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"Something that helped the whole picture": Experiences of parents offered rapid prenatal exome sequencing in routine clinical care in the English National Health Service

Running title: Parent experiences of rapid prenatal exome sequencing

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What's already known about this topic?

- Prenatal exome sequencing increases diagnosis of genetic conditions in pregnancies with a fetal structural anomaly.
- To date, prenatal exome sequencing has largely been offered in research settings and England is the first country to offer this test routinely within a national healthcare system.
- Clinical utility of prenatal exome sequencing has been demonstrated, but more information is needed to understand parents' experiences, information and support needs.

What does this study add?

- Parents valued the offer of prenatal exome sequencing, because of the possibility of receiving more information for current and future pregnancies.

- Prenatal exome sequencing results are being used to inform parents' decision making around termination of pregnancy, however, additional information from ultrasound and other tests continue to be important for personalised genetic counselling.
- Emotional support, clear options for contact with professionals and appropriate signposting are needed.

Abstract

Objectives

In October 2020, rapid prenatal exome sequencing (pES) was introduced into routine National Health Service (NHS) care in England. This study aimed to explore parent experiences and their information and support needs from the perspective of parents offered pES and of health professionals involved in its delivery.

Methods

In this qualitative study, semi-structured interviews were conducted with 42 women and 6 male partners and 63 fetal medicine and genetic health professionals. Interviews were transcribed verbatim and analysed using thematic analysis.

Results

Overall views about pES were positive and parents were grateful to be offered the test. Highlighted benefits of pES included the value of the additional information for pregnancy management and planning for future pregnancies. An anxious wait for results was common, often associated with the need to make decisions near to 24 weeks in pregnancy when there are legal restrictions for late termination. Descriptions of dealing with uncertainty were also common, even once results had been returned. Many parents described pES results informing decision-making around whether or not to terminate pregnancy. Some professionals were concerned that a non-informative result could be overly reassuring and highlighted that careful counselling was needed to ensure parents have a good understanding of what the result means for their pregnancy. Emotional support from professionals was valued, however some parents felt that post-test support was lacking.

Conclusion

Parents and professionals welcomed the introduction of pES. Results inform parents' decision making around termination of pregnancy. When there are no diagnostic findings or uncertain findings from pES, personalised counselling that considers scans and other tests is crucial. Directing parents to reliable online sources of information and providing emotional support throughout could improve their experiences of care.

Introduction

Prenatal exome sequencing (pES) has been shown to increase the diagnostic yield of genetic conditions where there is a structural abnormality and other prenatal tests, such as karyotype and chromosomal microarray are uninformative.[1-3] In unselected pregnancies pES improves diagnostic rates by 8-10%.[1, 2] Diagnostic rates can be further increased with selection of specific phenotypes, trio (parents and fetus) versus singleton (fetus only) sequencing, and pre-selection of cases following multi-disciplinary review.[3, 4] The clinical utility of pES has been demonstrated[5-7] and guidelines from professional bodies provide direction for the use of this test.[8-11] Results from pES can guide counselling about prognosis, direct clinical management during pregnancy, birth and beyond, inform parental decision making about whether to continue the pregnancy or opt for termination, and allow accurate counselling about recurrence risk for future pregnancies.[12-14]

pES for the diagnosis of fetal anomalies was implemented in the English National Health Service (NHS) in October 2020 as part of its national Genomic Medicine Service (GMS).[15] Testing in the GMS is based around seven regional Genomic Laboratory Hubs (GLHs) and a national Genomic Test Directory sets out which genomic tests are available.[16] pES is offered to parents when anomalies identified on fetal ultrasound are considered likely to have a genetic aetiology and will impact pregnancy management, as determined by a multidisciplinary team that includes fetal medicine experts and clinical geneticists.[15] Testing is preferably performed as trio sequencing with analysis currently using a panel of more than 1200 genes.[17] Results are returned within 2-3 weeks. Exome sequencing is also available if there is fetal demise or termination of pregnancy through a non-urgent pathway where turnaround times may be longer as there is no longer the possibility of influencing

pregnancy management. Incidental findings with implications for child or parental health are reported, but additional findings, for example cancer susceptibility genes, are not looked for. Variants of uncertain significance (VUS) are reported in some circumstances when multidisciplinary team review considers minimal additional information during pregnancy or after birth would allow reclassification to pathogenic.

There are a number of challenges when offering pES including interpretation of results,[18] counselling parents around the range of possible findings, discussing the implications of results and supporting parents when there are uncertain findings.[19] The timing of pES also poses challenges. When pES is offered for fetal structural anomalies, the majority of referrals are made following the 20 week routine fetal anomaly scan and parents can face an anxious wait for results as the pregnancy progresses.[14, 20] In England, this timing is also close to the 24-week limit, after which termination is only permitted when there is 'substantial risk' of serious disability in the child.

Notably, research exploring parent[13, 14, 20-25] and professional[14, 26-28] views and experiences of pES has largely been conducted when testing was hypothetical or when offered in a research setting. Further research is needed where pES has been offered within routine clinical practice. Moreover, when offering pES at a national level, as is the case for the NHS GMS, ensuring equal access and high standards of care across the country is crucial. Optimising EXome PREnatal Sequencing Services (EXPRESS) is a national study examining the delivery of pES across England through the NHS GMS.[29] The aim of this study was to explore parent experiences and support needs when offered pES through the NHS GMS. The study includes the perspectives of parents offered pES who can reflect on their own personal experiences and support needs and the perspectives of health professionals who can reflect more broadly on the experiences of all of the parents that they have seen when delivering the pES service..

