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Impact of fetal or child loss on parents' perceptions of non-invasive prenatal diagnosis for autosomal recessive conditions

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Abstract

Objective: To explore parents' personal attitudes towards non-invasive prenatal diagnosis in the context of their own experiences caring for a child affected with a genetic condition or after the loss of a fetus, infant, or child due to the condition.

Methods: We collected in-depth data from parents via either focus groups or individual interviews.

Design: This was a cross-sectional interpretive study based on grounded theory.

Setting: United Kingdom

Participants: Seventeen parents (13 women and four men) who were carriers of a serious autosomal recessive condition: spinal muscular atrophy, cystic fibrosis or thalassaemia. All had a child (living or deceased) with the condition.

Findings: Parents experienced changes in reproductive self-identity due to their experiences of having an affected child: this influenced their views of non-invasive prenatal testing. They began their reproductive journeys 'naively', but described feelings of reproductive vulnerability after the diagnosis of the child and consequent realisation of risks to future children. They viewed non-invasive prenatal testing as a way to reduce threats to unborn children, while allowing prenatal diagnosis.

Key conclusions:

When parents lose a child they may use emotional guarding, delayed pregnancy disclosure and avoidance of harmful activities to cope in future pregnancies. Parents who want to consider early

prenatal testing are less able to utilise these strategies, but non-invasive methods allow them to reduce the risk.

Implications for practice:

Midwives should be sensitive to parents' reproductive vulnerability after genetic diagnosis of a child and ensure they are supported to consider the option of non-invasive prenatal testing if appropriate.

Key words: carrier status, parent, psychological impact, genetic disease, non-invasive prenatal testing.

Highlights

- Parents who have a child diagnosed in pregnancy or after birth with an autosomal recessive genetic condition experience changes in reproductive identity
- Their feelings about themselves may shift from a position of invulnerability to reproductive vulnerability because of the realisation of serious risk to their future children
- Their wish to protect future children from harm may conflict with their wishes for prenatal testing
- Use of non-invasive prenatal testing is seen as a way to mitigate threats to fetal health, while allowing them to prepare for an affected child or consider termination of pregnancy.

Introduction

The constant and rapid improvement in genetic and genomic science, technology and information has increased the variety of genetic tests available for those at risk of rare diseases (Kingsmore, Dinwiddie et al. 2011). Genetic testing may be classified into four primary domains: diagnostic (Shashi, McConkie-Rosell et al. 2014), prenatal (Roa, Pulliam et al. 2005), carrier (Vallance and Ford 2003) and presymptomatic testing (Paneque, Sequeiros et al. 2015), with the present study focussing on prenatal testing. Several procedures are available to obtain samples to enable fetal testing. Invasive procedures such as amniocentesis and chorionic villus sampling (CVS) have been the most common and widely used (Simpson 2012), while non-invasive prenatal testing (NIPT) or diagnosis (NIPD) has been more recently introduced for use in some prenatal testing situations (Hill, Barrett et al. 2012). Clinical indications for prenatal testing include advanced maternal age (35 and older), family history of an inherited disorder, indications of fetal abnormality, such as an abnormal ultrasound examination (Lo, Cori D et al. 2014) or high risk prenatal screening result (Ekin, Gezer et al. 2014). The recognised advantages of invasive prenatal diagnostic procedures, such as obtaining definitive diagnostic results, are balanced against the associated health risk to the fetus, specifically, pregnancy loss rates following amniocentesis and CVS are typically around 1% (Mujezinovic and Alfirevic 2012).

The use of a non-invasive method to obtain samples is seen as an innovative technique that will change the prenatal diagnosis options available for couples. This technology is based on the presence of cell-free fetal DNA/RNA (cff DNA/RNA) in maternal plasma that is detectable as early as four weeks of gestation (Hill, Barrett et al. 2012), although sufficient levels for testing do not accumulate until around nine weeks of pregnancy. Currently non-invasive testing is available clinically for a limited range of conditions, for aneuploidy (Lo, Boustred et al. 2014), some single gene disorders such as thalassemia (Lo 2013) and for fetal sex determination for sex-specific disorders (Hill, Compton et al. 2012). Opinions about NIPT and NIPD are generally very positive and couples value both the chance to reduce the risk of miscarriage associated with testing and the confirmation of fetal status earlier in the pregnancy (Lewis, Hill et al. 2012, Hill, Compton et al. 2014). Conversely, some stakeholders have expressed concerns about the need for accuracy of results that may be used for subsequent decision making about termination of the pregnancy (Skirton, Goldsmith et al. 2014). Stakeholders were also concerned about the ease with which a blood sample can be taken and how this may affect the consideration given by parents as to the outcome and consequences of the test (Skirton, Goldsmith et al. 2014).

