Research

Integrating genetic risk assessment for multi-factorial conditions into primary care

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The genetic basis of many common, multi-factorial conditions is increasingly being understood but use of the knowledge created, raises major dilemmas for primary care. Identification of individuals that may be genetically predisposed to serious medical conditions provides the opportunity to offer screening or prophylactic treatment, for early detection or prevention and delay in disease onset in many complex conditions. We describe a new pilot service development to introduce genetic risk assessment for a wide range of conditions to primary care, and discuss the findings from its evaluation. The evaluation highlighted the issues about the incorporation of genetic risk assessment in primary care. The results of the evaluation along with findings from other studies, juxtaposed with the implications of developments in genetics suggest that changes are required to accommodate the integration of genetic risk assessment into primary care clinical practice. We discuss what these changes are, the benefits and drawbacks, and whether primary care can and is ready to make the changes required, further shifting the focus from disease treatment to disease prevention.

Key words: family; genetics; prevention; primary care; risk; screening

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Background

The rapidly developing corpus of scientific knowledge is providing greater insight into the role of genes in influencing the development and progress of disease. This includes common diseases, regularly observed on a daily basis in primary care, such as cancer, cardiovascular disease, diabetes mellitus, osteoporosis, polycystic kidney disease and hypertension, where there are multiple risk factors involved in causing the condition but genes can often be a principal component in predisposition.

Recognizing individuals that may be genetically predisposed to serious medical conditions has potential to enable the manipulation of contributory factors to reduce or minimize the increased risk (Qureshi and Kai, 2008). Co-factors that might be engineered to reduce risk include environmental iatrogenic causes such as smoking and obesity, cultural aspects such as number of sexual partners or consanguinity in marriages and diagnostic procedures such as repeated exposure to radiation from mammography or dental X-rays. Alternatively, high-risk groups (eg, BRCA1, BRCA2 gene mutations which predispose to
breast and other types of cancer) can be more closely monitored to enable the identification of disease at an earlier stage to maximize therapeutic interventions to reduce the potential impact of a disorder and where feasible, facilitate preventative therapies.

Reducing the impact may result in reduction of the acute and chronic long-term complications that often develop as an outcome of disease progression (Scheuener et al., 2004). This has major benefits for the individual in terms of their quality of life, their sustained economic earning capacity and the impact this has on their family members. The societal gain is a productive member of the workforce, and a reduced economic burden of treating serious disease and incapacity along with all the repercussions that late onset disease-related disability can bring to individuals and their families.

To detect individuals that might be predisposed to a particular disease, ideally a three-generation family history is required which includes all family members, illnesses that have affected them, age on onset and their current age or age of death. Based on the information obtained, it is possible to undertake an assessment allowing stratification of patients into differing genetic risk categories: population risk (an average risk similar to that of the general population), moderate or high risk. Those at population risk can be given the health and lifestyle advice that is applicable to the general public. Those found to be at increased risk require more ‘bespoke pathways’ or alternatively referral to specialist genetic units where a more detailed risk assessment can be made and personalized programmes of lifestyle advice, screening and monitoring and prophylactic treatment measures may be offered. This is based on the Kenilworth model devised for managing patients in primary care concerned about their family history of cancer (Eeles et al., 2007).

The use of genetic risk information to improve health has been a central tenet of the Department of Health policy and planning for several years (Department of Health, 2003). Many National Service Frameworks and guidelines highlight the importance of taking a family history for both diagnostic purposes and for recognition of other family members, who may share an increased risk, to allow primary prevention measures to be implemented (eg, lipid modification; NICE Clinical Guideline 67). However, identifying those individuals at risk has training and resource implications. Specialist genetics services or secondary care do not have the capacity to undertake a risk assessment of all people potentially at risk. Therefore, many consider primary care as the most viable setting for detecting and triaging these individuals (Kinmonth et al., 1998; Watson et al., 1999; Department of Health, 2003; Qureshi et al., 2005), similar to the model successfully applied to the field of cancer genetics.

