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Impediments to DNA Testing and Cascade Screening for Hypertrophic Cardiomyopathy and Long QT syndrome: A Qualitative Study of Patient Experiences

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Abstract
Background/Aims
This paper reports data from a qualitative study of patient experiences of DNA testing and cascade screening for hypertrophic cardiomyopathy and long QT syndrome, cardiac conditions that place sufferers at risk of sudden death. The paper particularly focuses on potential impediments to testing and screening.
Methods
Semi-structured interviews were undertaken with a purposive sample of 27 people in the UK who had undergone testing.
Results
In the context of the uncertainties that can characterize experiences of these disorders, the majority of participants in this sample embraced testing and screening as a way of providing health information for themselves or their relatives (particularly children). There was nevertheless evidence of ambivalence about the value and impact of the DNA test information which could influence participants' dispositions toward testing, and play into dilemmas about family communication. Other concerns arose in relation to communicating about these disorders, decisions to involve elderly relatives and pressures relating to family responsibility.
Conclusion
The evidence of ambivalence provides insight into why some people may be resistant to testing, screening and sharing information. The findings about communication processes indicate potential areas of concern for the cascading process.

Keywords
DNA test, cascade screening, hypertrophic cardiomyopathy, long QT syndrome, patient experience, family communication.

Introduction

This paper reports data collected from an exploratory, qualitative study of 27 people in the UK who had been DNA tested for a heritable cardiovascular condition that places them at risk of sudden cardiac death. Three key research questions were investigated: peoples' experiences of (1) the disorders and their treatment, (2) the DNA testing process, and (3) sharing information in family groups. There is a growing body of work on patient experiences of such disorders (Anderson et al. 2008; Christiaans et al. 2009a,b; Cox et al.1997; Farnsworth et al. 2006; Hintsa et al. 2009; Ingles et al. 2008; Morgan et al. 2008). Previous studies show that DNA technologies are widely embraced, although

acknowledge the existence of ambivalence, reticence or resistance. This paper particularly focuses on interview data that highlight some of the issues that may impede the use of DNA testing as part of a cascade screening strategy. Such a strategy involves "systematically approaching relatives of patients affected by genetic disorders" (de Wert 2005, p.397), and offering a predictive DNA test to those are potentially at-risk (based on information about a causal genetic mutation identified from a confirmed (index or proband) case).

There are a number of cardiovascular conditions that place people at risk of sudden cardiac death; hypertrophic cardiomyopathy (HCM) and long QT syndrome (LQTs) are among the most well known (Chiang 2004; Maron 2002). These are distinct and different kinds of cardiac disorders, yet there are sufficient similarities in their presentation to legitimate examining them jointly in a study of patient experience. Symptoms of both conditions often become evident in teenagers and young adults, and as fatalities can result the first time the disorders present themselves there are tragic stories of unforeseen deaths. Their incidence usually shows a familial pattern, and their heritable forms are usually autosomal dominant (Chiang 2004; Maron 2002). To date, HCM has been connected to mutations in at least thirteen different genes (Alcalai et al. 2008; Lind et al. 2006) and mutations in at least twelve different genes have been related to LQTs (Hedley et al. 2009). When it is useful to refer to HCM and LQTs together in this paper, they will be termed inherited cardiac conditions.

Importantly, there can be a degree of uncertainty surrounding diagnosis, prognosis and therapy (Michels et al. 2007). These are disorders which display phenotypic heterogeneity, with a range of symptoms (including "none") (Ingles et al. 2005; Keren et al. 2008; Vincent 1998). Symptoms such as arrhythmias and fainting can be attributed to many causes, and heart muscles can become thickened due to other factors. Clinical examinations using echocardiograms, electrocardiograms (ECGs) and 24-hour Holter Monitors can result in complex "borderline" cases (Crotti et al. 2008). Interventions to reduce symptoms and risk of dying include implantable defibrillators (in high-risk cases), drug therapies, lifestyle advice and routine clinical monitoring (Chiang 2004; Maron 2002). Nevertheless, some common interventions can themselves be sources of uncertainty in patient experiences (Andersen et al. 2008; Farnsworth et al. 2006; Henriks et al. 2005; Maron et al. 2004; Sola and Bostick 2005).