Methods

Study design and approvals

This was a qualitative study using semi-structured interviews with parents and health professionals. Ethical approval to conduct parent interviews was given by the Health Research Authority (HRA) and the East of Scotland Research Ethics Service REC 1 (21/ES/0073). Interviews conducted by RM as part of her PhD project were approved by the London Bromley Research Ethics Committee (20/LO/0987). The HRA classified the professional interviews as Service Evaluation and research ethics committee approval was not required. The service evaluation was registered with Research and Development at Great Ormond Street Hospital for Children NHS Foundation Trust.

Patient and public involvement

The EXPRESS study's patient and public involvement (PPI) advisory group includes representatives from several parent and parent support organisations, and a researcher with relevant personal experience. The PPI Advisory Group worked closely with the research team on study design and development of parent-facing documents, such as participant information and topic guides. The PPI advisory group have also inputted into interpretation of findings and development of suggestions for best practice.[30]

Setting

Parents over 18 who had been offered pES in the NHS GMS were recruited through the parent support charity Antenatal Results and Choices (ARC) and Fetal Medicine Units (FMUs) at six NHS hospitals across five GLHs, with two hospitals located in North Thames and one hospital located in each of London South, South West, East, North East and Yorkshire and North West. Professionals were recruited from services across all seven GMSAs.

Recruitment

Parents were recruited to the study after their pES results were returned. For recruitment through ARC, a study invitation was posted on the ARC parent forum asking parents who had been offered pES to contact the research team if interested in taking part. Potential participants were then sent the participant information and invited to arrange an interview time. For recruitment through NHS hospitals, parents offered pES were identified by local clinical teams and a study invitation and participant information were sent by mail. If no response was received after two weeks, a local clinical team member telephoned potential

participants to discuss the study. If potential participants agreed, their contact details were shared with the research team to arrange the interview. Parents were offered a £10 gift voucher to thank them for their time. Professionals from a range of backgrounds involved in offering pES were identified by the research team and were sent a study invitation and participant information by email. Potential participants were invited to contact the research team if they wanted to take part. Written or audio-recorded verbal consent was obtained from each participant prior to the interview.

Interviews

For the interviews with parents, 50 families across six NHS hospital sites agreed to share their contact details with the researchers. When invited to participate, 31 took part in an interview, 14 did not respond and four actively declined (62% recruitment rate). A further 11 families contacted the research team to take part in an interview as they had seen the advertisement on the ARC forum. Forty-two interviews were conducted with 42 women and six male partners. The interviews were conducted by HM, RM and MPeter between October 2021 and May 2023 (25 by video call and 17 by telephone) and lasted between 18 and 113 minutes (median duration 46 minutes).

For the professionals, 134 professionals were contacted by the research team and invited to participate: 63 took part in an interview, 70 did not respond, and one actively declined (recruitment rate: 47%). Interviews were conducted by HM, RM, MPeter and MH between November 2020 and December 2022 (53 by video call, six face-to-face and two by telephone) and lasted between 23 and 80 minutes (median duration 44 minutes).

Interview topic guides were first drafted by MH and revised following feedback from HM and MPeter (experienced qualitative researchers), LSC and RM (clinicians with experiential knowledge of pES) and the PPI Advisory Group. Topic guides explored; 1. Parent experiences with pES; 2. Parent information and support needs pre- and post-pES; 3. Benefits and concerns around pES; and 4. Impact of pES results on decisions to continue or terminate the pregnancy (Suppl Information). Professionals were also asked about the structure and delivery of the pES service and these findings will be reported separately. Standard demographic questions were included for both parents and professionals (Table 1).

Data analysis

Interviews were audio-recorded and transcribed verbatim. One parent declined audio-recording and notes were taken during the interview. All data was pseudo-anonymised prior to analysis. Analysis and coding were facilitated by NVivo version 13 (QSR International, Pty Ltd). Analysis followed the principles of thematic analysis.[31] Findings were generated using a team-based codebook approach[32] that combined inductive and deductive approaches.[33] Parent and professional interviews were initially treated as individual data sets. An initial draft codebook was developed for each data-set that was informed by the aims of the study, the interview topic guide and published literature (deductive component). The researchers then read and independently coded two transcripts, adding codes not covered by the original codebook (inductive component). Additional codes were discussed, and the resulting revised codebooks were used to code the remaining transcripts. For the parent interviews, a draft codebook was developed by HM, MPeter and MH who then used the codebook to independently coded the same two parent interviews. Coding was discussed and a revised codebook was agreed that was used to guide coding of the remaining transcripts, which were coded by one researcher (HM: n=28, MP: n=10, MH: n=10). For the professional interviews, a draft codebook was developed by HW that included codes relating to patient experiences of pES and the structure and delivery of the pES service, reflecting the broader topic guide that was used for the professional interviews. In the first instance, HW, MD, MPeter and MH independently coded the same two professional interviews. Coding was discussed and a revised codebook was agreed that was used to guide coding of the remaining transcripts; divided equally between the researchers (HW, MP, MD and MH). Throughout coding of both data-sets, additional codes were added when appropriate, according to an inductive approach. As the themes and sub-themes from the parent interviews were reviewed and revised, they were compared to the themes from the professional interviews that had been generated to reflect parent experiences of pES. The theme structures from the two data-sets overlapped and quotes from both the parents and the professionals have been used to illustrate the themes described here.

Results

Participant characteristics

Interviews were conducted with 48 parents, the majority were female (88%), White or White British (81%) and educated to a degree level or above (77%). The 63 professionals who took part in an interview were from backgrounds in genetics (clinical geneticist (38%) and genetic counsellors (11%)), fetal medicine (clinicians (33%) and midwives (10%)) and clinical science (8%). All seven GMSAs were represented. Participant characteristics are presented in Table 1.

The pES results and pregnancy outcomes for the 48 parents (42 pregnancies) are summarised in Table 2. pES was declined in two pregnancies. For the 40 pregnancies where pES was accepted, this test led to a diagnosis or partial diagnosis for 16, VUS for 1 and no findings for 23. Decision making about whether to continue the pregnancy or have a termination of pregnancy is summarised in Figure 1.

