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ORIGINAL ARTICLE

A qualitative study of patients' perceptions of the value of molecular diagnosis for familial hypercholesterolemia (FH)

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Abstract For many years, familial hypercholesterolemia (FH), an inherited disorder, has been diagnosed using phenotypic features plus family history of early onset cardiovascular disease (CVD), and has been successfully treated using statin therapy. DNA testing is now available and this has been incorporated into familial cascade screening programmes in many parts of Europe. Little is known about patients' perceptions of the value of undergoing molecular diagnosis for FH. In-depth interviews were carried out with patients (n = 38) being treated for FH who were the first in their family to undergo DNA testing for FH. Data were analysed thematically. While interviewees regarded DNA testing as an unexceptional event, it was seen as a positive innovation because it confirmed that their family carried a particular disorder, offered an aetiological explanation for their hypercholesterolemia and provided information about their own and family members' future risks. From the patient perspective, the main benefit of molecular diagnosis lies in its ability to provide information which allows (younger) family members to access genetic screening and, thus, timely treatment. The implications for future developments in genetic services and the need to investigate further the provision of molecular testing in mainstream specialties are briefly discussed.

Keywords Familial hypercholesterolemia (FH) · Molecular diagnosis · Patient experience · Qualitative interviews · Genetic screening

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Introduction

Diagnosis organises and classifies corporeal states, identifies treatment, provides prognostic and aetiological information, determines what is "normal", enables access to services, sanctions and creates social roles and structures relationships between patients and healthcare professionals. As such, diagnosis is a fundamental aspect of medical care (Jutel 2009). The relationship between diagnostic procedures and diagnostic categories is dynamic, with diagnostic categories being constantly refined in light of changes in knowledge and technological advances (Jutel 2009). This can be clearly seen in the field of inherited disorders; indeed, Hedgecoe (2003) describes how certain diseases or bodily traits have come to be redefined as genetic following the introduction of molecular diagnostics. DNA technologies have not only changed the ways in which we perceive some diseases but also our view of diagnostic processes (Lippman 1991, 1992; Miller et al. 2006). As various studies have highlighted, healthcare professionals and patients can regard DNA testing as providing immutable or definitive diagnostic categories and more authoritative predictions of future risks of disease in individuals (Miller et al. 2005; Horstman 2008).

This paper describes patients' perceptions of molecular diagnosis for familial hypercholesterolemia (FH), an inherited cardiovascular disorder, which, until relatively recently, was diagnosed using a combination of phenotypic features and family history of cardiovascular disease (CVD). Like diagnostic DNA testing for other late onset disorders, DNA testing for FH often takes place outside of clinical genetics; in this instance, within the lipid clinic. Earlier research has looked at the impact of genetic diagnosis for FH on individuals' beliefs about the aetiology of disease and their preventative behaviours (Senior et al. 2002; Hollands et al. 2012). Senior et al. (2002) interviewed patients with FH who subsequently underwent genetic testing as part of the GRAFT (Genetic Risk Assessment for FH Trial, Marteau et al. 1999) study, which compared the impact of molecular versus non-molecular diagnosis; they found that this group attributed their FH to genetic causes, which many saw as absolving them of responsibility for causing their disease. However, this research has failed to specifically explore individuals' views about the value of obtaining a molecular diagnosis. It can be argued that it is important to look at patients' perceptions of the value of molecular testing as a diagnostic tool, particularly within mainstream specialties, not least because it is predicted that DNA testing for common and/or complex disorders, like hypercholesterolemia, cancer and type 2 diabetes, may become a major part of the diagnostic repertoire in many clinical specialties in the near future (PHG Foundation 2011).

Familial hypercholesterolemia

FH is an autosomal dominant disorder affecting 1 in 500 people (DeMott et al. 2008). It is characterised by high levels of low-density lipoprotein (LDL) cholesterol, which, if left untreated, greatly increase individuals' risks of CVD—50% for men aged 50 years and 30% for women aged 60 years (DeMott et al. 2008). Individuals who carry a pathogenic mutation may have coronary events at an earlier age, with those under 40 years having a nearly 100 times increased risk of fatal heart attack (Marks et al. 2006). FH is usually treated by statin therapy, which significantly reduces morbidity and mortality from CVD (DeMott et al. 2008). The severity of the consequences and the treatability of hypercholesterolemia means that familial screening for FH has been actively promoted by WHO for nearly 20 years (WHO 1998).