Research on patient experience of inherited cardiac conditions highlights worry and uncertainty. With respect to LQTs, Farnsworth et al. (2006, p. 285-6) report sources of uncertainty and anxiety to be not only the diagnosis of a "potentially lethal" condition but also the "vast spectrum of clinical presentation" and the "stressors" relating to their "treatment and management." In Anderson et al.'s (2008, p. 492) study of coping with the disorder, uncertainties included worries about not knowing "what was happening", difficulties in interpreting physical feelings and the potential loss of control. With respect to HCM, Cox et al. (1997, p. 187) conclude that worry is a "widespread problem, and possibly one that is inherent in the condition. For despite reassurance and education, uncertainties about prognosis inevitably persist." It has been argued that those living with a familial risk of HCM, but without symptoms, may face so much uncertainty that even a positive DNA test has the potential to restore a sense of control or provide reassurance (Christiaans et al. 2009a), as has been recorded in relation to DNA tests for other disorders (Marteau and Mitchie 1995). Another area of significant concern for those at

risk of inherited cardiac conditions are issues relating to children (and grandchildren) and reproduction (Anderson et al. 2008; Charron et al. 2002; Farnsworth et al. 2006; Hendriks et al. 2005; van Langen et al. 2004, Yu et al. 1997). It has been shown with respect to HCM, however, that worry can be alleviated by attending specialized cardiac genetics clinics (Ingles et al. 2008), and this has also been recommended for those at risk of LQTs (Anderson et al. 2008).

The effectiveness of molecular genetic testing and cascade screening for inherited cardiac conditions is under discussion (Charron et al. 2002; Christiaans et al. 2008; Langen et al. 2004; Michels et al. 2007; van Yu et al. 1997). Pinpointing the causal genetic mutation in probands can confirm a diagnosis and may influence their clinical care. This knowledge can then also be used to screen relatives with a greater degree of certainty than clinical examinations alone (Yu et al. 1997), allowing for the discharge of those without a mutation (people who would otherwise have been treated as at risk) and the identification of clinically unaffected but genetically at risk individuals (with the potential for preventing sudden cardiac death). However, as the genes involved in these disorders have variable expressivity and penetrance (Vincent 1998; Yu et al. 1997) being diagnosed as "genetically at risk" does not necessarily provide insights into variability in phenotype and symptoms (Farnsworth et al. 2006). Also, the "predict and prevent" strategy relies on information about the disorder and the possible inventions being communicated within families – a responsibility which usually falls to the proband. These issues of continuing uncertainty and communication will be addressed in the subsequent discussion.

Methods

This research was affiliated with a program of work developing molecular genetic testing and cascade screening for HCM and LQTs in the UK, conducted by the Inherited Heart Disease service in Oxford as part of the Genetics Knowledge Park programme. This exploratory qualitative study aimed to investigate the experiences of people who had been offered testing. A qualitative methodology, using semi-structured interviews, was the most appropriate approach for gaining in-depth information.

Sample

Twenty-seven interviewees were selected purposively (Ritchie et al. 2003) on the primary criterion that they had undergone a DNA test for an inherited cardiac condition, with diversity sought on differences in the condition (HCM/ LQTs), route into testing (proband/ cascaded) and test result (positive/ negative). The participants were "recruited" via their medical practitioner (cardiac specialist, clinical geneticist or genetic counselor), following an ethics protocol approved by a Multi-centre Research Ethics Committee (MREC) which also specified processes for data collection and storage. Twenty four information packs sent from the clinic where the study originated generated fifteen participants (the reasons why nine people did not volunteer are unknown). To gain sufficient participants to ensure diversity in the sample, information packs were also distributed to seventeen other UK hospitals that had requested DNA testing during the study time-frame (it is not known how many practitioners gave information packs to patients, or how many patients refused the invitation to take part and why). All potential

participants who expressed an interest in taking part in the study were interviewed, resulting in an additional twelve participants from seven locations. Table 1 (Participant Characteristics) and its accompanying footnotes describe some key variations within the sample: condition (14 HCM, 13 LQTs), clinical status (20 treated as affected, 7 treated as unaffected), DNA result (17 positive, 7 negative, 3 no known mutation) and test status (15 proband, 9 cascade, 3 research).

Interview protocol and procedures

Data collection took place during 2005-06. Interviews were conducted in a setting chosen by the participant (usually their home) and were preceded by MREC agreed informed consent processes. All of the interviews were conducted face-to-face by the author, a trained social science researcher with 10+ years experience. Two interviews included multiple participants from the same family group (one involved two people, and one involved three). The median interview length was 49 minutes (Range: 27 minutes to 84 minutes).