Interview findings

Our findings are described within three overarching themes. 1. Searching for answers: Parent decision making when pES is offered, 2. Parent experiences of pES results and 3. Parent information and support needs.

1. Searching for answers: Parent decision-making when pES is offered

The introduction of pES into routine care was welcomed by participants. Parents described being *"incredibly grateful"* or *"lucky"* to have been offered testing, regardless of whether they had accepted or declined, or the type of result received. Professionals used terms such as *"fantastic"* and *"a great thing"* to describe the test and appreciated being able to offer parents an additional pathway to find a diagnosis using *"the most detailed information that we have access to"* (Professional 13, FMU Clinician).

Motivations to accept or decline pES

The opportunity for more information was frequently cited by parents as the main reason for accepting pES, as they were *"desperate for answers"* that could clarify prognosis (Table 3: Q1). Wanting information to gain more certainty was also common, and several parents accepted pES because they wanted to know that they had *"done everything physically possible in*

pregnancy to try and get an answer" (Parent 2). Other motivations for accepting pES were to inform decision-making around whether or not to continue their pregnancy (Table 3: Q2 and Q3) and gathering information that could inform clinical care for birth and the neonatal period as parents may *"just want to continue but know what the future the child has and prepare"* (Professional 4, FMU midwife). pES was also accepted to inform family planning as parents wanted to know the likelihood of a condition recurring.

Several professionals suggested that parents who decline pES generally fall into two categories: 1) parents that would not put the pregnancy at risk with an invasive test, and 2) parents prepared to end the pregnancy because other investigations indicate a very poor prognosis and who do not feel they can wait 2-3 weeks for pES results. These suggestions were reflected in the decisions of the two parents we interviewed who declined pES. One couple declined pES to avoid the miscarriage risk associated with an invasive test and, while they acknowledged the information from pES would be welcome, they were prepared to wait and *"do the test once he was born"* (Table 3: Q5). The second couple, who had already had an invasive test, declined pES to avoid waiting for further results when they had already decided to end the pregnancy (Table 3: Q6). Some parents who accepted pES described being *"slightly hesitant"* when making this choice, due to the potential to receive results about their own or their family's health as incidental findings with implications parental health are reported. Professionals noted that on rare occasions parents declined because of concerns around introducing further uncertainty as pES is "*still a new technique and there may be findings of a non-significance"* (Professional 9, Clinical Geneticist).

Parents face decisions about a complex test at an anxious and emotionally charged time

Parents' distress at the initial identification of fetal anomalies and the *"rollercoaster"* of emotions felt during this period was clear in our interviews. Parents struggled to cope with ongoing uncertainty and faced the stress of multiple tests and clinical appointments (Table 3: Q7). Some parents also talked about the difficulty of being able to engage with their pregnancy during this time, with one parent describing how she was "*starting to pretend he wasn't there because I didn't want to get attached"* (Parent 3).

When parents described decision making about pES in this setting, many said that their desire for more information made accepting testing an *"easy"* decision or *"a no-brainer"*. Participants noted that a key factor that simplified decisions was that pES is often offered after parents have had invasive testing and "*it was just taking bloods*" (Parent 17). A clear urgency to obtain answers was expressed, with parents often reporting that they *"agreed straightaway"* to pES, just wanting "*to get it over with so we didn't stress"* (Parent 25). Parents were acutely aware of the time pressures of pregnancy, and one parent explained that her decision to accept pES felt "*very rushed, but at the same time that was because our pregnancy was so far down the line*" (Parent 40). Even when clinicians encouraged parents to take their time with decisions, parents felt there was no time and they had to decide quickly (Table 2: Q8). Participants noted that the time it takes for testing could impact decision making. For example, one parent commented, *"we know it takes a while to go through… And so we just wanted to get the ball rolling"* (Parent 25). Some parents found it difficult to decide whether to have pES and then wait 2-3 weeks for results or to go straight to termination based on other clinical indications and have testing on the non-urgent pathway.

Most parents felt well informed, but challenges for pre-test counselling were noted

The challenge of describing a complex test and conveying the "*many possible results that can be uncertain or difficult to interpret, or maybe unanticipated*" (Professional 17, Genetic counsellor) was highlighted by professionals, who also noted the importance of clinicians having a good understanding of the test and the possible results and limitations when discussing with parents. The pre-test discussion about pES was often described by parents as *"a bit of a blur"* and that they felt *"bombarded with loads of information"* and professionals noted that many parents seem overwhelmed and struggle to take in information (Table 3: Q9). Some professionals described the need to have more than one appointment, so information does not become overwhelming and the importance of counselling skills when speaking to parents about pES because of the "*emotion and trauma that's mixed up with what they're going through*" (Professional 45, Clinical geneticist).

An additional source of stress and confusion linked to pre-test discussions centred on eligibility for pES. Sometimes, parents were told about pES and then had to wait to find out if they were eligible (Table 3: Q10). One parent felt confused about the eligibility criteria and

described the process as *"opaque"*. Professionals also highlighted that it is *"quite hard"* for parents who are told about pES, to then find out they are not eligible.

In general, the parents we interviewed felt they had a good understanding of pES, the possible results they could receive and the limitations, reporting that clinicians had explained the process clearly and had often shared written information. For some, however, it was evident that there were gaps in understanding about whose samples were tested and what genes were included. Parents could also miss or dismiss the possibility of uncovering information with implications for their own health because their primary focus is obtaining a diagnosis for their baby (Table 3: Q10). One parent described the discovery of possible health complications as *"a future me problem"* and that her decision to undergo pES was more about *"the here and now"*.

Many parents reported seeking information and support outside of clinic appointments. Information-seeking included reaching out to family and friends who were medical professionals and searching on Google. Some parents wanted detailed technical information and some reported researching academic papers to learn more about the test or about the suspected condition. Several parents volunteered that they had contacted the parent charity ARC, finding the organisation through their own research or through signposting by a clinician. This additional emotional support and information for decision making was described as *"superb"* and *"a godsend"*.

