditary genes, that the tumour is a genetic disease, a genetic abnormality, it's not inherited (Oncology consultant)*

A lack of understanding of genomes, and the potential of genomic medicine underlies some of the confusion evident in later responses; without this knowledge, it can be challenging for potential participants to imagine what the goals of this project might be, or what potential it could have.

## **C.2 Understanding the overall concept and aims of the project**

The PIL frequently failed to communicate a clear overview of the Project. In some cases, this was due to a lack of clarity within explanations of specific issues, but the dense, repetitive nature of the document also had an impact, as participants seemed to forget, or not pick up on, key elements of the Project's remit, and their commitment. This included:

- Not understanding the ongoing database nature of the Project, that access will be given to wider research teams, and who will have access, and how access is controlled:

*I have a question – who has access to the samples? If it's part of this Project, then fine, but I wonder how*

*far it goes. If I'm giving permission of the 100,000 research, then someone else wants a look – at what point do they stop asking permission? .... Just because I give you my DNA to map it for this project, doesn't mean I'm comfortable with you having a look at how you're going to clone me (Genetic participant, female)*

- Not understanding the goals of the Project; in particular failing to appreciate how different this study is to those that have gone before, and therefore lacking a clear sense of what conditions/types of patient this will benefit and why:

*I want to hear more about what they're aiming to do, what diseases they're going to help, what they think they might find out (Genetic participant, female)*

*Well, they've got a team of scientists ... surgeons or whatever they are ... working on projects within this company... that could relate to any kind of research, couldn't it? I mean ... drugs, or cures...? (Cancer participant, male)*

*I suppose the goal is to find links between those extra cancers [list within Additional Findings] – if you're prone to other diseases – it seems quite general (Cancer, female)*

A small number of participants had been onto the 100,000 Genomes website to read more about the project, and had encountered the introductory video, so could focus on issues mentioned within this (e.g. bowel cancer, diabetes):

*I assume they're mainly looking at things like diabetes, because that's what they were talking about on the website (Genetic participant, female)*

It will clearly be vital that all available support materials – on and off line – have a coherent message for potential participants.

- Not understanding the nature of their commitment, including what type/how many samples are needed (e.g. tumour sample plus blood sample for cancer participants; only one sample for genetic participants); that personal health records would also be part of the project, and that both genetic and health records would be combined on the database; that the access to health records/remit of the Project is ongoing/for their lifetime and beyond:

*A lifetime's commitment of samples – they weren't clear about how many (Genetic participant, female)*

*I want to know what will happen to me, do they really want tissue from me, where I've got to go to? (Genetic participant, female)*

- Not understanding that the project is government run/linked to the NHS:

*I'm not sure who is running the project? NHS or someone else? The language needs to be clearer (Cancer participant, English as a second language, female)*

*I'm not sure who Genomics are. I read it 3 times before seeing it's an NHS company. (Cancer participant, English as a second language, female)*

*Who are Genomics England then? I've assumed they're a new research company coming in (Cancer participant, male)*

### **C.3 Feedback**

There was a high degree of confusion around what feedback would be available to participants, and few, if any, potential participants showed clear understanding of the different levels of feedback in operation.

The distinction between the different types of feedback (Pertinent, Additional, Incidental), and whether each was optional or a core element of the Project, was extremely unclear. Whilst most could grasp that there would be some feedback available on their specific condition/diagnosis, many struggled to understand what might be included within Additional and Incidental findings, and what each would comprise:

*So, actual findings are what they've found about your condition ... the additional findings are other things like if they were looking at the common cold or whatever (Genetics participant, mother of proband child)*

The similarity in the words themselves does seem to contribute to this, especially for those with lower literacy/English as a second language, but there is also a lack of clear explanation of each:

*[Additional Findings] I'm not clear - a bit confused as to what they are saying here (Genetics participant, English as a second language, female)*

*I don't understand 'additional' [findings]? It would be better to have an alternative description. Feels like they are trying to find something which is not there (Cancer participant, English as a second language, female)*

*So I think they're telling me that if I have something else, like diabetes, they would pass that on. I would expect to be told anything they find out (Cancer participant, male)*

Many participants reading the list of **Additional Findings** assumed that the list of 'Looked for' conditions was the focus of the Project, rather than a list of feedback areas:

*I saw that list of conditions and I said to my daughter, well, they might not choose you, because you're not on here. These are the kinds of things they are looking to do research on (Genetic participant, mother of proband child)*

*I've assumed this table is the conditions they're looking at – it looks so official and your eye is drawn to it. So I'm wondering now whether the study would include me as I don't have one of those, unless one of them is our gene (Genetic participant, female)*

Others were unsure why the list is being included, but assume that it is an important element of the research remit:

*So what are we talking about? This could be something else that I could have, or this is what you're looking for, or this is generally what anyone could have? I don't understand why that was popped in*

*there (Cancer participant, female)*

As nearly all conditions on the list of Additional Findings were relatively meaningless to potential participants, they struggled to understand why this list was present, or to gauge the value of being tested for such conditions:

*I don't know what these are [list of conditions]. Just that they are cancer. I can't even pronounce most of them (Cancer participant, with English as a second language, female)*

*These are meaningless. Poly-whatever-it-is ... I didn't read that. I didn't know what it meant so it sort of went in one ear and out the other (Cancer participant, male)*

*This list left me cold, I can't pronounce them. I really didn't think I was that weird, but if I'm included on a list like that then I must be (Genetic participant, female)*

However, the list was felt to detail worrying, and serious diseases, and (when noticed) the mention of child onset can be especially worrying for parents:

*We might find all these nasty things that are wrong with you, or with your children. Bit scary (genetic participant, male)*

As such, many felt they would need to understand the list, either by Googling or by talking to an HCP:

*I'd just have to Google that list – otherwise it doesn't really mean anything (Genetic participant, male)*

Those with a more recent diagnosis within our sample seemed to find the idea of this list especially uncomfortable – as they had recently experienced being given unexpected bad news:

*That is just too much information, you don't want to scare people because you can look things up on the internet and really scare yourself. When I was diagnosed with bone cancer I went and googled it and I just got scared by everything I was reading (Cancer participant, female)*

We would therefore hypothesise that participants who had recently been diagnosed with cancer might find this list especially challenging.

For all respondents, the inclusion of specific genes was meaningless, with the exception of BRCA, which was familiar to some. Those who were aware of BRCA could see the opportunity to be tested for this as a real benefit:

*I had friends who wanted to be tested for BRCA and couldn't get it, so there will be some people who would really benefit from that. (Cancer participant, female)*

*They've not let me have the test despite my mother having breast cancer and so I'd really welcome the opportunity to have the test (Cancer participant, female)*

In line with participant concerns, some HCPs were also very concerned that the ‘Looked for’ conditions list would require them to provide time-consuming explanation and reassurance for participants:

*This is a catastrophe. I don't want to be held up explaining things which are unlikely to happen ... Please don't name them! (Genetic consultant)*

*I would really prefer this table not to be in there, it's gobbledygook, patients won't understand it, what's the point (Oncology consultant nurse)*

A significant minority of HCPs strongly suggested excluding the list of conditions– and detailed information on genes – in order to make it easier for participants to assimilate, and lessen their stress levels around diseases that they were highly unlikely to be carrying:

*I would certainly stop at telling them the genes – the vast majority really won't care (Oncology consultant)*

Understanding of ‘**Incidental Findings**’ was even lower than understanding of Additional findings amongst potential participants. As this is only mentioned in a short paragraph, coming after the complicated list of Additional Findings, many seemed to ‘skip’ this, or assume it to be a continuation of Additional Findings.

For potential participants studying this section, there was a lack of clarity around what Incidental Findings might include. Whilst the example of non-medical findings is usually well understood, and appreciated, the mention of ‘increased risk of common diseases’ is not clear and raises questions – not least around what might constitute ‘common diseases’. As outlined in Section 2.1, B4 some potential participants felt strongly that any increased risks should be fed back to the patient, and therefore believed that if this was not the case, this information should be given much greater prominence:

*I'd expect them to tell me everything. If they find anything, it should be passed on (Cancer participant, male)*

In general, there was often some discomfort with the idea that scientists/HCPs could be aware that you were at greater risk (and could potentially take preventative action) but would not be informing you:

*I don't like the idea that someone else might know, and you wouldn't (Genetic participant, male,)  
Genomics England won't contact me directly. But I'd like to know any result they have - even if there is nothing new (Cancer participant, English as a second language, female)*

In addition to these levels of more general confusion around feedback, the phrase ‘Your clinical team will not routinely tell you the results of any research undertaken using your samples...’ was



frequently misunderstood, with many patients thinking it was suggesting there would be no feedback at all, even around their condition, in contradiction to earlier points.

Finally, some of our BME participants were especially keen to be provided with a full report – and especially concerned by any suggestions that this might not be possible – as they were being treated both in the UK and overseas:

*We should get an update as soon as they have the result (Genetic Participant, English as a second language female)*

*I will want to know positive, negative or inconclusive (Cancer participant, English as a second language, male)*

#### **C4: Involvement of family members:**

The PIL was not felt to give a clear explanation of the commitment required from family members of patients with genetic conditions, or of the reasons for their involvement. Proband participants reading the PIL could be completely unaware of the need for family involvement, and felt this information would be vital in making decisions around participation:

*So, hold on, does a family member have to be included. Could this be my husband? I'm not sure who else I would ask. I can't imagine my brother doing something like this (Genetic participant, female)*

Both proband participants, and family members, felt that the information contained within the PIL was not sufficient, or tailored enough, to be of use to most family members. They were keen to be provided with more detail on which family members were most appropriate, and how many family members were required to participate; what family members would need to agree to; and what feedback family members would receive, and how this would be delivered (given that family members might be geographically distant and/or would not have a clinical/hospital team:

*I don't have a clinical team, so how would they feed anything back to me, would it be through my GP? (Mother of Genetic participant)*

#### **C.5: Insurance**

The PIL unambiguously states that samples and data will not be used for insurance, marketing or any other purpose unrelated to healthcare. This clear statement is welcomed (although it does appear a little late in the document), but can be undermined by later statements around insurance.

The implications for insurance of taking part in such a project were a key concern for some, especially amongst higher SEG groups. However, it is worth noting that those from lower SEG groups/less privileged backgrounds often failed to appreciate why insurance was relevant to this issue:

*I don't see why insurance would come into it – unless someone is looking to sue? (Cancer, male, with low*

*literacy levels)*

The wording around existing agreements with Association of British Insurers in the PIL suggested to many potential participants that insurers could access information after 2017, and that Genomics England has not yet resolved the issue beyond the short term. (*“The Association of British Insurers have agreed not to use genetic data to assess personal insurance until the end of 2017”*)

As the Project is understood to be a lifetime and beyond commitment for participants, this could be a source of frustration and concern for patients:

*So what happens after 2017 – have they just not thought about it? Surely that can’t be the case? (Cancer participant, male)*

Some genetics patients were more informed about this issue, and were aware that the current agreement runs out in 2017 and that it may not be renewed. They wanted to see this more clearly explained:

*There’s no guarantee that the insurers will stick to this. It’s just an agreement, it could all change (Genetic participant, female)*

There were also concerns that the PIL did not explain clearly enough that preventative treatment, which might occur due to results from testing for the Additional Findings, would have to be declared to insurers. A minority of potential participants realised that this could hold implications, not just for patients, but also for participating family members. They felt this needs to be mentioned as a consideration when thinking about whether to receive Additional Findings.

*They’ve got to make a link here with the eight conditions, if that’s going to be an issue and affect the insurance (Genetic participant, female)*

#### **C.6: Continuity between PIL and Consent Form**

It was very challenging for participants to cross-reference between the PIL and Consent Form, given that issues were not covered in a consistent order, in clear consistent sectioning, or even, in some cases, with the same terminology across the two documents (e.g. terminology used for feedback). In real terms, this tended to cause issues when potential participants encountered issues they were unsure about in the Consent Form, and looked to confirm their understanding in the PIL. Participants felt it would be very challenging to find the relevant section within the PIL, which therefore decreased confidence.

Creating more cohesion, and ideally active option to cross-reference between the two documents would allow potential participants to feel more confident, when completing the Consent Form, that further information was readily available.

#### **C.7: Mention of NHS involvement**

Across all participant types, but especially for those from a BME background, mention of NHS involvement, and the benefit that the project would generate for the NHS, was felt to be highly involving. Many saw this as a way to ‘pay back’ the NHS for the excellent treatment they had received, or to improve treatment if they felt their experiences had not been optimal. Mention of the NHS also helps reassure participants that the goals and aims of the Project are entirely legitimate:

*Genomic medicine will be a big help. There are no such projects right now. If it helps NHS - good. New discoveries and new products – the NHS will get a boost to help people out. Sometimes NHS is worse than 3rd world country (Genetic participant, English as a second language, female)*

*This data will help NHS directly and indirectly with genetic data. This is what NHS needs (Genetic participant, English as a second language, female)*

In comparison, mention of Department of Health – associated more with government and party politics – was less effective.

Whilst most noticed reference to the NHS within the PIL, further focus on the involvement of, and benefit to, the NHS, would be helpful in reassuring potential participants:

*Not sure who Genomics are. I read it three times before seeing it's an NHS company. Not clear (Cancer participant, English as a second language, female)*

*I think that would make more sense to people, if they thought it was being reinvested in the NHS, that's a plus (Oncology consultant nurse)*

### **C.8: Commercial Companies**

As explored in Section 2.1, B3, the issue of commercial involvement can be a concern for potential participants, especially in the context of the PIL. The lack of reassurance around the company types, and their goals/remit can leave participants feeling under-confident, and the focus given to the UK economy and supporting companies (‘in ‘What is the 100,000 Genomes Project, and what will it do?’) can also feel inappropriate.

The PIL also failed to clearly reassure participant that all data viewed by external researchers would be anonymised; it could be difficult for participants to appreciate how data could simultaneously be anonymous, and for feedback to be provided to their clinical care teams.

### **C.9: Language specific issues:**

In addition, there were a number of more minor wording issues, and expressions that either confused potential participants, or left them feeling under-confident. e.g. mention of ‘(Suspected) cancer’ could lead some to assume those with a definite diagnosis are not included; phrases such as ‘Clinical team’ and ‘social care records’ were not always immediately understood;. Fully detailed feedback is provided in Appendix 1, which captures the detail of all responses.

## D. Specific issues and concerns: HCPs only

In addition, to the issues above, which were highlighted by both HCPs and potential participants, certain areas were pulled out as concerns only by HCPs/potential participants with a HCP background:

### D1: Data protection

As explored in Section 2.2 B, HCPs expected this to be a significant concern for patients, especially in the light of the Care.data programme. They wanted to see this information clearly pulled together towards the beginning of the leaflet for reassurance, as currently the various points relating to security and confidentiality felt scattered throughout the leaflet/have relatively little prominence:

*I think the project's going to be a really hard sell, given my experience of Care Data ... A lot of this information [about security] comes too late. I think it needs to be said right at the beginning, so that patients are reassured from the start (Oncology consultant nurse)*

In comparison, whilst some potential participants were keen to be reassured about security, and felt that this issue was not currently well structured within the PIL, it was less of a major concern. Many participants felt they would be happy with well organised, but relatively low-key reassurance.

### D2: Feedback timings and mechanisms

Some of the statements in the Stage One PIL especially around the timescales for feedback and the potential for future analysis in the light of further findings prompted concerns from HCPs, especially those working in rare genetic diseases.

HCPs were worried that the PIL appeared to be making unrealistic commitments to patients around the turnaround ('within a couple of weeks') and regularity ('these results may periodically be updated and returned') of feedback (although they acknowledged that the PIL also included contradictory statements in these areas). Those in consultant positions were aware that they simply are not able to offer appointments within a short timescale. They felt that over-promising would lead to disappointment and frustration amongst potential participants, who would not be able to schedule appointments within the promised time:

*This raises lots of concerns. Even if Genomics England can do this, I could not offer an appointment in anything like two weeks. I really don't want people to be phoning up every two weeks asking for their results (Genetic consultant)*

The PIL also appears to make a commitment to provide regular, updated feedback to patients ('Depending on research findings these results may be periodically updated and returned to you...'). Genetic counsellors were surprised by this, reporting that this is an ideal which they have never actually managed to deliver to patients, due to the way their systems are set up, and the complexities involved in achieving this:

*It's a big promise, a bit responsibility and we've never been able to do it (Genetic counsellor)*

In addition, there was some concern around exactly how the results might be updated, especially the phrase ‘if there is new knowledge about how to interpret your results, we will re-analyse your data, perhaps on an annual basis’, as HCPs working in genetics explained that proactively going back to genetic samples in the light of new discoveries is logistically very difficult, and would be extremely time-consuming:

*Reviewing and getting information to a patient is a big deal, we need to know how that will happen, what the process is for Genomics England to keep in touch with healthcare professionals, we’re worried about what this is promising (Genetic counsellor)*

Genetic counsellors questioned who would be feeding back results from the Project, as they were aware that a lot of clinicians with patients participating in the study may actually know very little about genetic medicine. They felt it was vital that it is genetic counsellors who handle this feedback and expressed concern that patients who are not under the care of a geneticist may not get proper feedback/a thorough explanation of the results:

*What if they’re under the care of an ophthalmologist, for example, who may have no idea what the results mean. The feedback really needs to come from a genetic counsellor, but there is a limit to how many people we can see (Genetic counsellor)*

At the same time, they pointed out that it was simply unfeasible for every patient to receive their feedback via genetic counsellors, given their limited numbers across the health service:

*One thing we’ve always been slightly uncertain about is actually how this is going to happen. We’ve gathered that certainly we can’t handle all these people coming to the genetics clinic ... but I’m not convinced other clinicians could enlighten the patients much (Genetic counsellor)*

In general, participants seemed to be relatively relaxed about time frames for feedback, once they understood that it might not impact upon their personal treatment plan.

### **D3: Tone**

Many HCPs were very keen to ensure that the tone of the literature is non-coercive, and does not ‘promote’ the Project. Whilst the language in the PIL was generally felt to be less promotional than some other literature encountered, HCPs were concerned to ensure that all language used is neutral (e.g. use of ‘groundbreaking’ to describe the Project was questioned).

### **D4: Family commitment**

As explored in Section 2.2B, the issue of how HCPs should deal with family members was raised by a number of HCPs (with regards to both the PIL and PIB). Whilst not seen as a core issue for the information literature, they were keen for Genomics England to consider the implications for feedback to family members, whom they as HCPs might have very little contact with. Oncology specialists also raised the issue of responsibility to feedback to family following their patient’s death.

