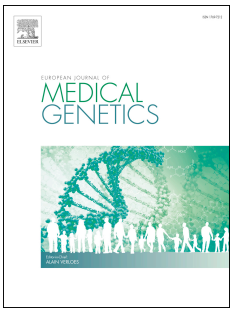

Young people's understanding, attitudes and involvement in decision-making about genome sequencing for rare diseases: A qualitative study with participants in the UK 100,000 genomes project

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PII: S1769-7212(19)30698-6

DOI: https://doi.org/10.1016/j.ejmg.2020.104043

Reference: EJMG 104043

To appear in: *European Journal of Medical Genetics*

Received Date: 14 October 2019

Revised Date: 18 August 2020

Accepted Date: 18 August 2020

Please cite this article as: C. Lewis, J. Hammond, M. Hill, B. Searle, A. Hunter, C. Patch, L.S. Chitty, S.C. Sanderson, Young people's understanding, attitudes and involvement in decision-making about genome sequencing for rare diseases: A qualitative study with participants in the UK 100,000 genomes project, *European Journal of Medical Genetics* (2020), doi: https://doi.org/10.1016/j.ejmg.2020.104043.

Author statement

Celine Lewis: Conceptualization, funding acquisition , methodology, formal analysis, investigation, writing - original draft, project administration.

Jennifer Hammond: formal analysis, writing – review and editing.

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Young people's understanding, attitudes and involvement in decision-making about genome sequencing for rare diseases: A qualitative study with participants in the UK 100,000 Genomes Project

Running title: Young people's views about genome sequencing

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Conflict of interest: C.P. has been on a secondment with Genomics England as Clinical Lead for Genetic Counselling since October 2016. The other authors declare no conflicts of interest.

Data Availability Statement: Excerpts of interview transcripts are available on request to the corresponding author.

Abstract

Genome sequencing (GS) will have a profound impact on the diagnosis of rare and inherited diseases in children and young people. We conducted 27 semi-structured interviews with young people aged 11-19 having GS through the UK 100,000 Genomes Project. Participants demonstrated an understanding of the role and function of genes and DNA, however the terms 'genome' and 'genome sequencing' were less well understood. Participants were primarily motivated to take part to get a diagnosis or identify the gene causing their condition. The majority of participants understood they might not receive a diagnostic result. Most were unconcerned about data security or access, however anxieties existed around what the results might show and the potential for disappointment if the result was negative. Signing an assent form empowered young people, formalised the process and instilled a sense of responsibility for their choice to participate. Most young people (≥16 years) had consented to receive secondary findings and had come to that decision without parental influence. Our research suggests that at least some young people are capable of making informed decisions about taking part in GS, and that involving them in discussions about testing can empower them to take responsibility over healthcare decisions that affect them.

Keywords: whole genome sequencing, secondary findings, young people, motivations, concerns, decision-making, rare disease

Introduction

The majority of rare diseases affect children and in many cases there is an underlying genetic cause for their condition (Wright et al., 2018). Many children with rare diseases, particularly those with developmental disorders, are undiagnosed (Firth and Wright, 2011). However, the advent of next generation sequencing technologies has revolutionised the way genetic testing can be conducted, enabling multiple genes or entire exomes or genomes to be sequenced simultaneously (Sun et al., 2015; Wright et al., 2018). Genome sequencing (GS) has been shown to increase diagnostic yield almost twofold compared to conventional panel testing (Lionel et al., 2017) and fourfold compared to chromosome microarray (Stavropoulos et al., 2016). The possible clinical benefits of a genetic diagnosis include ending the 'diagnostic odyssey' (Basel and McCarrier, 2017), access to information on management and therapy, a clearer prognosis, reproductive planning and opportunities to make contact with other families through disorder-specific support groups (Griffin et al., 2017; Thevenon et al., 2016). GS is therefore set to have a profound impact on children and young people with rare diseases and its implementation is being evaluated in a number of paediatric settings (Bowdin et al., 2016; Green et al., 2016; Turnbull et al., 2018).