Much of the current evidence on use of NIPT or NIPD has been based on populations of pregnant women (Lewis, Silcock et al. 2013, van Schendel, Kleinveld et al. 2014), health professionals (Hill, Fisher et al. 2012) and women and their partners who might be offered fetal sex determination prior to diagnostic testing (Hill, Lewis et al. 2012). One recent study has focussed on the views of carriers of life-limiting single gene disorders, reporting attitudes towards and preferences regarding clinical services associated with the test (Skirton, Goldsmith et al. 2014). However, there is little evidence on how the loss of earlier pregnancies, the birth of children with life-limiting illness or the death of children influences perceptions of non-invasive prenatal diagnosis.

The grief of parents who have experienced the death of a child is well-documented (Titus and de Souza 2011, Harper, O'Connor et al. 2014). Similar grief may be experienced as a result of fetal loss during pregnancy (Van and Meleis 2010, Cowchock, Ellestad et al. 2011), in fact in some cases the bereavement may be more difficult to manage when the loss occurs during pregnancy (Schaap, Wolf et al. 1997). It has also been reported that women who have undergone prenatal testing due to a high level of risk of fetal abnormality or detection of potential abnormality in pregnancy (e.g. during ultrasound) have been found to experience distress and many were still suffering the symptoms of anxiety six months later (Leithner, Maar et al. 2004). It is likely therefore that the experience of loss of either a child or fetus will influence parental beliefs and attitudes to prenatal diagnosis in a future

pregnancy and this is of importance to midwives who will be offering care, including discussion and organisation of NIPD, to families in subsequent pregnancies.

In this study we focused on parents who were healthy carriers of an autosomal recessive genetic condition. The aim was to explore parents' personal attitudes towards NIPD in the context of their own experiences caring for a child affected with a genetic condition or after the loss of a fetus, infant, or child due to the condition.

Methods

This was a cross-sectional interpretive study based on the qualitative paradigm, which enables the researchers to develop rich explanation from an individual's reported experiences (Willis 2007). Grounded theory was chosen as the most appropriate method due to its ability to identify social process in an inductive way (Strauss A 1998). Semi-structured interviews were used to collect data from the participants. The interview schedule was prepared by researchers who are experts in the field of prenatal diagnosis, genetic counselling and midwifery. We recruited carriers of three recessive conditions (cystic fibrosis, spinal muscular atrophy (SMA) and thalassemia) by approaching the relevant patient support groups and organisations, for example the Cystic Fibrosis Trust. Potential participants were invited via personal letter or email (from the support group staff) or via information sheets placed in relevant web pages. The three conditions were chosen to represent a range of different impacts on the affected child: the infantile form of SMA results in neonatal or infant death, while children with cystic fibrosis and thalassaemia require extensive supportive treatment and may die at a young age as a result of the condition. To obtain a maximum variation sample, we recruited carriers from a range of ethnic groups, of both genders and with a wide range of ages. Due to the rarity of some of the conditions and the geographical spread of potential participants, we offered telephone interviews where attendance at a focus group was not practical.

Both individual interviews and focus groups were facilitated by the same interviewer and these were audio-taped and transcribed in full. Data analysis was undertaken using an inductive coding technique (Strauss A 1998). Initially, transcripts were read several times to ensure familiarity with the content. Each part of the transcript was then coded independently by two researchers. After consensus was reached on the content, the codes were organised into categories and then several broad themes. All names and personal details have been altered to protect the confidentiality of the participants.

This work formed part of the larger RAPID study, for which National Health Service Research Ethics Committee approval was obtained in June 2010.

Findings

Demographic characteristics of the participants

A total of 17 people (13 women and four men, including four couples) were interviewed between October 2012 and October 2013. All but one couple was of White European origin and all the respondents lived in the United Kingdom. All were married or living with their long term partner. Demographic characteristics can be found in Table 1.