*What happens if the patient is dead, after the gene is found? ...Do I need to make contact with the wife and family, who I may not know well? What if his wife is estranged? Who takes the responsibility there?  
(Oncology consultant)*

They wanted to ensure that the responsibility for these long term implications was fully thought through by Genomics England.

## 3.2 Responses to the Patient Information Booklet (PIB)

This section summarises key themes in response to the original Patient Information Booklet, explored in Stage One. More detailed wording issues are covered in Appendix 2.

At the first stage, the PIB was explored as an alternative key information source to the PIL, and was explored in detail in 8 interviews, who all looked at the document in advance of the discussion. Paragraphs were also looked at in comparison to the PIL within the PIL interviews (to explore differences in tone and expression). All HCP interviews were also pre-tasked to read the PIB as well as the PIL.

### A. Overview of Findings

Participants found the PIB substantially easier to navigate and assimilate in comparison to the PIL, and the cancer version seemed to communicate particularly effectively. Potential participants who read the PIB as their first introduction to the Project gained a broader grasp of key elements of the Project, and were more confident about their understanding. Those reading sections as an alternative to the PIL wording nearly always found them clearer and easier to assimilate (including those with English as a second language). In particular, the PIB did a better job of clarifying:

- The involvement and role of commercial/pharmaceutical companies, and the benefits of their involvement:

*The National Health Service and the government are funding it, and they're going to let other people in – like drug companies, but they [i.e. NHS/Government] keep hold of it (Cancer participant, female)*

- The potential benefits to participants, and to other patients, now and in the future:

*To be able to understand why an individual develops a type of cancer, and be able to use medicine more specifically to that person – more individualised (Cancer participant, female)*

*Testing all your genes – to find out how you'll react to different treatments, and which are the best for you ... personalised (Cancer participant, female)*

*The point is to make it better for people in the future – to understand who's got these genes – to help my daughter and lots of other people (Cancer participant, female)*

- The need for both genetic information and healthcare information:

*They want your DNA – from tissue left over, and blood I think ... and your hospital or doctor's records*

*(Cancer participant, female)*

- That this is a Project with potential to make a real difference:

*We're the guinea pigs – we need this knowledge to go forwards (Cancer participant, female)*

- The 'database' role was also clearer, although not explicit/missed by some.

In comparison to the PIL, the language was generally felt to be clearer and more straightforward and accessible:

*It's clearer, more explicit (Genetic participant, male)*

*It's got detail, but at the same time it's simple, it makes you want to read (Genetic participant, mother of proband child)*

Both participants and HCPs thought that the tone was warm, engaging, even appreciative (rather than legalese): they felt that the PIB was talking directly to potential participants:

*It's reassuring – there's a warm, fuzzy feeling (Genetic participant, male)*

*Overall, it's friendly, professional – good (Genetic participant, male)*

*It sounds less corporate, it's more friendly ... It's as though someone really wants to try to explain it and make sure you understand it, they're not just telling you things because they have to (Genetic counsellor)*

The structure was substantially easier to navigate, due to clear sections, Q&A format, even the use of coloured text for questions.

As such, participants came away with a clearer understanding of the Project and their commitments and, in comparison to the current PIL, tended to feel more positive about the Project and their involvement.

However, the length of the document raised strong concerns among both HCPs and potential participants, especially if this document is positioned as the main information source for informed consent. More detail on this issue is outlined below (section B.1)

## **B. Specific issues and concerns: potential participants and HCPs**

Whilst the language is much clearer, and understanding is greater, outlined below are areas where the document was not felt to be working optimally.

### **B.1: Document Length and Structure**

The document length was a substantial issue for both HCPs and potential participants. Whilst the document was explored in full only within one depth with a participant with low literacy/English as a second language, feedback from HCPs suggests that the length would be a particular issue for

potential participants with low literacy skills, despite the language itself being substantially clearer and easier to assimilate.

The document length impacted on responses in a number of ways:

- Important details could get lost due to the amount of information being taken in; in some instances it was not clear to participants which elements were key/a priority. Overall understanding of the Project seemed substantially higher amongst potential participants who read the PIB, but even so, the core project remit was not always totally clear and potential participants could miss one or more vital elements including: the database role, and who has access to the data; the inclusion of both genomic and health record data; family involvement for genetic participants; or the ongoing commitment contained within consent.

*It hadn't been totally clear that this (access to records) was in perpetuity (Cancer participant, female)  
I'd completely missed that there needed to be family members taking part. Until you pointed that out to me, I hadn't taken that in at all (Genetic participant, female)*

*It was very wordy ... I just found there were so many words on each page, I wanted it better laid out, more bullet points (Genetic participant, female)*

- In practical terms, the length made the document somewhat off-putting to read. HCPs were especially concerned that potential participants would disengage and often felt the level of detail contained within the PIB is not required for informed consent. They also felt that its length would hinder its use as an aid to briefing potential participants on the Project. A number of HCPs spontaneously suggested that this document might be more effective in a secondary role, providing supplementary information, for patients to read either prior to, or after, agreeing to participate in the Project.

*That booklet would be overwhelming – it should be a few pages only (Biobank technician)*

*I'd use the shorter document to go through with the patient in the clinic, but I'd anticipate giving the longer document to patients in advance, or perhaps even while they're waiting, to read in their own time. Then that means they can come to clinic with any questions they've got, and having thought about it in advance (Genetic counsellor)*

*I'd use the shorter one to go through with patients together, and then refer families to the bigger booklet to look at in their own time (Genetic consultant)*

- There was a danger that the length of the document could suggest a complex, lengthy commitment which might put participants off engagement with the Project (although HCPs felt that in patient activity terms, Genomics England are asking for a relatively low level commitment of participants, in comparison to other trials/research projects).
- Some HCPs also felt that the length was suggestive of Genomics England covering itself, rather than patient-centric simplicity:



*Information sheets for trials have ended up being so long that people don't read them. I really feel they shouldn't just be there to cover ourselves but to empower patients (Oncology consultant nurse)*

- Tonally, a long document can also feel inappropriate, especially for cancer participants thinking back to the time of their diagnosis, when they were engaging with large amounts of vital information about their treatment and diagnosis. Many talked about not being able to deal with large quantities of information at that time:

*It would be too much at the early stage, when you're coming to terms with things (Cancer participant, female)*

*For 6 months I just spent a lot of time lying on the settee. There were things I had to do like speak to my insurance company and that was a huge effort. I wouldn't have had the energy to read something like this which was just optional (Cancer participant, female)*

In order to overcome these concerns around length, potential participants (who did not see both the PIL and PIB) suggested that a stripped out version of the PIB might work well, with two (even three) clear sections: a clear summary of the Project and their commitments; further detail for those who want to know more; and possibly a final FAQ section.

The table format at the beginning of the PIB was often disliked and did not appear to be performing this 'summary' role effectively. Whilst the Infographic was strongly appreciated for its explanation of the overall Project aims, it was felt to lack specific details about what would be expected of individual participants/the commitment required, and is featured too late in the overall document (more detail on the Infographic is available in section 3.4):

*I wonder if the pages at the beginning could be tightened up to make them shorter and snappier, more to the point. If they gave a really clear overview of what the project is and what it involves for you and then the rest of the document could have all that detail that you would only read if you wanted more explanation (Genetic participant, female)*

*What's missing is an overall idea of the process and how it affects you (Genetic participant, female)*

Those who felt there might be a role for a third FAQ section at the end expected this to cover specific elements, which might only be of interest/relevant to a minority (e.g. police access, whether companies could look at information not in their application, who will make money from this).

*I'm not interested in this [whether police can access the database] but I can see it might be important for some people, so it should probably be in there somewhere, just for reference (Genetic participant, female)*

More detail on how participants envisaged this staged document can be found in Section 3.10, A2)

In addition to the length, there was also a belief that the PIB was somewhat repetitive on some issues, although it was felt to be much clearer than the PIL in terms of its structure and organisation.

## B.2: Content coverage: level of detail

For some potential participants, especially those who were more engaged with and interested in the Project itself (often participants with genetic conditions), the highly detailed approach of the PIB was felt to be a strength. It demonstrated that all issues have been thought-through, and suggested an (unusually) transparent and open approach:

*It's the right amount of information – not too long (Cancer participant, female)*

*It's good to have the detail – it's more explicit – I prefer to understand why (Genetic participant, male)*

*There's more space, so it sounds clearer – because of the examples, because it's friendlier. Some of the clarity is lost in the 5 page one, because they're trying to cram so much in (Genetic participant, male)*

However, for many, the information level was somewhat overwhelming, making it difficult to split out vital from 'nice to know' elements of information. The level of detail could also get in the way of participant engagement, as the amount of text meant the Project's core goals were not sufficiently strongly pulled out:

*You are over-reassured, there's information there that you don't need to give (Cancer participant, female)*

*The questions [i.e. format] were clear; it's just hard to take everything in (Cancer participant, female)*

Those who liked the level of detail suggested structuring the information more clearly and making greater use of bullet-points and smaller paragraphs to help in communicating the essential points. This was particularly suggested for Sections 1 and 2 where some key elements could be overlooked.

There were also frequent suggestions for a Contents Page to aid navigation. The introductory section in the genetics version (signposting different sections for different audiences), which could have played this role, was not working to aid navigation or to signpost patients towards key sections, as the text was felt to be dense/heavy, and patients felt they were getting bogged down in detail before they had engaged with the main body of the document.

HCPs were particularly uncomfortable with the level of detail included within the PIB. They felt that much of the information was not necessary in order to generate informed consent, and that most participants would probably prefer lower levels of information:

*It's too much information – no-one would care (Biobank technician)*

HCPs often also felt strongly that the level of information contained in the PIB might impact negatively if used as the key piece of information literature. They believed that the PIB raised issues that would not otherwise be considered by potential participants, and would therefore create problems and concerns:

*It's almost convincing patients not to take part ... the risks and disadvantages ... the possibility that your*

*confidentiality could be breached in the future – that’s a bit ridiculous .... It answers questions that no one would ask, and answers them beyond what people need (Biobank technician)*

*The booklet mentions that samples may go to the US – I think that may raise concerns ... it sets up questions around ownership ... Some things are better left unsaid (Genetic Consultant)*

*I never even thought that a law enforcement authority might ask me for data ... so if it’s not a genuine issue, let’s not scaremonger (Oncology consultant nurse)*

There was certainly evidence that the mention of some issues in the PIB can prompt concerns among patients that might otherwise not have arisen – for example around insurance, commercial use or use after death. However, the concerns generated by the PIB were not noticeably different, or more strongly expressed, than those generated by the vaguer wording of the PIL.

### **B.3: Feedback**

Feedback is a complex issue, and one that certainly seemed to be better understood by potential participants who read the PIB rather than the PIL. Whilst the language used is not yet totally transparent, or consistent across PIB/Consent Form, the PIB language and explanations are substantially clearer than the PIL:

In particular, the following issues seemed substantially clearer:

- The rationale for the list of conditions included within Additional Findings. The PIB provided a clearer explanation of why these particular conditions/genes would be looked for (that they are serious, treatable and rare). However, even amongst participants who read the PIB, confusion was still evident, and, as with the PIL, the list of ‘additional, looked for findings’ could be a focus point, with some assuming these were the conditions being researched:

*This says to me they’re focusing on cancer and cholesterol and these are things which already have a lot of attention (Genetic participant, female)*

- Titles used are more immediately understandable (‘Additional Looked for findings’), and give more detail on the different feedback types;
- That findings will be returned in time to benefit some but not all participants;
- What actions might be taken based on the findings;

However, participants can remain either unclear, or unconfident of their understanding of:

- The different types of feedback – especially the distinction between Additional and Incidental findings;
- Which are optional, and which are not;

- The implications of opting in/out of various levels of feedback;
- The practicalities of how feedback is going to occur (for example, who will pass information back; in what format);
- Although not mentioned by many, frequency of ongoing feedback was also not clear, and HCPs felt it was inconsistent with promises made in the PIL.

#### **B.4: Genomics/Genomic medicine**

As already identified in the PIL feedback (Section 3.1, C1), neither of these terms are well known or understood and even more educated/informed participants could be unconfident:

*What's a genome? I had to stop there and look it up on the internet (Cancer participant, female)*

*I didn't know what this genome is – I Googled it – it needs to be on page 1 (Cancer participant, female)*

All audiences (including those with English as a second language, or with low literacy) were substantially more used to talking about DNA, genes/genetics.

As such, the term 'genomics' needs to be explained when first used, to help participants understand the basic remit of the Project. The 'What is a Genome' Infographic (explored only at low level) was often too detailed: a clear description in one sentence would be preferred (cf. sentence in Infographic 'Your genome is one whole set of your genes, plus all the DNA between your genes').

Genomic medicine also requires an explanation, so that participants can imagine what this could mean; some HCPs, and potential participants with expert knowledge suggested 'personalised/targeted medicine' as a way of communicating the idea, and breast cancer patients who may have come across this approach in their treatment also seemed comfortable with thinking about it in this way.

#### **B.5: Information for family members**

NB Very small number of non-proband participants involved in research

It was felt to be vital that the role of family involvement (for genetic participants) is made very clear up-front. Whilst the expression of the involvement of family was clearer in the PIB than the PIL, it was felt to come too late within the document. The introduction, which outlines the sections that different family members should read, did not actually appear to aid clarification of involvement per se. As such, the first time many participants appreciated the involvement of family members was via the Information is Beautiful Infographic.

Participants, and family members, believed that this important issue needs greater coverage, and were keen for clear explanation of the following issues:

- What commitment is required from family members and why (access to health records of family members was not clearly set out);
- Who can participate as a family member, especially as Infographic mentions parents only, which can be inappropriate for adults (e.g. parents, siblings, adult children);
- The feedback that will be available to family members, both in terms of what feedback should be expected, but also in terms of the logistics: if family members are not existing patients, how their feedback will be passed on was not communicated (via the proband participant's medical team, or via their own GP?). Whilst not explored in detail, a number of our proband participants also suggested that family members might feel more ambivalent about receiving feedback, as they had less to 'gain' in terms of understanding and treatment, and might be more fearful of hearing bad news if they were currently healthy.

It is worth noting that the pairs who participated in the interviews were all mother/daughter, and that there were some indications, both in these and interviews with young people, that siblings may be less willing to engage.

#### **B6: Versioning and balance of communication: cancer vs. genetic disease**

In general, versioning of the literature seemed to work well. It allowed for more relevant examples to be included for each potential participant type, for example in terms of how genomic information would benefit each disease area. However, the cancer version was felt to be slightly stronger than the genetic version:

- Expression of benefits around cancer version were clearer (p4);
- Greater use of cancer examples (e.g. in examples on p18);
- Majority of Additional 'looked for' findings are cancer.

As explored in Section 2.1, B genetic participants could be very aware of the amount of funding put into cancer research, in comparison to what they see as lower funding and research levels amongst rare diseases. As such, they can be especially sensitive to any perceived bias in focus, and ensuring a clearly even-handed approach is important.

*It gave me the impression that they were mainly looking for rare cancers ... The leaflet left me feeling disappointed, maybe they won't include us, maybe they're missing out whole groups of people (Genetic participant, female)*

In particular, the introductory explanation of how genome sequencing might help rare diseases was not felt to give enough detail, in terms of the impact the Project could have on understanding genetic conditions and on pushing forward the development of therapies:

*The other thing they haven't said, is that as I understand it, this is the first project of its type – it's groundbreaking – that doesn't come across. If you're doing something for the greater good, the fact that it's ground breaking is good to know (Genetic participant, male)*

A minority also wanted to see specific conditions or types of condition mentioned here in order to feel that this might make a difference to them and others like them.

### **B.7: Commercial Companies**

The issue of access to the 100,000 Genomes database by commercial companies seemed substantially less problematic for those encountering the idea within the PIB compared to the PIL. The explanation given under the title 'Why are you letting commercial companies access the data' was often praised for its clear and honest tone. It prompted many patients to reconsider their initial (negative) responses to this issue, and, in combination with the examples on the following page of the PIB, was generally felt to positively demonstrate how the involvement of commercial companies will create better outcomes for patients:

*I was wondering why they needed to be involved, but reading that makes me think I've got to be realistic. How else are drugs going to be developed? I'd rather companies weren't doing this kind of work, but it is the world we live in (Genetic participant, female)*

Even within this more positive context, different attitudes emerged to the phrases 'commercial companies' and 'pharmaceutical companies' (as explored in Section 2.1, B3 for more detail).

The term 'commercial companies' suggested a focus on moneymaking and profit (possibly over ethics). It feels quite vague and could create unease over the types of organisations that might be involved.

Most potential participants struggled to understand what other kind of commercial (non pharmaceutical) companies might be involved in medical research of this type and why. Although the examples certainly helped to illustrate the wide range of companies that might use the data, some of the terms/examples remained rather technical or unclear, so the benefit to patients was not always well communicated (e.g. 'an annotation company', 'a small devices company'):

*Commercial companies – there's a bit of a mistrust – maybe unfounded ...but giving examples of what they do is reassuring (Genetic participant, male)*

The examples also come a little late in the document and would benefit from being moved earlier so that patients are more positively inclined towards the Project's role and purposes from an earlier stage.

In contrast, potential participants have a general understanding/knowledge of who pharmaceutical companies are, what they do, how they would be relevant to this kind of project and how that would benefit patients.

Whilst cynicism was evident around the motivations and business practices of pharmaceutical companies (who can be associated with high profit levels, and exploitation of the NHS in terms of charging structures), this audience had a pragmatic acceptance that the involvement of such companies is the only way to bring new treatments to market:

*You've got to – who else would have the money to develop new medicines? (Cancer participant, female)*

That said, the explicit mention within the PIL that the drugs developed by commercial companies might not be available to NHS patients, could raise people's hackles once more. Ensuring that the section around commercial involvement does not end on this point would be worthwhile.

A few HCPs also expressed the opinion that these types of patients are likely to be less concerned about pharmaceutical organisations than a broader audience might be because given the higher value they would give to the development of treatments, and even higher awareness of the processes around drug development.