Interviews were conducted using a topic guide that was checked with an advisory panel of academics, a cardiac genetics counselor and a patient support group organizer to ensure that it was appropriate (See Appendix). The interview guide was structured around five topics: experiences of the condition; the process of DNA testing; sharing information in families; benefits and drawbacks of testing and screening and the provision of information. This guide was used flexibly and participants were encouraged to discuss issues that had the greatest significance to them.

Data Analysis

Interviews were audio-recorded and fully transcribed (and then cross-checked to ensure accuracy). Data analysis was developed by the author using an "analytical hierarchy" approach which begins with processes of coding, sorting and summarizing and links these to higher levels of analytical abstraction such as establishing typologies, detecting associations and developing explanations (Spencer et al. 2003). Transcripts were closely read and annotated to develop codes to sub-divide and categorize the data (Dey 1993), with sub-codes developed inductively from within the topics in the interview guide. Initial codes were developed and iteratively revised using the data from the first fifteen participants that had been imported into *QSR NVivo* qualitative data analysis software (Bazeley and Richards 2000). An interim "thematic analysis" (Gomm 2004) was developed to consolidate the coding frame and provide an analytical framework for exploring the areas of commonality and divergence within the dataset (this analysis was read and validated by a cardiac genetics counselor). Each additional transcript was then analysed to check consistency with (or difference from) the findings therein. The cross-sectional analysis presented here draws attention to commonalities and differences across the sample as a whole (Spencer et al. 2003).

Results

Psycho-social responses to test results

Before considering issues of ambivalence and communication, some findings relating to predictive DNA tests should be noted. Two of the nine participants tested in a cascade screen were DNA positive. One participant (R23), who reported no history of symptoms, appeared outwardly unconcerned by her positive test result. The explanation for this somewhat surprising reaction appeared to be that she had children who were clinically affected and receiving treatment, and claimed that she had thus expected a positive result. The other participant, however, explained that he was "a bit shocked really" and showed some evidence of having subsequent feelings of health anxiety and guilt relating to other members of his family; "when I found out I thought: '*oh, it's me that's causing all this trouble*'" (HCM, treated as unaffected, DNA positive, Cascade: R06).

Five of the seven cascaded participants who were DNA negative were clinically unaffected, and thus the "all clear" result was reported as largely expected (although a sense of relief was sometimes evident). The other two participants who received negative DNA results in a cascade screen had been treated as if they were affected by an inherited cardiac condition, and both reported a sense of shock at their result. One of these participants also exhibited distress (anger and regret) about the extent to which her (now over-turned) diagnosis had impacted life experiences:

> So it was yeah quite a shocker, in fact very, very shocking. So I'd spent 20 years on medication and living, potentially, I could have lived a life you know in cotton wool so to speak" (LQTs, treated as affected, DNA negative, Cascade: R13).

The other participant appeared more sanguine, although notably she still perceived herself as unwell, with her symptoms having a different cause: "I've got the condition but I haven't got the gene, my condition is caused by high blood pressure" (HCM, treated as affected, DNA negative, Cascade: R05).

Viewpoints on DNA testing

There were broadly two types of response to the potential of DNA testing and screening. One outlook was to embrace the potential for reducing uncertainties This response was usually accompanied by a belief that the outcomes of a DNA test could give greater certainty in diagnosis (participants used terminology such as "definite", "absolute", "certain" or "conclusive"). The desire to predict who was at risk was sometimes accompanied by a sense of urgency in relation to younger relatives; for example, one participant pressed to get her young children DNA tested because she "wanted to know now" (HCM, treated as affected, DNA positive, Research: R03). This welcoming response to the potential of DNA technologies was the most common attitude in this sample of participants.

However, a notable minority of participants (6/27) - while not entirely against DNA tests - expressed concerns about them, or the benefits of knowing their results. It is possible to identify five (potentially interlinking) sources of ambivalence, which together had the potential to influence attitudes to testing and screening. These are reported below to demonstrate the potential *range* of patient concerns and as such, no judgement is offered by the author about the clinical "accuracy" of the participants' views, and no comment can be made (given the sampling strategy) about how widespread these perceptions might be.