All participants had experience of having a child suffering from cystic fibrosis, thalassemia or SMA. The five children affected with SMA died before the age of two. One child was affected by thalassemia, and four by cystic fibrosis, both life-limiting conditions. Among the participants a number of women had experienced miscarriages (up to eight losses for an individual woman), either before or after the birth of the affected child and some were using assisted reproductive technologies such as pre-implantation genetic diagnosis (PGD).

Main themes

The core category emerging from the analysis was called the 'altering self-identity'. Within this category there were several themes: reproductive experiences, changes in self-identity, pressure to be tested and attitude to termination. Direct quotations are labelled with the pseudonym of the participant and the condition their children were affected by.

Theme 1: Reproductive experiences

All of the parents had been deeply affected by their previous reproductive experiences. Living with a child with a genetic condition or having lost a child due to a lethal genetic condition had led them to view prenatal testing as helpful. However, some participants highlighted the dilemma between taking an invasive test, with the unpredictable chance of a miscarriage, compared to knowing whether the fetus was affected.

'For, while you want to know, it's a risk that you don't necessarily have the mental ability to cope with' (Rachel, SMA)

Some expressed the view that the risk of miscarriage was worth obtaining the information:

' Yes I guess but I suppose I was prepared to take that risk to get the information... [but it] would be a big advantage not to have to take that risk or contemplate that risk (Jenny, SMA).'

'We wanted an amniocentesis for information, we were going to pursue the pregnancy regardless of what those results were. That's why we went for an amnio rather than CVS, to minimize the risk of miscarriage, and um, we were really blessed.' (Jakki, CF)

For some, the non-invasive prenatal test represented the only safe way to access either a positive or negative result in order to be prepared for the consequences.

' I can't see any disadvantage of this. If it is the case that you want to know if your child does have a terminal disease then for you to have a simple blood test which is no different to any other blood test that you might have. I think is absolutely marvellous because you are always concerned about results... (Tessa SMA)'

Pre-implantation genetic diagnosis (PGD) testing enables detection and re-implantation of unaffected embryos that do not carry the specific mutation connected with the condition. This was seen as an advantage as it avoided termination of an affected pregnancy, which for some parents felt like betraying their own affected child.

'.....felt that it would be a very difficult decision to be tested at sort of 12-13 weeks and whether to abort the pregnancy or not, having a child with CF, it would be very much like we would be getting rid of her [first affected child], so it wasn't really an option...so we are going down the PGD route (Phillip, CF).'

Theme 2: Changes in reproductive -identity

In spite of the different experiences of the parents involved, the analysis indicated that all parents appeared to move through a transition in their own identity. This comprised three main phases: initially reflected in a sense of invulnerability or naivety, followed by a growing awareness of vulnerability with optimism, and finally by a sense of reproductive vulnerability.

Initially, parents reported a lack of awareness of specific risks to their children.

' ...Because you know before this happened I wouldn't have dreamt of something like this having happened to me or to anybody that I knew, so I didn't even know that I would have, not that I wouldn't

have taken it seriously, but sort of taken on board what it could mean. I think this is probably the same for most people because we go through life thinking or hoping that it won't happen to us and not there are so many different things to think about you can possibly consider everything and take it on board.' (Amelie, SMA).

This lack of awareness made the diagnosis more of a shock.

'.....so pleased and happy that you are pregnant, ...we didn't know at the time, any of these conditions- you just look at them, and think, - Oh that sounds horrific – and you don't think anything more of it and then the result comes back and it's like your world's fallen apart' (Phillip, CF).

Health professionals were seen as a vehicle, leading parents through the cognitive process of their transition. For some, this felt almost coercive:

'Well, when I was pregnant, the midwife insisted that I was tested for sickle cell purely because of my ethnicity.it was my first pregnancy and I was happy to be pregnant really, I and I said I don't need to have it done because there is not history of it in my family, and I thought that even if the baby does have it, does it make any difference now? I was about 21 weeks pregnant, and I thought, well , I just didn't see the point' (Ayse, CF).

Among parents there were some who, despite being aware of their carrier status, preserved an optimistic attitude. While they felt their own vulnerability, the profound desire to create their own family influenced their decisions not to have prenatal testing.

' we knew there was a chance that he could have thalassemia before he was born. We chose at that stage not to get him tested because it was our first born and we knew in our hearts that even if he had it we weren't going to do anything about it. We wouldn't have terminated, so we went ahead' (Rita, thalassaemia).