### **B.8: Security and anonymity**

In general, this issue was covered well within the PIB, and potential participants understood the anonymous nature of the database – with the reference to barcoding working especially powerfully to explain how samples could simultaneously be anonymous, and tracked back for feedback purposes – and also feeling reassured by the security measures in place:

*The confidentiality was clear - that you can't be identified by the samples, it can't be linked back (Cancer participant, female)*

However, structurally the points were scattered throughout the document, which both felt repetitive, and could slightly unsettle potential participants, as they were unsure if points were direct duplication, or intended to cover subtly different aspects.

### **B.9: Samples**

Further detail on the nature of the samples themselves, and also the process of sample collection were requested by some potential participants. This was especially in terms of practicalities, which could have a substantial impact on potential participants' likelihood to engage with the Project.

In particular, the following issues were raised:

- Ensuring that information around 'tissue' samples is clear – particularly in terms of who has to give tissue samples (just cancer patients?), where the tissue is collected from, and whether an additional operation is required. HCPs could feel that this was likely to be an especially key issue for potential participants;

- Where possible, outlining whether samples could be collected within routine appointments, or whether a separate appointment would be required;
- Even, whether samples can be taken at local hospital, or via a GP, or whether they need to be taken at a specialist centre (e.g. for genetic participants who may visit specialist facilities for their treatment on an occasional basis only).

#### **B.10: Insurance**

This issue was substantially more reassuring within the PIB, as opposed to the PIL, and the concern that the issue of insurance companies would create problems from 2017 onwards was not raised.

However, HCPs, and those with more expert knowledge could still feel that the fact that preventative treatment might impact on insurance was not clear, and that as such, potential participants would not fully understand the implications of this choice. They therefore wanted to see greater clarity, and these implications made explicit when potential participants are deciding about opting into additional findings:

NB As mentioned in section 3.1, C5, not all potential participants seemed to understand the implications of insurance in this context. Certainly some in lower socio-economic groups felt that insurance was not relevant to them, and these groups may not be clear on the wider implications of these decisions across different financial products.

#### **B.11: Language: HCPs only**

While the warmer tone and more accessible language of the PIB were generally very much welcomed by potential participants, some HCPs, and some patients with a healthcare background, expressed unease about elements of the tone/language. At times the document was felt to adopt a persuasive tone, and to come close to being coercive. Particular concerns were raised by parts of the introductory section 'About the 100,000 Genomes Project' which were felt to slip into a promotional approach (e.g. 'this is a world first'). Throughout, though, some HCPs felt that the language could be too casual and inappropriate for a document intended to inform the consent process.

*'Your oncologist thinks that your involvement will benefit people who have the same cancer as you in the future'. I've written here that's too coercive, because if they like their consultant then we're saying here 'your consultant thinks this is something you should do'. So I would change that 'we'd like to be able to offer this as something you might wish to consider alongside your normal care' rather than saying your oncologist thinks your involvement will benefit people because basically, you're then saying you've got a moral obligation (Oncology consultant nurse)*



### 3.3 Responses to the Consent Form

This section summarises key themes in response to the Consent Form, explored in Stage One. More detailed wording issues are covered in Appendix 3.

#### A. Responses to language and structure: Potential Participants

Potential participants' expectations for the Consent Form were relatively low, in that they anticipated that it would need to take the form of a legal, official document, rather than acting as a particularly informative or accessible piece of literature. As such, whilst there were areas where they were confused or unclear, some tended to accept the document as fitting with their (low) expectations:

*There's a lot in here, lots of nit-picky stuff. It feels like a mortgage application, having to sign all this. It's very legalese (Cancer participant, female)*

*I had no problem with the consent form – it didn't bother me (Cancer participant, female)*

They also tended to position the Consent Form as Genomics England 'covering themselves', and as such, expected it to be written to cover all eventualities, but more from the standpoint of entering a legal contract, rather than in order to ensure that participants are fully informed and understand all aspects.

*It just fits with my expectations. It seems to me they've covered themselves ... It's definitely more geared up for covering them, rather than informing you (Cancer participant, female)*

While some potential participants were accepting of this, others found the dense technical language and the complicated phrasing off-putting and criticised the form for not being clear enough; they felt that, although it may not stop them signing it, they would need further clarification to be confident of exactly what they were agreeing to:

*I think this is a fairly standard consent form for research etc. However it's a bit intimidating and very wordy ... I'm not sure most people would take the opportunity to fully read all of this before they signed it (Genetic participant, female)*

*I got past the first three points and then I didn't take it in (Genetic participant, female)*

However, some criticisms did emerge. Potential participants commented on the challenge of cross-referencing between the consent form and main booklet. They criticised the lack of consistency in language used, and also in the basic structure of the two pieces of literature, making it very challenging to go back to the information literature and find more detail, should any issue on the consent form be unclear:

*... If I'm going through [the consent form] and I've got to refer to [the PIL], but then I've got to read it through to find out where the hell it is, I've forgotten what I'm doing ... and you get nowhere with it and at the end of the day, you get so frustrated, you either bin it, throw it away or don't bother (Cancer participant, male)*

As such, a more consistent, cross-referenced format across both pieces of literature was called for, and the techniques used in other complex forms (e.g. social service or taxation forms) cited:

*I would want some consistency, so the same subheadings in the booklet... and the consent form ... so you can cross-reference it (Genetic participant, male)*

*I've come across that before – especially with government forms. You know, you get an instruction leaflet to go with it and you read part of it and it says something like, 'Check item 3' ... If you're stuck in that, between those two... then you've got to wade through all that other thing again to find out what they're talking about (Cancer participant, male)*

Finally, in terms of tone, whilst the more legal approach is expected, frequent references to 'including after my death' (points 7, 8, 9) were emotionally uncomfortable for some, especially for cancer patients, who could feel this is a real possibility, and some younger genetic patients who were not ready to engage with the idea of their own death. 'During and beyond my lifetime' was suggested by one participant as a less abrasive wording. Ensuring that this idea is clear, but not repeated/felt to be a focus seems appropriate. Softening the legal tone with a thank you at the end of the document was also suggested by a small number of potential participants.

*A little 'thank you, we're very grateful' at the end might be nice (Genetic participant, female)*

## **B. Responses to language and structure: HCPs**

HCPs were often highly critical of both the document's length and the complexity of the language used. This was especially true of those who were aware of moves to improve the clarity and accessibility of language used in consent forms in their own setting. As such, they positioned the consent form as an 'old fashioned' format that didn't prioritise potential participants' needs and desires:

*I find this consent form to be quite daunting ... it feels like 'God I'm signing my life away, I've just signed so many things, it would just look less daunting if there were few things to initial (Genetic counsellor)*

*The language is at a high level and it's quite legal ... it just doesn't sound friendly, and I don't mean touchy-feely friendly, just friendly-accessible, yeah (Oncology consultant nurse)*

Many wanted to see a much simpler form, in order to help patients genuinely understand what they are consenting to. In particular, there was often felt to be a high degree of repetition, both within the document itself, but also repeating points that had already been explained, or giving detail that had already been provided, in the main patient information literature. For example, points 4 and 5, and 7 and 8, each seemed to cover similar ground and there was some feeling they could be amalgamated or, if they are different, then the distinctions need to be more clearly drawn out. In point 8, listing out the types of health records in brackets was deemed unnecessary, as they have already been listed in the PIL.

HCPs felt that a number of points could be compressed and simplified, especially as it appears that everything on the form has to be agreed to/signed (i.e. why offer so many individual boxes for initialling if there aren't any options/opt-outs):

*The things is, people don't have a choice, there's only one thing they can opt out of, isn't there (Genetic counsellor)*

*The whole form needs looking at again to be shorter and more straightforward. This is just a check that you've understood it, it doesn't all need to be said again (Genetic consultant)*

The version of the consent form used in the pilot (8-10 points) was felt to be much more appropriate by many HCPs:

*It's too long and it's repetitive, there should be no more than 8-10 items to consent to and initialise, as we had in the pilot (Genetic consultant)*

Small font size and style (Cambria) were also criticised by both HCPs and potential participants as difficult to read, and increasing the lack of accessibility:

*I don't like the font and there are just too many words on each page (Genetic participant, female)*

Some of those who had taken part in the pilot also questioned whether there would be separate consent forms for different kinds of participants, for example, parents of proband children, as they had had in the pilot. Although not essential, they felt this was preferable in helping to make the different issues clear for different kinds of participants.

The point was also made that those taking consent need to be properly informed about all aspects of the study so that they can discuss it accurately and confidently with potential participants. This came through particularly strongly from an Oncology consultant, who was aware that with cancer patients, oncology nurses will probably take consent and they are unlikely to have a strong understanding of genomics (vs. genetics patients who are more likely to be talked through the Project by a genetic counsellor or specialist consultant):

*You have got to concentrate on information for the consenter. They are such a key part of this (Oncology consultant)*

### **C. Specific issues and concerns: potential participants and HCPs**

In addition to these general concerns around language and structure of the PIL, particular elements were pulled out as especially unclear:

#### **C.1: Feedback**

The issue of feedback was particularly confusing in the consent form, and was criticised widely by both potential participants and HCPs.

The range of feedback types, and the alternative consent options were rarely, if ever, fully understood within the consent form; indeed potential participants were often more confused by the feedback options in the consent form than they were in the PIL. The heading just before point 16 'Optional Feedback of additional results' is not helping with comprehension as it is not clear

whether all the points that follow come under that heading or not (i.e. including Incidental Findings). In addition, it was not clear to potential participants or HCPs why some words are in brackets, (e.g. '(only)', '(Possibly)', '(any)' and this increased the sense of confusion around these points.

In particular, potential participants found it very difficult to disentangle the differences between 'Looked for additional findings' and 'Conditions beyond the pre-agreed list of looked-for findings' (points 16 and 17). The sentence construction used for these two points was felt to be very complex and difficult to untangle, making key points difficult to assimilate. Similarities in the language and layout of the two feedback types also made it extremely challenging to fully appreciate the difference. In addition, the language used was not consistent with the language used in the PIL (or PIB), which meant it was very difficult for participants to carry their knowledge across from the PIL (for example, Consent Form title point 17: '(Possibly) conditions beyond the pre-agreed list of looked-for findings' was not used in either the PIL or the PIB):

*I think it would be better if you put it all together [16 and 17] and either you agree to it all or you don't (Genetic participant, female)*

*I don't get this one [17] at all. I think it must be about other conditions that they're looking for. So other genetic conditions that are a bit like mine that they want to understand more. I don't know (Genetic participant, female)*

Point 17 generated a degree of concern among HCPs: it was regarded as very unclear, and some felt that asking patients to consent to something so ill-defined and nebulous was unfair and bordering on unethical:

*People have got no frame of reference to even think about that possibility ... It's mind-blowing and I worry that we'll mind blow them and so a knee jerk reaction could be 'oh God I can't take all this in' and they won't want to do it (Oncology consultant nurse)*

*I think it's terribly worded ... Could we not just say 'as the project goes on we may add some genes to the original list' and then we can combine it with the one before [16] (Genetic consultant)*

The idea of consent around carrier status/unborn children was both confusing, and emotionally challenging for some (points 16 and 17). A number of participants found it difficult to comprehend the different genetic statuses that could be identified; for example carrier status, in comparison to an as yet unexpressed gene that could still be expressed later in life. Translating this to (unborn) children was especially confusing; participants were unclear how definitive the genomic information would be (e.g. will they be told about a risk of a disease/given a definite diagnosis/given a concrete idea of the level of risk) and therefore exactly what information they would be consenting to receive here. Whilst some participants can appreciate the importance of encouraging thought and discussion around this issue, it was not felt to be sufficiently explored within either the PIL or PIB to allow for an empowered/informed decision to be made. In particular participants thinking back to this time in their cancer diagnosis could feel they were not ready to think about such issues, and deal with the emotional complexity they generate.

Turning to point 18, the focus was felt to be firmly on **not** feeding back findings, but it was unclear to respondents what might be included under 'Incidental Findings'. A number were confused about how this related to the feedback already promised, meaning that they could question their interpretation of all feedback types and whether their understanding had been accurate to date:

*I don't understand this [18], it's just too long and 16 and 17 have already dealt with feedback, so I don't see what 18 could be about (Genetic participant, female)*

*I really didn't understand this [18]. I read it three times and I just didn't get what it was on about (Cancer participant, male)*

Given the lack of clarity around what is included under Incidental findings, some assumed this meant a wide range of different types of information would be understood by scientists, but not fed back to potential participants. This focus on what is not being fed back could lead participants to think about the ethical implications of this issue, and whether it is appropriate for this feedback not to be given to potential participants, an issue that had not always been fully considered when reading the PIL/PIB:

*If they find something wrong with you through your samples you've given them, I would have thought they would... be obliged to tell you that there's a health issue... but if they find something that you could sort out and they don't bother to tell you about it, it doesn't make any sense; it's crackers. It's like them saying, 'Well hard luck, we're not going to bother.' (Cancer participant, male)*

*I don't understand – why are they not feeding that back? Why not – if it's going to help (Cancer participant, female)*

Whilst this was the majority viewpoint, others saw this point as a catch-all/final legal get out, enabling Genomics England to abdicate responsibility for any issues not explicitly covered.

Finally, those remembering details from the PIL could assume Incidental Findings refers only to paternity issues, and possibly other genetic family relationships; this is worth bearing in mind if participants are to be fully informed about what they are consenting to here.

## **C.2: Completing the form**

From a practical point of view, there could be some confusion over how to complete the form. Whilst the introduction explains the need to initial each box, it was unclear what to do where consent was not required, or if consent was withheld on a specific issue (for example for optional feedback areas). Potential participants were unsure if simply not initialising would be sufficient, or whether they would need to make their lack of agreement more explicit. It was also unclear if every point had to be agreed to in order to participate in the study:

*Do I have to agree to this [point 14]? Could I say no? Would I still be able to take part? (Genetic participant, female)*

## **C.3: Issues introduced only within the consent form**

There were a number of issues that were not mentioned in the PIL. Encountering elements of the Project, and required commitments, for the first time within the consent form could be destabilising, leading participants to wonder what other information they had missed. The following issues were mentioned in this regard:

- Access to records by 'study monitors' (point 8):

*Who are these study monitors, they haven't been mentioned anywhere else? (Genetic participant, female)*

- Consenting to access 'now and into the future (including after my death)' (points 8 and 9): the Consent Form explicitly refers to access continuing after death, which can be the first time that some potential participants fully assimilate this point. The PIL wording 'lifetime and beyond' is less explicit;
- Access by international researchers (point 11): whilst the PIL describes 'organisations coming from anywhere in the world' the mention of international researchers in the Consent Form seems more obvious, so can feel new to participants;
- Mention of processing other than genomic sequencing (point 5).

#### **C.4: Samples and versioning of the consent form**

For Stage One the Consent Form was not versioned. Whilst this was not hugely problematic, the reference to samples (point 4 and point 9) could be off-putting for genetic participants, who could be concerned that they were required to donate tissue samples, and were concerned about the invasiveness of the process.

As the nature of sample donation can be a key element in decisions to participate, ensuring clarity here is vital.

#### **C.5: Specific wording concerns, and strengths**

Point 7 ('Together with my donation of access...') created particular confusion. The wording and sentence construction was felt to be extremely difficult to unravel, but in addition the words and phrases used in the first sentence ('donation of access', 'parts', 'death', 'medical') combined to suggest to some respondents organ donation, or the donation of posthumous body to medical science. Ensuring that the meaning here is clear and unambiguous would help lessen any possible concerns.

*'Donation' seems a funny word here (Genetic participant, female)*

Some wording was ambiguous, and would benefit from further clarity, e.g. 'self-reported health information' (point 6); social care records (point 8); 'extended clinical care team' (point 15).

*I don't have an extended clinical care team, could it just say specialist instead (Genetic participant, female)*

As in the PIL and PIB, reference to commercial (for profit) organisations could be concerning, and in general, explicit reference to pharmaceutical companies and/or the goals of the Project could help reassure. 'Scientific and medical purposes' (point 9) was a strong phrase to reference the goals of the Project, and reassure potential participants of the value of the research being conducted. Mentioning the NHS, where possible, would also be reassuring.

Throughout, HCPs and some potential participants, felt that more frequent use of the words 'anonymous' or 'non-identifiable' when referring to samples/data (e.g. on Point 3) would be helpful, and would help patients understand more clearly when information will be identifiable (e.g. for purposes of feedback) and when it won't.

### **3.4 Responses to the Infographic**

This section summarises key themes in response to the Infographic, explored in Stage One, and briefly in the YPAG. More detailed wording issues are covered in Appendix 4.

#### **A. Overview of responses**

In general, responses to the Infographic were extremely positive. Both HCPs and potential participants felt that the Infographic offered a clear introduction, and a very helpful overview of the Project's remit and goals, and, to some extent, the process of being involved in the Project. Participants in Stage One, who were struggling to understand key elements of the 100,000 Genomes Project, often felt that the Infographic did most to help them grasp and engage with it. The Infographic worked especially well for BME audiences with poor English skills, who anticipated using the visuals in tandem with explanation from HCPs, helping them to follow the process and the core elements of the Project.

Whilst potential participants were generally positive about the tone, this was a concern for some HCPs, who felt that the language and expressions of the benefits of the Projects were somewhat too coercive to be used as information literature.

We encountered a small number of non-visual thinkers who found this format un-engaging and difficult to grasp, but they were firmly in the minority.

