INNOVATIVE HEALTH TECHNOLOGIES PROGRAMME

Genetic Screening for Susceptibility to Disease: The Case of Haemochromatosis

E·S·R·C ECONOMIC & SOCIAL RESEARCH COUNCIL

KEY FINDINGS

- How significant is an adult population screening approach to understanding disease?
- What is the relationship between genetic screening and clinical practice?
- With respect to population screening are larger claims being made?
- What is the fundamental distinction between risk and susceptibility?
- To what extent is adult population screening the future of biomedicine and new genetics?
- Asymptomatic and symptomatic individuals' accounts of diagnostic process
- The personal impact of being given the diagnosis
- Their understanding and use of the genetic and risk information they have been given, including
- The transmission of this information to other family members

RESEARCH FINDINGS

- The research demonstrates the variability of risk perceptions by emphasising how empirical findings rarely produce a unified notion of risk.
- In addition we have established that conceptually the distinction between clinical categories such as risk and susceptibility is fundamentally unclear.
- Such lack of clarity has direct bearing on self perceptions of individuals and their engagement with the disease.
- The research shows that communication within family members which is very often not free flowing and this lack of information sharing within family can impact upon uptake of screening and testing within families.
- We have particularly focused on the developing clinical description of haemochromatosis and how this relates to and departs from individual subject's definitions and understanding of their own experience of the disease.
- The research has successfully demonstrated how clinical/professional encoding and 'lay' decoding of risk whilst linked produce divergent interpretations.
- The research has established need for more robust information and genetic counselling support for haemochromatosis patients.
- The research also shows how population screening puts an additional strain on primary and secondary health care provision by necessitating continuing follow-up. Haemochromatosis sufferers in our research found most GPs to be totally unaware of the condition.
- In the context of government's white paper on genetics and our health these findings assume added significance.

RESEARCH TEAM

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The research has shown how the relationship between the molecular and the clinical is often indeterminate and generates 'uncertain risks'. Uncertainties are complex and at many levels. The category of disease, haemochromatosis, itself has emerged as an uncertain one. The ambiguity permeating clinical diagnosis and the lack of clarity on the question of critical parameters that separate carriers (genotypes) from frank disease episodes (phenotypes) remains uncertain. While it is possible to screen individuals with the view to predicting their personal susceptibility to developing the condition, such risk prognostications are often tentative. A positive test result for the mutation identifies an otherwise healthy individual only as susceptible to the development of the disorder. There is as yet no clinical basis for the prediction of when and how a healthy susceptible individual develops frank disease or overt iron overload. This leaves clinicians and geneticists grappling with the multifactorial complexities underlying the condition. Even as clinicians are struggling to understand and differentiate both the category of normality and pathology and the finer processes of transition from the former to the later, this uncertain knowledge is being passed on to individuals/populations and assessments of their personal susceptibility is being predicated on the as yet tentative, uncertain understanding of genetic predisposition to haemo-chromatosis. Thus, as our research suggests, this uncertainty on the one hand puts additional pressure on the monitoring of populations to ascertain their risk of developing haemochromatosis, while on the other since the science of genetic screening is still in its infancy, inevitably exposes populations to tentative risk projections without contributing any definite information on their personalised genetic futures.

Our research shows that the impact of genetic uncertainty and tentativeness on individuals is another dimension that needs urgent attention both at the level of health policy and planning. Those with disease and related complications, such as arthritis, surprisingly have very little or no access to genetic counselling. Their healthier counterparts who have tested positive for the mutation similarly have had no genetic counselling sessions. In both cases, individuals get information about the condition from their consultant haematologist in often crowded and busy clinics, which is a poor substitute for professional genetic counselling support, given the level of stress and anxiety amongst individuals with frank disease.

Another important dimension is in the realm of communication within family members which is very often not free flowing. As our interviews with asymptomatic individuals and clinical research at Cardiff show the lack of information sharing within family can impact upon uptake of screening and testing within families. This makes population screening even more problematic since even in smaller population cohorts the uptake of screening cannot be assumed. Even when the knowledge that genetic disease runs in the family is openly shared across and between generations people do not always take measures to establish their own risk. This is not to suggest that they suffer from some kind of fatalism or feel some kind of powerlessness in the face of an inevitable bad genetic outcome but rather the clear absence of any symptoms or signs and a general sense of wellbeing on a day- to- day basis informs their actions. Our research further suggests that those individuals who are undergoing active screening and surveillance tend to remain indifferent about their genetic make-up. This is a finding of concern as healthy individuals often understand personal risk and susceptibility information as the 'system' keeping an eye on them.