For others though, once the risk to their children was known, they were forced to acknowledge their own vulnerability and engage in a decision making process.

'When we found out, I was like, Right we can't have any more children because you know I don't want to pass this on to another child. I don't want them to have to go through that. But um, you know, as time goes on, I do want another child, and I know that not a lot of people get funding for PGD and it costs' (Marie, CF).

In some cases the clear change in reproductive identity caused them to modify their planning for future children after the birth of the affected child.

' well it was a bit complicated, the full story is that after Felix [died] we basically decided we weren't going to have any more children. We had my older son and he was healthy and we just felt very fortunate to have him. I think neither of us could make a decision that we would try for another child. I think secretly there was this sort of what we had planned to have two kids. But I say we couldn't bring ourselves to even think about that, but then very unexpectedly I ended up pregnant after my one and only drunken night out and then I just kept it to myself. I had to go into complete denial about it just to carry on functioning because I couldn't contemplate any scenario really in terms of what would happen in the pregnancy. There was part of me pleased and part of me in dread about it all' (Jenny, SMA).

Alongside the changed perspective regarding having more children, the experience of parenthood was depicted as different from other parents. According to these parents in fact, caring for a sick child implied a lifetime commitment, a total devotion to him/her.

'we are gonna do this, cos this is for our baby, but the idea that you've got to do it forever, is, that's what, that gets you, and you think, actually this is a lot for a child to deal with and for us as well' (Rose, CF).

The life limitations expressed by the participants were perceived differently when considering the composition of the family. If the affected child was the first child, the difficulties were perceived as more bearable because of ignorance about what it involved.

'I think it's just a special one, your first pregnancy as well, because you have never been in that situation...even if they had told me then at 12 weeks, 'your baby has got CF', I wouldn't have changed my mind, because it's my first baby. I don't know anything about CF...going forward, I think I would possibly consider abortion if my next baby had CF, only because my daughter's got CF and I know that for the rest of my life I'm going to dedicate more time to her than I would if she didn't have CF.'(Ayse, CF).

In addition, attitudes of parents towards prenatal diagnosis were related to a personal reproductive history.

'Yeah absolutely. Um I think especially if you have been trying for a long time, or if you have had problems previously or anything like that, I think, you know if you had miscarried say, two pregnancies and then you finally got pregnant, I think your view on the pregnancy is very different to if it was your first child and you got pregnant within a week.' (Phillip, CF).

Theme 3: Social pressure to accept prenatal diagnosis.

In term of pressure to be tested, parents described both internal and external sources of pressure. Internal sources were described as generated by personal feelings/emotions.

Internal pressure was felt when considering the immediate family and extended family.

'To be honest, I think really affected our parents more than it did us in many ways because we had a dying child which was enough to cope with, but I think on Jenny's parents' side there was a stupendous amount of guilt particularly from her dad I think, because it seemed to be from his side as his sister had this and he didn't mentioned it and all sort of stuff' (Rob, SMA).

A significant factor leading to an increase in internal pressure to be tested for parents who already had an affected child was feeling unable to cope with more than one affected child in the family

'Obviously, if I go on and hopefully have other children I would be having testing because we decided that we couldn't cope with more than one child with the condition' (Rita, thalassaemia)

Another motivation for having prenatal diagnosis was to protect the suffering child and to give him or her as much attention as possible.

'It's the severity as well. With CF you just don't know what....the baby could be born with all sorts of problems, you know if you do carry on and have a second child with CF, they could be ten times worse than the first child... if we did have a termination, that would have to be a justification behind it, that we've got to prioritise our first child.' (Marie, CF).

The prospect of having an affected child was also the cause of internal anxiety. Parents spoke of wishing to avoid having another child with a lethal or life limiting condition.

'...we didn't want to go through not knowing and then find out when the child was born because obviously there is a lot of pain and suffering that they go through as well we didn't want them to be put through that. So it was a risk [of miscarriage] to take and it was fine, it was fine.' (James, SMA).

Furthermore, some parents undertook prenatal testing to avoid other siblings suffering from the possible loss of an affected brother or sister.

'...Clearly it wasn't an expected pregnancy so given that it was not long, I mean only a year or so after Felix [died] I think roughly, still fresh in mind, do we want to go through that again.... I don't think that we would have wanted to put anybody through that really. With Liam it was pretty hard telling your 3 year old that their brother is going to die all sort of stuff. Why would we want to put anybody involved in all this again let alone the actual child involved' (Rob, SMA).