Historically, the diagnosis of *probable* FH was based upon raised levels of LDL cholesterol and a family history of early onset CVD, whereas a *definite* diagnosis also required the presence of tendon xanthomata (visible cholesterol deposits) (Simon Broome 1999). DNA testing for FH mutations is now available, and this can be used to confirm pre-existing clinical diagnoses (diagnostic testing) and identify (younger) pre-symptomatic individuals as carrying a mutation (predictive testing) (Civeira et al. 2008; van Aalst-Cohen et al. 2006). It has been argued that familial screening for FH may be a cost-effective way of reducing premature death from CVD, hence DNA cascade screening programmes have been implemented in some European countries and some parts of the UK (Finnie 2010; Marks et al. 2002).

In Scotland, patients attending specialist lipid clinics, who have a clinical diagnosis of FH, have been asked to provide blood samples for molecular testing since 2010. If a pathogenic mutation is identified, the index patient is referred to clinical genetics to discuss their result and identify relatives for cascade screening. Family members are diagnosed by DNA testing in the genetics clinic and then referred to specialist lipid services for their clinical management (see Hallowell et al. 2011, Box 1). The qualitative study reported in this paper was carried out following the implementation of the Scottish DNA cascade screening programme. We sought to investigate index patients' experiences of undergoing DNA testing as part of the screening programme. We have previously reported their perceptions of the organisation of familial cascade screening (Hallowell et al. 2011) and the impact of DNA testing on risk perceptions and health behaviours (Jenkins et al. 2011). This paper reports data on their views of the value of obtaining a molecular diagnosis for FH.

Methods

Recruitment

One hundred and fourteen patients, who had a clinical diagnosis of FH and had undergone DNA screening in two lipid clinics in SE Scotland, were invited to take part in an interview. Patients were sent an invitation from the lead clinician, a study information sheet and an expression of interest form to return to the qualitative research team in a pre-paid envelope.

Sampling

DNA testing of index patients who have a clinical diagnosis of FH produces one of two results; a *positive* result which confirms the individual carries an FH mutation or an *inconclusive* result, which reveals they do not carry any of the pathogenic mutations covered by the test. The latter is not a negative DNA result, as it is possible that the individual's (and family's) hypercholesterolemia is caused by another genetic mutation, which can give rise to the FH phenotype. Given our interest in individuals' experiences of undergoing molecular diagnosis, we purposively sampled two groups; patients receiving a positive result and patients receiving an inconclusive result. Within each group, we tried to achieve a balanced sample with regard to gender and age profile, in line with

earlier research (Weiner 2009; Weiner and Durrington 2008). Recruitment ceased once data saturation occurred.

Data collection and analysis

NJ conducted the interviews at a time and location chosen by participants. With one exception, an online interview using instant messaging, interviews were carried out face-face. Interview topic guides were informed by the literature, observations of consultations in both lipid and genetics clinics previously undertaken by NH and NJ for familiarisation purposes, and findings emerging from an analysis of initial interviews. The interviews explored personal and familial disease histories, experiences of managing hypercholesterolaemia, experiences of DNA testing and obtaining and interpreting DNA results; and, the impact of DNA testing on risk perception, risk management and health behaviours. Data collection and analysis took place concurrently, allowing issues identified in early interviews to inform the areas explored in later ones (Strauss and Corbin 1990). Data collection ceased at the point where no new themes emerged from the analysis of new interviews.

Interviews were recorded, transcribed, anonymised and analysed using a thematic approach (Strauss and Corbin 1990). The research team systematically compared the transcripts of those receiving different types of DNA results to identify crosscutting themes and to highlight common and divergent experiences. A coding frame was developed to capture data relating to the primary research aims as well as emergent themes. Data were managed using NVivo 8 (QSR International, Victoria, Australia). Although not explicitly asked to comment on the benefit of DNA versus biochemical diagnosis, interviewees' perceptions of the value of DNA diagnosis emerged as a substantive theme in the analysis. As the analysis suggests, both those who received a positive result and those who received an inconclusive result identified a number of benefits of DNA diagnosis.

Results

Participants

Thirty-eight individuals were interviewed. The gender split (women:men) was 55%:45%. Most interviewees (79%) were aged over 45 years, 42% had university level education and the majority were working/had worked in a higher socio-economic occupation. Roughly a third were long-term (>10 years) clinic patients, while a third were novices, having been referred to the lipid clinic within the last 2 years. Most interviewees (31, 82%) reported a family history of CVD/hypercholesterolemia and 31 (82%) had biological children. Twenty-three (61%) received a positive result following DNA testing and 15 (39%) of these had attended the genetics clinic to discuss their result prior to their interview.

