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Genetic unexceptionalism: Clinician accounts of genetic testing for familial hypercholesterolaemia

Catherine M. Will [a], David Armstrong [b], Theresa M. Marteau [c,*]

[a] Department of Sociology, Friston Building, University of Sussex, Falmer, Brighton BN1 9SN, United kingdom
[b] Division of Health and Social Care Research, King's College London, 7th Floor Capital House, 42 Weston Street, London, SE1 3QD, United Kingdom
[c] Department of Psychology (at Guy's), Health Psychology Section, Kings College London, 5th Floor, Thomas Guy House, Guy's Campus, London SE19RT, United Kingdom

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ABSTRACT

This paper considers the implications of genetic testing in the case of familial hypercholesterolaemia, drawing on twenty semi-structured interviews with general practitioners (family doctors in primary care), nurses and specialists in hospital clinics (secondary care) in the UK. Though these professionals appear aware of and interested in the genetic component of the condition, and DNA testing is underway in at least some centres, their accounts suggest that the genetic test is not having a major impact on clinical work. Instead we find that professionals report that they generally rely on other information when making a diagnosis, especially cholesterol levels understood as a key risk factor, while the results of DNA tests, if used, come late in a much longer series of clinical investigations, judgements and interventions. In addition to elaborating professional views of genetic testing, the research provides a way of understanding other studies that describe lay people as not necessarily privileging genetic explanations of familial hypercholesterolaemia.

Introduction

Until recently a genetic disease was often understood in biomedical discourse as one in which patients with a genetic mutation experienced a specific illness, in which the genotype was assumed to lead inexorably to the phenotype. Huntington's disease, sickle cell disease and cystic fibrosis are all established exemplars of this model. But since the emergence of routine genetic testing in clinical settings, understandings of the relationship between the genotype and phenotype have been expressed in terms of association rather than determination. In other words, genetic mutations and polymorphisms may now appear as one risk factor among others in the aetiology of multifactorial diseases. Yet social scientists have suggested that genetic information may still have a special significance for policy makers, doctors, and patients. The human genome has a foundational status that seems different from other environmental risk factors; genetics underpins the very essence of being a human being; genes, unlike other risk factors, are immutable. Genetics seems both to lie at the cutting edge of modern science and to map onto older yet still influential lay models of inheritance and constitution (Rose, 2006).

The fact that genetic risk factors seem different has led to them being labelled as 'exceptional' in that a genetic risk factor is often perceived to carry more weight for doctors and patients than an equivalent environmental one (Murray, 1997). This has resulted in genetic information being handled with more caution, requiring more safeguards during and after its communication to patients. It has been argued that these claims to genetic exceptionalism simply serve to maintain a privileged position for genetic information in the clinic that it does not deserve or need (Ross, 2001). Indeed, the promotion of genetic exceptionalism seems to underpin a political position that supports genetic determinism and its primacy over other hazards of life that are more amenable to change and control.

In part the debate about genetic exceptionalism depends on the type of genetic test. If the genetic test is for a variant with high penetrance, that is, its presence results in a high probability of disease, then it may be expected to have greater significance than if the test is for a gene with a lesser impact. In fact the former might be said to be exceptional in the sense of unusual because most disease variants confer only a modest impact (Holtzman & Marteau, 2000). Yet for patients, a genetic label might carry significance irrespective of the size of risk it confers, a question that has underpinned a number of qualitative and quantitative studies which have tried to assess how patients react to genetic information: do they treat it as 'exceptional'? In the study reported here interviews with clinicians were used to explore the question of genetic exceptionalism from the perspective of professionals working with patients with familial hypercholesterolaemia (FH). As

* Corresponding author. Tel.: +44(0)20 7188 82590.
E-mail address: theresa.marteau@kcl.ac.uk (T.M. Marteau).

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its name implies, this is an inherited genetic mutation that results in high blood cholesterol, a recognised risk factor for heart disease.

Patient responses to genetic information

Evidence from qualitative studies suggest that patients' reactions depend on the strength of the probability of disease, such that the few genetic tests which have a high predictive value are seen as different (Hedgecoe, 2004; Miller, Ahern, Ogilvie, Giacomini, & Schwartz, 2005). Quantitative and qualitative studies have shown that behavioural responses are affected by the provenance of the risk estimate (Marteau & Weinman, 2006; Saukko, Richards, Shepherd, & Campbell, 2006). For example, when risks are estimated using genetic tests, this is associated with greater confidence in medication as a means of risk reduction. Qualitative work has also suggested that, in general, patients feel greater responsibility for and involvement with their condition when it is presented as having a genetic basis (Hallowell, 1999; Novas & Rose, 2000), though responses also appear to vary according to other factors, including whether or not the carrier feels ill (Bharadwaj, 2002) and whether they have experience of the disease in family members (Hallowell, 2006; Walter, Emery, Braithwaite, & Marteau, 2004).