Although a significant body of work has emerged in recent years exploring adult patients' experiences and attitudes towards GS, (Boeldt et al., 2017; Mackley et al., 2018; Roberts et al., 2018; Sanderson et al., 2015) very little empirical research in this area has included young people (Pervola et al., 2019; Raghuram Pillai et al., 2019) (sometimes referred to as 'adolescents' and defined as aged 10-19 years by UNICEF (UNICEF, 2019)). To date, the limited work that has been done has primarily used hypothetical scenarios (Hufnagel et al., 2016; McGowan et al., 2018), or assessed adults' perspectives on sequencing in the paediatric setting (Fernandez et al., 2014; Levenseller et al., 2014). Young people with health-related issues are likely to face significantly different physical, psychological and social challenges from those of both young children and adults (Frederick, 2016). They may

have specific information and support needs including peer support, provision of age-appropriate information and healthcare providers who proactively raise salient issues (D'Agostino and Edelstein, 2013) Therefore, it is important to give them a voice regarding their understanding of the benefits and potential risks of GS as well as their preferences for involvement in decision-making.

The current legal position in the UK is that children under 16 years cannot make decisions about their healthcare without parental consent, unless they prove to have sufficient maturity and intellectual capacity (referred to as “Gillick competence”) (Griffith, 2016). In other European countries, the age at which children can consent varies between 14-16, 18 or is dependent on maturity (European Union Agency for Fundamental Rights, 2017). In the United States of America, children’s consent authority differs across states (Coleman and Rosoff, 2013). In some States no particular age is required, in some it is aged 14 and over and in others in is aged 18 and over. Studies have, however, shown that young people, particularly adolescents, do frequently have the capacity to be actively involved in discussions about their healthcare, including genetic testing (McGill et al., 2018; Pervola et al., 2019) and participating in research (Kuther and Posada, 2004) The American College of Medical Genetics and Genomics recently issued a statement in which they highlighted the importance of engaging young people in meaningful conversations about the goals and implications of genomic testing and potential findings, and consideration of its personal benefits and limitations (Bush et al., 2018). Engaging young people in medical decision-making has also been shown to be associated with lower decisional conflict (David et al., 2018).

In the 100,000 Genomes Project, a United Kingdom (UK) national programme charged with preparing the National Health Service (NHS) for the introduction of genomics into clinical practice, much attention was focused on involving young people in the decision-making process, including the development of age appropriate information materials and written

'assent' forms for participants under 16 years (Genomics England, 2015). Of the rare disease proband participants in the 100 000 Genomes Project, around a quarter of them were 15 years of age or under at the time of taking part (data accessed from the Genomics England Research Environment, 11th November, 2018). In that project, consent to take part included consenting to receive a clinical diagnosis where one is found, and allowing de-identified, individual clinical and genomic data to be used for research purposes (Turnbull et al., 2018). In addition, participants aged ≥16 years were able to opt in to receive clinically actionable 'secondary findings' such as hereditary breast and ovarian cancer (BRCA1/2) and hereditary colorectal cancer (Lynch syndrome) (Genomics England, 2015). Parents of children < 16 years could also consent to receive secondary findings, which have symptoms which onset in childhood, to be looked-for in their child. These conditions include retinoblastoma, Von Hippel-Lindau syndrome, child onset multiple endocrine neoplasia types 1 and 2, and childhood onset familial hypercholesterolaemia (Genomics England, 2015).

We sought to characterise the understanding, motivations, concerns and experiences of decision-making among young people having GS in relation to both the main findings and the secondary findings.

Methods

This was a qualitative study using a semi-structured interview format to enable in-depth exploration of young people's views.

Ethical approval

NHS Research Ethics Committee approval for this study was obtained from West Midlands (15/WM/0258).

Sampling and Recruitment

The study was conducted in the UK with young people affected by rare diseases taking part in the 100,000 Genomes Project. Participants were not eligible for the Project if they had a molecular diagnosis. For many recruitment categories, it was expected that patients had already undergone clinically appropriate genetic testing, but that no molecular diagnosis had been found (Genomics England, 2015).

Participants were recruited through a children's hospital in London specialising in rare diseases. Potential participants were identified by a member of the healthcare team recruiting participants into the rare disease arm of the 100,000 Genomes Project. The inclusion criteria comprised: young people aged between 11-19 years (including probands as well as siblings undergoing GS), not affected by intellectual disability, and able to read and communicate in English. Siblings were invited to take part in the study as they were participants in the 100,000 Genomes Project and assented/consented to take part. They also had the potential to learn about secondary findings. A cut-off of 11 years was chosen as this was the age from which young people were invited to sign an 'assent' form in the 100,000 Genomes Project.