General practice has always emphasized its role in caring for the family as well as the patient. This has previously meant treating the patient and sustaining their family unit with information and psychological support in times of physical or mental illness. However, there has been relatively little focus on genetic disease and family history. Family history taking in primary care has traditionally been rudimentary (Rich et al., 2004), primarily focusing on social structures and superficially on first degree relatives of the patient, namely parents, siblings and offspring. It often does not provide sufficient information to undertake a fully informed genetic risk assessment (Murff et al., 2004; Qureshi et al., 2005) and where it does, this tends to be used in isolation, without considering the environmental factors and the gene–environment synergy that causes disease (Hall et al., 2007).

Incorporating genetic risk into family history taking in primary care enables clinicians to take a holistic review, combining gene, environmental, cultural and iatrogenic factors in their assessments of disease risk for individuals and families. Family based strategies for identifying family members at risk contributes to further extending the role of primary care in disease prevention and health promotion, and provides opportunities to identify those individuals who are most likely to benefit from, and need to be targeted for, increased screening and improved access to health checks as outlined in the Government agenda for the NHS (Brown, 2008).

General practitioners (GPs) also have an important role in the successful utilization of genetic risk assessment by patients because they can initiate and catalyze health behaviour changes by individuals (Rubak et al., 2005; Qureshi and Kai, 2008). Primary care also has the best and most widespread access to the traditionally difficult to reach groups and are the best positioned health professionals to monitor continued concordance.
with health behaviour and screening recommendations, and prophylactic treatment regimens. Therefore, successful utilization of genetic risk assessment is often dependent on embedding this within primary care. However, following an evaluation we recently undertook as part of a pilot service development, to ascertain the most effective way to integrate genetic risk assessment into primary care for a range of common, multi-factorial conditions including cardiac, renal and endocrine diseases, a number of issues were identified.

The purpose of the evaluation was to:

i) describe the acceptability and feasibility of genetic risk assessment tool specifically designed for primary care (called ‘the family history screening questionnaire’ (FHSQ)), the guidelines for the assessment and two different referral pathways;

ii) evaluate patient anxiety and worry regarding family history and the risk of inherited genetic disease;

iii) ascertain primary care health professionals’ opinions on the role of primary care in the provision of genetic risk assessment;

iv) identify the barriers and facilitators to routine provision of genetic risk assessment in primary care.

Briefly, 13 GPs from 13 practices (14% of practices invited to participate) in a local primary care NHS trust initially volunteered to participate in a project to integrate genetic risk assessment into their practices, but only eight practices finally introduced the pilot project to their practice (see Table 1).

The practices were varied in terms of the number of GPs, their list size and Townsend scores (Townsend et al., 1992) ranged from 18.58 (greatest level of material deprivation) to 4.2 (lowest level of material deprivation). The pilot service development was deliberately aimed at a district with many potential barriers to such programmes, including high levels of socio-economic deprivation and high levels of non-English speaking residents so that a realistic range and scale of potential problems could be identified.

A variety of data collection tools were used to meet the objectives. Qualitative semi-structured interviews and focus groups were conducted to ascertain health professionals’ opinions, views and experiences of integrating genetic risk assessment into their practices. Some practices also completed a feedback questionnaire about the feasibility and practicality of the genetic risk assessment form, guidelines and appropriate referral of patients.

All participating patients were asked to complete validated assessment tools (six-item short form Spielberger State-Trait Anxiety Inventory (STAI) and an adapted six-item worry scale (Marteau and Bekker, 1992)) pre and post their genetic risk assessment to collate self reported changes in psychological well-being. Patients also completed a nine-item questionnaire which restricted them to yes, no or other categorical responses about the views and experiences of genetic risk assessment.

An initial FHSQ (see Appendix 1) consisted of a series of questions regarding family history and age of onset of cardiac, endocrine and renal disease, devised by a team of medical consultants with expertise in these fields in conjunction with a medical geneticist. The follow-up second questionnaire was developed to ascertain a more detailed family history to include at least three generations of both affected and unaffected family members, age of diagnosis and current ages or age of death for all family members. This second form is based upon those used for identification and management of patients at risk of developing cancer in the West Midlands (West Midlands Cancer Strategy (WMFACS) form, 2003).