External pressure to be tested was mentioned frequently. Respondents frequently reported being guided by health professionals to undergo a genetic test, sometimes without taking into account the parents' beliefs or intentions.

'So it wasn't a very, my impression was it not being a neutral conversation from the consultant's point of view as in this is the information, evidence, off you go and make a decision, but sounded a little bit steering and this may have struck us because it was probably steering in a way we wouldn't have gone, and if you were thinking of tests because you wanted to make a judgement on termination or not, maybe that wouldn't have occurred to you because he would have been speaking in a way that you were thinking anyway. But I remember that quite clearly an assumption built in there that is why you have the test and you know depending on the result that will determine whether you have a termination or not.' (Rob, SMA).

Societal pressures were also mentioned.

'...you will be surprised, you will get some shocking comments from people like – you shouldn't have another baby..you do get that from people...' (Jakki, CF).

Theme 4: Attitude to termination.

Many parents expressed a positive attitude to PGD in order to avoid a termination. Some of them justified this as a consequence of their painful experience with losing an affected child.

'...because we had seen what had happened with Felix that if the test had come back positive I don't think there would have been a great deal of discussion about termination' (Rob, SMA)

Great attention was given when discussing the abortion of a fetus suffering from a fatal condition or a life limiting/ non-fatal condition. The diagnosis of a non-lethal condition compared with a fatal one was considered as forcing the choice.

'I certainly found that when I was pregnant with Frankie, that I didn't want any of the tests that I could have had because I've always felt that I would look after a baby even if it had [an abnormality]. I think the only exception was in my head was if a baby had such a severe, you know, disability, that they were to die soon after birth, you know, very serious spina bifida or something like that, but in terms of finding out the chances of having Downs or any of that stuff, I chose not to because I would have, you know, gone ahead with the pregnancy' (Rose, CF)

A lot of interviewees pointed out the importance of timing when considering a termination. The growing attachment occurring between the mother and baby while the pregnancy proceeded was clearly expressed.

'...because the later on it is the more you have got to think time is marching on and you know what I mean it's like going along and it's obviously it's just getting more and more developed as well, they are developing more inside her so it ends up looking like a little person as well the longer you leave it'(James, SMA).

Personal beliefs such as fatalistic or religious views also had an impact.

'You know for a child's point of view I don't think it is fair for a child to be born with that. But then I'm Catholic so from that point of view I shouldn't really I guess have that kind of feeling but yes I don't believe that it is fair for a child to be born intentionally with such a life'(Amelie, SMA).

Discussion

All the participants in this study had family experience with parenting an affected child with an autosomal recessive genetic condition. Some had lost a child to a heritable disease, and some had experienced a life-time commitment caring for their affected child(ren). While we initially conducted the study to explore parents' perceptions of the use of NIPD, it became clear that their experiences had a profound impact on perceptions of themselves and themselves as reproductive beings. Although there is much literature available on the grief that accompanies the diagnosis of a child with a life-limiting condition ((Harper, O'Connor et al. 2014), an important contribution of this study was its capacity to report the experiences of parents who were prone to changes in their self-identity as a consequence of their own experience. This centred around their perception of the likelihood of them having a child with serious health problems. Their journey began from the 'naïve' concept of invulnerability. The lack of awareness of being at risk of passing on a genetic condition to their child made them comparable to other parents, with the same probability of giving birth to a healthy child. A sudden change happened when a parent became aware of the risk, usually as a result of the birth of an affected child. The implications of the birth or prenatal diagnosis of one affected child led to a perception of being vulnerable to further reproductive losses, a parent different from others. Between these two conditions, there was sometimes an intermediate step, where the parent involved was, for example, diagnosed as a carrier, but was able to maintain some optimism about the pregnancy. In this case, the parents could be cognitively aware of the risk but not necessarily emotionally prepared for the diagnosis in the child. It is clear that self-concept can change in a range of situations, including through the reproductive process. Darvill et al (Darvill, Skirton et al. 2010) showed that childbearing women experienced changes to their self-concept, especially during the first pregnancy, and this related at least partially to feelings of lack of control over the process. However, with a successful outcome to the pregnancy, they regained self-confidence. In the case of parents who have been made aware that their child is at risk of a genetic condition, and the loss or birth of an affected child, the restoration of self-confidence is likely to be delayed.