. At the end of the 100,000 Genomes Project consent discussion, potential participants were told about this interview study, and asked if they (and their parent(s) for participants aged 11-15) were interested in taking part. If so, they were asked to complete a consent to contact form. CL (first author, behavioural scientist and research lead) then sent the potential participant or parent(s) a participant information sheet explaining the study and followed up via email or telephone a few days later to determine whether the young person was willing to participate and if so arrange an interview (telephone or face-to-face). Consent was required from both the parent and participant when the young person was aged under 16 years, but only the participant if over 16 years. None of the participants had received a GS result at the time of interview.

Interviews

Interviews were conducted by CL. The semi-structured interview guide was developed by an advisory team comprising genetic counsellors, a fetal medicine expert and genetic research scientists and explored the following topics: 1. knowledge and understanding of the term 'genes and DNA', 'genomes', 'genome sequencing' as well as the study procedure (that it is voluntary, timeframes, data access etc), 2. motivations for assenting/consenting to GS, 3. concerns around GS, 4. Motivations and concerns regarding secondary findings, and 5. involvement in the decision-making process. Interviews were audio-recorded, transcribed, anonymised and participants were given pseudonyms.

Data analysis

An abductive approach for coding and analysis was employed starting with codes derived from the topic guide and allowing new codes to emerge from the data(Robert et al., 2015). Data analysis was conducted following the principles of thematic analysis(Braun and Clarke, 2006). A draft codebook was devised by CL informed from the topic guide. Three transcripts were then independently read and coded by CL and SS and additional codes added. Coding was compared and a second codebook devised. Remaining transcripts were then coded by CL using this second codebook with a subset coded by SS to ensure inter-rater agreement. Once all transcripts had been coded, CL and JH reviewed and refined the themes and sub-themes (constant comparison). A Framework matrix was also created as a way of ordering the data to facilitate recognition of patterns such as contradictory findings(Gale et al., 2013). In particular, we were interested to see how frequently codes concerning participants' motivations and concerns occurred and explore whether they were influenced by factors such as age, gender or whether they had a 'working diagnosis'.

Results

Participant characteristics

Between June 2016 and March 2018, 40 young people (and their parents) were approached about this study, and 27 agreed and participated (68% recruitment rate): 19 were female, 25 were probands and two were unaffected siblings. Participants ages ranged from 11-18 years (mean = 14 years). The most common condition types for affected probands were skeletal (including osteogenesis imperfecta) (n=8) followed by renal (n=4) and dermatological (n=3). Fourteen probands had no diagnosis, 11 had a working diagnosis (e.g. epilepsy) but no known genetic aetiology (Table 1). Interviews lasted between 15 minutes and 49 minutes (median = 34); 25 were conducted by telephone, two were conducted face-to-face.

Qualitative findings

Theme 1: Knowledge

1.1 The terms 'gene' and 'DNA' are well understood

Participants frequently described the function of genes and DNA using analogies including "an instruction manual or an encyclopaedia of you" (Rowena, 13 years) and "like a fingerprint" (Alice,13 years). Genes and/or DNA were described as "what makes you, you" (Laura, 13 years),) and "control how your body performs" (Craig, 16 years). Around half of participants understood that genes and DNA are "passed down", and nearly all expressed an understanding that genes can cause health problems:

> "I know that I've got a fault somewhere in there, I got told it was like spelling. If the specific gene, it's like a letter, if that's not in the right place the spelling is wrong so that means my genes for that specific thing would be wrong." (Harry, 13 years.)

Some participants displayed more advanced knowledge. For example, two spoke about inheriting “two sets of genes, one from each parent” (Emma, 13 years), two participants, aged 16 years and 18 years, referenced the letters A, G, T and C, and two participants (13 and 17 years) mentioned the terms recessive and dominant inheritance, although only the older participant (Martin, 17 years) was able to articulate how these genes functioned in practice: “there are loads of genes that are recessive, which don’t show but they’re still there”. This participant also expressed an understanding of gene-environment interaction; “Certain things with your genes you can’t help, but it’s still a lot about your lifestyle decisions as well”. In most cases, participants commented that their knowledge of genetics had been acquired at school, but in some cases had been reinforced through the 100,000 Genomes Project. A few of the younger participants (11-13 years) had not heard of terms such as DNA and gene prior to the consent appointment.