The first concern is that a "negative" DNA result in a symptomatic patient was not necessarily an "all clear," and that this may add to experiences of uncertainty. One participant, whose echocardiogram had revealed a "possible thickening of the heart muscle" but who knew of no experiences of the disorder in her family, described the results of a DNA test that she had taken in an attempt to confirm her diagnosis:

> […] they tested three genes and they all came back negative. But as [the genetic counselor] said, it doesn't mean that I haven't got it. [..] because, I mean it was made very clear that if the results all come back negative it's, you know, it's maybe. I don't even think they said it's inching towards having not got it. (HCM, treated as affected, No known mutation, Proband: R27)

The participant reported that the potential for an inconclusive outcome had been explained to her. Nevertheless, her admission that "I'd like to have a concrete yes or no rather than a '*we don't know, but live like you've got it*'" indicated her continuing dissatisfaction. Indeed she reported: "the main problem is because they still haven't told me definitely that I've got [HCM]." Despite her awareness of this scenario, the "negative" DNA test result was a disappointment because it failed to remove uncertainty.

A second concern was the finality of DNA test results. This next participant was asymptomatic, but had relatives diagnosed with LQTs and had experienced sudden cardiac death in his family. He reported that he was searching for a conclusive diagnosis and, when asked, revealed a degree of hesitancy about his (negative) DNA result being the end of the matter:

> R10 […] nobody was prepared to say I haven't got it. Along the line they were all saying less likely, no symptoms, less likely, no symptoms, not conclusive you know, all the way along. So when this thing [the DNA test] came up at Oxford, seemingly conclusive, I said '*we'll have a bit of that.*'
>
> AS Okay, you say seemingly conclusive?
>
> R10 Well, you know, until next time somebody says: '*well, actually it's not conclusive*' and then we'll do some …, another test. (LQTs, treated as unaffected, DNA negative, Cascade: R10).

Interpreted at face-value, this apparent expression of cynicism was related to the inherent uncertainty and evolving nature of medical knowledge and testing (it is unclear whether this is cynicism in general, or specific to LQTs). An alternative or supplementary interpretation, however, is that despite a negative DNA result the participant was revealing underlying feelings of denial (expressing doubt because he still fears that he has LQTs), or even "survivor guilt" (expressing doubt as a mechanism for coming to terms with the knowledge of not having LQTs, while his relatives do).

The third source of ambivalence regarding DNA testing concerned the impact of a positive DNA diagnosis on quality of life. The following account is from the same participant quoted previously:

> You get to a stage where you're thirty-eight years old, which is my age, and you think okay it hasn't bothered me up to now and do I want to reduce the quality of my life in the future by finding out and possibly having to take beta blockers [..] I don't want to, didn't want to go on beta blockers because you know two of my [siblings] are on them, they've both put on a lot of weight, they weren't able to do the sport things that they were able to, it's a whole change of life and so I didn't want that. (LQTs, treated as unaffected, DNA negative, Cascade: R10)

His decision to take a DNA test, at least as he reviewed it in retrospect following a negative DNA result, was framed by two appraisals. The first was a risk assessment based on symptoms and age (this participant perceived that he might be less at-risk because of he was thirty-eight and asymptomatic, reflecting a common view that LQTs often affects younger people). The second weighed any potential benefits of "finding out" (i.e., a positive DNA diagnosis) against fears that potential treatments may affect his "quality of life" (represented by weight and lifestyle).

Discussions with parents about DNA testing their children revealed two further interrelated sources of ambivalence. One was that a positive DNA test did not give certain knowledge about prognosis, and this was linked to a second worry that knowing one was at risk of sudden cardiac death could be an emotional or psychological burden. The following participant reflected on the different experiences of two of his siblings who had died (only one of whom had known that he was at risk):

> With the benefit of hindsight [..] it might well have been better if he hadn't known because he'd have just got on with his life. You know for [my sister] of course it was tragic that she didn't have…, but she didn't know anything about it, she lived a fully active life until suddenly something happened but [my brother] knew about it for 7 years, the most informed 7 years of his life knowing that this was hanging over him as a threat and the advantage of knowing it was there didn't translate [..] I don't think that was a great improvement to his life. (HCM, treated as affected, DNA positive, Proband: R08)

This participant, unconvinced of the benefits of knowing (because this had not improved his brother's life, or prevented his death), concluded that his children's DNA test results were not the "real answer," as he still did not know full implications. Another participant similarly reported ambivalence about getting his children DNA tested for HCM:

> I've got very mixed thoughts about that because I think, you know, if it is possible to know about these conditions at such a young age, I think that could really have a hugely life changing impact. [..] And so if my son is given that definite label, you know at the age of twelve or whatever, then I'm sure it's definitely going to have an impact on him. I mean one of the things that is said is that if children have got this diagnosis, they ought to be directed away from very competitive sports and things like that. But you know I think if you have enough of a family history and a suspicious enough background then you can probably direct your children away from those things anyway without giving them the label, because at the end of the day we don't have a …, you see one of the things that is frustrating

> about this condition is that there's no definite treatment that's going to prevent the sudden death and there's no absolute way of picking out who will get the sudden death. (HCM, treated as affected, DNA positive, Proband: R11)

This participant felt that not only did a positive DNA test fail to provide more certain knowledge about disease prognosis or treatment, but also it carried with it a label that was a burden in everyday life (in insurance and other bureaucratic realms, and also as an emotional and psychological influence). It is notable that, in this sample and from the point of view of some participants, concerns about the lack of treatment options pertained to HCM rather than LQTs.

Viewpoints on family communications

The range of information that interviewees reported having shared with others in their family included details about: the disorder, DNA tests and the processes of cascade screening. Experiences of sharing information in family groups were variable. Some participants considered the process to be unproblematic: they thought they knew who to contact, how to contact them, what they needed to say and were confident that they could provide the necessary information. (It should be held open to question whether participants' ideas about these areas necessarily coincide with those of practitioners). Data analysis also revealed a range of difficulties in communication, including "knowledge" issues (knowing which family members could have inherited the gene alteration, and explaining the medical / genetic aspects to someone else) and loss of contact for either mundane or complex/ sensitive reasons (e.g., not having a contact address or phone number, or not wanting to speak due to previous disagreements).

The following extract, from a participant who reported a particularly difficult experience, illustrates how a variety of factors can become interlinked in decisions about sharing information:

> R19 The biggest issues that have come up are people [*health practitioners*] saying to us that you should be telling certain members of the family and certain members of the family saying, you know; '*no, don't bother people with it*' […] My mum's side of the family didn't want me to get in contact with that side of the family. I sort of think, well why I am worrying with it? I don't know, I don't know what to do. We're still trying to decide on whether to contact them. […] But it's very difficult going to strangers and saying '*Look sorry to tell you this, you might have this condition, do you want to know?*' when they could just go through, well they could get on quite happily with their lives basically. […] I just feel like, you know, if I could just tell them, that you can have the test, then it would just be nothing to do with me anymore and I could just not…, you know, it's nothing to do with me anymore. I don't know. Mum just doesn't think I should get involved.
>
> AS Right, and what does your husband think?

> R19 He thinks, he thinks yes, we should do it, definitely; because of the children, yeah their children. (LQTs, treated as affected, DNA positive, Proband: R19)

The dilemma expressed here reveals the intersection between: a "complex" and geographically dispersed family network; weak relationships with some family members (some of who she did not know, or know how to contact); competing advice or pressures (from health professionals and kin including "blood" relatives and spouse); personal guilt and anxiety; and, the difficulties of communicating information about the condition.

Of the difficulties in communication that were reported, those that were more specific to inherited cardiac conditions were rooted in the sudden and extreme nature of the health threat to other family members, particularly children. While for most this was a motivation to communicate, in some instances it was experienced as a burden of guilt and anxiety (particularly where there were other barriers to communication). The difficulties involved in speaking with relatives about inherited cardiac conditions were: how to start the conversation about being at risk of sudden death; how to tell people they (or their children) would have to stop playing sports or doing strenuous exercise; the worry that they (or the recipient) would find it an emotional or stressful conversation, or that the recipient might not want to know, particularly because the knowledge could be a burden. This last issue is encapsulated by the question that Participant 19 (quoted earlier) imagines she will have to pose to her relatives: "*do you want to know?*", to which she then adds "when they could just go through, well they could get on quite happily with their lives basically." As reported in the previous section, there is a possibility that some people might *not* want to know – that they might think they are better off not knowing. The above extract suggests that people who are ambivalent about the benefits of the knowledge can worry that they are going to force unwanted knowledge on others.