In this study, parents discussed the pressure they felt to accept prenatal testing where this was available to them: pressure was exerted by both health professionals and by those around them in wider society. However, Garcia et al (García, Timmermans et al. 2012)(2015) studied women who were offered prenatal screening in the Netherlands and concluded that women overall did not feel obliged to accept screening as part of their parental duty to the fetus. However, this may reflect cultural values and attitudes in the Netherlands, compared with those of women in the UK and also the different situation where women who are offered screening are perceived as low risk, while our participants were at high risk of having an affected child and had already experienced loss or illness in their offspring.

In a review of parental responses to the loss of a child during the perinatal period, Lamb (Lamb 2002) refers to the coping strategies used by parents in a subsequent pregnancy. These include emotional guarding, delaying announcement of the pregnancy and avoidance of activities that are perceived as potentially harmful to the fetus. However, parents who have experienced previous losses due to a genetic condition are unable to utilise many of these strategies. Due to the need to obtain medical

advice early in the pregnancy if they wish to consider prenatal diagnosis, they are forced to disclose news of the pregnancy at an early stage. In addition, invasive prenatal diagnostic techniques expose the fetus to risk of miscarriage. It is unsurprising therefore that the use of NIPD, which does not carry any risk to the fetus, is an acceptable method of testing for these parents. However, to make best use of these techniques, it is vital that parents are referred to specialist genetic or fetal medicine services before conception or failing that, very early in the pregnancy to maximise the chances of NIPD being available to them.

Strengths and limitations of the study

The results of this study are based on in-depth interviews with parents who had experienced loss, and the data are therefore reflective of those experiences. However, none of the parents had been offered NIPD at the time of the study, therefore they were reporting their intentions and attitudes, rather than actual use of NIPD.

All data were collected by one researcher to ensure consistency, but the analyses were conducted independently by three researchers and discussed in depth by all of the authors. The last author is a midwife and genetic counsellor by profession, which influenced the research question and may have influenced the selection of data that have been reported here.

Conclusions

Midwives and other health professionals are aware that loss of a child during pregnancy or after birth is a significant event for the parents and previous authors have reported an increased incidence of mental health problems (Chojenta, Harris et al. 2014) and psychological distress (Giannandrea, Cerulli et al. 2013) in mothers in subsequent pregnancies. However, the change in parents' reproductive identity due to losses connected with a genetic condition is not well documented. It is clear that additional support from midwives during subsequent pregnancies, with an acknowledgement of the additional feelings of vulnerability experienced by parents whose fetus is at high risk of a disorder may be helpful in allaying some of the distress felt. In addition, midwives should be aware of the options for non-invasive prenatal testing that may help to reduce risks to the fetus and make appropriate referrals so these options can be discussed in a timely manner. As NIPD becomes available for a greater range of conditions, studies of parents who have considered and/or used these methods of testing are required.