Indeed, some were so positive about this style of presenting information that they called for more use of visuals/'flow-charts' through the literature:

*They could do with more of these types of diagrams (Cancer participant, female)*

#### **B. Key Strengths: Potential Participants**

The overview provided by the Infographic was especially praised. The concise wording, clear visual presentation and sense of flow and structure were welcomed, and the use of visuals meant the information was easier to assimilate:

*I think it's good – it's not too much writing and it doesn't repeat everything (YPAG, Liverpool)*

*I think it was nice and clear and straight to the point and I think the layout's very good. (Genetic participant, female)*

*This is really clear, like a flow chart. I like that it's visual, you can look at the steps as you're going along (Cancer participant, female)*

Potential participants felt that the Infographic worked very well to give them an understanding of what the Project involves, and what the benefits could be:

*I looked at this and thought 'It's pretty, I understand, it's such a relief' – because I was interested in it ... I just think it's brilliantly done (Cancer Participant, female)*

*I got a better idea of the project from this (Genetic participant, parent of proband child)*

*It's a medical summary. I don't see how you could say that any better. It's very precise ... I like that very much ... it's nice and simple... (Cancer Participant, male)*

In particular, the following elements were felt to cut through very powerfully:

- Included clear explanation of genomes:

*It immediately tells you what genomes are ... I mean I looked at this and thought, 'Oh, I really do understand it now' (Cancer participant, female)*

- The use of both genetic information and health records was very clear;
- The involvement of family members for genetic participants was felt to cut through most strongly here, along with a clear explanation of why these are important:

*I hadn't noticed [in the PIL] that parents were also involved – it makes it clear why here (Genetic participant, parent of proband child)*

Only one potential participant was confused and questioned whether cancer participants also needed family involvement;

- The process of comparing genetic materials worked especially well with the visualisation – this was easy to understand, but also underlined the anonymous nature of the comparisons taking place:

*'We compare many patient's genomes, and try to find similarities and differences' ... OK ... I like that ... the process... is perfectly straightforward (Cancer participant, male)*

- The clearly distinct approach for potential participants with cancer vs. rare diseases meant that both cohorts had a strong sense of the project working for 'people like me';



- Featuring understandable examples of potential benefits for the individual, as well as clear expressions of the overall goals of the Project, helped potential participants see the benefits for them as well as for people with similar issues in the future:

*Real opportunity ... important scientific discoveries ... I like that, it's a nice powerful clear message (Cancer participant, male)*

The use of (predominantly) clear visuals and icons helped participants to navigate and feel in control:

*I would pick this up first ... it's to the point and it uses pictures (Genetic participant, parent of proband child)*

*Good pictures – they make sense, it's relevant (YPAG)*

The visual approach was especially popular within participants for whom English was a second language. They felt that the Infographic offered a clearer route into the Project, with less intimidating text, and the use of visuals helped them to follow the 'flow' of the Project as it was explained to them:

*It would be better if the clinician gave this first and explained it (Genetic participant, English as a second language, female)*

For continuity, and especially for these audiences, it might even be worth considering including visual links to the Infographic within other documentation (e.g. PIL) to help potential participants make connections between documents.

Participants were also very positive about the emotional tenor of the approach. Focusing on individuals and following their story through made the literature feel more engaging and personal. Potential participants also responded positively, in the most part, to the more enthusiastic and benefit-focused text (vs. the PIL), including the description of the potential benefits to the individual, as well as the great potential offered by the Project:

*That's a very strong statement – that information about predictions, and finding treatments... it should go at the beginning ... this is what we want to do (Genetic participant, male)*

The final statement ('Now there is a real opportunity to turn...') and the statements about treatment for Tom and Amy were especially powerful in demonstrating the potential of the Project. However, some could feel that the introductory paragraph was tonally less ideal, and verged on self-congratulation.

*It's just saying 'aren't we wonderful', it's boastful ... Just tell me what they've done (Genetic participant, female)*

*I just find that initial paragraph too emotional, and it's irrelevant, why are they telling us this (Genetic participant, female)*

There were also a small number who questioned the apparent certainty of 'Tom' and 'Amy' benefiting from the Project:

*I think they're being a bit optimistic about Tom. This is what they're hoping to do isn't it. I don't think anything's guaranteed (Cancer participant, male)*

Overall, though, the impact of the Infographic was to encourage potential participants to feel more positive about being involved. This was particularly due to its concise, benefit-orientated nature.

These opinions were very much shared by young people – both in the YPAG and in our depth interviews – who felt that the Infographic would offer a strong option for young people (aged 11/12 years upwards). They were very positive both about the content and the level of communication, and found the visually-focused presentation style of the Infographic highly appealing. More detail can be found in Section 3.7.

*It's a really good balance of picture and text, and it just gives the information straight to you ... I really prefer it (Genetic participant, 15 years)*

However it is worth pointing out that this literature was only explored briefly with young people, so detailed feedback on improvements to specifically target this group were not sought.

### **C. Key Strengths: HCPs**

Many HCPs imagined this would be a useful tool in introducing the Project to potential participants by providing a quick overview of the Project set up/remit, and the potential benefits:

*I love the infographic – it's so easy! ... It's laid out so well, it's literally walking you through the leaflet – and the graphics are brilliant (Genetic Consultant)*

*If you do nothing else, use these because they explain a lot (Genetic counsellor)*

As with potential participants, they praised its concise summary of key elements, and easy visual accessibility. One consultant working regularly with patients for whom English was a second language felt it would be especially useful for this audience.

### **D. Specific issues and concerns: potential participants and HCPs:**

A number of HCPs (and potential participants with a healthcare background) were concerned that the language used, and references to potential personal benefits, were inappropriate for consent literature (e.g. mentioned benefits that not every individual would experience). They felt that at points the text was overly-emotional and coercive, especially the introduction:

*I'm not sure it's fair to talk about 'painstaking research' and 'thousands of dedicated scientists' (Genetic consultant)*

In addition, the research identified a small number of key issues requiring greater clarification:

#### **D.1 'Observable traits'**

This phrase, and the ‘eyeball’ visual used were very unclear to respondents, and the lack of mention in any of the other literature added to their confusion:

*An explanation of what observable characteristics or traits are would be good here (Cancer Participant, female)*

*Why would her characteristics or traits be observed; can they give a lot away? Only because to me I’m thinking, ‘Well are they just going to sit and watch me or see how I act or react?’ (Genetic Participant, family member of proband adult)*

## **D.2: Practicalities of viewing on and offline**

Whilst the visual presentation is very strong, the blue background was challenging for a wide range of potential participants (and identified as especially poor for dyslexia sufferers):

*The diagram [Infographic] was good, but on the screen it was hard to see – I don’t think blue was the right choice of colour (Cancer participant, female)*

It is worth mentioning, however, that the blue could be strongly, and positively, associated with the NHS (especially mentioned by those from BME backgrounds in our sample).

The document is substantially more effective when viewed on screen than in (A4) printed format, where the text is too small and the colour contrast insufficient. When inserted into the PIB the Infographic also suffered from being divided to fit onto an A4 page; it was re-ordered to be read in a clockwise direction but this was not explained and nearly all participants read it downwards in columns. This was frequently confusing and meant that some of the strengths of the communication were lost. :

*This is very important, but it’s just too small. If I was feeling ill, I’m not sure I’d be bothered to be honest (Cancer participant, female)*

*This is good but it’s not in order and it just seems very odd the way they’ve laid it out (Genetic participant, female)*

*The order just doesn’t work for me. Could they perhaps put it in landscape? (Genetic participant, female)*

Those who saw the Infographic as it was originally designed (a long diagram in portrait format) responded very positively and felt that a lot of its appeal would be lost if it was ‘squeezed’ to fit into an A4 document.

## **D.4 Focus on figures**

The focus, in the Infographic, on numbers of participants created confusion as these ‘don’t add up’ (25,000 participants with cancer; 15,000 participants with rare diseases; but 100,000 genomes in total) – participants could therefore wonder if they had misunderstood, or if the numbers were inaccurate:

*That doesn't add up to 100,000 – it's a con! (Genetic participant, male)*

*I just think it looks a bit odd that the number of patients doesn't add up to 100,000. I think they need to explain why that is, otherwise people might wonder what's going on (Genetic participant, female)*

For genetic participants – who may already be sensitive to the (perceived) greater research budgets given to cancer over genetic conditions - there can be particular interest in, and concern around, the focus of priorities for the 100,000 Genomes Project:

*I still would probably want to know why it's 15,000-25,000. I don't understand that ... all the time you're bombarded with something to do with cancer and to be fair, ... if I was in that position, that's all I would care about also; but the condition that my daughter has, you know, it's not everywhere... (Genetic participant, family member of proband adult)*

#### **D.5 Family Involvement:**

The Infographic makes clear the need for involvement of family members for genetics patients, and this is a real strength. However, although it stipulates that these will be the patient's closest relatives, and it appears to specify parents. As this can be the first/only time that genetics participants appreciate the need for family involvement this can be interpreted very literally, with some assuming it needs to be their parents; mentioning other possible relations here (siblings, adult children?) would be reassuring;

#### **D.6 Practicalities of involvement**

The Infographic does not cover the practicalities of participation – how and where samples will be taken, exactly what samples are required, what happens next for those individuals taking part etc. As these practicalities are key to decisions to participate, both adult and YPAG were keen for this information to be available in an equally appealing and accessible format:

*I think it's great; but I'm still curious as to how they would do it. Like if you'd given me this, if you were recruiting me, I would still put that down and be like, 'OK, cool, so how are you going to do it?' (Genetic participant, female)*

#### **D.7 Some unclear icons**

As well as the eyeball visual (Observable traits), the DNA icon was confusing to some. For some, this was due to a lack of connection between this visual and their mental associations with DNA (would a classic helix be more recognisable?) and for others, there could be an expectation that the visuals for the normal and abnormal DNA variants would be different (i.e. to represent the mutation of the cancer genome or of the genetic condition).

### 3.5 Children's and Young People's information literature: Context and ideals

This section begins with some general findings on the attitudes of children and parents, and their needs in terms of literature, before summarising responses to the literature and Assent Form for young people and children developed for Stage One.

It is worth mentioning that whilst most children interviewed with their parents were aware of their diagnosis, and expected to be involved with the decision to take part in the Project, we did encounter a minority of families where children had not been informed of their diagnosis, or whose developmental delays meant that they would not be expected to be involved in decisions around participation.

#### A. General attitudes

##### A1: Format and style

Children, and in particular young people, within the YPAG had a number of suggestions for the optimal presentation and format of information:

- At an overall level, YPAG tended to suggest more creative, multi-media, and interactive formats where possible. More specifically, this included formats such as interactive apps or screens, radio or short video clips, or in one of the YPAGs, an animated/interactive version of the current Infographic or mind-mapping:

*Imagine if that one [the Infographic] was interactive, so that points opened up when you clicked onto them (YPAG, Liverpool)*

*Something on TV or radio – less reading (YPAG, Liverpool)*

They did, however, recognise that these options may not be practical or cost-effective.

- Even in paper format, it is worth stressing that this age group had high expectations and standards around look and format – for example, they could often have strong opinions about the ideal typography, or card type. Ensuring that the literature looks contemporary and appealing will be important:

*You could imagine something like this [Infographic] on really nice matt card, something that makes you want to pick it up and actually keep it (YPAG, Nottingham)*

Amongst younger children, simple formats could be preferred, but one suggested a more story-based format, following characters you could associate with and get to know – a format they had encountered in literature for a previous operation:

*When my 7 year old had grommets ... he had a book with Molly ... now Molly is doing this – a character you could follow through so it was more like a story (Genetic participant, parent of 13, 9 and 7 year old)*

- Even if written, more interactive format can be suggested, especially for younger children (e.g. including quizzes/colouring/stickers, to both engage interest and check understanding). For older children, a blank space for recording their own questions was suggested as part of the document.
- For a number of parents, written literature was not appropriate, given their children's situation (including children with visual impairment, developmental delays, and children who were not aware of own diagnosis). Consideration will need to be given to inclusivity across these types of issues.

In terms of any written literature, the format priorities identified within the YPAG were:

- Clear, non-technical language;
- Concise and focused expression – not too lengthy;
- Contained format – fold-out A4 booklet was mentioned on a few occasions as optimal size:

*I don't think the format should be like this – it should be like a fold out leaflet ...then it doesn't look like it's a lot (YPAG, Liverpool)*

- Visually engaging – with age relevant visuals, and colourful approach;
- Not patronising, in terms of both language used, and concepts explored - especially for 11 years+.

There was some debate within the YPAGs over the number of literature versions for under 16s that would be optimal, with some suggesting a version for 11-13, and 14 years plus, given the large shift in terms of scientific understanding, and the increase in personal identity and independence that occurs across this age bracket.

#### **A.2: Ideal content:**

In terms of content, thinking about all ages of potential participants, YPAG felt that it was vital that all children and young people were informed about:

- Who is running the Project;
- What the goals of the Project are;
- What commitment is asked of them – including detail on any samples required;
- Things they should think about/consider before agreeing to take part;

- What feedback they will get and what else they will hear about the progress/results of the Project.

Thinking about literature for Young people (aged 11 years +), particularly clear priorities emerged in terms of their priorities for content and tonality:

- There can be a strong desire for reasonably detailed and sophisticated information both about the Project's goals, and the scientific approach and background. As genes and genetics currently covered in curriculum at this age (in KS3 currently), young people could have reasonably developed understanding:

*You do genes in KS3 now, so most 11 or 12 year olds would have covered it (YPAG, Liverpool)*

In addition, it seems likely that young people with genetic conditions will have greater understanding than the general public, as for adults with genetic conditions.

*My children know a lot about this because they've been interested in their condition, it's something we talk about, so some of this seems quite basic to us, although I can see it might not be to the average child (Genetic participant, parent of 11 and 15 year old)*

- Young people also wanted to be enthused by the Project and what it might achieve. It was important for them to hear that a Project of this type has never happened before, and has real potential to help other young people like themselves. As such, they felt that participation would be something participants could be proud of:

*I think it sounds amazing. I want to know more about what it could achieve. Is this something I'm going to look back on when I'm older and say 'I did that'? (YPAG, Nottingham)*

- As young people anticipated playing an active role in deciding on participation, understanding the practicalities of their commitment can also be really important – what will happen, when, who will be involved: to help them understand what they are committing to/inform the reality of consenting:

*They need to tell us right at the beginning what is being asked of someone taking part (YPAG, Nottingham)*

- Tonally, a 'straightforward', but not simplistic, tone was expected, and they imagined the literature would be positioned as opening conversations up, and prompting discussion and thought, rather than taking a didactic approach – they were keen for the literature to respect their control and autonomy. By 11years+, potential participants seemed to expect the decision to participate to be one that they would very much input into, with family discussion around the important ideas. Parents also supported this approach, with one parent in particular, welcoming a questioning approach that would encourage conversations within the family about participation.

*I don't want it to be too simple. I want them to come and ask me questions about what they're reading because then that gives me a way in of talking to them about it. Otherwise, if it's too simple, they'll just sit there and read it by themselves and think they've got it all (Genetic participant, parent of 11 and 15 year old)*

One parent, and one group of YPAG suggested that in addition to the Children's Literature, it would be valuable to provide an accompanying leaflet outlining parental guidance. They envisaged that this would give advice on how to talk through the important issues with children of different ages. In one YPAG, they also felt that this (parent guidance) literature should include topics (e.g. managing feedback on Additional Looked for findings) that may not be appropriate for young people's literature, but that could form a valuable part of family discussions:

*That [additional findings] might be worrying if it was in the young people's literature, so it might be better in the parent leaflet, so they can talk about it with you (YPAG, Birmingham)*

It was assumed that the parental leaflet would work in tandem with the Children's Literature, using consistent vocabulary and structure.

One parent felt it was also very important to encourage parents to make sure that their children felt fully informed, allowing them to ask questions, giving them time to think. They also felt it was important to stress to parents that it was acceptable for their children to refuse to be involved:

*I think they have got to give some advice about how to talk this through with your child, read it with them, let them ask questions. And to say that it doesn't matter if your child doesn't want to take part. I'd be really worried about the pressure some children might be under from their parents (Genetic participant, parent of 7 and 4 year old)*

This parental leaflet was expected to include guidance both for proband children, and siblings.

### **A.3: Other issues of importance to Young People:**

The issue of **sibling involvement** was also important to the YPAGs, especially as some within the groups had family health issues, so were heightened to this scenario. They usually felt that a separate leaflet aimed specifically at siblings would be beneficial, as they expected siblings to have different perspectives, priorities and needs:

*If a sibling was 15, they might not want to know if they are predisposed to something (YPAG, Birmingham)*

*They might need additional support ... someone to talk to (YPAG, Birmingham)*

The **transition from child assent to adult consent** was an issue that the YPAG felt was important, and needed to be thought through by families, so that young people would feel adequately informed to make this decision when they turn 16.

*What happens when you are 18, or 16? It might not align with your views, or you might want to move on*



*(YPAG, Birmingham)*

They also felt that a 'tiered' contact process would help children build up to the idea of informed consent gradually, by increasing their information and therefore their understanding as they get older. Young people felt that for anyone who joins the Project as a child (i.e. under 11) or even at 11 or 12, turning 16 would feel a long way away. During that time, as understanding grows, and as children develop their identity, it was felt likely that they would want to know more about what they were participating in, how their data is being used, and what the Project is achieving. Young People suggested Genomics England re-contacts children, for example proactively sharing the literature aimed at 11 years plus, or even talking proactively to young people approaching the age of consent:

*If I joined this when I was 8 or 9 then 16 would feel like such a long way ahead. I think they should contact them again at 11 and send them the next leaflet, and maybe again a bit later on as well (YPAG, Nottingham)*

*From about 14, I think you want to start giving people a bit more information (YPAG, Birmingham)*

Interestingly, one YPAG felt that young people with serious illnesses were sometimes more mature, having coped with complex issues, so would be especially likely to want to understand their consent process.

Whilst not a focus for this research, there was some suggestion that **recruiting siblings** might be a challenging process. Many felt that it would be vital to have a separate document for siblings under 16, who would have different priorities and contexts:

*You'd need a separate version for siblings I think (YPAG, Liverpool)*

### 3.6 Responses to Literature for 6-10 year olds

*Caveat: due to the ages represented at the YPAG, and the ages of children who participated within the interviews, most of our feedback comes from parents/children aged 7-8 years, or from YPAG members who were aged 10years+.*

#### A. Overview

Parents with children 7/8 years, and participants in the YPAG felt that the language, tone and broad visual approach were largely appropriate:

*It explained it so people my age could understand it, and learn more about if they want to do the science thing, and about what they do, and that it doesn't matter if you don't want to do it (Genetic participant, 8 year old)*

*I thought that was fab – really clear, at the right level ... bright colours, the pictures help, and the people look happy, good simplicity of vocab (Genetic participant, parent of 7 year old)*

There were some indications it may be slightly simplistic for 10 year olds, especially in terms of language. However there were also some 11/12 year olds with lower/average literacy levels in the YPAG who seemed more comfortable with the Children’s leaflet than with the older-oriented document. Some flexibility might therefore be required in terms of choosing the most appropriate leaflet for children at the top of the 6-10 age bracket and at the lower end of the 11+ bracket.

In terms of format, (literature was shown in printed PowerPoint format) a more compressed format would feel even more accessible – a small booklet (e.g. folded A4), even a small book format were suggested.

## **B. Specific Issues and Concerns**

Detailed feedback can be found in Appendix 5, but the following outlines the core strengths, and areas that children, young people and parents felt needed further development.