Contrary to some scholarly assumptions that stress and anxiety emanating from the knowledge of being predisposed to genetic disease may turn individuals into 'potential perpetual patients' our interviews with asymptomatic individuals clearly show how people do not feel anxious and seek much comfort in surveillance. Individuals' misconceptions that they are under scrutiny and surveillance can, however, be problematic for two reasons. First, the individual is part of a much larger population awaiting her or his turn and second, current uncertainty about the likely onset of the condition means individuals cannot always be identified in time for preventative phlebotomy.

Our interviews with symptomatic patients show high levels of concern: individuals struggling with uncertainty in the absence of any persuasive information about the symptoms and signs that underscore haemochromatosis. The main reason for this uncertainty lies within the clinical domain. As yet no systematic description of the disease exists. It is often very difficult to get a diagnosis where genotype and phenotype can be identified and clarified to an individual. Whilst there are descriptions of symptoms and signs that relate to the onset of the condition and its progression, the diverse individual manifestations of the disease continue to confound experts. Symptomatic individuals therefore are labouring hard to have their personal experiences of the disease and their body's everyday struggles with iron overload acknowledged and validated by the clinic. Since reported symptoms and signs can sometimes depart from the accepted clinical description of the disease consultants either ignore their persistent insistence on being taken seriously or resist their claims using the laboratory test results as evidence.

The research also shows how population screening puts an additional strain on primary and secondary health care provision by necessitating continuing follow-up. In addition to screening people and identifying them as being at risk, screening places a considerable demand on health care providers, many of whom have never seen a case of hereditary haemochromatosis. Haemochromatosis sufferers in our research found most GPs to be totally unaware of the condition. It is not uncommon for GPs to fail to diagnose the condition and thus not refer individuals to appropriate facilities for treatment, which in some cases results in irreversible cirrhosis of the liver. In the light of our findings the role of 'primary care in genetics' as outlined in the government's White Paper becomes exceedingly problematic. The White Paper places considerable demand on health care providers like GPs and practice nurses by suggesting that they are best equipped to manage patients' concerns and expectations; identifying genetic conditions, assessing risk, managing risk, screening, testing, providing and co-ordinating long-term care and gatekeeping to specialist care. This emphasis will only compound the pressure on primary care as an increasing awareness of the molecular basis of disease causation is putting additional pressures on general practitioners who are struggling to cope with a plethora of emergent syndromes and diseases that are either new or were previously thought to have no basis in molecular genetics.

About the Project

DNA-based population screening techniques are often seen as the 'future of biomedicine'. There is significant scientific and media interest in how future molecular genetics will identify and personalise risk and susceptibility assessments of individuals through genetic testing. The recent government White Paper is a good example of such 'promissory' futures. Genetic haemochromatosis, a common inherited blood disorder in populations of Northern European descent, has emerged as a recent example of population screening techniques in Australia and to a lesser extent in the United States. In Britain, however, this model has remained contentious and genetic haemochromatosis is viewed less favourably as evidence showcasing our 'geneticised future'.

The main aim of this project was to document consequences of population screening for genetic disorders based on the case of haemochromatosis. The main objectives of our research have been to study:

(1) A series of clinicians and other experts to establish the expert opinion concerning the value and implications of population screening.

(2) Asymptomatic informants who have been identified (through routine blood donation) as being at risk of developing the condition, and a series of informants with frank symptoms. We have carried out in-depth semi-structured (focused) interviews with all three series of respondents.

This research has sought to make a significant contribution to the current and ongoing debates about the desirability of population screening. While these argue about the desirability of giving risk or susceptibility information to healthy individuals, as such information may create anxiety and distress, our research has shown the actual process of disclosure and its personal consequences not only remains poorly understood but also produces varied responses to such risk assessments and disclosure. The research therefore demonstrates the variability of risk perceptions by emphasising how empirical findings rarely produce a unified notion of risk. Thus the main thrust of our research is to demonstrate both theoretically and empirically the variability underscoring the science of genetics and how reductionist arguments make little sense when the actual practice and meaning of genetic diagnosis is so varied and therefore such interventions seldom produce unified risks and single consequences. The research has therefore emphasised how in order to understand genetic population screening the discourse of risk, as both managed and projected by medical science and its users, must be understood.

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