Several qualitative studies have investigated patient understandings of and responses to genetic information about FH in particular. The condition appears in two forms: heterozygous and homozygous. Heterozygous FH occurs when the mutation is on one chromosome for that gene; homozygous when it is on both. The frequency of the heterozygous genotype is said to be in the region of 1 in 500 in the UK population, a group with a high chance of developing cardiovascular problems in middle age. Homozygotes are much rarer, and may die very young without treatment. In the specific case of newborn screening, parents' beliefs about the provenance of the information appeared important (Senior, Marteau, & Peters, 1999). When the information was interpreted as a measure of raised cholesterol parents saw the condition as controllable, but where they associated the test with genetic information they were more alarmed. Adults receiving information about their own genetic risk were more likely to see the results as routine and no more or less significant than other risk factors (Senior, Smith, Michie, & Marteau, 2002). This chimed with work by Weiner (2009), who suggested that existing lay models of 'coronary candidacy' (Davison, Davey Smith, & Frankel, 1991) already led people to expect a familial component to cardiovascular disease, and that genetic information was accommodated within these models. More ambiguity was apparent in relation to the specific question of responsibility (Weiner & Durrington, 2008). In Weiner's study, patients distinguished between their high cholesterol and cholesterol problems in other people associated with lifestyle. However they also used the interviews to emphasise efforts to change their lifestyle, especially diet. As in other cases, it seems likely that patients' representations of genetic risk and responsibility in the case of FH will partly depend on the context, setting and manner in which they receive such information (Bharadwaj, 2002).

Clinical contexts

FH patients are rarely seen in the kinds of dedicated genetic clinics that have taken on some of the work of testing and informing patients about other conditions with a genetic component but rather, in lipid clinics which manage patients with abnormal blood lipids whatever their origin. It might appear that that a genetic clinic would be more likely to elicit a reaction informed by genetic exceptionalism, as genetic counsellors give a special priority to this information and its fundamental character (Scott, Prior, Wood, & Gray, 2005). However, variability in genotypes mean that genetic tests rarely appear to present doctors with a clear guide to action (Miller et al., 2005). In a range of conditions, researchers have failed to identify rapid changes in practice attendant on the introduction of genetic testing (Cox & Starzomski, 2003; Hedgecoe, 2003; Kerr, 2004). In this context, Hedgecoe (2003) suggests that in many conditions the main impact may come in shifting the classification of particular conditions, and thus be felt on diagnostic practice rather than treatment (but see Hedgecoe, 2004, for the effects on Alzheimer's).

This leaves open questions about the integration of 'genetic' and 'clinical' information in particular diagnostic practice. In some cases the work of classification appears most strongly inflected by clinical judgement based on 'clinical' signs and symptoms (Featherstone, Cox, & Starzomski, 2004; Latimer et al., 2006; Prior, 2001). However where testing is provided through collaborative work between clinicians and researchers, it has been suggested that new forms of expertise may be being brought into play and codified in conventions and rules (Bourret, 2005), so that clinical care and research may become somewhat problematically combined (Hallowell, Cooke, Crawford, Lucassen, & Parker, 2009).

In the case of FH little is known about the impact of genetic testing on professional practice at the present time. In the Netherlands genetic screening was introduced in the 1990s, but continues to exist in uneasy relation with general practitioners' focus on global risk of heart disease associated with lifestyle (Horstman, 2007). Nevertheless, advocates for genetic testing successfully presented the FH mutation as widespread in the Dutch population, informative in being both directly and reliably linked to heart disease, and an important trigger for early treatment regardless of cholesterol levels. In the UK genetic arguments have been entering the medical literature but are frequently countered by alternative models of cardiovascular disease, expressed by different disciplinary stakeholders (Weiner & Martin, 2008). Staff working in lipid clinics may themselves have been trained in a range of specialities, including chemical pathology and biochemistry in addition to cardiology or endocrinology. Referrals to these clinics come from primary care as well as secondary specialities including cardiology and endocrinology or diabetes medicine. These clinics tend not to employ 'genetic nurses' found in other settings described in the literature (Wierzbicki, Dermott, Ratcliffe, [on behalf of the Medical Scientific and Research Committee Heart UK], 2008), and have often been established before the introduction of DNA testing.

In these settings FH may be diagnosed with reference to a range of clinical signs and symptoms including cholesterol deposits on the Achilles tendon, known as tendom xanthoma, which were formalised as the 'Simon Broome' criteria following observational studies in the 1980s and early 1990s (NICE, 2008a; Scientific Steering Committee on behalf of the Simon Broome Register Group 1991). Some clinics, however, have now got access to, and chosen to incorporate DNA testing, into their work, providing the basis for a comparison in this paper between different organisational settings and the ways in which different staff report making a diagnosis.

To investigate the meaning of genetic testing within clinical practice, this study draws on interviews with general practitioners alongside interviews with doctors and nurses working in the lipid clinics themselves. After exploring statements made by these different groups about the value of genetic testing, we offer a reconstruction of the place of the test within the spatial and temporal organisation of care within these different settings, paying particular attention to the salience of diagnostic or classification practices. In this context it is important to note that referrals to lipid clinics tend to be for patients requiring further investigation, including those with raised blood lipids which are ultimately believed to have a genetic basis and those whose high