2. Parent experiences of pES results

Value and meaning of pES results

Waiting for results was described as *"excruciating"*, and *"a horrible state to be in"*. For some parents the wait was made more difficult as the differences in termination law before and after 24-weeks was viewed as *"a ticking deadline"* (Table 4: Q1). Professionals also highlighted the *"rushed decisions"* and stress for parents who *"pin their hopes on a diagnosis to justify the option of a termination"* (Professional 4, FMU midwife) when a no informative findings result might mean the option of termination is no longer available.

Most parents reported that their results had initially been returned by phone by a health professional they already knew followed by an in-person appointment (Table 4: Q2). Participants emphasised the significance of pES results, highlighting a diagnosis from pES was helpful for management of the pregnancy and immediately after birth (Table 4: Q3), but those who terminated a pregnancy following pES felt they avoided added distress and delay of a searching for answers after birth and were able to avoid having a post-mortem (Table 4: Q4). Finding out a condition was *de novo* brought relief and reassurance to parents who were "*so grateful to have that reassurance that I'm not a carrier"* (Parent 47). However, for parents who found they were carriers of the condition, there were feelings of *"guilt"* and *"blame",* and one parent described feeling *"crushed"* by *"the information that we are genetic carriers"* (Parent 9).

Even when pES gave a no informative findings result, its potential to provide parents with more information was still viewed favourably (Table 4: Q5). Some parents felt relief when there were no informative findings from pES, with parents describing it *as "a massive weight lifted"* and *"the opportunity to relax"* (Table 4: Q6), but others expressed disappointment and frustration as many had pinned their hopes on finding a diagnosis (Table 4: Q7).

pES results influence parents' decisions about termination of pregnancy

Many parents reported that their result from pES had been helpful for decision-making about whether to continue or end the pregnancy (Table 4: Q8) and for coming to terms with their choices as a diagnosis could give "*peace of mind that we made the right decisio*n" (Parent 39). Findings from scans and other tests were also key factors in many decisions, especially when there were no diagnostic findings, and pES results were sometimes described as *"something that helped with the whole picture"* (Parent 44).

Of the 16 families who received a diagnosis or partial diagnosis from pES, 13 opted for a termination and three chose to continue their pregnancy. Many who terminated the pregnancy said that they were already considering this decision based on scan findings but had hoped for *"certainty"* from pES about whether to proceed. For the three families who continued their pregnancy after a diagnosis, relief was felt that it was a condition where they

felt positive about continuing with information to prepare for the future: *"knowing what we're dealing with has been really, really helpful"* (*Parent* 19).

Professionals described the challenges of returning VUS, reporting that parents find these results *"really stressful"*. They noted that not being able to provide parents with definitive answers led to further uncertainty and parents often decide to end the pregnancy if a VUS is identified (Table 4: Q9). However, the one parent we interviewed with a VUS result continued the pregnancy but felt this would have been their decision regardless of the result.

There were 23 parents who received a no diagnostic findings result, 16 of whom chose to continue their pregnancy. For these parents, the no informative findings result was described as giving them *"confidence", "reassurance"* or *"peace of mind"* around their decision to continue the pregnancy. Seven parents with a no informative findings result chose to terminate their pregnancy, primarily guided by the findings of other tests such as MRI or ultrasound (Table 4: Q10).

From their reactions and decisions around termination, it was evident that parents conceptualised their no informative findings results in different ways. Many viewed this result as reassuring. For some of these parents the no informative findings result was additional information that confirmed reassuring findings from other investigations. However, some parents expressed optimism that was almost entirely focused on their pES result. For example, one parent embraced the hope that *"there probably isn't anything hugely genetically wrong… sometimes things are just unexplained*" (Parent 38). In line with this, some professionals raised concerns that parents can be falsely reassured by a no informative findings result and worried that parents do not always understand the limitations of the test and that optimism about this result as indicative of no genetic cause for the condition is sometimes misplaced, especially when other findings, such as ultrasound or MRI, still suggest a poor prognosis (Table 4: Q11).

Uncertainty beyond the testing journey regardless of the result

Although most parents accepted pES in the hope of obtaining definitive answers, several remained anxious and uncertain after results were received. One parent talked about how,

even though she had received a diagnosis from pES, the uncertainty around the spectrum of disability that her child could be born with was the most difficult thing to manage. Uncertainty could also continue for some parents with a no informative findings result. One parent explained how they felt "*relief and then still a little worry as we really still had no answers"* (Parent 43), and another parent described being hyper-vigilant about their child's development (Table 4: 12). These parents talked about ongoing anxiety that "*we still don't have an explanation… and that will always be in the back of our minds"* (Parent 21).

3. Parent information and support needs

Suggestions for improving parent care

Parents and professionals were asked for their suggestions on ways to improve information, counselling and support for parents offered pES. Parents were generally very positive about the care they had received. Emotional support and warmth from clinicians were considered important (Table 5: Q1). Several parents described fetal medicine midwives being *"always open to speak to us*" and a great source of emotional support, with one father noting that the midwives were *"sensitive, and they showed a lot of care whenever we got a call and they really looked after you"* (Parent 32). The need for continuity of care was also highlighted; one parent suggested that a professional such as a midwife should take responsibility for a particular case (Table 5: Q2). Having a point of contact for follow-up questions and support, including after results were returned, was also particularly valued by parents. Even those who did not use it felt reassured knowing there was someone to contact. However, some parents felt reluctant to bother professionals with questions for fear of being *"a burden"*. Several parents felt communication and support was lacking, especially those without a named contact after results were returned: "*I feel like there was support in the hospital, like on appointments, but as soon as you left the hospital there was nothing*" (Parent 33). Some parents reported feeling *"abandoned"* and described the challenges of long waits for appointments.