DNA diagnosis for FH: an unexceptional event or unexceptional test?

Most interviewees described DNA testing as "a bit of a non-event" (FH04, Positive) or as having had little or no impact on their lives, with two patients failing to recall the outcome of their DNA test. This lack of engagement was justified by the fact that genetic test results had not altered pre-existing disease management regimens (see also Jenkins et al. 2011).

> *FH06 I'm taking statins now so whether I, whether I'd had the genetics test or not I was already on a course of statins and statins have reduced my cholesterol level. Positive*

> *FH07 I need to manage my condition for me, and I've been doing that and I don't see that any sort of genetic imbalance there or genetic issue would have changed how I would have had to manage that. Inconclusive*

When discussing their reactions to undergoing DNA testing, most interviewees compared molecular diagnosis for FH, not with their earlier clinical diagnosis, but with DNA testing for other conditions. Drawing these comparisons led them to conclude that, when compared with other types of genetic testing (e.g. for Huntington's disease (HD) or inherited cancers), genetic testing for FH appears to have less threatening (potential) consequences.

> *FH11 It [DNA testing for FH] is not predicting what ghastly things are going to happen to you if you get this thing in the future … You don't have to plan your life around it. You don't have to wonder, can you have children or not. Inconclusive*

> *FH04 I mean, it's not that bad, you know, particularly given the good medication that's around. It's not like having something like Huntingdon's or something like that, you know, where you've got a 50% chance of having some terminal and incurable condition. It's not the same. Positive*

Thus, interviewees' views of DNA testing for FH appeared to be influenced by their wider perceptions of FH. Many commented that hypercholesterolaemia is easily managed with medication, unlike cancer, which, as FH18 (Positive) reflected, "[bowel cancer]…carries many more implications for your future." Thus, DNA testing for FH was constructed as a more benign intervention than predictive testing for colorectal or breast cancer, primarily because having a

predisposition to elevated cholesterol was not perceived as "life-threatening".

FH09 I don't truly see high cholesterol as being treated as life-threatening. …different if you had a form of cancer that's hereditary and it's going to kill you or it's going to have fairly serious consequences to you. Inconclusive

The perceived usefulness of DNA diagnosis

If interviewees have already obtained a clinical diagnosis and are successfully managing their hypercholesterolemia with statin therapy, what is the value of a molecular diagnosis? Does receiving a molecular rather than a clinical diagnosis have any perceived benefits for patients, or is it, as FH04 (Positive) commented, just regarded as a more expensive "… sledgehammer to crack a nut"?

FH04 I still can't see the point of this expensive test to do something that a simple blood test [serum cholesterol test] will do. Positive

FH04 was in a minority, for most interviewees saw molecular diagnosis as having some value over and above receiving a clinical diagnosis based on phenotypic markers. In discussing the perceived benefits of DNA testing for FH, interviewees described molecular testing as performing a number of the accepted functions of diagnostic tests, namely classifying or relabeling symptoms, providing aetiological explanations and providing information about the future, i.e. prognostic or risk information.

Classifying symptoms

While for some DNA testing merely confirmed their pre-existing clinical diagnosis, for a small group it provided a new, and definitive, diagnostic label. Before undergoing DNA testing, a couple of interviewees had been diagnosed as having "high cholesterol" or some unspecified hyperlipidemia. Molecular diagnosis, therefore, identified them as having a particular condition—FH.

FH37 [Dr] says "we've got a name for what you've got!" He was quite chuffed, and he said "oh, after all these years of seeing you I now have a name for what you've got, after all these years of just treating you for high cholesterol and here we go, it's a genetic thing" Positive

Thus, for a minority, molecular diagnosis resulted in the classification of pre-existing symptoms as a specific disease entity. While the classificatory function of DNA testing may have had little impact on the majority, many interviewees observed that receiving a molecular diagnosis was important because it provided them with a clear aetiological explanation for their hypercholesterolaemia.

Providing aetiological explanations and removing uncertainty

Many interviewees who received a confirmatory result described their DNA test result as providing an explanation for their own (and their family's) hypercholesterolemia.

FH13 it's confirming what we thought … it's definitely confirming it, you know what I mean, as opposed to "I think you've got it", as opposed to what maybe the lipid clinic said, "your results show that you've a tendency" but it does actually confirm that it is a family problem. Positive

Indeed, molecular diagnosis was constructed as a positive development because it provided individuals with a degree of certainty or undisputable evidence about the genetic cause of their hypercholesterolemia.