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References

- Chojenta, C., S. Harris, N. Reilly, P. Forder, M.-P. Austin and D. Loxton (2014). "History of pregnancy loss increases the risk of mental health problems in subsequent pregnancies but not in the postpartum." *Plos One* **9**(4): e95038-e95038.
- Cowchock, F. S., S. E. Ellestad, K. G. Meador, H. G. Koenig, E. G. Hooten and G. K. Swamy (2011). "Religiosity is an important part of coping with grief in pregnancy after a traumatic second trimester loss." *Journal Of Religion And Health* **50**(4): 901-910.
- Darvill, R., H. Skirton and P. Farrand (2010). "Psychological factors that impact on women's experiences of first-time motherhood: a qualitative study of the transition." *Midwifery* **26**(3): 357-366.
- Ekin, A., C. Gezer, C. E. Taner, M. Ozeren, M. E. Avci, I. Uyar and I. E. Ertas (2014). "Cytogenetic analysis of 6,142 amniocentesis cases: A 6-year single centre experience." *Journal Of Obstetrics And Gynaecology: The Journal Of The Institute Of Obstetrics And Gynaecology* **34**(7): 571-575.
- García, E., D. R. M. Timmermans and E. van Leeuwen (2012). "Parental duties and prenatal screening: Does an offer of prenatal screening lead women to believe that they are morally compelled to test?" *Midwifery* **28**(6): e837-843 831p.
- Giannandrea, S. A. M., C. Cerulli, E. Anson and L. H. Chaudron (2013). "Increased Risk for Postpartum Psychiatric Disorders Among Women with Past Pregnancy Loss." *Journal of Women's Health (15409996)* **22**(9): 760-768 769p.
- Harper, M., R. C. O'Connor and R. E. O'Carroll (2014). "The relative importance of avoidance and restoration-oriented stressors for grief and depression in bereaved parents." *Psychology, Health & Medicine*: 1-10.
- Hill, M., A. N. Barrett, H. White and L. S. Chitty (2012). "Uses of cell free fetal DNA in maternal circulation." *Best Practice & Research: Clinical Obstetrics & Gynaecology* **26**(5): 639-654.
- Hill, M., C. Compton, M. Karunaratna, C. Lewis and L. Chitty (2014). "Client Views and Attitudes to Non-Invasive Prenatal Diagnosis for Sickle Cell Disease, Thalassaemia and Cystic Fibrosis." *Journal Of Genetic Counseling*.
- Hill, M., C. Compton, C. Lewis, H. Skirton and L. S. Chitty (2012). "Determination of foetal sex in pregnancies at risk of haemophilia: a qualitative study exploring the clinical practices and attitudes of health professionals in the United Kingdom." *Haemophilia: The Official Journal Of The World Federation Of Hemophilia* **18**(4): 575-583.
- Hill, M., J. Fisher, L. S. Chitty and S. Morris (2012). "Women's and health professionals' preferences for prenatal tests for Down syndrome: a discrete choice experiment to contrast noninvasive prenatal diagnosis with current invasive tests." *Genetics In Medicine: Official Journal Of The American College Of Medical Genetics* **14**(11): 905-913.
- Hill, M., C. Lewis, L. Jenkins, S. Allen, R. G. Elles and L. S. Chitty (2012). "Implementing noninvasive prenatal fetal sex determination using cell-free fetal DNA in the United Kingdom." *Expert Opinion On Biological Therapy* **12 Suppl 1**: S119-S126.

- Kingsmore, S. F., D. L. Dinwiddie, N. A. Miller, S. E. Soden and C. J. Saunders (2011). "Adopting orphans: comprehensive genetic testing of Mendelian diseases of childhood by next-generation sequencing." Expert Review Of Molecular Diagnostics **11**(8): 855-868.
- Lamb, E. H. (2002). "The impact of previous perinatal loss on subsequent pregnancy and parenting." The Journal Of Perinatal Education **11**(2): 33-40.
- Leithner, K., A. Maar, M. Fischer-Kern, E. Hilger, H. Löffler-Stastka and E. Ponocny-Seliger (2004). "Affective state of women following a prenatal diagnosis: predictors of a negative psychological outcome." Ultrasound In Obstetrics & Gynecology: The Official Journal Of The International Society Of Ultrasound In Obstetrics And Gynecology **23**(3): 240-246.
- Lewis, C., M. Hill, H. Skirton and L. S. Chitty (2012). "Fetal sex determination using cell-free fetal DNA: service users' experiences of and preferences for service delivery." Prenatal Diagnosis **32**(8): 735-741.
- Lewis, C., C. Silcock and L. S. Chitty (2013). "Non-invasive prenatal testing for Down's syndrome: pregnant women's views and likely uptake." Public Health Genomics **16**(5): 223-232.
- Lo, J. O., F. Cori D, M. E. Norton and A. B. Caughey (2014). "Noninvasive prenatal testing." Obstetrical & Gynecological Survey **69**(2): 89-99.
- Lo, K. K., C. Boustred, L. S. Chitty and V. Plagnol (2014). "RAPIDR: an analysis package for non-invasive prenatal testing of aneuploidy." Bioinformatics (Oxford, England) **30**(20): 2965-2967.
- Lo, Y. M. D. (2013). "Non-invasive prenatal testing using massively parallel sequencing of maternal plasma DNA: from molecular karyotyping to fetal whole-genome sequencing." Reproductive Biomedicine Online **27**(6): 593-598.
- Mujezinovic, F. and Z. Alfirovic (2012). "Technique modifications for reducing the risks from amniocentesis or chorionic villus sampling." The Cochrane Database Of Systematic Reviews **8**: CD008678.
- Paneque, M., J. Sequeiros and H. Skirton (2015). "Quality issues concerning genetic counselling for presymptomatic testing: a European Delphi study." European Journal Of Human Genetics: EJHG.
- Roa, B. B., J. Pulliam, C. M. Eng and S. W. Cheung (2005). "Evolution of prenatal genetics: from point mutation testing to chromosomal microarray analysis." Expert Review Of Molecular Diagnostics **5**(6): 883-892.
- Schaap, A. H., H. Wolf, H. W. Bruinse, S. Barkhof-van de Lande and P. E. Treffers (1997). "Long-term impact of perinatal bereavement. Comparison of grief reactions after intrauterine versus neonatal death." European Journal Of Obstetrics, Gynecology, And Reproductive Biology **75**(2): 161-167.
- Shashi, V., A. McConkie-Rosell, B. Rosell, K. Schoch, K. Vellore, M. McDonald, Y.-H. Jiang, P. Xie, A. Need and D. B. Goldstein (2014). "The utility of the traditional medical genetics diagnostic evaluation in the context of next-generation sequencing for undiagnosed genetic disorders." Genetics In Medicine: Official Journal Of The American College Of Medical Genetics **16**(2): 176-182.