Participants felt that information in different formats, such as written information, animations and videos, would be welcome to "*complement the face-to-face consultation"* (Table 5: Q3). Signposting was also highlighted as important so that parents know where to find appropriate information (Table 5: Q4). Professionals also emphasised the need for

information in multiple languages and, ideally, opportunities for parents to speak to clinicians in their preferred language (Table 5: Q5).

Discussion

In this study, we used qualitative interviews with parents and professionals to understand the experiences and support needs of parents when pES was offered in clinical practice through the NHS GMS. Overall, parents and professionals were positive about pES. In line with previous studies considering parent experiences of pES conducted in a research setting,[13, 14, 20, 24] parents were grateful for the opportunity to have a test that increased the likelihood of receiving a diagnosis during pregnancy. In addition, parents valued the information from pES that guided management of their current and/or future pregnancies and could help them come to terms with their pregnancy experience. Our study also highlights some of the challenges for offering pES which have also been seen in previous research with parents,[13, 14, 20, 24] such as supporting parents through decision-making around a complex test during an anxious and time pressured period. Conducting our research in a clinical setting where pES has been implemented nationally has also emphasised the variation in parents' experiences of accessing follow-up and signposting for support after results are disclosed.

When parents discussed their motivations for accepting pES, their need for answers was evident. At a stressful and anxious time, decisions to have pES were made quickly, the time pressures of pregnancy could make decisions feel rushed and the focus on the baby meant that parents may dismiss the possibility of findings related to their own health. In turn, professionals worried that this could sometimes result in parents opting for pES without understanding the wider implications of the test. Similar findings around the challenges of decision making were observed in our previous study looking at parents experiences of pES when offered as research.[14] In addition, these challenges mirror those seen in studies exploring parental decision making about rapid genomic sequencing for critically ill children which also take place in a stressful, time-pressured setting.[34, 35] Notably, Lynch et al[35] have called attention to the importance of individualised pre-test counselling to address the variation in parent decision making and offset the tension between decision making about a complex genomic test and needing to make decisions quickly.

In our study, professionals highlighted that expert pre-test counselling from someone with a good understanding of pES and the limitations was necessary to support parental decision-making. Our data suggest that additional training for clinicians not yet familiar with genomic tests is required. Training on eligibility and the care pathways for offering pES is also important for all clinicians involved in delivering pES to mitigate against parents being put in the position of being told about the test only to find out they are not eligible.

Parents in our study did report feeling well informed about pES through pre-test counselling. However, it is important to note that the majority were highly educated and spoke English as a first language – factors known to facilitate understanding and the ability to engage in discussions about genomics with health professionals.[36, 37] To meet the individual needs of parents who will have different levels of education and who may better understand their testing options in their native language, an adaptive and culturally sensitive approach to counselling is needed. Consideration of practice models to support cultural competency in genomics[38] and the recruitment of professionals who speak languages prevalent in the local community will facilitate support for more parents. Furthermore, presenting information about pES in alternative formats should be considered; this could include web-based decision aids, which have been shown to be successful for other prenatal tests,[39, 40] or an animation or video, which has been well received by patients offered genomic tests in other settings.[41, 42]

Ongoing parental support and follow-up after pES results are returned is also needed. Several parents noted that follow-up care and communication post results disclosure could be improved. This is particularly important as parents are often unprepared for the increased uncertainty brought about by results from prenatal testing.[19, 43, 44] In our study, many parents continued to experience uncertainty long after results were received - especially when there was not a diagnostic result from pES. To support parents and help them to cope with uncertainty, the parents and professionals we spoke to suggested that parents would benefit from access to a named clinician via email, phone or a patient portal for test-related queries. It could also help to offer parents a 'check-in' with a known clinician. Routine signposting to

specialist parent support services would also be a welcome option for parents to discuss their feelings further.

A key finding of our study was that pES tests were frequently pivotal for parental decision-making about whether to continue or end the pregnancy. Notably, many parents felt unable to move on, both clinically and emotionally, without a result from pES. In previous studies, parents' decisions to terminate the pregnancy often occurred before pES results came back, but a diagnosis from pES did impact decision making when parents waited for their results.[13, 25] For parents in our study, diagnosis from pES indicating a poor prognosis gave parents more confidence about ending their pregnancy, supporting findings from studies considering the clinical utility of pES.[5] Similarly, a no informative findings results, when viewed with other findings could bring relief and confidence to continue the pregnancy. Those that terminated the pregnancy after a no informative findings result described pES as one part of a bigger picture and being guided by other scan and test findings in their decision to terminate. Concerns that parents sometimes interpret a no informative findings result as a good outcome, even in the context of a poor prognosis on scan findings, highlight the importance of considering pES alongside scan and other test results to build a full diagnostic picture. This is line with professional guidance that recommends clinicians ensure parents understand that a no informative findings pES result does not necessarily rule out the presence of a genetic condition.[8]

Strengths and limitations

A major strength of this study is that our interviews with parents, which provide an in-depth exploration of their personal experiences, have been combined with the wider perspective of professionals who shared their views on parent experiences. Including the professional interviews has been particularly valuable to obtain insights into the reasons parents might decline pES and the support needs of parents across a range of different backgrounds, as these experiences were not represented in the sample of parents that we interviewed. Another strength is the sample size and that the parents and professionals included were diverse in terms of their geographical locations across England. There are limitations to the generalisability of this study as participants were self-selected, and responder bias may be an

issue. In addition, because some test outcomes were self-reported, we have not included the pES results of the parents we interviewed in the paper, which limits interpretation of parental experiences and decision making. Parents also self-reported when they were offered pES, so we have not reported the time period between being offered pES and taking part in an interview, which limits the understanding of how long feelings such as anxiety and uncertainty may change over time. Another limitation is that the majority of parents we interviewed chose to have pES, reported being White/White British and were educated to degree level or above. As a result, our participants do not represent the full range of views and experiences of parents offered pES. More targeted research is needed on the views and experiences of those who have declined pES, and of participants from underrepresented groups. Future research could also consider the use of validated tools to look at constructs such as decisional conflict[45], decisional regret[46] or anxiety (eg GAD-7[47]).