Three participants voiced disquiet about involving their elderly parents in screening, or they had already declined to involve them. They offered a number of reasons. First, they did not want to worry them with information about a heart problem, particularly where they had other health concerns. Second, it was suggested that a diagnosis of the condition would not be directly beneficial to people in the later stages of life. Some participants thought that as these disorders most often develop in young people, elderly parents were less likely to be at risk. Third, there was also a desire to protect parents from the potential guilt of passing on a "faulty" gene. These decisions by "adult children" to protect their parents could pose a barrier for taking cascade screening beyond first degree relatives (as will be discussed in the following section).

There was also evidence of pressure from relatives to get other people in the family tested, based on fears or anxieties about the disorders. For example, one person reported actively "persuading" a sibling to undergo DNA testing by arguing that she had a duty to protect the younger generations of her family. She explained how she had convinced her sister of the "logic" of cascade screening by persuading her that if she took a DNA test and was clear, she could then protect her children and grandchildren from ever having to worry about the disorder. In another example, a participant had complained that her parents had applied strong pressure on her to get tested, and had only realised afterward "that all this pressure that they were putting on me, was probably fear in them that I may have it, and their granddaughter" (HCM, treated as unaffected, DNA

negative, Cascade: R25). These instances reveal that cascade screening for inherited cardiac conditions can open up feelings of responsibility about health to the wider family unit, with some family members using the interests of younger generations to exert pressure on decision-makers.

Discussion

For the participants in this study, DNA testing and cascade screening were commonly embraced as ways of reducing uncertainties in diagnosis. The ambivalent responses (albeit in a small proportion of participants) were a main focus of the findings as they provide an insight into the challenges that might face those promoting or implementing DNA testing and cascade screening. Anderson et al. (2008, p. 496) note that we "can only speculate about the reasons why some individuals do not want to be tested […]", but in the absence of studies of such individuals, the evidence presented in the research study can play a role. The findings regarding ambivalence reveal the kinds of concerns held by people who were faced by choices regarding DNA testing, and included the perceptions that it might be better not to have to live with the knowledge that you are at risk of sudden cardiac death, that a positive DNA result might not relieve uncertainties about personal risks, and that testing might actually have negative social and psychological consequences of its own. These sources of ambivalence may (even if only in part) contribute to understanding other evidence of reticence, such as relatives not welcoming information about their genetic status for LQTs (Andersen et al. 2008), reports of a limited uptake for genetic counselling for HCM (Christiaans et al. 2008), and a small minority of people who had been DNA tested for HCM admitting they would rather have not known (Christiaans et al. 2009b).

The findings of the present study concerning family communications also have implications for providing services for DNA testing and cascade screening. Perceptions about disease severity, interventions and the certainty offered by testing, were influential factors affecting the sharing of information in families, as they are in previous studies (Wilson et al. 2004). In the context of inherited cardiac conditions (at least in this sample of participants), the risks of sudden death in the young contribute not only a particular sense of compulsion and urgency for sharing information, but also a potential for anxiety and guilt, particularly where there were perceived barriers to communication. These barriers were reminiscent of other studies (Gaff et al. 2007; Wilson et al. 2004) but were specific to inherited cardiac conditions in so far as they related to the challenges of talking about sudden death, and the effects of a diagnosis on lifestyle.

It is know that non-disclosure dilemmas can stem from concerns about causing harm, distress or alarm to relatives (Clarke et al. 2005; Keenan et al. 2005), but a notable aspect of this study is evidence suggesting that a lack of conviction about sharing information could relate to an ambivalent attitude toward the "benefits" of the knowledge. Underlying this ambivalence was the dilemma of whether knowing that you are at risk of sudden death was a good or a bad thing. Where participants thought that treatments were available and effective, the common refrain could be paraphrased as: "Why wouldn't you want to know?" Where participants were more skeptical about interventions, there was ambivalence about the value of DNA tests which could impact on thinking about getting tested, getting children tested or passing on information to other family members.

In this study there was a notable inversion of the usual pattern of parental-child decision-making (Gaff et al. 2007; Keenan et al. 2005), as some children (albeit adult children) were taking responsibility for decisions about their parents' involvement in testing. Judgements about obligations and the vulnerability of the recipients with respect to information were evident in this sample, as part of the well-known disclosure dilemma: Is the emotional harm of disclosure lesser than the medical benefit (Gaff et al. 2007; Wilson et al. 2004)? Some participants thought that the tangible health benefits for some vulnerable older relatives were not particularly clear cut, weakening the imperative for sharing the information with them. These results could have implications for cascade screening for inherited cardiac conditions, as, in some instances, testing elderly family members can contribute to assessing the risks faced by people in the extended family group.