Two different potential pathways for genetic risk assessment were developed: a proactive pathway and a reactive pathway. For the proactive route, a member of the practice staff initiated discussion about family history of cancer, cardiac, endocrine or renal disease during routine consultation, clinics or new patient checks. The reactive pathway displayed posters in general practice waiting rooms asking in lay terms whether...
patients had a family history of a series of diseases. If interested in having their family history reviewed for inherited genetic risk, patients were asked to leave their names and addresses for a health professional to contact them. The four practices that instituted the proactive pathway also displayed posters in waiting areas. During a time frame of six months, from January to June 2006, FHSQs were completed for 42 patients by six out of original eight participating practices, of which 41 were returned to the evaluation team. Table 2 provides a breakdown of which health professionals were involved in the completion of FHSQs.

Twelve patients reported no family history of any of the conditions described, nine said their family was affected by one of the conditions listed and 16 reported a family history of more than one condition. Five FHSQs were not fully completed. From this initial screening tool (FHSQ), health professionals identified 12 patients who required a fuller genetic risk assessment of which only two were followed up and a full family history was obtained and referred to the local clinical genetics service.

The relatively poor response rate from GP practices that had volunteered led to an exploration of some of the reasons for this outcome. A number of factors began to emerge which can begin to explain the responses received.

### Practice feedback

Primary care professionals completed 23 practice feedback forms of which eight (34%) described problems with patient completion mainly due to language barriers.

Eleven primary care professionals were interviewed or took part in focus groups including five GPs, two practice managers, two practice nurses and two health care assistants, and these participants discussed the practicalities of integrating genetic risk assessments into primary care practice.

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**Table 2** Implementation of family history and genetic risk assessment pathways

<table>
<thead>
<tr>
<th>Discipline health professionals</th>
<th>Approach to identification</th>
<th>Variation of pathway</th>
<th>FHSQ administered to patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health care assistant</td>
<td>Proactive</td>
<td>No variation pathway fully implemented as designed</td>
<td>1</td>
</tr>
<tr>
<td>Two practice nurses</td>
<td>Proactive</td>
<td>Receptionist administered FHSQ to all patients attending one of three nurse-lead clinics. Patients were asked to complete them in the waiting room and return to nurse during their consultation</td>
<td>17</td>
</tr>
<tr>
<td>Two health care assistants</td>
<td>Proactive and reactive</td>
<td>Poster displayed in waiting room and health care assistant initiated discussion regarding family history during consultations</td>
<td>3</td>
</tr>
<tr>
<td>Two health care assistants</td>
<td>Proactive and reactive</td>
<td>No new patients approached. Discussion initiated with patients attending chronic disease clinics. Poster displayed in waiting room and chronic disease clinic</td>
<td>15</td>
</tr>
<tr>
<td>GP</td>
<td>Proactive and reactive</td>
<td>GP initiated discussion regarding family history during routine consultations</td>
<td>0</td>
</tr>
<tr>
<td>Practice nurse</td>
<td>Proactive and reactive</td>
<td>Poster displayed in waiting room and practice nurse initiated discussion regarding family history during routine consultations</td>
<td>6</td>
</tr>
<tr>
<td>None identified</td>
<td>Reactive</td>
<td>Poster displayed in waiting room, names and contact details of interested patients recorded. Clinical genetics unit sent family history screening questionnaires to patients on the list</td>
<td>7</td>
</tr>
<tr>
<td>None identified</td>
<td>Reactive</td>
<td>Poster displayed in waiting room and chronic disease clinic. Arrangement with the project co-ordinator for review of family history when required</td>
<td>0</td>
</tr>
</tbody>
</table>

FHSQ = family history screening questionnaire; GP = general practitioner.
Perceived patient demand

The findings from the interviews showed that GPs perceived little demand for genetic risk assessment for cardiac, endocrine or renal disease and suggested that patients have other priorities. This was assumed by GPs because they said issues of family history and inherited disease were rarely raised by the patients during routine consultations. The only exceptions were for concerns for an inherited predisposition to cancer or antenatally during pregnancy. Where concerns were raised about family history and genetic predisposition or causes, it was suggested that this was triggered by the occurrence of disease or a death in the family. Some also thought that patients did not want information about the causes of disease because many believed its occurrence was due to fate or God’s will. Many believed that patients were not interested in advice on preventing disease but were concerned only with having their symptoms treated.