### **B.1: Visuals**

The visual style was generally deemed a real strength. The simple, cartoon style used, with a friendly, positive tone, was felt to be entirely appropriate. Use of recognisable characters (e.g. Disney), or a single/couple of specific characters that children could follow through their ‘journey’ were suggested for additional engagement by a minority:

*The pictures are good for the age range (YPAG, Liverpool)*

In particular the visual of the family in hospital was praised (p.3) as showing a realistic, but positive depiction of hospital stays. However, children and parents felt that too many visuals were included, and that a visual for every point made the document feel too long, without adding sufficient value:

*When you’re halfway through it feels like there are still loads of pages to go (a shorter version) would be easier to digest (YPAG, Liverpool)*

Using fewer visuals would help the document feel shorter and easier to navigate.

### **B.2: Language**

In general, the language was praised, in terms of the age suitability, and also the approachable and reassuring tone:

*She read it herself – there weren’t too many hard words ... it was easy to read, very understandable ... I felt it hit the right spot (Genetic participant, parent of 8 year old)*

*It was simple, easy to understand (YPAG, Birmingham)*

However, there were a few occasions where it was slightly over-simplistic, and also a few specific words where alternatives were suggested. The following are the most important, but more detail can be found in appendix 6:

- In general, the word 'ill' was preferred to 'sick', which can be associated with vomiting rather than long term illness:
- Wording around samples strongly suggested that children would have the choice of giving blood or spit:

*Is there a choice? Is it blood or saliva? (YPAG, Liverpool)*

This was welcomed if the choice was real, but if sample format is not a choice, it is vital that this is clear. Children and parents saw the two as offering very different commitment levels, given the potential pain involved in blood samples (especially important for those undergoing regular, invasive treatment). A children's HCP also called for an unambiguous statement here, as they were aware that parents could be uncomfortable with putting children through additional blood tests – indeed one parent of a 7 year old within our sample was especially uncomfortable about participation if blood samples are required:

*My daughter's never had blood taken. I actually think that would be quite traumatic for her and I don't think I'd be prepared to put her through that (Genetic participant, parent of 7 and 4 year old)*

- Free time (p9) was not felt to be a concept that most children would understand.
- The **cake analogy** used on p4 was generally very well liked, and felt to be clever:

*I learnt that if you had lung problems, it would help them and tell them about how the genes work, and how they are like ingredients in a cake ... some bits were funny – like the Victoria Sponge (Genetic participant, 8 year old)*

*I liked the baking analogy – being able to connect to it (Genetic participant, parent of 8 year old)*

The idea seemed to require some discussion and explanation for younger children (e.g. 7/8 years) but parents felt this was useful in generating discussion, rather than being a concern. We suspect the analogy might be a challenge for a 6/ 7 year old (none within our sample).

One YPAG suggested using an alternative to 'burnt' within the cake analogy, as that was felt to have negative connotations.

### **B.3: Anonymity, consent and tonality**

The literature was felt to work well to reassure children that they are allowed to say no, and that they have some control over the process (p7). This was considered important and appropriate for younger children, who might be nervous of expressing their opinion:

*You can tell the doctor, and it doesn't matter if you don't want to do it ... that was good (Genetic participant, 8 year old)*

However, the issue of anonymity was slightly more problematic (p. 10). Whilst not generally picked up on as an issue by children, parents of proband children often felt that the wording suggested secrecy, and that involvement in the project is something you (as a participant) need to keep secret. Clarifying that children are free to talk to anyone they want to about the project might help the balance here:

*Actually children want to tell people when they're doing something like this, and they should be encouraged to talk about it! (Genetic participant, parent of 7 and 4 year old)*

For children aged 6-10, turning 16 was felt to be too distant an event to imagine or associate with, and YPAG also felt that children of this age were unlikely to understand the age of consent. Given this, it might be beneficial to simplify the language and expression around this idea e.g. 'When you are 16years old, we will need to ask you again if you are still happy to take part. You will be an adult then, so it will be up to you if you still want to take part in this study'.

#### **B.4: Practicalities of commitment**

In general, the implied flexibility of approach, and focus on children's priorities within the literature was praised (e.g. appointment times to suit child, availability of pain relief during sampling process). Any further flexibility would be welcomed (e.g. potential to use samples gathered as part of existing treatment regime):

*Sometimes they take blood when they do her IVs – that would be good (Genetic participant, parent of 8 year old)*

### **3.7 Responses to Literature for 11-15 year olds**

#### **A. Overview**

At an overall level, the literature for 11-15 year olds was much further from the ideal identified by both YPAG, and proband children and their parents, and was felt to require substantial reworking.

In particular, the literature was insufficiently complex, in terms both of language and the concepts discussed. Certain important issues were not covered in sufficient detail (e.g. basic concept of the Project, its goals and database format; the nature of individual feedback; and who the Project is being run by).

The structure of the leaflet and the layout of information on the page were also less effective, impacting on understanding and engagement. Whilst visuals were only intended to be draft, again, there was strong criticism of the style and approach.

## B. Specific Issues and Concerns

Detailed feedback can be found in Appendix 6, but the following outlines the core strengths, and areas that young people and parents felt needed further development.

### B.1: Level of communication: language

In general, young people in the research, especially those 13 years+, found the literature insufficiently complex and even rather patronising, in terms both of language and content.

Firstly, to explore the language:

Frequently the vocabulary and expressions were criticised for their simplicity, with research audiences wanting to see more scientific, even professional language e.g.:

- Including words and phrases such as ‘characteristics’ rather than ‘tell our body things’ (p.4); ‘parent or guardian’ rather than ‘mum or dad’ (p7):

*It should be slightly harder language (YPAG, Liverpool)*

- Using more technical language e.g. sequencing DNA, anonymity:

*They’re very keen on scientific language in Key Stage 3 (Genetic participant, 13 year old)*

- Avoiding ‘over’ explanation of simple ideas (e.g. flexibility in appointment scheduling).

Where technical language might not be understood by all across the age range, young people suggested providing tools to help them to unpick more complicated ideas themselves – for example a glossary of key terms, or hyperlinks to more detail within the website. The idea of being in control in this way seemed very appealing.

A few other language suggestions were made e.g.:

- Some terms need clear explanation: e.g. ‘genome’, difference between assent and consent;
- As for children’s literature, ‘ill’ was preferred to sick, as sick suggested vomiting only.

### B.2: Level of communication: content

Based on the type of information that young people expected to be included, there were often high levels of disappointment, and a sense that a number of important issues were not covered at all, or not in sufficient detail for potential participants to make an informed decision:

*I would have liked more detail (Genetic participant, 13 year old)*

- Practical detail around participation: e.g. the number/length of appointments. Young people could assume this will be quite a high time commitment, and were surprised that the core

commitment was for a single sample (NB focus on fitting around your time may contribute to these perceptions):

*How many times you have to visit the hospital and how long each visit will be (YPAG, Liverpool)*

*That's how I would decide if I want to take part or not (YPAG, Liverpool)*

*How many visits and how long – I've got no idea! (YPAG, Birmingham)*

*That it's not invasive – you're not going to be cut to pieces (YPAG, Birmingham)*

*How often will I be in hospital and how far will I have to travel (YPAG, Nottingham)*

*Will they have a party at the end of it, after a few months, when everyone who has been involved in it can get together and say what they thought of being part of it? (Genetic participant, 11 year old)*

- The basic nature of the project, especially the ongoing commitment/database role, and the implications of this, and the use of health records as well as genomic information (the literature focuses on the sample, and only mentions health records on p.13).

*Is it just me giving some blood? Is it just a one-off or are they going to want something more from me? (Genetic participant, 15 year old)*

- Some wanted to know more about what would actually happen to their samples, and the kind of work that the scientists might be involved in; there was a curiosity around understanding (in appropriate language) some of the nitty-gritty of how the Project will work:

*I want to know what they're actually going to be doing in the laboratory. How will they use my sample, what are they going to be doing to it (Genetic participant, 11 year old)*

- Who is running/controlling this project – both in terms of NHS links; and the involvement of commercial/pharmaceutical organisations;
- Goals of the Project, and what it hopes to achieve: what sort of issues might the Project be looking at; how will genes/genomic medicine help us moving forwards.

*Who's going to benefit – if it's not going to help that person, then say it'll help other people in the future (YPAG, Birmingham)*

*Why are they screening – what are they trying to do? (YPAG, Birmingham)*

- The nature of feedback that you (and your family) would get (N.B. although some feeling that this may be better dealt with in detail within parental literature, to avoid unnecessary stress);
- More information about role and importance of sibling/parent samples – exploring differences in genes/why this is important.

In addition to information that was simply missing, young people also felt there was an unnecessary ‘dumbing down’ of concepts: ‘experiments that you might do in science at school’ (p17) was especially criticised: young people are aware that processes will, and should be, substantially more complex:

*I hope it's not really like what we do in school. These should be proper scientists (Genetic participant, 15 year old)*

### **B.3: Visual approach**

Exploring visuals was not a key focus for this stage of research. However the mismatched visual styles and lack of consistency were often criticised, and it will be vital that the visual approach in the final document is highly consistent in order to appeal to this sophisticated audience.

The visual on p. 6 was consistently pulled out as hitting the optimal tone: reasonably scientific and technical looking, with more sophisticated visual references e.g. view of cells; enhances and works with text, rather than merely illustrating it:

It was notable that any visuals showing Young People could be criticised; it seems likely that finding visuals featuring young people that feel truly inclusive for all would be a challenge:

In addition, young people felt that the overall document was substantially too visual-heavy – this could feel somewhat patronising (no longer require visuals illustrating every point in order to remain engaged), but more importantly, was felt to be adding little, other than greatly increasing the document’s length:

*They should condense it a bit – it feels like it's a lot – because it feels like a big huge book because of how they've presented it ... the pictures are really big (YPAG, Liverpool)*

*There doesn't need to be a visual for everything (13 year old)*

### **B.4: Structure**

The structural approach was criticised in two major areas:

- Firstly, the overall flow was not felt to take potential participants clearly through the core elements of the Project and their commitment. The document comes across as repetitive (e.g. p. 2-4); in particular, repeating the simple idea that the document needs to be read carefully/that potential participants should talk to their parents was widely criticised:

*On the first page, where it says please read this leaflet very carefully – I don't think you'd need to tell that to a 13 year old (YPAG, Liverpool)*

*It's so patronizing, it just keeps going on and on saying it's OK not to take part (YPAG, Nottingham)*

The early section in particular was felt to be very long (still ‘introducing’ leaflet on p.7). As mentioned in the ‘Content’ section above, the order and focus of the document could also lessen clear communication of the commitments involved.

- Secondly, on any individual page, text was often presented in a number of different formats, e.g. boxes, speech bubbles and ‘flashes’. This created frustration and confusion: young people were unclear why the different formats were used, so tried to use these cues to assess if they represented different types of information, or suggested a reading order on the page. The use of these different formats made it challenging to disentangle the reading hierarchy and be confident of the order in which to read the elements

*There’s so much going on here. Why is that in that flash thing? I really don’t know what to read first. It looks like something a Year 6 might put together in PowerPoint (YPAG, Nottingham)*

*The speech bubbles just look really immature. It needs a more professional look if you ask me (YPAG, Nottingham)*

### **B.5: Tone**

As per comments on the language, young people were keen for the literature to treat them as ‘adults’ – i.e. with a responsible, direct tone. In certain areas, the tone was felt to be inappropriately didactic, telling young people what to do or think (e.g. p.2). The expression of the option to opt-out/not be involved was also criticised here; most wanted the focus on involvement being their choice, rather than on the fear of consequences.

In addition, the document failed to capture the excitement that initial information about the Project generated among some young people. For those that appreciated the Project’s groundbreaking nature and distinctiveness the literature could feel somewhat pedestrian. The idea that the Project would make a difference and help others in the future was felt to be a highly motivating concept, and one that would benefit from greater prominence. Young people felt that creating a greater sense of the potential of the Project could create greater engagement overall.

*When you first talked about it, it sounded amazing, but this [the document] doesn’t tell me about any of that (YPAG, Nottingham)*

## **3.8 Responses to Infographic among Young People**

The Infographic was shown briefly in YPAG and some of the interviews with young people with a genetic condition. In comparison to criticisms of the literature, young people (especially 13 years +) consistently preferred the language and complexity level of the Infographic, praising its highly engaging and coherent visual approach:

*I think it’s good – it’s not too much writing and it doesn’t repeat everything (YPAG, Liverpool)*



*Good picture – they make sense, it's relevant (YPAG, Liverpool)*

*Its not too complicated – it's in the middle of the scale (between patronising and too technical) (YPAG, Liverpool)*

*It's very neat – with the arrow and the follow-through (YPAG, Birmingham)*

*That's nice, I really like that. They should just use that to tell you about it (YPAG, Nottingham)*

In particular, the use of personal examples which can be followed through to understand the Project's goals and benefits, as well as the clear explanation of how genomic samples would be compared, (aiding understanding of how scientific breakthroughs could occur), were praised:

*The case studies – real examples – it makes you relate to it (YPAG, Birmingham)*

The Infographic was a familiar and engaging format for most, providing a strong overview of the Project, although, it was felt to lack practical information around what participation involves (indeed, a second Infographic laying out exactly what is required of participants was suggested):

*It doesn't talk about the blood test, and what you have to do (YPAG, Birmingham)*

One YPAG were keen to create even greater engagement via the Infographic by making the format interactive, so that the process could be followed step-by-step; but also that any specific point could be clicked into to learn more.

Certain issues and language elements in the Infographic would need simplifying for the younger end of the age bracket, and the detail of this was not explored in the session. However but the overall approach and information level seemed appropriate for 11-15year olds.

### **3.9 Responses to the Children's and Young People's Assent Form**

This section summarises key themes in response to the Assent Form, explored in both Stage One and Stage Two (no changes were made between stages). More detailed wording issues are covered in Appendix 7.

#### **A. Overview of responses**

At an overall level, the Assent Form was felt to work well. Language, font and layout were clear and tonally appropriate, format was concise, and the issues covered were felt to capture the key elements of consent. Relatively few suggestions for optimisation emerged across both stages.

*It feels very clear and transparent. It seems quite safe, there's no small print (YPAG, Nottingham)*

It is worth mentioning however, that as outlined in section 3.5 A.3, Young People and parents were keen to understand the difference between assent and consent, as they were often not aware of the meaning

of the two terms. However, this may be best explained within the literature rather than on the form itself.

Some parents of younger children as well as some young people made the point that it is unusual for young children to be asked to sign a form. Parents could feel that signatures are not a concept they will understand, so children might need some support, as well as careful explanation of what they're doing; young people also indicated that emotionally this might feel like a significant issue and that it would be important for the literature to support and explain this process.

One parent was particularly concerned about the ethics of asking a 6-10 year old to give their assent. She felt that a child this young probably wouldn't be in a position to fully comprehend what they were doing and she therefore questioned the legal status of the assent form. She was keen for more information about this so that she could understand the role/status of the assent form within the overall consent process:

*I'm a bit concerned about what this means in terms of a 6 year old signing it – is that even meaningful ... Ultimately it is the parents who will make the decision, so what does it even mean for a child to sign something like this (Genetic participant, Parent of 6 and 4 year old)*

## **B. Specific issues and concerns: children, Young People and parents:**

### **B.1: Practicalities of completing the form**

Some minor suggestions emerged in terms of completing the form:

- Ensure that it is clear how the 'Yes'/'No' boxes should be completed – should these be ticked or initialled?
- Consider reformatting so that the space to sign is clear – currently positioning on page two could be missed or some assumed they should sign on page one. Parents with younger children felt they may need a larger space to complete this;
- A minority suggest making it clear that the child/young person only needs to complete one signature on page two (e.g. box around this section).

### **B.2: Tonality and language issues**

Again, a small number of minor issues were raised:

- Introductory sentence ('Young person to circle all they agree with please') would benefit from a warmer, more accessible expression – 'Please circle if you agree with these statements' was suggested in one YPAG;
- A small number of parents were keen to see simpler and more open questions in the assent form; suggestions were made to reword 'have you asked all the questions you want' with 'have

you had the chance to ask all your questions’; and ‘have you had your questions answered in a way you understand’ with ‘do you fully understand the answers’;

- One parent also wanted the assent form to be more explicit and more reassuring about the possibility of saying ‘no’, as she was concerned that children might feel pressured into signing the form in order to please their parents. She felt that including phrases such as ‘you can change your mind later on’ and ‘if you’re not sure about this, do say no’, even explaining that children could have the option of taking part in the study later in their lives, would soften the approach, and encourage children to engage with the form and think about what they were doing;

*The key for me is giving parents time to talk this all through with their children in their own time, and just making sure that parents aren’t pushing their children into it (Genetic participant, Parent of 6 and 4 year old)*

- ‘...it’s OK...’ in the final assent bullet point could feel somewhat jarring – ‘you can’ was suggested as an improvement

### **3.10 Summary of Suggestions for Optimisation: Stage One**

#### **A. Patient Information Leaflet/Booklet**

The following suggestions are drawn from responses to both the PIL and PIB, amongst potential participants and HCPs.

**Firstly, some overall developmental guidance in terms of the approach of the documents:**

##### **A.1: Simplification of expression**

The more straightforward language, sentence construction and warmer tone of the PIB were consistently preferred. Potential participants both found this style easier to understand, and felt that it spoke more directly to them. As such, maintaining this simplicity and approach through all development is strongly recommended – avoiding both complex sentence structures and ‘legal’ terminology.

As part of this simplification, a large and legible font is also important – the font used in the PIL was felt to be both small and hard to read.

##### **A.2: Structuring and information organisation**

Given the complexity of the information being communicated, a clear structure is vital to take potential participants through the information they need to absorb. A number of recommendations emerge in terms of improving the structure and information organisation:

- **Sectioning the document:** many HCPs and potential participants suggested a brief **overview** – that can be flicked through to give a context to the whole project, and allow participants to gauge their levels of interest; for HCPs, this overview could also be used as the basis for an initial explanation of the project:

*I'd have a short information sheet at the beginning – then all the detail behind it (Oncology consultant)*

This would need to cover those core issues that all participants 'need to know': core commitments from participants, the project remit and role, as well as some basic detail around governance/ anonymity. In particular, the following issues were felt to be key by potential participants, and are not yet always assimilated from the PIL, or even the PIB:

- Project goals: clear, engaging goals would help participants engage;
- The nature of potential participants' commitments;
- Ongoing data usage/beyond lifetime commitment ('In your lifetime & beyond' was the strongest expression here);
- Database role, who may have access, how access is controlled;
- How information can be anonymised but also made identifiable for the purposes of feedback;
- Different types of feedback available.