Conclusion

Our research shows overall positive parental responses to the introduction of pES in clinical practice. Parents valued the offer of the test and the possibility of receiving more information for current and future pregnancies. Results were useful for pregnancy decision-making, and in helping to come to terms with pregnancy/baby loss or preparing for the birth of their baby. High quality communication and the offer of ongoing support with a named contact throughout the pES pathway will improve parent experiences of the distressing time after fetal anomalies are identified, and continued education and training for professionals is required to improve knowledge of genomics and understanding of the eligibility criteria.

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Conflicts of interest

None to declare.

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Table 1. Participant characteristics

	N	(%)		N	(%)
Parent participants					
Gender			**Main language spoken**		
Female	42	88%	English	36	75%
Male	6	13%	Other	4	8%
			Unknown	8	17%
Ethnicity			**Religion**		
White/White British	39	81%	Christian	12	25%
Asian/Asian British	4	8%	None	25	52%
Other	2	4%	Sikh	1	2%
Black/Black British	2	4%	Agnostic	1	2%
Mixed	1	2%	Unknown	9	19%
Education			**Age (years)**		
Degree or above	37	77%	Mean	34.5	
Vocational	5	10%	Median	35	
GCSE/O-level	4	8%	Range	(28 - 49)	
A-level	1	2%			
No qualification	0	0%			
Unknown	1	2%			

	N	(%)		N	(%)
Professional participants					
Professional role			**GMSA Region**		
Clinical genetics clinician	24	38%	North West	8	13%
Fetal medicine clinician	21	33%	North East and Yorkshire	8	13%
Fetal medicine midwife	6	10%	East	10	16%
Genetic counsellor	7	11%	Central and South	11	17%
Clinical scientist	5	8%	North Thames	12	19%
			South East	4	6%
			South West	7	11%
			NA	3	5%

Note: The above numbers reflect the inclusion of 48 parent participants; only 42 parent interviews were conducted since six interviews included a couple.

Key: GMSA = National Health Service Genomic Medicine Service Alliance (there are seven GMSAs that coordinate the embedding of genomics into mainstream clinical care in England); NHSE/I = NHS England and NHS Improvement

Table 2. Pregnancy characteristics at time of interview.

Participant ID	Accepted pES	pES result	Outcome	Decision to terminate/ continue pregnancy based on
Parent 1	Yes	Partial diagnosis	ToP	Scan findings
Parent 2	Yes	No findings	ToP	Scan findings
Parent 3	No	-	ToP	Scan findings
Parent 4	Yes	Diagnosis	ToP	pES findings
Parent 5 & 6	Yes	Diagnosis	ToP	pES findings
Parent 7 & 8	Yes	Diagnosis	ToP	pES findings
Parent 9	Yes	Diagnosis	ToP	pES findings
Parent 10 & 11	Yes	No findings	Live birth	Scan findings
Parent 12	Yes	No findings	ToP	Scan findings
Parent 13	Yes	No findings	ToP	Scan findings
Parent 14	Yes	No findings	Live birth	pES findings
Parent 15 & 16	Yes	Partial diagnosis	IUD	Scan findings
Parent 17	Yes	No findings	ToP	Scan findings
Parent 18	Yes	Diagnosis	ToP	pES findings
Parent 19	Yes	Diagnosis	Live birth	pES findings
Parent 20	Yes	No findings	Live birth	Scan findings
Parent 21	Yes	No findings	Live birth	pES findings
Parent 22	Yes	No findings	Live birth	pES findings
Parent 23	No	-	Live birth	Scan findings
Parent 24	Yes	No findings	Live birth	Would not have considered ToP
Parent 25	Yes	No findings	Live birth	pES findings
Parent 26 & 27	Yes	Diagnosis	ToP	pES findings
Parent 28	Yes	Diagnosis	ToP	pES findings
Parent 39	Yes	Diagnosis	ToP	Scan findings
Parent 40	Yes	No findings	Live birth	pES findings
Parent 41	Yes	No findings	Live birth	pES findings
Parent 42	Yes	VUS	Live birth	Would not have considered ToP
Parent 43	Yes	No findings	Live birth	pES findings
Parent 44	Yes	No findings	Live birth	Would not have considered ToP
Parent 45	Yes	No findings	Live birth	Information unavailable
Parent 46	Yes	Diagnosis	NND	pES findings
Parent 29	Yes	Diagnosis	ToP	pES findings
Parent 30	Yes	No findings	IUD	Not applicable
Parent 31 & 32	Yes	Diagnosis	ToP	pES findings
Parent 33	Yes	Diagnosis	ToP	pES and scan findings
Parent 34	Yes	Partial diagnosis	ToP	pES and scan findings
Parent 35	Yes	No findings	Live birth	pES findings
Parent 36	Yes	No findings	Live birth	pES findings
Parent 37	Yes	No findings	ToP	pES findings

Parent 38	Yes	No findings	Continuing pregnancy	pES findings
Parent 47	Yes	No findings	ToP	Scan findings
Parent 48	Yes	No findings	ToP	pES and scan findings

Key: pES = prenatal exome sequencing; ToP = termination of pregnancy; VUS = variant of uncertain significance; No findings = no diagnosis from pES; IUD = intrauterine death; NND = neonatal death