Many professionals from the project reported limited confidence and competence in carrying out a genetic risk assessment, from ascertaining a suitable family history to assessing and stratifying the risk for a wide range of conditions which may arise as the result of a genetic predisposition. The majority of professionals reported limited experience of genetic disorders and making referrals to the regional genetics service. However, some professionals said they routinely took a family history during new patient consultations but it was they, rather than the patient, who initiated discussion about family.

It was thought that more guidance and support was required to enable primary care health professionals to identify patients and families that might benefit from a referral to genetic specialist services. There was a view that practice health care assistants should incorporate family history taking into the new patient registration consultation and genetics specialists should review them and provide risk assessments to be followed up in primary care clinics, if necessary.

Utility of the family history screening tools in routine primary care

Based upon their previous experience, most professionals believed that patients would not know and be able to accurately report their family history and therefore would be unable to complete the FHSQ without significant input from health professionals. Language and literacy were specifically perceived to be a problem for some patients. Some GPs also suggested that patients would not recognize a number of the conditions listed on the FHSQ (sudden cardiac death, heart failure and osteoporosis) and they expressed concerns about asking patients to take home and complete the full family history questionnaire, which they thought they were unlikely to be able to do.

Patients’ perspective

Half of the 41 patients \((n = 22; 54\%)\) completed anxiety and worry scales. The mean STAI state anxiety was 37.69 at baseline and following risk assessment increased to 45.11. Worry scores barely altered, 8.95 at baseline rising to 9.50. The change in anxiety and worry observed between risk assessment and baseline however was small and unlikely to be clinically relevant (ie, a seven unit change in anxiety on a 40-point scale and one unit change in worry on an 18-point scale). Out of the 20 patients surveyed with a patient perceptions questionnaire, 15 (75\%) thought it would be useful to know their genetic risks.

Implications of the emergent issues

The evaluation from this service development, despite its limitations of size, identified a number whether it is possible to screen everyone in their practice, including the feasibility of reaching all patients on their lists, and the resource requirements. Many of the health professionals felt there was a limited role for primary care, especially as there were so many other competing requirements and clinical priorities in the sector. GPs particularly recognized genetic risk assessment would have benefits for patients and thought primary care was best placed for collecting family history information.
of issues which have not been fully explored in the literature in primary care genetics; the only exception being that related to education and training. The continued limited capability of primary care clinicians to carry out genetic risk assessment due to a lack of genetics education and training supports previous findings that better education and increased awareness in relation to genetics is required (Emery et al., 1999; Burton, 2003). There was a perceived need for greater support and guidance from specialist genetic services despite the simplicity of the assessment pro formas designed for both patient and clinician, which were similar to versions currently used by health professionals and patients in cancer genetic risk assessment, where risk triaging is now well established in primary care.

One problem identified for primary care relates to the practicalities of carrying out genetic risk assessment. Some patients will not necessarily know what illnesses and conditions have affected other family members beyond their parents and siblings, and even then they may not full recognize the condition. Therefore, it was thought that health care assistants, as a minimum, would be required to assist patients with completing genetic risk assessment forms, which can be time consuming. GPs were also concerned that carrying out a genetic risk assessment, even if the relevant information had been collated by other health professionals, would be time consuming. Experience from cancer genetic pathways however has shown that a small proportion of people have a problem completing a family form, but in most instances people are able to complete it if they have time to contact relatives to obtain more details. However, language and literacy barriers would need to be considered in the assessment process.

Many of the participating clinicians thought that most patients are not really interested in knowing whether they are at an increased risk from illness based on their family history. These views contrast significantly with referrals made for a family history of cancer, which are most commonly generated by patient request or GP instigation, rather than hospital based referrals. This may suggest that the problem to overcome is one of perception or knowledge in relation to genetics and other types of disease. The barrier is more likely to be a lack of knowledge and access to appropriate information. Patients have different beliefs and understandings about disease and causative factors (Walter and Emery, 2005; 2006) and these require consideration in discussing genetic risk information with them. Often, lay people think that illness is inherited to some degree, sometimes incorrectly so (Walter et al., 2004). There is evidence that some patients are interested in knowing more about the role of their genes in causing a serious disease or having a test for their susceptibility to serious diseases (The Harris Poll, 2002; Buchanan et al., 2005; Vries et al., 2005), but that when they raise it with their GP, they are not necessarily given appropriate information or advice (Metcalfe et al., 2007). Patients may not raise the issue themselves for several reasons, including limited awareness of options to prevent or delay onset of multifactorial conditions and expectations that their doctor will tell them if they need to consider their family history. Further work to ascertain patients’ level of interest in having their genetic predisposition identified may be relevant for informing future service developments, sub-stratified by gender, ethnicity and disease type (based on associated morbidity and mortality), and the availability of preventative therapies.