1.2: The terms ‘genome’ and ‘genome sequencing’ are less well understood

Only a quarter correctly referred to the term ‘genome’ as being “all the genes” (Kathryn 16 years) or “all the DNA letters” (James, 18 years), and these participants were generally older (15-18 years). Regarding the term “genome sequencing”, half spoke of looking at the “order” (Ash, 14 years) or “pattern” (Craig, 16 years) of the genes, ten participants explicitly stated they did not know what the term genome sequencing meant (median age 13.5 years), and five did not remember hearing the term during the consent appointment.

When asked why their parents were also asked to provide their DNA for the study, four participants (13-16 years) understood that it was for comparative purposes. One participant, aged 13 years, articulated how her unique DNA sequence would be compared to her parents’ DNA and also potentially other people’s with the same condition;

> “Everyone’s got their individual sequence so everyone is different, so you can look at your own [genome] and compare it to other people’s. So they might compare mine to

> my mum or other people with JDM [juvenile dermatomyositis] to see what the links are" (Elli, 13 years).

Notably, when asked whether they would definitely get a result from having their genome sequenced, most correctly understood that "some people get a diagnosis but not everybody." (Emma, 13 years).

Theme 2: Motivations

2.1: Young people cited multiple practical benefits

All participants in the study were motivated to take part in the 100,000 Genomes Project because there was, potentially, a perceived benefit to them. These motivations included wanting to get a diagnosis, to identify the gene causing their condition, or to find out if the condition was genetic.

When exploring the importance of a diagnosis, some spoke of wanting to know if they had inherited the condition, or whether they might pass the condition on to their own children, a concern notably raised by some of the younger participants in the study:

> "Also, if I ever have children when I'm older, will they get it and will the doctors be able to help them?" (Rowena, 13 years).

A prognosis was raised as being important by around a third of participants, for example, Mazie (13 years) spoke about wanting to know "if I will develop anything else". Some thought a diagnosis would "help doctors to know what medication might be better than others" (Elli, 13 years). A couple spoke of wanting a diagnosis to "end all of the testing" and a few participants discussed that an important practical benefit of a diagnosis was being "able to explain to people what's actually wrong" (Louisa, 13 years).

Participants were realistic about the limitations of GS, with around half articulating that a diagnosis was unlikely to have a significant impact. For example, Elliott commented that "it'd be nice, but I don't think it'll change my life" (Elliott 15 years). Only a few participants (aged 13, 15 and 16) spoke of being motivated because they wanted to "cure" their condition.

2.2: Potential emotional benefits were also important

A third of participants cited motivations of a psychological nature. These included wanting an "answer…to put a few questions to rest" (Elliott, 15 years), to "stop me from keep on wondering how I got it" (Elli, 13 years), to gain "closure" (Emma, 13 years), and for reassurance "that it's not something I've done to cause it" (Katrina, 16 years). Amy spoke of the importance of a diagnosis in validating to others that she did have a genetic condition:

> "I'd like to put a label on it, because it's hard to explain to other people and it's almost like people think 'Oh, she hasn't got a diagnosis so she hasn't got anything wrong'" (Amy, 16 years).

2.2: *Young people are also motivated to help other people and contribute to science*

Almost all participants cited altruistic motivations. This included the potential benefits that taking part could have for others with the same condition, such as treatment or a quicker diagnosis. Rowena reflected on the research that had gone before which had subsequently benefited her:

> "The reason I have been given the medication so quickly, is because they've done this sort of thing on other people which has helped me to be served in this way." (Rowena, 13 years).

When comparing the motivations for taking part in the 100,000 Genomes Project, age appeared to be an important factor. Younger participants (11 to 13 years) cited nearly twice as many benefits directly related to them compared to benefits to others. Older participants (14 to 18 years) also cited more benefits to themselves compared to others, but the difference was less pronounced than that apparent among younger participants. No differences were observed when comparing across whether participants had a 'working diagnosis' or no diagnosis.

Theme 3: Concerns

3.1: Some participants were anxious about what the result might show and the potential for disappointment if the result was negative

When prompted, most participants commented that they did not have any concerns about having GS. However, a few participants did raise concerns about the potential emotional impact of the result, such as the potential for the result to reveal their condition was more serious than expected:

> "Maybe if it's life threatening, like if something comes back that might shock me or something I never knew before which would scare me" (Claire, 17 years).

Similarly, Kathryn (16 years) spoke of having concerns that the results might show "I've got another problem that I need to manage". A few spoke of potentially being disappointed if they didn't get a result, for example, Laura (13 years) said that "if they can't find it, like it's going to be a bit sad because you want to know".