Table 3. Searching for answers: Parent decision making when pES is offered

Quote number	Illustrative quote
Motivations to accept or decline pES	
Q1	*"Yeah, there was never a question that I wouldn't do it because it was literally 'this might give us answers'. No-one could tell us what was wrong with him".* Parent 15 – Mother, partial diagnosis from pES (continued pregnancy)
Q2	*"The main reason I wanted to know what it was so I could make a decision on whether we was going to continue with the pregnancy or not." Parent 39 – Mother, diagnosis from pES (termination of pregnancy)*
Q3	*"…for Muslims, if you're going to have a termination after the 120 days which is about eighteen weeks, you can only have it if the baby's going to have a very poor quality of life or if the baby's going to die – often when you do a scan you can't give that information…but having a prenatal result really helps some of my families because we could say we've found this and we know the prognosis for these babies."* Professional 5 - Genetic counsellor
Q4	*"It was quite easy to make that decision once we heard that it [invasive test] would affect the baby. Obviously we would want to know but once we heard it could affect the baby, there was no chance and we'd do the test once he was born."* Parent 23 – Mother, declined pES (termination of pregnancy)
Q5	*"The only concern was just the time it took to get the results, so in terms of actually doing the test, like, we would have gone ahead with it straightaway, but it was just because the results took a while and we kind of already had in our minds what we were going to do and I felt really uncomfortable being pregnant and kind of knowing that we were going to be hanging on to get the test results really."* Parent 3 – Mother, declined pES (termination of pregnancy)
Q6	*"we had the MRI, we had the heart test, we had the extra ultrasound scan week 21/22 and we went back in for another scan and I remember asking the consultant, I was like 'at what point are you going to say to us we've exhausted our tests and we can't give you any more certainty', because it felt really uncertain."* Parent 7 - Mother, diagnosis from pES (termination of pregnancy)
Parents face decisions about a complex test at an anxious and emotionally charged time	
Q7	*"they allowed us as much time as we needed but, for me, it made sense, it was just taking bloods from me, it was simple, it was a test that could potentially show us the cause … If we wanted to take our time, she was like there's no rush, but you can imagine time for us was not there, so we had to do things quite quickly." Parent 17 - Mother, no informative findings result from pES (termination of pregnancy)*
Q8	*"that's quite common for them to come back and say 'I don't remember a word you've said'".* Professional 29 - FMU midwife
Most parents felt well informed, but challenges for pre-test counselling were noted	

Q9	*"[the geneticist] was lovely saying she will do her absolute best to try and secure this testing for us and, yeah, that was an incredibly anxious time waiting for that decision, so we were very relived to be allowed.*" Parent 10 - Mother, no diagnosis from pES (termination of pregnancy)
Q10	*"to be honest, probably because of the emotions we was going through at the time, I didn't really worry about if they found anything to do with me and my partner…I was so focused on baby, and he was like my 100 % priority at that time."* Parent 2 - Mother, diagnosis from pES (termination of pregnancy)

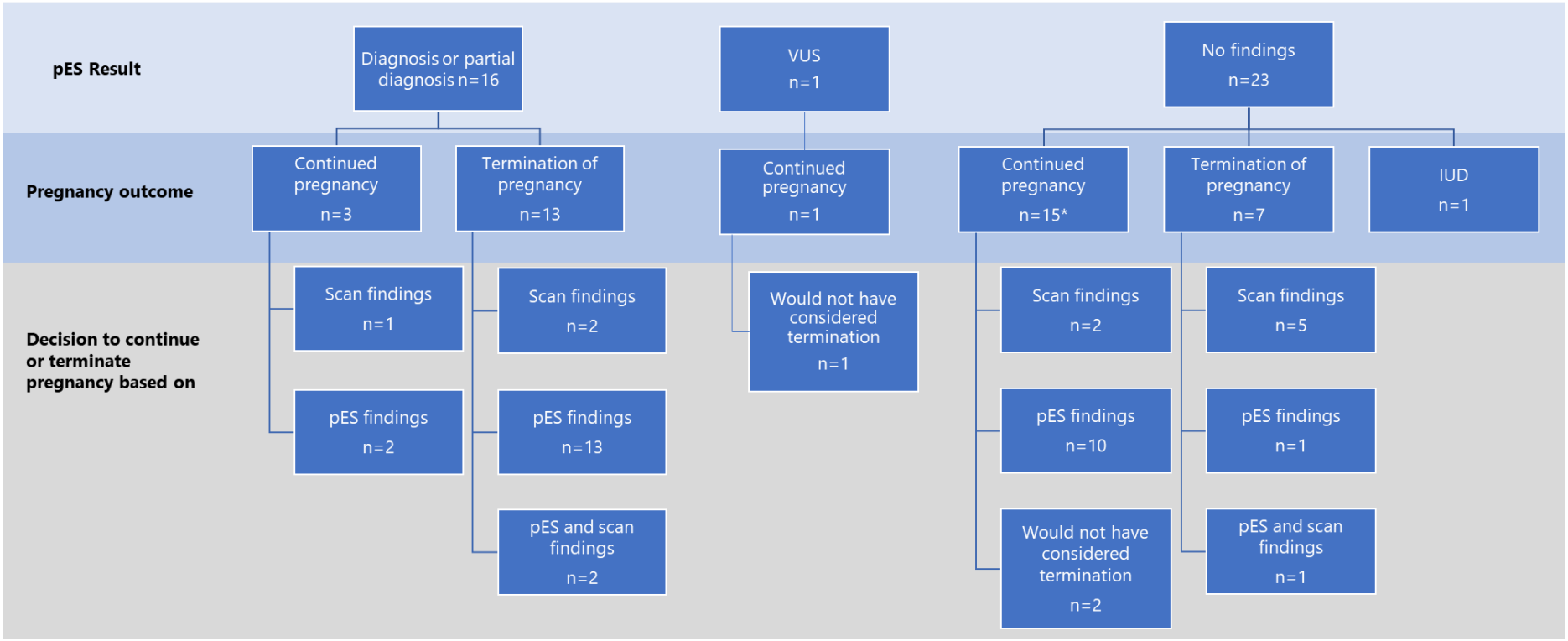
Table 4. Parent experiences of pES results