Potential participants assumed that this document would create interest and excitement, by explaining why this Project is different, and how it might help people in the future. Neither the PIL nor the PIB were entirely successful here, although 'What can working with the 100,000 Genome Project achieve' (Section 3, PIB) was acknowledged as an interesting section that comes too late in the document.

Overall, the Infographic was the most successful at communicating the vision for the Project, especially through core phrases such as: 'Now there is a real opportunity to turn the very important scientific discoveries about DNA and how it works into a potentially lifesaving reality for NHS Patients across the country'. However, depending on the role the Infographic plays in the consent process, the language and tone need to be carefully balanced with ensuring that the document fits with HCPs' needs to be non-coercive.

Potential participants assumed that the second part of the document would then contain **more detail around practicalities**, as well as answering specific worries or issues. Some who read the PIB even suggested a final '**FAQ**' section, covering those issues of interest only to a minority (see section A.3 below for more detail). Tiering information in this way would help participants to establish an initial understanding of the Project and to work out their attitude towards participating, before engaging with all the detail.

- **Ensuring consistency across literature:** potential participants wanted to see greater consistency across the information, and, in particular, felt it was important to be able to cross-reference between the Consent Form and information leaflet quickly and easily. Cross-referencing sections via the use of numbering, or even icons, was suggested to aid this process.

Especially for BME audiences, the inclusion of more visual elements throughout the PIL would help aid understanding, and break up the text. The Infographic went down well with this audience due to the use of icons and diagrams and accessibility of format; using those icons to link between the Infographic and information literature could be helpful, if the Infographic does have a key role in HCP explanations.

- **Discrete sectioning:** creating clear, discrete sectioning that decreases repetition and allows potential participants to easily navigate through the information literature seems essential. Many participants suggested greater use of bullet points to highlight key information, and make for a quicker reading experience.

### **A.3: Content and Coverage**

Whilst participants were keen to understand their commitment, ensuring that the document remains concise and easily readable was a key priority for both potential participants and HCPs. The Stage One PIB was felt to be substantially too long, whereas both potential participants and especially HCPs, felt that the length of the PIL was more appropriate for the core information literature. There does also seem to be potential for less detail in specific areas (from a participant and /or HCP point of view) e.g.:

- Security: whilst an important issue for reassurance, in both the PIL and PIB this is covered on a number of occasions and at times gives more detail than needed (e.g. preventing companies looking at something that wasn't in their application);
- Detail on Additional Feedback/Looked for diseases: ensuring that focus is upon the criteria rather than the details of the specific conditions seems sensible, and some HCPs felt the conditions should be removed altogether, as they could lead to confusion amongst potential participants.

Additional issues covered in the PIB were important only to a minority. To make the core information more targeted (depending on constraints in terms of ethical transparency) these issues could be sectioned at the end as FAQs for the minority who might want to explore them:

- Police use of the data;
- What if your samples are lost or stolen;
- Where will your samples be sequenced;
- Left over samples;

- Storage techniques for DNA;
- Could I be identified?

#### **A.4: Versioning and balance of communication: cancer vs. genetic disease versions**

If feasible, creating separate versions for cancer vs. genetic disease cohort does seem valuable.

Whilst participants were not explicitly aware that the PIB was versioned, the focus on relevant examples, and in particular the potential to explain how the Project could be helpful for ‘people like them’, contributed to making the document feel more meaningful. The versioned PIB also led to lower levels of confusion in areas where the commitment is different for different cohort types (e.g. around samples required, the need for family involvement).

In general, HCPs also felt that specific versions for genetic and cancer participants would be important – both to ensure that communication was clear and accurate, and also to reflect any different concerns.

One HCP questioned the direct references to cancer within the PIL and PIB. Given that some participants may not have a definite cancer diagnosis at the time of recruitment, the explicit mention of cancer might be off-putting for potential participants, and difficult for healthcare professionals recruiting them. This was not raised elsewhere, but is worth bearing in mind in future development.

Ensuring that both versions are equally strong will be important: in the Stage One versions, the cancer version seemed slightly stronger. Ensuring that the examples are relevant, and that the benefits to each cohort are clear, will be vital.

**Secondly, specific issues which were highlighted in terms of the need for further development and clearer expression:**

#### **A.5: Feedback**

Although the PIB is substantially clearer, the complexity of the layers of feedback suggests a more visual approach may be beneficial in helping to make the different types of feedback clear, and to help potential participants grasp the options available.

Any explanation of feedback needs to be in clear language, and absolutely consistent with the Consent Form. In particular, further clarity is needed on the distinction between Additional and Incidental findings, and on the exact nature of what constitutes Incidental Findings. The criteria for both Accidental and Incidental findings are not currently cutting through.

The list of conditions included within Additional Feedback creates some issues – as potential participants often felt they needed to understand the conditions better – and HCPs certainly felt that the inclusion of the list would require additional explanation. If this is to be retained, ensuring a clear focus on the role

of this list, the criteria used in determining which conditions will be looked for (serious, treatable and rare), and removing some detail (e.g. genes tested for) would be beneficial.

In addition, there would be benefit in greater clarity around the nature and frequency of reporting results. BME audiences especially were keen to receive a written report themselves (e.g. if spending time on subcontinent/being treated there in addition to NHS treatment). Clarifying the frequency of data analysis and feedback should ensure that potential participants have a realistic understanding of any (ongoing) feedback they will receive. HCPs are also keen to ensure that the feedback timings and mechanics are feasible from a logistical point of view.

The open, honest tone used in the PIB to explain Additional and Incidental findings was largely appropriate: one HCP suggested: 'in doing this kind of work it might be possible to also detect a potential risk for other (very rare) illnesses'.

HCPs/patients with greater knowledge also felt strongly that greater transparency is needed around the possible disadvantages of opting into Additional feedback, to encourage consideration of the issue and a more informed decision, particularly in terms of thinking about the personal impact/impact on family members and the possible implications for insurance.

Where possible, reassuring potential participants that counselling will be available would help both HCPs and potential participants feel that Genomics England is looking after potential participants.

#### **A.6. Inclusion of Family members**

Participants, and family members, felt that this important issue needs greater coverage, and needs to cut through early in the leaflet. They were keen for clear explanation of the following issues:

- What commitment is required from family members and why (in PIB, the need for access to health records was not clearly mentioned);
- Who can participate as a family member, especially as Infographic mentions parents only, which can be inappropriate for proband adults (e.g. parents, siblings, adult children);
- Clarifying whether genetics patients can *only* participate if blood relations are also taking part;
- The feedback that will be available to family members, in terms of content and channel – especially if family members themselves do not have access to a clinical team.

HCPs also mentioned the need for clarity (within policy, rather than as a focus for the information literature) around the responsibility for passing on feedback to family members, especially in the instance of the death of the proband participant.

#### **A.7. Genomics/Genomic medicine**

Both terms need immediate explanation, when first used, to help participants understand the basic remit of the Project. The 'What is a Genome' Infographic (explored only at a low level) was usually felt by both participants and HCPs to be too detailed, so a clear description in one sentence would be preferred (cf. sentence in infographic "*Your genome is one whole set of your genes, plus all the DNA between your genes*").

Genomic medicine also needs explanation, so participants can imagine what this could mean; some HCPs/breast cancer patients suggest/talk about 'personalised/targeted medicine' to help communicate the idea.

#### **A.8. Commercial Companies**

Use of specific language, which clarifies the role/remit of organisations accessing the data, and focuses on the benefits these may give, would help lessen potential concerns:

- 'For scientific and research purposes' works especially well to reassure;
- Focus on 'pharmaceutical' rather than 'commercial' companies seems to give a greater sense of containment;
- Use of understandable examples in PIB (e.g. drug development, understanding disease development) also works well, but more tangential examples(e.g. data handling /analysis) can encounter the same issues as mention of commercial organisations;
- Involvement in trials was especially motivating, so worth explicitly mentioning.

In addition, any mention of the NHS helps to reassure participants and adds to the positive context in which the Project is operating. All, including BME participants, seemed especially motivated by the idea of improving/contributing to NHS treatment, and are more likely to have high levels of trust in the NHS rather than government/Department of Health.

#### **A.9. Security and anonymity**

Whilst this is an important issue, generally HCPs were more concerned about this than potential participants.

In both the PIL and PIB at Stage One, repeated references to aspects of security throughout the document were destabilising, as participants were unsure if messages are being duplicated or subtly changed. One reassuring paragraph, referencing a list of security measures was felt to be sufficient:

- Mention of use of barcode (PIB), and that storage is not on the internet seemed especially reassuring;



- Unambiguous statement in PIB that ‘we will not allow access to companies wanting to assess insurance risks or to marketing or other consumer companies’ was also strong, although currently ‘buried’ in document (Section 3, ‘Who will have access to our data’);
- For the more sophisticated, there would also be a value in reassurance that security is ongoing/developing as technology developing (specific concerns may shift and evolve here and will need to be reflected);
- Specific mention of anonymity in any scientific journals (mentioned in PIL) is also valuable;
- Final point in Section 5 (What happens to my family’s data in 2018) can be very destabilising when noticed: potential participants want to feel confident data will be protected for the duration.

#### **A.10. Insurance**

The wording used in the PIB is reassuring, and overcomes most potential concerns. Potential participants want to feel that this issue has been thought through and resolved for the full length of the Project. However HCPs/potential participants with more knowledge question whether this information is completely accurate. They would like to see a clearer statement that the agreement with the ABI will run out in 2017 and that there is no guarantee it will be renewed. They also feel that an explicit link should be made between the implications of the Additional Findings, and the fact that insurers will have to be informed of any treatment arising from those findings. In order to ensure that potential participants are fully informed, it may also be worth including a clear description of what is meant by ‘insurance’ (e.g. would affect credit rating, ability to get a mortgage etc.).

#### **A.11. Samples**

It would be useful to include a brief summary of the practicalities of sample taking, as this can be key in making a decision about participation. This would include absolute clarity on: what samples are needed (not clear in PIL); whether a separate operation/appointment is required; where samples can be taken (GP/local hospital).

### **B. Consent Form**

Key recommendations for the optimisation of the consent form follow.

#### **B.1: Consistency across information literature and consent form**

Create consistency across information literature and consent form to ensure that it is simple for potential participants to cross-reference and to access further information when required. More specifically, this includes:

- Consider the use of numbering or icons to allow participants to cross reference between documents, along with a consistent structure;

- Ensuring complete consistency of language across PIL and consent form, so that no new concepts/ phrases are introduced in the consent form (e.g. explicit reference to ‘study monitors’, ‘international researchers’, processes other than genomic sequencing, and access after death are all more explicit/mentioned only in consent form and not in PIL).

## **B.2: Simplification**

- Simplify information provided as much as possible, to ensure focus on key issues, with additional information contained within the information literature only (e.g. lists of healthcare information sources);
- Ensure sentence construction throughout is as clear and unambiguous as possible;
- Consider larger font, and clearer font style.

## **B.3: Feedback**

Ensuring greater clarity and simplicity around feedback options is vital – current presentation and language used creates a high level of confusion and ambiguity. In particular, the following were suggested:

- More distinct descriptions of ‘Looked for additional findings’ and ‘Conditions beyond the pre-agreed list of looked-for findings’ – the similarity in descriptions used often created confusion;
- Clearer communication of the difference between Additional and Incidental findings, to ensure participants understand these thoroughly, and in particular what type of conditions are covered under ‘Incidental findings’ – currently the focus on lack of feedback here can lead some to assume they will be given no feedback at all;
- Ensuring that carrier status is clearly explained within the information literature, so that participants can make informed choices here.

## **B.4 Practicalities of completion**

In this version, potential participants could struggle to understand what they would need to do if not consenting to a particular item, and questioned whether not initialling would be sufficient to convey lack of agreement. This needs to be clarified, especially for points that are not obligatory (e.g. consent around carrier status).

## **B.5 Versioning**

If feasible, versioned documents would ensure that exact nature of samples could be referenced more explicitly.

Some who had been involved in the pilot also questioned whether versioned copies (e.g. for parents of proband children) would be available, to ensure each consent form is sufficiently ‘targeted’.

## B.6 Wording issues

A number of specific wording issues would benefit from reworking to clarify meaning:

- Point 7 ('Together with my donation of access'): can currently suggest organ/body donation;
- Self-reported health information' (point 6); social care records (point 8); 'extended clinical care team' (point 15)

As in the PIB and PIL, references to commercial organisations can be unpopular, and, explicit reference to the NHS, and to pharmaceutical companies and/or the goals of the Project could help reassure, with 'Scientific and medical purposes' (point 9) operating as a strong phrase to reference the goals of the Project.

Throughout, more frequent use of the words 'anonymous' or 'non-identifiable' when referring to samples/data (e.g. on Point 3) would also be helpful.

## B.7 Consider the broader process around the consent form

HCPs were keen to ensure that those administering forms were fully trained – given that this might not be senior clinical or specialised genetics staff.

## C. Infographic

Whilst the infographic was generally deemed very strong, a small number of optimisations emerge:

- For HCPs, the Infographic was not tonally appropriate for information/consent literature, due to the emotional even coercive language, and references to personal benefits
- **'Observable traits'**: this phrase, and the 'eyeball' visual need to be clarified or removed; language used needs to be consistent with that in other information literature
- **Practicalities of viewing**: Consideration needs to be given to the colour contrast between background and text, and also to the best presentation if used on paper. Currently the Infographic is substantially more effective onscreen.
- **Focus on figures**: Giving further justification for figures used, and why the total doesn't add up to 100,000 would be beneficial.
- **Family Involvement**: Ensuring that it is clear that other family members (e.g. siblings) can participate might be helpful
- **Practicalities of participation**: As these are not covered in the document, an additional infographic could be called for

- **Genome icon:** there is some suggestion that this may not be the clearest icon to use/does not immediately reference DNA for potential participants

## **D. Children's information Literature**

### **D.1. Visual approach**

Whilst the visual approach in general was felt to be tonally appropriate, lower use of visuals was suggested to ensure that the document feels quicker and easier to read.

### **D.2. Language and expression**

Whilst the language used was generally praised, a small number of suggestions emerged for optimisation:

- Replace the word 'sick' (which could be associated only with vomiting) with the broader 'ill'
- Ensure that it is clear if children can choose between blood or saliva samples;
- Whilst the cake analogy was liked, some suggested a more positive expression than 'burnt' to express genetic mutations;
- Ensure that stressing anonymity does not become suggestive of secrecy, and that children are encouraged to talk about the Project should they want to;
- More information on practicalities of sampling (e.g. whether samples can be gathered as part of routine appointments) would be welcomed.

## **E. Young People's Information Literature**

### **E.1. Language and complexity of ideas**

Young people were keen for more complexity in terms of language used (to reflect their growing scientific knowledge) and the concepts explored. More specifically, the following were suggested in terms of language:

- Use of more scientific, and adult vocabulary – e.g. 'characteristics' rather than 'tell our body things' (p.4); 'parent or guardian' rather than 'mum or dad' (p7);
- Including, and also providing explanations of, technical terms (e.g. genome) – glossary or hyperlinks to allow participants to explore these terms were suggested;
- Avoiding 'over' explanation of simple ideas (e.g. flexibility in appointment scheduling);
- As for children's literature, 'ill' was preferred to sick, as sick suggested vomiting only.

Young people felt many key elements were not sufficiently explored and were keen for more detail on the following aspects of the Project:

- The nature of the project, especially: the ongoing commitment/database role, and the implications of this; and the use of health records as well as genomic information;
- The Project's goals and aims;
- The scientific approaches to be used in the Project;
- The role and importance of sibling/parent;
- Practical detail around participation;
- Even, the nature of feedback.

### **E.2. Structure and format**

A more natural 'flow' was desired, as the Stage One literature was felt to be repetitive at times. The presentation of text in different formats was also criticised, for creating confusion around reading order, and a more coherent presentation style was desired

### **E.3. Visual approach**

Young people were keen for a lower use of visuals, and felt that it was not important to have a visual to illustrate every point. They were keen to see a consistent visual style, with a scientific and technical look, and sophisticated visual references, rather than simply seeing visuals illustrating every point, with one particular visual (p.11) felt to be hitting the right tone.

### **E.4. Tone**

Young people were keen to see a responsible, direct tone, and for the document to present them with information, but leave them to make decisions, so a non-didactic approach is vital.

Finally, young people also felt that the document failed to capture the excitement that initial information about the Project could generate, and were keen for the Project's groundbreaking nature and distinctiveness to cut through.

## **F Assent Form**

Only minor suggestions emerged in terms of optimising the assent form:

- Ensure that it is clear how the 'Yes'/'No' boxes should be completed e.g. ticked or initialled; and that the presentation of these is equal (No appeared bold in the current version);
- Ensure space for signature is very clear, and that sufficient space is provided for younger children;

- Consider rewording Introductory sentence to a warmer, more accessible expression – ‘Please circle if you agree with these statements’ was suggested in one YPAG;
- A small number of parents suggested simpler and more open questions and higher levels of reassurance around the option to refuse assent – but most children and young people seemed to feel current expression was appropriate.

Some did question whether children at the younger end of the age bracket would understand the process of signing, or have a ‘signature’.

### **G Additional themes from Children and Young People’s sessions**

A number of suggestions emerged at a general level in terms of Children’s and Young People’s literature:

- Providing the information proactively as participants reach age milestones, to ensure that their understanding of their commitments continues to develop (e.g. sending 11 yrs+ literature, and adult consent literature through to participants in advance);
- Consider parental leaflets, to help guide parents in conversations around the Project with proband children and siblings.

## 4. Stage Two Findings

### 4.1: Background and context issues

#### A. Issues of particular concern to participants

At Stage Two we returned to speak to a selection of respondents who had participated at Stage One. In the intervening period between Stages One and Two a number had reflected on the Project and the commitments involved, and as a result raised a small number of specific issues, which they felt strongly about, when we returned to speak to them again.

- As explored in Section 2.2, B2, the issue of what happens to findings beyond your lifetime/the 'legacy' of passing access to your information to future generations had come to the forefront for some. The Stage Two literature prompted further reflection on these issues, as the PIL and Consent Forms are considerably more explicit about the use of samples and information after participants' deaths (including the mention of benefiting family in point 20 of Consent Form). Some of those we spoke to were very keen to be able to 'pass their data on' so that future family members could continue to benefit.
- As explored in Section 2.1, A, (Differences between the cancer and rare genetics cohort), the issue of timing was raised again as an issue by a small number of cancer participants; they were very aware that consenting within the short time frame prior to operations could add stress and needs to be handled very carefully to avoid alienating, or over-burdening potential participants.