3.2: Most participants did not have concerns about data security or access

Most participants felt reassured by the data being deidentified so "they can't trace it back to me" (Kathryn, 16 years), and made comments signalling their trust the NHS: "I'm quite confident that they're going to keep it safe" (Emma, 13 years). Some older participants were

unclear how their data could be used against them, even if it was accessed without their permission.

Regarding data access, a number of participants articulated that the involvement of for-profit companies in research was “a good thing [because] medicines [are] produced from that” (Elliott, 15 years). Two participants were, however, ambivalent about ‘for-profit’ companies having access to their data, although both made comments in which they acknowledged the role of such companies in “help[ing] research, they can fund developing a cure” (Craig, 16 years).

Only one person raised concerns about health insurance companies accessing his genomic data. In this case, the participants had been reassured by his father who had “assured him that for now, at least until 2019 I think they said health insurance companies wouldn’t be able to access any of that information” (James, 18 years).

Theme 4. Decision-making

4.1 Most young people felt the decision to take part in the 100,000 Genomes Project had been patient-led or a joint decision with parents.

All participants were aware that taking part in the study was voluntary. Half of participants, and in particular the older participants, felt that the decision to have GS had been *their* decision: “My dad was there at the appointment but I think it was my decision because I wanted to try and find out what it was that was causing my problems” (James, 18 years). These participants frequently spoke about making their own decisions about many aspects of their healthcare. For example, Kathryn (16 years), spoke about how her mum had “taken a step back from dealing with hospital appointments” and that she now “manage[d] my own medication”. For her, the decision to take part in the 100,000 Genomes Project was a

continuation of being responsible for her own health: “the genomes thing, is kind of just a continuation of that, just managing like my own condition and stuff”.

In around a third of cases, the decision to take part in the project was a joint decision between the participant and their parent(s). Despite parents being the ones who ultimately signed the consent form for their child to take part, participants reflected on the importance of being involved in those conversations. For example, Emma commented:

> “I think ultimately it’s my parents’ decision but I should get a lot of say in it…a thing like that is going to impact me more than it’s going to impact them, so I think it is very important for me to be involved in conversations like that.” (Emma, 13 years)

In five instances (which included participants aged between 12 and 15 years), the decision to take part was made primarily by the parents. However, in these cases, the participant had agreed with that decision. Rowena, 13 years, spoke of not wanting to make the decision on her own, and was reassured that her parents were involved, suggesting that younger participants still relied on their parents to make important health-related decisions on their behalf:

> “I wouldn’t want to make the decision on my own without knowing that it was the right thing to do. My parents said I think this is a good idea for you to do this and knowing my parents they would generally always make good decisions and they know what they’re doing and I trust them.” (Rowena, 13 years).

None of the participants described not wanting to take part and their parents having exerted pressure on them to participate.

Theme 4.2: Involving young people in decision-making is empowering.

Involving young people the discussion about genome sequencing, including asking them to sign an assent form empowered young people, formalised the process and instilled a sense of responsibility for their choice to participate. This is highlighted through comments such as: "it made me feel important, not just a blood source" (Elliott, 15 years), "I feel like I have a responsibility in some way" (Charlotte, 11 years), and "I think it shows that it's not just about how old you are, it matters if you think you want to do this" (Rowena, 13 years). Notably, Fiona (11 years) commented that she hadn't been asked to sign anything but would have valued the opportunity to do so as it might have made her more inclined to understand the study: "If I signed it, the questions that were being asked on the form, I might have understood more what was going to happen". Moreover, where young people weren't being involved in the consent discussion, it resulted in them "just zon[ing] out" and not "really pay[ing] much attention…even though it was primarily about me". (Ash, 14 years)

Theme 5.1: Young people are motivated to receive secondary findings so they can take action and be prepared

Participants were primarily motivated to receive secondary findings for reasons related to taking action and "to be prepared", but also acknowledgedthat "just because there's a possibility, doesn't mean it will happen." (Rowena, 13 years). Other motivating factors included wanting to regain a sense of control over one's health when so much was outside of their control "The suddenness and unexpectedness of my tumours have caused a few mental health issues…it would be helpful to know if something like [cancer/heart disease] could happen." (Katrina, 16 years). Some participants who had consented to receive adult onset secondary findings, envisaged that they would adapt their behaviour e.g. "stop smoking…stop eating sugary foods" (Martin, 17 years) if they were found to be at increased risk. Two participants were in part motivated because there was a family history of cancer. One participant linked her motivation to being part of the 'information age'; ""the age in which I live, everybody wants to know as much as they can about themselves" (Claire, 17 years).