However, a more fundamental consideration emerged. The successful integration of genetic risk assessment into primary care is dependent on further changes in focus from treatment to prevention. A highly contentious point of debate in primary care at present is whether the budget and resource should shift to focus on prevention of disease and ill-health, or remain primarily focused on the sick and ill patients. The balance between resources for those affected by disease and ill health versus that of prevention is a complex debate; and to refocus on prevention requires the will and resource to enable it to happen. Many of the participants thought genetic risk assessment could potentially be useful to patients but they were unsure of how genetic risk assessment could bring benefits to primary care provision when there are so many other competing priorities. This raises important questions: what is the focus of primary care? And if the benefits to healthy patients are to be fully realized without detriment to those already sick, how does primary care turn its attention to integrating new technological developments that require a
Incorporation of genetic risk assessment into primary care is not new. In cancer, for example, many GPs carry out an initial risk assessment before deciding whether to refer patients to specialist genetics units because of their family history. However, there appears to be less inclination to carry out genetic risk assessments for other diseases, some of which have higher morbidity and mortality rates than cancer (e.g., cardiovascular disease), despite options of prevention and early detection being available which may reduce socio-economic costs related to the management of future disease.

Primary care would appear to be the obvious setting for carrying out genetic risk assessment. Primary care health professionals have regular contact with the majority of their patients and could routinely collate family histories and identify those who are likely to be genetically predisposed to common multi-factorial conditions. This ongoing contact means that GPs also have the most opportunities to influence healthy lifestyle behaviours and promote concordance with screening or prophylactic treatments. Also, as patients develop a growing awareness of genetic risk factors, it is from GPs that they are most likely to request further information. This was illustrated in the field of cancer genetics where service development was initially driven by patient demand. Secondary care activities increasingly use genetic testing (e.g., BRCA 1 or BRCA 2 mutation testing) to predict patients’ responses to some cancer treatments, thereby removing their choice about genetic testing. This has implications for all siblings and children of the person tested because they are at risk from carrying the same gene that predisposed them to breast cancer. Primary care is likely to be the first point of access for the family members who may want genetic testing to ascertain their own predisposition. In future, it is likely that the management of other diseases will include gene mutation studies to identify the best course of treatment with similar implications for the blood relatives of these genetically tested individuals.

Including genetic risk assessment in primary care does have further challenges. A way of recording, assessing and updating family histories of patients is required, and this has resource implications. There have been efforts to develop tools for genetic risk assessment in primary care but they have generally had only limited success (Qureshi et al., 2005; 2007; Emery et al., 2007). The focus of genetic risk assessment also has potential adverse effects in the medicalization of the healthy and raising anxieties, both of which have a resource implication in terms of time to support individuals and allay unnecessary fears and concerns, but also the costs of prophylactic treatment and screening for those individuals that might never develop the condition.

Despite the drawbacks, there are potentially many benefits of integrating genetic risk assessment within primary care. Better information of an individual’s risk of future disease that is derived from genetics and environmental factors can improve care through raised awareness of healthy lifestyle choices and prophylactic treatment in the individual, and allow targeted screening of individuals at increased risk rather than screening programmes for the general populous. With the present government focus on screening (Brown, 2008), family risk assessment including a genetic history will provide a strong evidence basis for cost-effective targeting of those individuals who are most likely to be at risk from a specific condition. Finally, better genetic risk assessment within family history taking will assist with identifying those at risk from monogenic conditions, pre-conception and prenatally to allow a more informed discussion of the risks associated with pregnancy and the health implications to both mother and child.