It was expected that the recruitment process would be approached with sensitivity. Beyond this, the possibility of a staged consent, that would allow cancer patients to reconsider participation after treatment/having come to terms with their diagnosis, or the idea of being able to revisit their commitment after treatment (e.g. by looking through a longer booklet/asking more questions) were both suggested.

#### B. Responses to the concept of a longer booklet

During Stage Two we explored with respondents whether the PIL gave them sufficient information about the Project, or whether they saw a need for a longer document that would cover a more extended set of issues/some issues in greater depth. Part of this discussion also looked at the role/timing that a longer document might play within the overall consent process.

The majority were positive about the idea of a longer booklet or FAQ document, which they could use as a reference tool, and seemed to envisage a number of potential roles for this:

- For those looking for more detailed information on specific issues, which they acknowledged may be of niche interest and therefore would not need to be included in the core booklet; suggestions for contents (largely based on issues they recalled from Stage One) included:
  - How data protection will continue to be developed;
  - The charging structure for private companies accessing data;
  - Why might Genomics England send samples overseas, and whereabouts;
  - Why samples might be banked for a long time (as well as retaining genomic data);
  - What is covered under 'digital images'.

*I think a third longer, more detailed document or booklet should be produced. So that people can dip in/out as suggested is a good idea, people can get answers to any questions they may have in more detail (Cancer participant, female)*

- For those who consent at speed (i.e. cancer participants) and want time afterwards to consider the project and think about the implications (this may be the case especially if PIL/consent form are in electronic formats):

*Your brain goes into freeze – you need to be able to absorb things when you're ready (Cancer participant, female)*

*You can appreciate it in your own time – if something's not clear, you can look at it and read it in your own time (Genetic participant, parent of proband child)*

- To provide more excitement and energy around participation. A few participants felt that the consent document – whilst clear – didn't capture the excitement generated by such a groundbreaking initiative, and could see a role for a more 'promotional' style booklet which could cover: more about the project's goals and aspirations; the reasons why the Project is only possible now; the kind of research that might be possible and the benefits it might lead to:

*I think people would be interested to know more about the project because it's such a new thing (Cancer participant, female)*

- Some participants anticipated that this could be a more visually engaging/glossy document which they would keep on file/for posterity to read for more general interest and to show to others:

*I would definitely want something that I can take home, to look at if I need to (Genetic participant, female)*

There was an expectation that any additional information would be available both on paper and online/electronically:

*I think the website would be better with more extensive FAQs – the documents are massive as it is and I think another monster document would put me off (Genetic participant, female)*



A few of those we spoke to were very clear that they wouldn't want or need to have any more information, and might even find it overwhelming, but these were in the minority (and, it should be noted, they generally still wanted something – in paper or online – that they could refer to in the future):

*I am not sure what value this would be. The new document is quite comprehensive and provides a good summary. Too much detailed, complicated information may confuse people. A copy of the patient information sheet should be provided for the patient to keep as it is informative and there is the option to ask further questions at any time in the future (Genetic participant, female)*

*I don't think there is a need for a third document, the patient information leaflet explains more than everything that I need to know (Cancer participant, male)*

## 4.2: Responses to the new PIL (VERSION 0.10)

### A: Overall responses

Encouragingly, the vast majority of those we spoke to at Stage Two felt that the new PIL represented a considerable improvement; it was deemed clearer and much easier to understand. This was particularly the case for those who had read the PIL at Stage One, although even those who had looked at the Stage One PIB often appreciated the shorter length and more structured, targeted communication of the new PIL.

Research participants identified the main improvements as being substantially more accessible language (especially compared to Stage One PIL); and greatly enhanced structure and flow making it easier to read and to assimilate. Most participants felt they had understood the core issues from reading this second stage PIL:

*I felt like I understood it a lot better this time, and it was a lot clearer (Cancer participant, female)*

*Everything's explained better now – with bullet points and the numbers that work across – rather than paragraphs and paragraphs of writing (Genetic participant, parent of proband child)*

*The difference was incredible ... about a thousand times better... The language makes you feel a lot more in control (Genetic participant, female)*

*It's a huge improvement – much clearer, it flows better, a good overall picture (Cancer participant, female)*

*I think this edit is a lot better than the first edit, it's clearer to understand what it's talking about ... It's understandable (Cancer participant, male)*

NB Participants certainly benefited from reading about the Project for a second time; however these improvements do also seem to be very directly driven by changes made to the document.

In general, the new PIL and Consent Form also work well together, with very few inconsistencies, and with a stronger feeling of coherence.

Tonally, the accessible language creates a more positive approach than the Stage One PIL, but can lack excitement for some.

In general, potential participants felt that the document treads a fair line between explaining that the project may not help participants directly (e.g. feedback may not arrive in time for your treatment), while also giving a sufficient sense of how your participation will help others/might even help you in the future. However, there was interest, particularly from genetics patients, in hearing more about how the project might impact on patient prognosis and on understanding rare disease, with the examples from the Stage One PIB and the Infographic favourably recalled.

It is also worth mentioning that some potential participants mentioned the Infographic and expressed surprise/regret that this appeared to be ‘missing’ from the re-worked document. This element was extremely popular at the first stage of research, especially because, as a visual overview of the Project, it quickly helps to establish an early understanding of the Project and the commitment required. It also played a role in the first stage of making potential participants feel excited about, and engaged with, the project. A number of potential participants also welcomed information being presented in a more visual format.

*I did find the flow charts [i.e. the Infographic] from the original document quite useful. One of the things I found with the original document was that it was quite wordy and the flow charts split that up a bit (Genetic participant, female)*

## **B: Responses to language and structure**

As noted above, the **structure** of the new PIL was felt to be an improvement over both the PIL and the PIB looked at in Stage One.

In particular, the following structural elements were praised:

- The addition of ‘key point’ boxes, which make the document feel well-organised, logical, and give focus to key issues; the issues pulled out were generally felt to be the most appropriate ones. They helped participants to scan, as well as to check their own understanding:

*They highlight the important information and draw your attention to the bits you really need to know (Genetic participant, female)*

*I think the boxes are really good. I was reading them after I'd read the main bit of detail just to make sure I'd understood it all (Cancer participant, female)*

*I like the addition of the key points. I feel like this breaks up the document more (Genetic participant, female)*

*These (key points) worked so much better – people want to be able to scan (Genetic participant, parent)*

*of proband child)*

- The much greater use of bullet points contributed to making the document more digestible, and easier to skim. The bullet points also work to identify the key pieces of information, enabling patients to focus on what they need to know:

*Bullet points make such a difference – you can scan (Genetic participant, parent of proband child)*

- The use of numbering to cross-reference sections across the Consent Form and PIL enhanced the impression of accessibility, although it is worth mentioning that it seems more likely that cross-referencing will occur from the Consent Form to the PIL (i.e. ideally both documents would be cross-referenced to each other):

*Linking the documents is a good step and improves the intelligibility of the consent form (Genetic participant, female)*

Although the structure is much improved, at points the document could still feel somewhat repetitive. This was especially around sections 6 and 7 vs. sections 9 and 10, even into 11 and 12, which all appear to be covering issues around data protection/who will access your information. Sections 6 and 7 were also criticised as they are both covering the remit/commitment of the Project (i.e. setting out what health records will be accessed), as well as touching on issues of access and security; ideally potential participants wanted these dealt with separately.

The top level sectioning (e.g. ACCESS TO DATA AND CONFIDENTIALITY; RESULTS 2) was often missed. Titles at this level do not appear to be used consistently in the document, although they could help with navigation and sectioning if given a clearer/more prominent role:

*'Results 2'. That's a bit odd, have I missed Results 1 somewhere? Is this something to do with what's gone before? (Cancer participant, female)*

*I think that it may be quite difficult to navigate this document alone, as I still found myself not quite sure which sections went with what (Genetic participant, female)*

The new PIL was regarded as quite **lengthy** and was certainly longer than many potential participants ideally wanted. However many acknowledged that this length may be unavoidable for consent to be fully informed. The level of detail given was generally felt to be appropriate, and respondents struggled to identify sections/issues that they would be happy to see cut:

*It is very long ... but it's a very serious thing you're entering into, so it needs to be detailed (Cancer participant, female)*

*On the second read I was glad – it felt like you were being fully informed... (Genetic participant, female)*

Respondents praised the document for its much more straightforward, even reassuring, **tone**, in comparison to the legalistic or technical approach of the Stage One PIL that many had criticised. The

language was felt to be warmer and more accessible, and most found the document much easier to read:

*The language is less academic and more accessible to the average person (Genetic participant, female)*

*I feel like this is definitely aimed at Joe Bloggs (Cancer participant, female)*

*It felt like they were thinking about me, rather than getting things from me (Genetic participant, female)*

However, especially for those potential participants who had seen the PIB (or loved the Infographic) there was a feeling that some of the excitement – around the uniqueness of this project, and what participation can achieve – had been lost:

*I missed the first really bright and sparkly paragraph that made it sound exciting. This feels a bit flat [in comparison to PIB] (Genetic participant, female)*

One participant with a HCP background felt this was entirely appropriate and preferred this flatter, more straightforward style.

*I feel like it's less promotional, less like it's trying to market something, which I like (Genetic participant, female)*

## **C: Specific issues and concerns**

Despite these significant improvements, the research identified a number of aspects where further development of the PIL would be beneficial to ensure full clarity and understanding. More detailed feedback on specific aspects of the document is provided in Appendix 8, but here we pull out the key areas where further content/explanation would be helpful.

### **C1: Family Involvement**

- With the genetics version, potential participants still felt that the involvement of family members was not clearly explained, and wanted more explicit detail on:
  - The need for family member involvement, and which family members this could be;
  - What form their involvement would take;
  - What feedback they would get, and how this would be disseminated to them:

*It wasn't clear to me that I would need to get members of my family involved at all (Genetic participant, female)*

*I am confused by this as suddenly other family members are involved. Does this mean participants need to nominate two relatives to have blood tests? There is nothing else about this in the rest of the document which covers getting participants' blood tests but nothing about relatives and their consent to use their genomes for comparison. Very confusing. (Genetic participant, female)*

Whilst our focus was on proband participants, they questioned whether family members would glean sufficient information/feel that this document was tailored to their needs. One parent of a pro-band child interviewed also felt that the PIL is firmly 'adult only' information. As per stage one, guidance for parents (e.g. how to talk to your child about the project; what this will mean for your child/your family) could be suggested as a separate/additional document.

## **C2: Different types/levels of findings**

- **Distinction between different types of Findings:** overall, the treatment of this issue seemed much clearer than the original version: more participants tended to pick up that there are two types of feedback – one on their condition, and one on 'other issues' – and that they had a choice whether or not to receive the latter.

However, as explored in Stage One (see Section 3.1, C3) the words 'Additional' and 'Incidental' suffer from sounding/looking relatively similar; this was highlighted when looking at the Consent Form, as participants were frequently confused by incidental findings at this stage and couldn't recollect what they had read in the PIL. In particular, the phrase 'incidental findings' did not seem to be a phrase that potential participants immediately understood or were able to play back with any confidence.

As such, a clear, introduction box that outlines the different feedback types (three for cancer, four for genetics) and broadly what each covers, might help participants to hold the different types of feedback clearly in their heads.

- **Understanding Additional Findings:** while some were certainly positive about the simplicity generated by removing the list of conditions, a number then felt it was difficult to get a sense of what Additional Findings might include.

*I really like the fact this doesn't have a long list of cancers. But I'm just not sure that this explains it as clearly as the first leaflet [PIB] did (Genetic participant, female)*

The key point box for this section was felt to be somewhat wordy and unclear. Understanding was also hampered by the fact that the issues were not then re-stated within the main body, meaning there was no opportunity to read them again/see them set out with a different wording (as is the case with most of the other boxes through the document).

The focus here needs to be on communicating the most important points:

- That these conditions are rare (although care needs to be taken with expression here to ensure that there are no references to the likelihood of having/not having one of these conditions at an individual level);
- They can be serious or even life threatening;

- They are treatable under the NHS;
- And that more detail can be obtained from HCP taking consent (some suggested online availability would be helpful here too).

The Consent Form wording could be praised as clearer than the new PIL here:

*This is a clearer explanation than there was in the main leaflet (Cancer participant, female)*

In particular, the Consent Form communicated more explicitly that the person taking consent would have a list of the conditions and would be happy to discuss them. It may be worth highlighting the availability of this list within the PIL.

Most of our participants didn't notice that they were now not being asked for explicit consent for new additions to the list, and the removal seems to make understanding easier. However, one participant with a HCP background had ethical concerns about the level of disclosure here.

- **Understanding Incidental Findings:** this continued to be challenging and the current expression (in both PIL and Consent Form) failed to clarify. Potential participants were unsure what results this might include and questioned why they would not be informed of this information.

*I really don't understand 'Incidental findings' at all - I'm guessing it means it won't affect my health, but it's not clear and I would need clarification (Genetic participant, female)*

Moreover, 'Incidental findings' could be missed in the genetics PIL, as the insertion of the section on 'carrier status' feedback tended to dominate.

- **Carrier status:** (NB Genetics patients only; not explored at Stage 1.): a few in our sample had already considered this issue due to their particular personal circumstances and for them this was an interesting and engaging additional option.

However, it was not clear from the literature that this type of feedback would only be offered to existing parents who are taking part in the Project with their child, and as a result a number of questions were raised about the logistics and process of consent. Clarifying the criteria for eligibility, and ideally offering a versioned document for parents/non-parents, would help to overcome many of the points raised here. If a versioned document cannot be offered, then the research suggests that there may be a risk that some will misunderstand, or even challenge, the criteria determining who will be offered these tests/feedback.

The issues that were felt to be unclear included:

- Questioning how both partners could be participating in the Project (as they are not blood relations);

- Questioning why this is only being offered to those already in a relationship, and the exclusion of those who are currently single but may consider having children in the future. As such, a number of dilemmas emerged: what would happen if a participant develops a relationship after initial sign-up and then wants to be tested? Could an individual find their own carrier status? What about those in gay relationships/actively single parents who may be seeking to become parents?

*What happens if you're single, or if you're gay, would you still get the feedback? I just think it sounds a bit discriminatory. I'm a bit surprised (Genetic participant, female)*

- When it comes to consent, understanding more clearly what would happen if one participant consents and the other doesn't;
- A minority felt it would be important to give detail about the types of conditions that would be looked for here.

As this issue was not explored in detail, we feel that further exploration around the policy issue and how it can best be expressed/communicated might be advisable. As for many issues, some suggest that an overt offer of genetic counselling will be important here.

### **C3: (Future) health records**

Overall, the new document is more explicit in communicating that the Project includes access to health records, as well as sample-gathering.

*This is great as I didn't realise it would be medical records from birth so adds clarity and transparency (Genetic participant, female)*

However, not everyone understood that this includes ongoing access to (updated) health records and this still needs to be made more explicit.

The clearest expression here was *'This will include receiving annual information from your clinical team...'* which communicates both that the information will be updated and that this process will occur automatically. That said, this particular phrase suggests that this is only information relating to the patient's main condition, and so would need to be changed to reflect the fact that wider health information will be gathered (if this is the case).

Other phrases, including *'... continue to access your health records electronically into the future'/ 'you are agreeing that it can be continually updated in the future'* (used in Key Point) are less explicit and could be overlooked/not fully assimilated. The Key Point box here needs to set this issue out more overtly.

### **C.4: Confidentiality/anonymity:**

In general this was an area of real improvement, and most felt reassured about the processes in place. However, there was some confusion around how information can be simultaneously anonymous, and also fed back at an individual level to clinical teams. The explanation about the data being identified by a code (as per the Stage One PIB) is included, but comes late in the document (pg. 6). The expression used in the Stage One PIB (also used in the new YP Literature) - 'Your samples will have a barcode attached for identification' – seemed to work especially well. In addition, inserting the word 'anonymous' when talking about access throughout the document, especially commercial access, would help provide reassurance.

#### **C.5: Commercial/profit-making companies:**

As explored in Stage One, this phrase could be off-putting, especially as, for some, it brought to mind database sales techniques. Ideally, when commercial companies are first mentioned (P1), it would be helpful to either provide a brief explanation, or to reference a later section. The current explanation (on P6) comes too late for many. Communicating (as per the Stage One PIB) that commercial companies are vital to developing many of the drugs and therapies that go on to be used by patients in the NHS would be valuable:

*No examples of commercial companies, so I can only think mailing lists/junk mail sort of arrangement (Cancer participant, female)*

*It implies to me that results can be sold – and makes me think of junk mail mailing lists (Cancer participant, female)*

Given this, sections 11 and 12 overall could benefit from slightly more explanation and reassurance. In particular the sentence in the third sub-point – 'Profit making companies.... large amounts of data' – would benefit from re-working to make clear that the goals will be for the benefit of patients and to state who can and cannot access information and in what format (covered in preceding section so may just need cross-referencing/reminding).

*I want to know that me taking part is going to be valuable and worthwhile. Is the data going to be available to the people who are going to make the best use of it in that field and not just going to the highest bidder (Cancer participant, female)*

As previously mentioned, the phrase 'for scientific and medical research purposes' worked well in Stage One, and might be usefully deployed here.

#### **C.6: Practicalities**

As at Stage One, potential participants sought more information about how samples would be taken, and where/by whom. A sentence explaining whether sampling will take place within a separate operation/appointment would be beneficial ('part of your routine care' is not sufficiently explicit).

#### **C.7: Versioning for cancer vs. genetics**



In comparison to the Stage One PIL, the Stage Two PIL was versioned which was welcomed. In particular, versioning around the samples required, the explanation of why they are looking at the whole genome, and the fact that cancer patients may not benefit from results being returned in time, resulted in clearer communication, with participants more confident about what was being asked of them, and why. The only exception here was a few minor references to results not being returned in time to impact on treatment, which was not felt to be appropriate for the genetics version.