Of the eleven participants eligible to consent to adult onset secondary findings, only one participant declined to receive these. His decision was in part related to the advice he had been given by the health professional consenting him into the 100,000 Genomes Project, that he would be "too young to do anything about it", and that he could receive secondary findings results at a later date.

When participants were questioned as to how they might feel if they were to find out they were at increased risk for certain conditions, six participants reflected that they would find the information "worrying", with Kathryn (16 years) raising concerns that "it would be another thing wrong" that she would have to deal with alongside her current genetic condition. Nevertheless, all six who did articulate concerns, commented that they still wanted to know.

Theme 5.2: Young people are making independent decisions about adult onset secondary findings without parental influence

Most participants who had consented to receive adult-onset secondary findings described making decisions without parental influence, and justified this approach with comments in which they were keen to exert their autonomy around decisions related to their health e.g. "I feel like I was responsible enough to make that decision myself" (Amy, 16 years) and "in the end it's about my body" (Seeta, 17 years). Two participants had, however, included their parents in the decision-making process. In one instance, there were divergent views amongst family members, with a father raising concerns "that if something comes up and it's really bad" he didn't want his daughter to " have to deal with it yet." (Claire, 17 years). Nevertheless, despite her father's reluctance, Claire had exerted her agency over the situation; "it's up to me and I wanted the information to come back".

Theme 5.3: Young people under 16 years of age want to be involved in decisions around childhood onset secondary findings

When it came to decision-making about childhood onset secondary findings, around a third of participants under 16 years did not recall the discussion. Of those that did remember, some had been actively involved in the discussion and clearly valued the opportunity to be involved in those decisions as highlighted by Rowena (13 years) who said "I wanted to know and so I said to my parents 'yes I do want to do this'". Those that hadn't been involved commented that they would have liked to have been involved in such discussions as highlighted by Emma (13 years) who commented that "It does affect me the most…I should get a lot of say in it".

Discussion

To our knowledge, this is the first study to explore the attitudes of paediatric rare disease patients being offered GS. In the new UK NHS Genomic Medicine Service, around half of the rare and inherited disorders for which GS will be routinely available are conditions that affect young people (NHS England, 2019). Collecting empirical evidence about young people's understanding, attitudes and preferences regarding decision-making can inform recommendations and best-practices.

Young people in our study demonstrated an understanding of the role and function of genes and DNA including a basic understanding of inheritance. However the terms 'genome' and 'genome sequencing' were less well understood, particularly amongst younger participants. These findings echo those from our quantitative survey study examining knowledge of genetics and genomics amongst 554 school pupils (Lewis et al., 2020). This finding is likely to reflect the National Curriculum in England where concepts such as genetics and DNA are

introduced from age 11 and the concept of genomics from around age 15 (Department for Education, 2015). The majority of participants in the present study understood that a limitation of GS is that they might not receive a diagnostic result. This is important given that currently around only 40% of paediatric patients get a result from GS (Lionel et al., 2017). Our data suggest that in the new NHS Genomic Medicine Service, it is important that health professionals check young people's understanding, particularly around what GS is and the current limitations of the technology to ensure they do not have unrealistic expectations about what results they might receive. Educational resources such as animations may be an effective way of supporting and enhancing young people's understanding during the in-person appointment.

A notable finding from our study is that young people were able to project how they might respond to a diagnostic result or a negative result and articulate their potential emotional reaction (fear, anxiety, disappointment etc). Such concerns may be realistic: Werner-Lin et al. found that parents and adolescents who had received non-actionable paediatric exome sequencing results initially experienced emotions including frustration, disappointment and fear (Werner-Lin et al., 2018). Giving young people the opportunity to discuss the potential emotional impact of GS findings in more depth including the option to discuss these separately from other family members, might be good practice going forward.

One area where our findings differ to research conducted with adults (McCormack et al., 2016; Robinson et al., 2016) is that young people did not have concerns about data security or insurance. A similar finding was reported by Pillai et al. who found that parents were more likely than adolescents to indicate that concerns around privacy and confidentiality influenced their decision to learn secondary findings results about their children (Raghuram Pillai et al., 2019). Young people had confidence that the NHS would protect their data and did not know how their data could be used against them. This is perhaps not surprising given most young people in this age group have not yet had to think about insurance, but may also

reflect a lack of awareness regarding the potential for genomic data to be used to discriminate against them in the future (e.g. employment). In other contexts, research has also shown that in the context of online personal information, young people feel they have "nothing to hide" and therefore do not consider privacy relevant for them (Adorjan and Ricciardelli, 2019). Further research could further explore whether this mindset applies to young people in the context of genomic data.