**Future work required**

In light of the issues raised by GPs, there is clearly further work required to examine the implications of integrating genetic risk assessment into primary care practice. Some steps have been taken to improve education and awareness of genetics in general practice; GPs with a special interest in genetics (GPwSI Genetics) were appointed to develop ‘professional leadership, education of peers and provide strategic advice to PCTs’ (NHS National Genetics Education and Development Centre, 2007). This ‘snapshot’ suggests there is still much more education and training required. Further studies are required to
establish the patients’ need for genetic risk assessment, where it is required, examine different models of service delivery in collating family (including genetic) history information and assessment of risk, including utilization of new information and computing technologies. A variety of models have been described earlier, ranging from use of specialist nurses in primary or secondary care to the use of information technologies (Eeles et al., 2007; Elwyn et al., 2005). However, there would appear to be a consensus that the success of different models is variable because it depends on the needs of the local community, resource availability and motivation of clinicians to engage in this area of practice. Therefore, further work is required with local communities to establish their priorities and service model preferences and long-term work is also required to establish whether genetic risk assessment is beneficial and effective clinically and economically to individuals and wider society.

Summary

In this paper, we have tried to discuss the development of new services to integrate more genetic risk assessment in primary care, in the context of a discussion about the benefits and drawbacks of its introduction for a range of diseases that might be prevented or their onset delayed, if risks are identified and prophylactic actions taken.

As a result of our evaluation findings, we highlight a number of factors that need to be considered, including an increasingly difficult dilemma of balancing the care of the sick and preventing future disease, and consideration of the resources required to carry out a genetic risk assessment and education and training of primary care health professionals to undertake it. Simple pathways and triggers will also be required so as not to burden primary care with resultant unmanageable workloads or unrealistic knowledge requirements.

We conclude that primary care is the most appropriate place to undertake an initial genetic risk assessment to identify those who are at increased risk and who would benefit from referral to specialist genetics centres. However, primary care will need to evolve to incorporate and integrate the developments in genetics, which are increasingly being applied to clinical practice.

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References


The Harris Poll® #26 2002: If genetic tests were available for diseases which could be treated or prevented, many people would pay to have them. Retrieved 18 August 2008 from http://www.harrisinteractive.com/harris_poll/index.asp?PID=304


Appendix 1

Coordinated by the West Midlands Regional Genetics Service
Birmingham Women’s Health Care NHS Trust

In collaboration with
Heart of Birmingham Teaching Primary Care Trust
University Hospital Birmingham NHS Foundation Trust

Family History Short Form

TO BE COMPLETED BY INDIVIDUALS AGED 18 AND OVER ONLY

Please fill in your personal details below:

<table>
<thead>
<tr>
<th>Full name:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of birth:</td>
</tr>
<tr>
<td>Post code:</td>
</tr>
</tbody>
</table>

Please indicate whether you or any of your close blood relatives* have had any of the following medical conditions at (or under) the age specified.

*Close blood relatives are your mother, father, brothers and sisters (full or half), aunts and uncles and grandparents

<table>
<thead>
<tr>
<th>Medical condition</th>
<th>Age</th>
<th>Please circle ‘Yes’ or ‘No’</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Heart attack</td>
<td>50 or under</td>
<td>Yes / No</td>
</tr>
<tr>
<td>2 Sudden cardiac death</td>
<td>50 or under</td>
<td>Yes / No</td>
</tr>
<tr>
<td>3 Cardiomyopathy (enlarged heart)</td>
<td>Any age</td>
<td>Yes / No</td>
</tr>
<tr>
<td>4 Any other type of heart disease e.g. heart failure</td>
<td>50 or under</td>
<td>Yes / No</td>
</tr>
<tr>
<td>5 Kidney disease and/or had kidney dialysis</td>
<td>Any age</td>
<td>Yes / No</td>
</tr>
<tr>
<td>6 High blood pressure</td>
<td>50 or under</td>
<td>Yes / No</td>
</tr>
<tr>
<td>7 Stroke</td>
<td>50 or under</td>
<td>Yes / No</td>
</tr>
<tr>
<td>8 Osteoporosis (soft, fragile or brittle bones)</td>
<td>75 or under</td>
<td>Yes / No</td>
</tr>
<tr>
<td>9 Hip fracture</td>
<td>75 or under</td>
<td>Yes / No</td>
</tr>
<tr>
<td>10 Diabetes</td>
<td>Any age</td>
<td>Yes / No</td>
</tr>
<tr>
<td>11 Have you or any of your blood relatives had a genetic test or attended a genetic clinic?</td>
<td>Any age</td>
<td>Yes / No</td>
</tr>
</tbody>
</table>