A similar cost-benefit analysis of the value of the information may also deter some people from a DNA test. In this study there was evidence of reticence, persuasion and resistance, sometimes linked to a perceived lack of "personal benefit" from DNA testing. The primary motivation for DNA testing for an inherited cardiac condition is to gain health information relevant to oneself or to one's children or family, and it has been reported elsewhere that there can be family pressures to be involved in cascade screening, with elderly people often citing their (grand)children as the reason for testing (Christiaans et al. 2009b). The findings herein underline that, for some people, choosing (or refusing) to have a DNA test for an inherited cardiac condition (and/or to be involved in sharing information) could rest on perceptions and pressures concerning family responsibility rather than on overt personal health benefits.

Limitations of the Study.

The heterogeneity within the sample is notable and may influence experiences. While there were no consistent divergences among different "kinds" of participants (i.e., according to the characteristics in Table 1) in the data analysis, such differences could be masked within a small sample. Other potentially important sources of variation include age (this information was not collected), symptoms and experiences of the disorders (in the individual and the family group), the time that had elapsed since testing and the influence of testing and counselling processes and practices (participants here received care in various locations, at different times and had different routes into testing). The extent of variation in this research is not unusual for an exploratory qualitative study, and actually provides an important benefit by helping to reveal a wider range of experiences than in a more homogenous sample.

A second limitation is potential sampling biases: health practitioners who were well-disposed toward a DNA testing service chose which (if any) of their patients received information packs; and, the interviewees "self-selected." These constraints, common in qualitative research, were in this instance a consequence of requiring "gatekeepers" to facilitate access to a small number of potential participants. It could be noted, however, that these biases could potentially work in contradictory ways, leading not only to a high representation of "positive" views of testing but also for interviews becoming a platform for voicing dissatisfaction about treatment. Also, a number of participants were from the same families and therefore may share similar views of or

experiences with the disorders and genetic testing. While a purposive sampling technique ensured relevant data were collected, no claims are made for the representativeness of the sample.

Research Recommendations

Further research is needed (if possible using more generalizable sampling techniques) to establish the frequency of the viewpoints reported herein, to assess whether they are more or less likely to be expressed by different "types" of participants, and to determine whether they have any real effect on the uptake of, or satisfaction with, health service provisions. Research could also investigate clinical interventions and counseling strategies designed to address such concerns. As the ambivalence reported in this study represents the experience of people who underwent testing despite their misgivings, it is necessary to investigate the extent to which these reservations match those of individuals who resist involvement in testing (although accessing potential participants is recognized to be a significant challenge).

Implications for practice

Although the experiences reported herein are not claimed to be generalizable to the wider patient population, they could alert health practitioners to areas for further consideration. First, the positive reception to DNA testing is arguably related to its potential to alleviate uncertainties. Nevertheless, DNA tests do not necessarily meet all desires for certainty, and this disjuncture may be either a source of ambivalence in decision-making (to undertake testing or share information in families), and/or a potential source for disappointment post-results. Second, other fruitful grounds on which to investigate reticence about, or resistance to, testing and sharing information could be: perceptions about the social, psychological and lifestyle effects of a diagnosis and skepticism about interventions (and the overarching issue of how to cope with living with a threat of sudden death).

Third, facilitating a cascade screen in a family group may require going beyond individuals' instrumental health concerns to confront questions of family responsibility (which have the potential to raise ethical dilemmas about the duty of care and the duty to warn). On a practical level, a cascade screen may be supported by finding the most appropriate ways of supporting patients in their discussions with their relatives. Fourth, there is potential for those involved in predictive testing for inherited cardiac conditions to experience shock and distress at negative results as well as guilt and health anxiety in relation to positive results. Also, if those who are DNA negative still perceive themselves as unwell, any shift in care patterns (i.e., outside of specialist genetics/cardiology) needs to be handled sensitively. Fifth, it is possible that the sense of urgency that accompanies the threat of sudden cardiac death and concern for others (often young people) might lead to ongoing anxiety during the testing and screening process, and a desire for fast service provision.