Simpson, J. L. (2012). "Invasive procedures for prenatal diagnosis: Any future left?" Best Practice & Research: Clinical Obstetrics & Gynaecology **26**(5): 625-638.

Skirton, H., L. Goldsmith and L. S. Chitty (2014). "An easy test but a hard decision: ethical issues concerning non-invasive prenatal testing for autosomal recessive disorders." European Journal Of Human Genetics: EJHG.

Strauss A, C. J. (1998). Basics of Qualitative Research: Techniques and Procedures for Developing Grounded Theory, Sage Publications.

Titus, B. and R. de Souza (2011). "Finding meaning in the loss of a child: journeys of chaos and quest." Health Communication **26**(5): 450-460.

Vallance, H. and J. Ford (2003). "Carrier testing for autosomal-recessive disorders." Critical Reviews In Clinical Laboratory Sciences **40**(4): 473-497.

Van, P. and A. Meleis (2010). "Factors related to dimensions of grief intensity among African-American women after pregnancy loss." Journal Of National Black Nurses' Association: JNBNA **21**(2): 1-8.

van Schendel, R. V., J. H. Kleinveld, W. J. Dondorp, E. Pajkrt, D. R. M. Timmermans, K. C. A. Holtkamp, M. Karsten, A. L. Vlietstra, A. M. A. Lachmeijer and L. Henneman (2014). "Attitudes of pregnant women and male partners towards non-invasive prenatal testing and widening the scope of prenatal screening." European Journal Of Human Genetics: EJHG **22**(12): 1345-1350.

Willis, J. (2007). Foundations of Qualitative Research: Interpretive and Critical Approaches. Thousand Oaks, California, Sage Publications, Inc.

Table 1. Demographic characteristics of participants

Pseudonym	Gender	Age	Children	Condition	Prenatal tests in the past
Rita	Female	30-39	Two children, one affected.	Thalassaemia	CVS x1
Mushtaq	Male	30-39	Two children, one affected.	Thalassaemia	Wife had PND
Deidre	Female	30-39	Three children, one affected.	Cystic fibrosis	No
Ayse	Female	20-29	One child, affected.	Cystic fibrosis	No
Philip	Male	30-39	One child, affected.	Cystic fibrosis	Considering PGD
Faye	Female	20-29	One child, affected.	Cystic fibrosis	No
Rose	Female	30-39	One child affected.	Cystic fibrosis	No
Matt	Male	30-39	One child, affected.	Cystic fibrosis	No
Jakki	Female	40-49	Two children, one affected	Cystic fibrosis	Yes. CVS x1
Marie	Female	30-390	One child, affected.	Cystic fibrosis	
Jenny	Female	30-39	Three children, one died of SMA at 5/12.	SMA	Yes
Rob	Male	30-39	Three children, one died of SMA at 5/12.	SMA	Wife had PND
James	Male	40-49	Three children, one died of SMA at 5/12	SMA	Wife had PND
Tessa	Female	40-49	Three children, one died of SMA at 5/12	SMA	CVS x 2
Rachel	Female	40-49	Two children, one died at 7/12 of SMA. Two further miscarriages.	SMA	No 3 x PGD unsuccessful
Alexis	Female	30-39	Four children, one died at 21 months of SMA.	SMA	No
Amelie	Female	40-49	One child, died at 10 months of SMA	SMA	No, but unsuccessful PGD