FH21 If there hadn't been genetic testing there then I probably would have been sitting here going, well, maybe it's lifestyle, maybe it's genetic, can't really tell. We think it's probably passed down, but we can't prove it. And you'd be sort of sitting there with more questions than answers. Positive

Moreover, it confirmed that they were managing their hypercholesterolemia correctly.

FH40 And certainly the genetic testing takes that element of uncertainty out. It hasn't changed the treatment in any way because I was already getting treated, but it has taken that element of uncertainty away…. Positive

By providing a genetic explanation for disease, DNA testing potentially reallocates blame, in the sense that disease becomes an internalised or individual, rather than a social or environmental, problem. In this instance, the individualising effect of receiving a molecular diagnosis was seen as working in the interviewees' favour, primarily because this aetiological explanation absolved them of the responsibility for causing their hypercholesterolemia. Thus, for some, obtaining a DNA diagnosis challenged the view that hypercholesterolemia is caused by bad habits or irresponsible living. This observation may partly explain why molecular diagnosis was so firmly embraced by those identified as carrying a pathogenic mutation, and is further supported by the reactions of

some who received an inconclusive test result, who said they felt disappointed as they still had to counter others' "mis"perceptions that they were in some way responsible for causing their hypercholesterolemia.

FH29 [I was] almost disappointed [to receive inconclusive result]. ….I don't think I'm causing my high cholesterol but it would be very easy then to turn round to people and say, well actually, it's in my genes and that's it. … So I was actually almost disappointed 'cause it would have been nice to say that it [genes] was the cause. Inconclusive

Although DNA diagnostics provided those who tested positive with some answers, this was not the case for those who had received an inconclusive result; as FH29 indicates, these individuals were left in a state of uncertainty. Some of these interviewees did appear to feel short-changed that they had not received a confirmatory DNA diagnosis; as FH19 (Inconclusive) said: "I would rather have found out that, you know, is it a genetic thing because if it's a genetic thing, there's nothing you can do about it."

Our interviewees not only drew upon discourses of responsibility when talking about the aetiology of FH within themselves but also when discussing the intergenerational transmission of FH mutations. A few, who had had their mutation status confirmed, acknowledged the familial aspects of genetic transmission and expressed a concern that their children may have (or had) inherited their FH mutation.

FH05 Yeah, because you think "well, that's something that I've passed on". That would bother me more than me having it because it doesn't affect me at all, but I would hate to think that I'd given one of my kids something like that. Positive

In sharing their worries about their children being at-risk, interviewees reflected upon the role of DNA testing in revealing future risks, and many regarded this as a major benefit of molecular diagnosis.

Revealing the future

While most of the interviewees in both groups did not see their own risks of CVD as altered by their DNA results, there were a couple of exceptions. FH13, for example, described how learning that he had FH, rather than just "high cholesterol" had heightened his risk perception.

FH13 I got maybe the impression that the hypercholesterolemia is really more to do with family connections, or the family side of it was important but I didn't quite realize… it is a more serious type of disease than just the straightforward hyperlipidemia… I suppose I do see myself as a higher risk now, obviously. Positive

Although DNA diagnosis appeared to have had negligible impact on personal risk perceptions for the majority, nearly all saw DNA testing as valuable because it presented them with the possibility of predicting disease risk within the wider family. Many interviewees with young children, like FH42, emphasised how a DNA diagnosis could help to establish definitively and early on whether or not their (asymptomatic) children had FH.

FH42 I'm very pleased to know that in the future – I've got two children … I intend to bring them up with healthy eating habits and healthy lifestyle but not having the stress of having the worry, I don't want them to have to worry about it. If you get the genetic test done, it takes the worry away, it's a definitive "yes" or "no". If it's a "yes" then you treat it …Positive

Others stressed the importance of obtaining a DNA diagnosis for other young relatives.

FH18 I suppose it was looking backwards, and I suppose particularly my uncle, with my uncle having five children, all of whom had children, I suppose I saw an opportunity there to tell all of them "look, don't worry! [you can find out] " you know. Positive

A few interviewees who had received an inconclusive result were disappointed their wider family was unable to have predictive testing. These interviewees said that they would have liked to have established their young children's mutation status, so that they could start to manage their risk at an early age; for example, by modifying the family diet.