The majority of young people in this study felt that *they* had made the decision to take part in the 100,000 Genomes Project and receive main findings related to their condition, or that it had been a joint decision with their parents. This reflects the ethos of the project which emphasised the importance of inclusive decision-making (Genomics England, 2015). Our findings also shed light on the choices, justifications and parental involvement in young people's decisions about secondary findings. Notable findings include that 1) participants (under 16 years) were keen to be involved in discussions around whether to find out about childhood onset conditions, and 2) most older participants (16 years and over) wanted to receive adult onset secondary findings, had made that decision independently of their parents, and expressed justifications regarding these independent choices that related to notions of autonomy and independence. Similar themes emerged in a previous study with adolescents aged 13 to 17 years old without a clinical indication for genomic testing in the USA (Pervola et al., 2019).

Four capacities have been described that are required for (medical) decision-making; these are (1) communicating a choice, (2) understanding, (3) reasoning, and (4) appreciation (Grootens-Wiegers et al., 2017). In this study we found that participants understood that participating was voluntary and were communicative and expressed a choice (capacity 1); they understood why they were undergoing GS (capacity 2); they were able to apply logical reasoning and weigh up the potential benefits and risks of taking part e.g. getting a diagnosis vs. not getting a diagnosis (capacity 3); and they were able to appreciate the

relevance of taking part for them as well as others (capacity 4). Thus, our findings suggest that many of the participants in our study *are* likely to have had the capacity to make an informed decision and felt empowered by being actively included in the decision-making and assent processes. This is an important finding as it has implications for clinical practice in that it underscores the importance of health professionals actively involving young people in the discussion and decision-making around GS. The finding that young people valued the opportunity to be involved in the decision-making process and in particular provide written assent is also notable and we recommend that this practice should continue.

Strengths and limitations

This study adds much-needed empirical data on a topic that has received relatively little attention to-date, namely the views and experiences of young people having GS. A strength of this study is the diverse range of condition-types that affected participants in the sample. As with all qualitative studies, participants were self-selecting; participants with negative experiences may have been less willing to take part. In addition, this study did not include participants with intellectual disability which makes up a sizable number of children who might be offered GS (Wright et al., 2015). Finally, no demographic data on the parents (socioeconomic background or education level) were collected and thus we are unable to comment on the background of the participants. Participants' background may have had an impact on their level of understanding and/or attitudes towards genome sequencing.

Conclusion

Young people understood the potential benefits of GS for both themselves and others, as well as the limitations of the technology. Our research provides evidence to show that there will be some young people with rare diseases that 1. are *capable* of making informed-decisions to take part in testing, and 2. that involving them in testing decisions *empowers* them to take responsibility over healthcare decisions that affect them. Further research with young people after they receive GS results will add to understanding of their overall

experience of this technology. In addition, future research could focus on the experiences of young people with intellectual disability, in particular whether and how to facilitate empowerment and inclusivity.

Funding: This research was funded through a Health Education England Fellowship Award. LSC is partially funded by the NIHR Great Ormond Street Hospital (GOSH) Biomedical Research Centre (BRC). The research was made possible through access to patients being recruited to the 100,000 Genomes Project. The 100,000 Genomes Project uses data provided by patients and collected by the UK National Health Service (NHS) as part of their care and support. The 100,000 Genomes Project is managed by Genomics England Limited (a wholly owned company of the Department of Health) and is funded by the NIHR and NHS England. The Wellcome Trust, Cancer Research UK, and the Medical Research Council have also funded research infrastructure. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

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757

Table 1: Participant characteristics

Participant characteristics	
Age	11-18 years, mean=14 years
11-13	12
14-16	10
17-19	5
Gender	
Female	19
Male	8
Proband or sibling	
Proband	25
Sibling	2
Condition type (probands)	
Skeletal	8
Renal	4
Dermatological	3
Autoimmune	2
Hearing	2
Ophthalmological	2
Congenital heart disorder	2
Neurological	1
Endocrine	1
Diagnosis (probands)	
No diagnosis	14
Working diagnosis but aetiology unknown	11