### **C.8 More minor issues:**

Below we outline a few areas where wording and expression could still be further optimised. These issues were mentioned by smaller numbers of participants/are less key:

- The introductory sections (P1) – ‘Your Genome’, ‘What can sequencing a whole genome tell us’, and ‘How this might affect patient care’ up front generally worked well, and helped to establish reasonable understanding among the potential participant audience from the outset; the focus on the NHS was also reassuring.
- However, it would certainly be valuable to explain the benefits of genomic medicine more clearly. As at Stage One, this was not a term that most were familiar with, and there is potential to generate greater understanding/support for the Project if potential participants have a sense of what the benefits will be for others like them.

*They're still not really explaining what genomic medicine is (Cancer participant, female)*

In addition, mention, at this early stage, of industry, commercial organisations and the UK economy could feel less appropriate, although an explanation here that the commercial organisations involved are predominantly those working in healthcare/pharmaceuticals would ensure this element felt more relevant.

*I don't understand where the economy comes into all of this, it just seems irrelevant, the Project is about helping patients and learning more about rare conditions (Genetic participant, female)*

- The Section ‘Why have you been invited to join’ was generally acceptable, although the cancer version could benefit from a slightly more detailed explanation to ensure that potential participants grasp the basic idea that the genome of their cancer is different to their healthy genome, and that this Project will compare the two. The explanation of this from the Stage One PIB was felt to be very clear.
- The options for leaving the Project (section 20) appeared rather lengthy and over-complex, especially at this point in the document. Some questioned whether this level of detail about leaving is required at the consent stage, when the primary need is to understand that they are free to leave if they want to. Some potential participants felt that they would only need to read about the various ways in which they could leave the Project if they were seriously

thinking about opting out. The point was also made that it would be beneficial to close the document with a positive thank you for potential participants.

- As in the first stage, some found the 'potential risks' trivial and unnecessary:

*A risk of bruising – that's pretty silly! If you've got cancer, that doesn't really matter (Cancer participant, female)*

- The phrase 'Condition regarding which you joined ...' was criticised as clumsy and unclear by a number. Alternative suggestions included: 'the condition that resulted in you joining', 'condition for which you joined'.
- Section 11 and 12 'Who can access my data': the sentence 'You can ask for a copy...charged for providing this' confused a number of potential participants. It wasn't clear to respondents what data is being offered here, so some assumed this was saying that they would need to pay for any feedback; it needs to be made explicit that this is referring to the full sequenced genome. The explanation from the earlier PIB which described the scale of the data involved (i.e. more data than can be held on a laptop) seemed to help potential participants accept this charge.
- Insurance: nearly all were accepting of the explanation and wording around this issue in this re-worked PIL. However, one participant with a healthcare background remained concerned that the literature does not make clear that the agreement might not be renewed/is not legally binding, and continued to question whether the implications of testing/Additional Findings would be fully thought through by potential participants.

*I was shocked to see it said that it will definitely be updated – they don't know that (Genetic participant, female)*

- Counselling: some felt that the offer of counselling should be a vital part of any agreement to participate, given the potential implications of the findings and the decisions that may have to be made as a result; among those who were more informed (genetics patients) the PIL was not felt to give enough reassurance that counselling will always be available at feedback stage (and one respondent felt that ideally counselling/greater prompts to consider implications should be available when deciding about whether to opt in to Additional Findings).

*There are lots of things that would normally be discussed before having a genetic test ... Normally if you have a genetic test on the NHS you're offered an appointment beforehand to discuss the implications of the results (Genetic participant, female)*

*I don't think 'signposting' you to support is good enough. They need to offer genetic counseling if they're giving you feedback about this kind of thing. I think they've got a duty of care here (Genetic participant, female)*

The inclusion within this document of carrier status further increased the importance of counselling being offered for some.

- Numbers of patients/100,000 Genomes: the document still left some people questioning the figure of 100,000. This was both in terms of understanding why this number of genomes has been chosen, as well as also understanding the context to this figure: is this a lot or a little; what will 100,000 allow the Project to do? There were also some who picked up on the mention of 70,000 NHS patients on pg. 2 and questioned how this could lead to the sequencing of 100,000 genomes. Further explanation/breakdown of the various numbers involved might be helpful.

### 4.3: Responses to Consent Form

#### A Overview

By and large, the Stage Two Consent Form, while still long, was felt to represent an improvement, with clearer and more accessible language.

*I feel like it's a good balance between the formality of a consent form, which you need to have, because it is an official document, and more accessible language (Genetic participant, female)*

In particular the points covering Main genetic findings and Additional findings (point 16 and 17), although still wordy, were improved. The distinction between them was frequently better understood on the Consent Form vs. the PIL. Two elements seemed to be particularly helpful here:

- The option to tick yes or no for Additional Findings;
- The explicit inclusion of the words 'optional' and 'non optional' on points 16, 17 (and 18).

Some suggested that, for further clarification, especially on point 17, it could be bulleted or broken into smaller paragraphs.

However, further other areas of feedback required further development, outlined below:

#### B: Specific issues and concerns

##### B.1: Points 18 & 19(Pre-symptomatic Carrier Testing and Incidental findings)

There was consistent and widespread confusion around points 18 and 19, in line with the lack of clarity thrown up by the PIL.

Part of the confusion around point 18 was generated by the lack of consistency with the PIL in some of the terminology used. For example, 'pre-symptomatic' and 'X-linked conditions' do not appear in

the PIL. Point 18 also made explicit the need for joint consent, which prompted some questions/doubts about how this process would actually work in practice:

*What happens if you're signing separate consent forms at separate times? What if one party doesn't consent? Surely consent needs to be an individual matter, you can't do it together (Genetic participant, female)*

Point 19 remained unclear, as potential participants were unable to imagine the kind of findings this refers to. Further clarification on the types of findings that will not be fed back would be beneficial so that participants fully understand what they are consenting to here.

## **B.2: Point 20 (Pre-symptomatic Carrier Testing and Incidental findings)**

Point 20 was particularly problematic, in part because it was not covered in the PIL, so respondents were rather taken aback when coming across it in the Consent Form. Broadly it raised high, but confused expectations, around proactive contact of family members in the event of (any) unexpected findings being generated.

For some this was an exciting option, but they questioned the logistics of how this might happen (e.g. how will family members be tracked/do family members themselves get a choice about which findings are fed back; how long does this option continue?).

For others, however, this felt like an unappealing loss of control, very much at odds with the assurances of confidentiality and security throughout the documents. Two issues around confidentiality seemed particularly problematic:

- Firstly the understanding that the proband participant could not name which family member/s they would be happy to be contacted;
- And secondly that there appear to be no assurances over how this process could be achieved without naming the proband participant and revealing the condition which led to them joining the Project.

A small number of those we spoke to were very concerned by this issue; this included one potential participant who was estranged from part of her family and who strongly objected to relations, whom she is no longer in contact with, learning medical details about her condition.

In addition it was not clear from this point, if this process would happen after your death or whilst you are still alive:

*They're saying it might benefit my family, and you will share the information with them – but there's nowhere where you have a choice ... it doesn't feel like you have control (Genetic participant, parent of Proband adult)*

*Oooh, that says to me that when I'm dead and buried then my family could access my carrier status. I*

*don't think that's what they mean, but it's a very open statement and leaves you to read between the lines. It needs to be much clearer what the implications are (Genetic participant, female)*

It should be noted that the reference to 'normal clinical practice' in this point is not helpful as potential participants are not aware of what this means.

There was also some confusion generated by the current layout of the Consent Form. Point 20 looks as though it follows directly on from, and is part of, point 19 – Incidental Findings. This underlines the importance of using headings, bolding and sectioning in a clear and consistent way throughout the Consent Form.

*So [in 19] ... they're saying it won't be fed back.... But here [20] they are saying it will get fed back to your family. So I had understood it might benefit my family, my daughter or grandchildren... but it's not quite adding up (Cancer participant, female)*

### **B.3: Additional issues**

Finally, we note a small number of more minor issues arising from the Consent Form:

- Point 4 needs to clarify if blood *and* tumour/tissue sample are required for cancer version and Point 8 needs to be versioned for genetics vs. cancer;
- Point 13 could still do with further editing/feels wordy;
- For the cancer version, 'missing' point (point 18) needs to be clearly explained, or fully renumbered, so participants don't feel anything is missing/they are being fully informed

## **4.4. Stage Two Recommendations (PIL and Consent Form)**

### **A. Recommendations for the PIL document**

#### **A.1: Structure and Layout**

- Key Point boxes: the structure and layout of the revised PIL work very well. In particular the Key Point boxes represent a considerable improvement over the earlier version. We would recommend reviewing the wording in the boxes to ensure that each one is as clear as possible and accurately presents the most important points, as the evidence suggests that in some cases, this may be all that some participants read.
- Cross-referencing: the ability to cross-reference between the PIL and the Consent Form was welcomed, although ideally, the cross-referencing would work in both directions, so that patients can easily check back to the PIL when reading the Consent Form.

- Length: although the document can feel quite lengthy, respondents struggled to identify areas which could be cut. That said, sections 6/7 and 9/10, even 11/12 could feel repetitive and would probably benefit from tightening up. Ideally the key issues around data security and confidentiality should be covered concisely in a single section, to provide maximum levels of reassurance to participants.

## **A.2: Content and explanation**

- Family Involvement: for genetics patients this remains a point of weakness in this document. It is not yet explicit enough about the need for two blood relations to participate. Beyond this, more information is required about what will be expected of blood relations (i.e. just blood samples, or health records as well?), what feedback they will get, and how they will receive this feedback. Some would like to see a separate document for family members, although if better information about family involvement can be provided and more explicitly flagged, then we feel that a single leaflet could suffice.
- Findings: this can still be an area of confusion. Although this version of the document is an improvement, a visual aid that clearly sets out the different feedback types and broadly what each covers would, we believe, help considerably with levels of understanding.
  - For Additional Findings specifically, the key criteria for the conditions being looked for here (that they are serious, treatable and rare) need to be emphasised in the body of the text and in the Key Points Box. While it seems sensible to have taken the list of conditions out of the literature, the research did suggest that patients would like to have a sense of the kinds of conditions included; stressing that the person taking consent has a list of the conditions and can discuss them would be useful here.
  - The section on Incidental Findings would benefit from some examples of the kind of results this might cover as currently patients are unable to envisage what this refers to and this can be a cause for concern or confusion.
  - Carrier Status also threw up a lot of questions. As this area was not looked at in Stage One, we would recommend further exploration around the policy issue. Certainly we would recommend greater clarification around who will be offered these findings (i.e. parents of proband children only); ideally a versioned document would be offered to parents vs. non-parents.
- Access to health records: although this document more clearly communicates that the Project will access health records, it would benefit from being more explicit that this includes ongoing access to updated health records.
- Other recommendations are more minor and include:

- Clarifying how data can be both anonymous and fed back to clinical teams (references in the PIB at Stage One to a barcode appeared to work well);
- Giving more (upfront) detail/reassurance around the kind of commercial/ profit-making companies that will be involved in the Project and why;
- More detail on the practicalities of how samples will be taken and where/by whom;
- A slightly more extensive explanation of what genomic medicine is and how it can benefit patients in the introductory section;
- Ensuring that the information around insurance issues clearly and honestly explains the situation and informs patients of any implications for them, including making a link with the potential implications coming forward from Additional Findings;
- Clearer explanation around the figure of 100,000, how that will be achieved, and what such a large number will enable the research to achieve.

## **B. Interest in more detailed information**

- There does appear to be a role for more detailed information about the Project to be made available to participants. Ideally this would be provided both in hard copy and via the website. This additional information needs to fulfil two quite distinct roles: firstly providing more detailed information on specific issues for those who have particular concerns/interests; secondly providing a more interesting and exciting overview of the Project, including why it was conceived, what it hopes to achieve; what makes it different to preceding studies etc. This is something that participants might want to have as a keepsake/reminder of what they are part of.
- If the patient information literature is presented only in an electronic format during the consent process, then the research suggests that offering this to participants via a hard copy to take away, or through the website, would be sensible so that participants can review and remind themselves of what they have agreed to in their own time.
- We recommend considering a role for an Infographic as part of the overall set of patient information literature. Many of those we spoke to at Stage 2 were disappointed that this had apparently been 'left out' of the leaflet, as they had appreciated seeing details of the Project presented in a more visual manner.

## **C. Consent Form**

- Points 18 (Carrier Status) and 19 (Incidental Findings): while the Consent Form was felt to have improved with clearer and more accessible language, and some points made more succinct, several points remained problematic. Issues around points 18 and 19 largely reflected the problems that the

PIL revealed in terms of understanding what kind of results might be included here and, in the case of Carrier Status, understanding who would be eligible for this and why. Care also needs to be taken to ensure that there is absolutely consistency in terminology across the PIL and the Consent Form.

- Point 20 (informing family): this was more challenging, in part because this hadn't been covered in the PIL, and therefore the Consent Form was the first time that potential participants had come across this issue. We would recommend further exploration of this, but certainly the research indicates that this will be a problematic area for potential participants who can be worried about issues of confidentiality and lack of control. The literature needs to clearly address: how this will happen; why it needs to be happen; what, if any, control the participating patient can have over this process (e.g. designating which family members they are happy/not happy to be contacted, putting a timescale on when they consent to this information being passed on); and what will be done to protect the confidentiality of the participating patient.

## 4.5 Children's and Young People's Literature

These are based on responses from the final YPAG (Birmingham) – all of whom were 11 years +. As there was only one session looking at these materials, all feedback is contained within the main report. A copy of the updated literature explored is attached in appendix 10 (Children's Literature) and 11 (Young People's Literature)

### A: Overall responses to Children's and Young People's literatures

Overall, the young people we spoke to regarded both the Children's and Young People's documents as strong and they suggested minor improvements only. The overall tone and language level were regarded as broadly appropriate, the literature covered most of the key issues judged to be important at an age-suitable level. Whilst they felt the YP document was too long (and the children's also slightly lengthy) the issues covered were felt to be important, so they found it impossible to suggest any cuts.

The group were particularly positive about the inclusion of a glossary – with only minor improvements – the inclusion of key points pulled out in boxes, which they felt focused on important issues, and really helped them navigate the literature, and the overall tone of the visuals used.

As explored in earlier sessions, they did however feel that a separate booklet might be important for siblings, who would be coming from a different start point and might have different concerns. In particular, they suggested that siblings might need more support (separate to the proband child) in thinking about the implications of genetic testing for conditions already diagnosed as present within the family:

*Additional support ... do they know that there will be someone there to talk to about the implications, what might happen (YPAG, Birmingham)*



They also felt that the issues of handling additional findings, and the implications of findings, would be challenging for any child, and ideally wanted to see parent literature that covers how to discuss this with children and young people, so that they are part of the decision-making process that would affect them. They did feel that this was probably best led by parents, rather than covered specifically in the YP literature, given the complexity of the issues.

Finally, as in Stage One, they were very interested in managing the consent process as children get older – to ensure that they are in a position at 16 to make an informed decision. The idea of tiered/updated information as children get older was well received.

They also had some more specific feedback which follows.

## **B: Children’s literature: 6-10 years: suggestions for optimisation**

### **B.1 Visuals Approach**

In terms of visual approach and format, the visual included was well liked and felt to hit an appropriate tone:

*That’s just the sort of picture we always like – really cute! (YPAG, Birmingham)*

The YPAG felt a slightly more visual approach would be appropriate (e.g. additional picture; more coloured text). In terms of the overall format, they felt that aiming for 2 sides of A4 should be a maximum, but preferred a smaller leaflet format (e.g. fold out A4):

*It needs not to feel like it’s too much to read (YPAG, Birmingham)*

### **B.2 Wording and language**

A small number of low key wording suggestions also emerge:

- In general, the word spit was felt to be challenging and slightly inappropriate –it was not language they expected to read in this type of document. They suggested using ‘saliva (spit)’ for the first reference, then saliva throughout. As for previous groups, they felt it was vital that it was clear if children would have a choice of saliva or blood samples;
- Point 11: a minor issue, but reversing the first two sentences was suggested, to better answer the question posed;
- Point 12: final sentence ‘Tell your mum or dad or the doctors and nurses’ was felt to be incomplete and either needed to be part of the previous sentence, or finished with ‘if you don’t want to take part anymore’;
- Point 14: as in Stage One (see section 3.5, A3) the YPAG were concerned about the focus on 16 years as the age you reach adulthood, and felt these age cuts offs were somewhat

arbitrary. Instead, they recommended focusing on this as an age where you can have autonomy over decisions in the Project - 'You can decide for yourself';

- Finally, they suggested the document finish with a friendly sign off – e.g. Thank you for reading this, and do ask any questions!

## C: Young People's literature: 11-15 years: suggestions for optimisation

### B1: The glossary

This was felt to be an excellent concept, which would ensure that the document is accessible to all, but also gives control to young people reading the document to look up only those elements they are less confident of:

*I was just thinking there should be a glossary for some of these words, then I turned the page and there was! (YPAG, Birmingham)*

To further improve the glossary, some suggested that glossary words should be in bold from pg.1, to draw attention to them.

There was some discussion around whether the bat/cloud example within the glossary was patronising, but most felt it was a clever way to explain the idea. Removing the explanations (e.g. 'cloud – fluffy white things in the sky') might help overcome concerns for some around tone. The only suggestion was reworking the phrase 'Then they have that illness for the rest of their lives' (end third paragraph, Genes section), which was felt to be rather negative, suggesting life-long limitation, and not needed:

*It sounds a bit depressing and I don't think it adds much (YPAG, Birmingham)*

### B.2: Blood samples

Some felt the box on pg.2 had slightly the wrong focus – that when and where blood samples are given is less important than the fact that you are giving blood (and medical records). Information about the option to numb the skin before taking blood, and parents staying with you, was felt to be reassuring, and they would also like to know if the sample can be taken as part of a routine appointment. However, they felt by 11 years old, reference to 'special' cream wasn't needed/was somewhat patronising.

### B.3: Age of Consent

As throughout the young people's work, many questioned the simplicity of tying 16 to adulthood, and suggested instead talking about 'you are old enough to consent by yourself'.

### B.4: Additional issues

- There were mixed opinions on the idea of a word search (with younger being more positive) but a page for notes was welcomed.

**General points on p. 3** were all felt to be well expressed, clear and reassuring. There was some discussion of whether 'confidential' (at the end of section 'will anyone else know if I'm taking part') was too complex for an 11 year old, but most of the group felt this was an appropriate term.

- Nearly all the questions they asked spontaneously were answered, but they suggested some minor additions:
  - Clarifying that the project is being run for/on behalf of the NHS;
  - Providing a rough sense of the wait for provision of results;
  - Providing external contact information/how to find out more.