FH07 …but that's what you give them, you give them whole milk, full-fat. Does that change if there is a genetic cholesterol issue? Do we need to start thinking about that now rather than giving them all the 'green milk' as I call it when they're six-ish, which again is the advice or...? So those are the things I've been thinking about. Inconclusive

Discussion

This paper has explored patients' views of the use of DNA technologies in the diagnosis of FH. The data suggest that undergoing molecular diagnosis only had a modest impact upon interviewees, which may be due to the fact that receiving a DNA test result (or not) did not change the ways they

managed their hypercholesterolemia (Jenkins et al. 2011; Senior et al. 2002; Hollands et al. 2012; Hardcastle et al. 2015). However, while DNA testing may have had little effect on risk management behaviour and intentions, it was perceived as having some benefits: it provided an aetiological explanation and diagnostic label, confirmed current risk management practises, absolved individuals of blame for their hypercholesterolemia and provided information which other family members could use to access timely diagnoses and treatment (See Hallowell et al. 2003). Thus, as far as our interviewees were concerned, DNA testing for FH was generally regarded as a worthwhile or valuable activity. These views contrast with those of healthcare professionals working in primary and secondary care who regard DNA testing for FH as inaccurate, time consuming, expensive and as adding little value to their clinical practice (Will et al. 2010).

The data suggest that DNA testing undertaken within a mainstream lipid clinic is not perceived as an exceptional or anxiety provoking experience (see also Jenkins et al. 2011; Hallowell et al. 2011). Saukko et al. (2006) similarly report that individuals undergoing screening for genetic susceptibility to thrombophilia in primary and secondary care see this procedure as generating useful information, but not as an unexceptional or unusual event. Indeed, like us, they observed that a substantial proportion of people they interviewed did not recall having had a "genetic" test (Saukko et al. 2006). These authors speculate that these reactions were influenced by the fact that the DNA testing for thrombophilia is for very low-risk genetic susceptibilities, which have little or no impact on health or its management. Our findings similarly support the hypothesis that perceived risks rather than objective risk estimates may influence patients' views of DNA testing. Indeed, despite the fact that FH objectively increases individuals' risk of CVD if left untreated, it was clear that our interviewees did not perceive FH as a particularly risky or threatening condition, when compared with cancer and neurological disorders, therefore, confirming their diagnosis of FH was not seen as personally threatening. This view may be based upon their experiences of successfully (and easily) treating their hypercholesterolemia with statin therapy (Jenkins et al. 2011; Hollands et al. 2012; Hardcastle et al. 2015); alternatively, it may be due to the fact that cultural conceptions of cancer and CVD are very different. Finally, it must be noted the drawing of downward social comparisons to modulate risk was also observed by Senior et al. (2002), who report that some patients in their study described the risks of CVD caused by FH as comparing favourably with those of other genetic diseases such as sickle cell disease.

Some of the findings reported in this study have also been documented by Weiner (2009, 2011), who investigated the views of patients being treated for FH, who had not been offered DNA testing and Hollands et al. (2012) who compared the views of first- and second-degree relatives of FH patients undergoing either clinical or molecular diagnosis. The participants in both studies similarly regarded a diagnosis of FH as absolving them of responsibility for causing their hypercholesterolaemia (Weiner 2009, 2011; Hollands et al. 2012; Senior et al. 2002). Furthermore, like our patients (Jenkins et al. 2011), the interviewees in Weiner's and Hollands et al.'s studies regarded their risk management activities as vindicated. Thus, it could be argued that phenotypic diagnosis in Weiner's and Hollands et al.'s studies performed a very similar function to molecular diagnosis in the current study. However, there is an important difference between our findings and those of Hollands et al. (2012) and Weiner (2011); namely, our interviewees' emphasis on the predictive value of molecular diagnosis for the wider family. Although Weiner (2011) reports that some of her interviewees acknowledged the familial aspects of their hypercholesterolemia, she suggests that their accounts of disease causation were not highly geneticised and that few regarded themselves as having an obligation or responsibility to ensure that other family members sought information about their risks of FH (Weiner 2011). In contrast to Weiner (2011) and Hollands et al. (2012), the predictive value of molecular diagnostics for other family members was emphasised by our interviewees, who, like those described by Horstman and Smand (2008), regarded it as one of its greatest assets, not least because they recognised that molecular testing is the only way to confirm that their younger relatives can be offered more timely access to treatment (Jenkins et al. 2011).