Quote number	**Illustrative quote**
Value and meaning of pES results	
Q1	*"I had the test at 21/22 weeks and were told it would take 3 weeks. It actually took less – I suspect because there was no result. I remember counting because we were just going to make it before the 24-week cut off. It was the most stressful time in my life."* Parent 35 - Mother, no diagnosis from pES (live birth)
Q2	"*I think the result had been emailed to them and they called immediately and basically she just said 'it's come up not showing anything, we haven't found anything of relevance in your tests' and she said 'we can discuss this further when you come up in a couple of days', she just wanted to let me know because obviously we'd been waiting the full three weeks to sort of ease our mind a bit*" Parent 2 - Mother, diagnosis from pES (termination of pregnancy)
Q3	*"The neonatal doctors would have had so much less information and all of the things that they did for her throughout the five days that she was with us, at least they had a diagnosis and they knew why they were seeing certain things or why certain features were present."* Parent 46 - Mother, diagnosis from pES (neonatal death)
Q4	*"One thing I was pretty anti- against is a post-mortem…So, you know, by having this, there's a clear – we didn't have to…have a post-mortem…we could use the cuddle cot…And within two weeks we were burying him…which was helpful.*" Parent 5 - Mother, diagnosis from pES (termination of pregnancy)
Q5	*"I say unfortunately, but you could feel either way about it, our test come back showing no relevant result, so we still never got any answers for us, but I'm still so grateful that we had it, because had it have shown something it would have given us so much more information as to prognosis and outcome and all sorts, so I was still really grateful to have it even though, in our case, it didn't really prove beneficial."* Parent 2 - Mother, diagnosis from pES (termination of pregnancy)
Q6	"*I think it just meant we can relax a bit more. So like we knew it didn't rule out everything and we made sure we both understood that. But the relief of the main things it was looking for which are the most common, was really reassuring, that he didn't have that.*" Parent 25, Mother, no diagnosis from pES (live birth)
Q7	*"Yes, she said I don't have very much to say because we didn't find anything, and I thought, I don't what this means…I thought I would be immediately happy, but what it meant was that I was in the same place as before with having to make a decision about what to do."* Parent 38 - Mother, no diagnosis from pES (continuing pregnancy)
pES results influence parents' decisions about termination of pregnancy	
Q8	*"we felt like OK well all the tests are clear so far, like, we don't want make a decision without having, sorry, without having a diagnosis. But the moment that we got the diagnosis I think we both knew pretty quickly what needed to be done" Parent 29* - Mother, diagnosis from pES (termination of pregnancy)
Q9	*"I think the VUS side of things actually, if there's no pointers on ultrasound or in their history to the meaning of that variant, then it just is a bit wishy washy and I find they just can't process it. I think*

	the cases I've seen, they've had termination anyway because there's just – this is just too much now" Professional 25 – FMU consultant
Q10	*"I guess in our specific circumstance, the exome test as a whole didn't really influence our decision in any way because we didn't get a result, but I think had it shown a result it definitely would have helped give us that extra information…but I think for us in our case the MRIs were the most influential diagnostic test that we had, because our second MRI at 27 weeks had showed that baby's brain just hadn't developed past about 22 weeks."* Parent 2 - Mother, no diagnosis from pES (termination of pregnancy)
Q11	*"So we definitely notice that people's understanding of that test is better news to not find anything, which may be true but isn't always true. And so I think the problem is, when people understand a little bit…you're spending more time unpicking what they actually understand already…and unpicking all of that is actually sometimes harder than starting from nothing."* Professional 51 - Genetic counsellor
Uncertainty beyond the testing journey regardless of the result	
Q12	*"like every time she does anything I'm like "Is that normal?" Should she have rolled last week?"* Parent 24, Mother - no diagnosis (live pregnancy)

Table 5. Parent information and support needs

Quote number	**Illustrative quote**
Suggestions for improving parent care	
Q1	*"So I think again, you know, when we got the news I think we should have had a counsellor there in the room or someone to talk to, anybody, I don't think we should have been sent home on our own. I don't think that should have happened."* Parent 12 – Mother, no diagnosis from pES (termination of pregnancy)
Q2	*"And I'd spoke to seven people to be asked to be taken off that list. And I wasn't. And every time that came up that upset me all over again…and I think I know you don't have a midwife anymore…I think you need a midwife, somebody who said I'm taking this case and I can go through it with them."* – Parent 12 – Mother, no diagnosis from pES (termination of pregnancy)
Q3	*"I think purely just going off of mine and my partner's experience, I think maybe like a video would have been really helpful, maybe some sort of animated or with some people actually talking on it explaining the process, I think that would have been good, because my partner's a very visual sort of person."* Parent 2 – Mother, no diagnosis from pES (termination of pES)
Q4	*"I mean I think we've been doing a lot of work about information before you come to the appointment so some signposting before the appointment either about the type of tests that might be available, easy access to links, online digital stuff as well as information in different languages is simple but key to what we can offer parents. Different formats of information so digital videos and media things as well as written information seems to go across quite well." P35*
Q5	*"I suppose having more access to people who are trained in genetic counselling who speak another language would be good and ideally, I mean, a lot of it is sort of community based as well and having those links with the communities that we serve, so I think we're doing a bit of work on that, I think involving the local communities and midwives and the patient groups probably – information in different languages" P10*



Key: pES = prenatal exome sequencing; ToP = termination of pregnancy; VUS = variant of uncertain significance; No findings = no diagnosis from pES

*One of 15 pregnancies had an intrauterine death before decisions on continuing or ending the pregnancy were made.

Figure 1: Summary of outcomes for all pregnancies were pES was accepted