These findings could help to guide practitioners as they develop appropriate forms of anticipatory guidance regarding information provision and genetic counseling. Such guidance might include considering the extent and value of information provided by a

DNA test (particularly in connection to perceptions of uncertainty); and, reflecting upon the implications that different test results may have for treating the disorders, and for living and coping with them. Cascade screening processes could be facilitated by identifying appropriate, effective and sensitive mechanisms for sharing information in families, and developing the means for supporting patients with communication. For example, practitioners could provide patients with a letter to share with their family members to document the diagnosis, symptoms, risk of cardiac events and potential for testing.

Conclusion

DNA testing and cascade screening is welcomed by many of those living in families at risk of inherited cardiac conditions as a means for reducing the uncertainties associated with these conditions. The evidence of ambivalence, however, shows that some important uncertainties can remain which may affect peoples' dispositions toward testing and screening. Potential impediments to cascade screening also arose in relation to issues of communication and family responsibility. The present findings could provide health practitioners with insight into why some people at risk of inherited cardiac conditions may be resistant to testing, screening and sharing information. Further investigations are necessary to test these exploratory findings using a more generalizable study design that considers the influence of different clinical protocols on patient experience and/or explores the views of people who have refused to be involved in testing and screening.

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APPENDIX: INTERVIEW GUIDE

Theme A. Experiences of the Condition and Treatment

Personal and family history of the disorder
What has happened during medical care?

Theme B. DNA Testing

Why offered the DNA test?
What were the results?
Key reasons for having the test?
Any difficulties in making the choice?

Effects of DNA test on how they think about the condition.

Theme C. Family Communication

Were they the first person to have a DNA test? Who else has had a test?
Did they contact other family members about the test? Who and why?
Were there family members they didn't contact? Who and why?
Difficulties in the process of communicating with relatives.
Amount of (and preferred) support/ advice/ information from the medical team.

Theme D. Benefits and Drawbacks

The positive and negative outcomes of DNA testing for them and their family.
Has participation in DNA testing left any lingering concerns or outstanding problems?

Theme E. Information Provision

What information was given about the implications of the results of a DNA test?
Was this given at appropriate times, and were there opportunities to discuss issues, concerns or problems?

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Table 1: Participant characteristics

Participant ID	Disorder	Clinical Status[1]	DNA test[2]	Test Status[3]
R01	HCM	affected	positive	research
R02	HCM	affected	positive	research
R03	HCM	affected	positive	research
R04	HCM	affected	positive	proband
R05	HCM	affected	negative	cascade
R06	HCM	unaffected	positive	cascade
R07	HCM	affected	positive	proband
R08	HCM	affected	positive	proband
R09	LQT	affected	positive	proband
R10	LQT	unaffected	negative	cascade
R11	HCM	affected	positive	proband
R12	HCM	affected	positive	proband
R13	LQT	affected	negative	cascade
R14	HCM	affected	no known mutation	proband
R15	LQT	unaffected	negative	cascade
R16	LQT	affected	positive	proband
R17	LQT	affected	positive	proband
R18	LQT	affected	positive	proband
R19	LQT	affected	positive	proband
R20	LQT	unaffected	negative	cascade
R21	LQT	unaffected	negative	cascade
R22	LQT	affected	positive	proband
R23	LQT	unaffected	positive	cascade
R24	LQT	affected	positive	proband
R25	HCM	unaffected	negative	cascade
R26	HCM	affected	no known mutation	proband
R27	HCM	affected	no known mutation	proband

[1] Classifying participants "clinical status" as affected or unaffected was somewhat problematic; this was based on participants' (sometimes unclear) accounts, not clinical records, and as previously noted, these are disorders in which there are "grey" areas. Those who reported being treated by health practitioners as at-risk were classified as affected (including two who took part in cascade screening and subsequently had negative DNA tests [R05, R13]). To recognize this potential ambiguity, the phrase "treated as affected/ unaffected" was used when labelling responses in this article

[2] The three DNA results of "no known mutation" were patients who were having a test to confirm a diagnosis, but who had not had a positive match against the three common genetic variants included in the screen (meaning that further research on their DNA would be required to confirm a diagnosis or facilitate a cascade screen for their family)

[3] The "research" test status denotes that three participants' DNA tests were part of historic HCM family research studies that were unrelated to the program of work that gave rise to this study. Despite this, the label "proband" was used for the purpose of classifying their "test status" in this article