There are a couple of explanations for these observed differences. First, none of Weiner's (2011) interviewees and only 50% of Hollands et al.'s (2012) underwent molecular diagnosis; therefore, it is hardly surprising that their interviewees did not reflect on the predictive value of DNA testing. Second, while half of Holland et al.'s interviewees did have a DNA test, it is unclear whether the predictive value of testing was addressed in the semi-structured interviews. Finally, we observed that when genetic testing was discussed in the lipid clinics and in genetic consultations in our study, healthcare professionals discussed the implications of receiving a diagnosis of FH for patients' relatives when they were advising them about initiating a familial cascade. Given that over a third of our interviews had attended a cascade consultation before being interviewed, it was perhaps unsurprising that our interviewees emphasised the importance of a receiving a DNA diagnosis for family members when questioned; although, it can be argued that they only did so because this resonated with their understandings and priorities. However, it can be speculated that perceptions of the usefulness of molecular diagnosis for self and other family members may be influenced by the ways the healthcare professionals' frame disease and DNA diagnostics, a point that has been acknowledged by Weiner (2011). While a number of studies have explored the ways in which genetic information is presented within the genetics clinic (see for example O'Doherty 2006, 2009 and

Arribas-Ayllon et al. 2011), we are unaware of research which has looked at the ways in which DNA testing is presented and framed by other clinical specialists within mainstream medicine. We suggest that there is a need for more research that looks at the ways in which (the value of) molecular diagnosis is presented within mainstream medicine by non-genetics specialists; particularly, as this group may be increasingly charged with providing these services in the future.

Finally, in contrast to Hollands et al.'s (2012) observations that some of their interviewees described their social identity as negatively impacted by a positive (clinical/molecular diagnosis) of FH, our study suggests that receiving molecular confirmation of a clinical diagnosis of FH can be seen as providing patients with some form of biographical reinforcement (Carricaburu and Pierret 1995). There was evidence that DNA testing had a positive effect on identity, it not only established one's identity as a person with a familial or genetic disease but also confirmed that one is managing hypercholesterolemia in appropriate ways (Hardcastle et al. 2015). Indeed, the implicit value of molecular diagnosis in this respect was reinforced by the responses of some of those who received an inconclusive result, who appeared to struggle with ongoing uncertainty about personal and familial risks and risk management.

Study limitations

Prior to concluding, it is important to reflect upon the study's limitations. While a qualitative design enabled the collection of rich data about patients' experiences of undergoing molecular diagnosis in a mainstream specialty, it could be argued that this study suffers from an ascertainment bias. All the patients had already been identified as having hypercholesterolemia and were successfully treating it, some for many years, thus while DNA testing could confirm their clinical diagnosis, it did not provide them with a new diagnosis per se. Given these observations, it could be argued that if we are interested assessing the perceived benefits of DNA testing, then it is important to gauge the views of those who have not been previously identified as having hypercholesterolemia or those who have a family history of disease. A prospective study of the perceptions and experiences of FH naïve individuals undergoing opportunistic DNA screening for FH during genome/exome sequencing as per the ACMG's recommendations (Green et al. 2013) could potentially overcome these shortcomings. We must also draw attention to the fact that our sample was relatively well-educated (42% University Education), compared with the general population. At the time of these interviews, only one person attending the lipid clinics, where we recruited our sample from, had opted out of DNA testing; this bias in our sample may therefore be due to the fact that those who attend lipid clinics are more likely to be of higher socio-economic status and more likely to be more highly educated (Jenkins et al. 2011; Weiner 2006).

Conclusion

In conclusion, this paper suggests that as far as index patients are concerned, the usefulness of obtaining a molecular diagnosis for FH lies in its ability to confirm their personal and family history of CVD and to predict (younger) relatives' future health risks. This observation raises a number of issues for future developments in genomics. If the perceived benefit of genetic testing for patients, who are successfully being treated for disease, lies in its ability to provide a seemingly conclusive aetiological explanation and predict other family members' future risks, how will patients perceive DNA tests which provide a less conclusive aetiological account and may have less personal predictive power or few, if any, implications for their relatives? In other words, how will patients perceive the value of DNA tests which may provide them with ambiguous results (for example, variants of uncertain significance) or testing for single nucleotide polymorphisms, which have little, if any, predictive power for biological kin? The increased use of direct to consumer DNA testing and the introduction of faster and cheaper whole genome and whole exome sequencing suggests that we may have to consider these issues in the near future.

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Compliance with ethical standards All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (South East Scotland Ethics Committee (ref: 09/S1102/66)) and with the Helsinki Declaration of 1975, as revised in 2000 (5). Informed consent was obtained.

Conflict of interest The authors declare that they have no conflict of interest.

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