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ARTICLE

BRCA1/2 predictive testing: a study of uptake in two centres

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Differences in reported uptake of genetic testing for mutations in *BRCA1* and *BRCA2* can largely be accounted for by different methodologies and by studying research *vs* nonresearch families. In our joint study of 75 nonresearch families from two UK centres in which at least 3 years had elapsed since the initial proband had been informed of the availability of testing, only 45 and 34% of eligible individuals from Manchester and London, respectively, had come forward for counselling. Final uptake rates using a non-proactive approach were 53 and 29% for women and 11–12% for men, but the figure among those attending clinic was 73 and 62%, respectively. Unlike previous studies, we did not find that uptake had stabilised after a year with 25% of those being tested more than 2 years after the family was informed, and several delaying a considerable time between genetics appointments. We believe that the particularly low uptake even of counselling in men may need to be addressed by improving family communication or providing information sheets for family members to disseminate.
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Introduction

Once a mutation of BRCA1/2 is identified in a family, every individual in that bloodline has, in theory, the opportunity to have a genetic test. Each person can choose to have the test, to refuse the test, to postpone, or not even to attend genetic counselling to discuss these options. Previous experience with other dominantly inherited adult-onset genetic disorders suggests that many at-risk individuals will decide not to pursue predictive testing, in spite of the potential advantages in terms of screening and early detection of tumours.

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Within publicly funded health systems, it is useful for service providers and budget holders to have an estimate of uptake of all the important steps of predictive testing: counselling, follow-up, and the genetic test itself. Previous studies of families participating in research programmes have demonstrated variable uptake rates,[1–3] but the results are hard to interpret because of methodological differences between the study protocols.

In the simplest terms, the level of uptake of a test is the number of family members who opt for testing, divided by the number of people at risk and aged 18 years or more. The ideal way to measure uptake would involve contacting all family members to offer counselling and testing. However, in routine clinical practice, family members unknown to the clinic are not approached directly about their risk or invited to attend. This practice respects the confidentiality of patients, and instead relies on family

members to disseminate the information in circumstances they judge best to avoid generating undue anxiety or distress. It is therefore impossible to know whether family members who are not in contact with the clinic have made an informed decision not to attend or whether they are simply unaware of either the family history or the availability of a predictive test.

These differences in clinical approach and research methodology, together with the usual variation in family communication and dynamics, may affect the numbers of persons attending for counselling, and therefore the size of the 'unknown' group, in different studies. While it is important to know what proportion of clinic attendees will proceed with testing, the 'unknowns' must also be considered, as they are potential future patients.

The most difficult aspect of measuring uptake is the definition of the population eligible for testing. Should it be defined in terms of the family, or those at-risk individuals seen at a particular clinic? In situations where a test is only offered as part of a study protocol, and an active approach is made to recruit family members to the study, these are one and the same. However, in routine clinical practice, mutations are found in one affected individual, and information is allowed to disseminate naturally through the family. Some studies attempt to estimate uptake at a specific time point, which fails to take into account other life events that may influence uptake. It may therefore be more revealing to consider the rate of uptake over time, and how this is influenced by factors such as age and life changes such as marriage and reproductive decision-making.

An alternative strategy would be to measure uptake as a proportion of those eligible individuals who have attended clinic, rather than of the whole family. This then ensures that an individual is aware of their family history and the subsequent implications. This method has the advantage that it is possible to record precisely the time taken from the commencement of counselling to a decision to proceed for each individual in the study.

Another difficulty is the decision as to who is eligible for presymptomatic testing? The simplest method is to count everybody in the bloodline of the family, but it is not usual practice to test those under the age of 18 years or those unable to give informed consent due to mental health or learning problems. When calculating uptake among patients of one particular clinic, family members resident in another region or country become ineligible for testing by that clinic. Furthermore, it is unnecessary to test the children (and grandchildren) of anybody found to be a noncarrier.

We have assessed uptake using different approaches in two NHS clinic settings and compared this to previous reports in the literature, bearing in mind the difficulties discussed above.

Methods

Subjects

Uptake was assessed in 75 families with mutations identified and communicated to the original affected proband (and other family members who had previously attended for counselling) before 1st September 1999. In all, 51 families were recruited from the genetic counselling clinics in Manchester and 24 from the Royal Marsden Hospital (RMH) in London.

Families were excluded if they had been involved in previous research where blood samples were taken from unaffected family members or where the majority of at-risk family members resided outside the regional catchment areas. Individuals under 18 or over 70 years of age, nonregional residents, and the children of those receiving favourable predictive test results were also excluded. Genetic counselling was based on a modified Huntington protocol with an initial information session, followed by a first pretest session in which the test itself was discussed and a second session at which blood could be drawn for testing. A results session during which follow-up is planned is also integral. All individuals undertaking tests prior to 1st September 2002 were included.

Families are initially informed of the possibility of mutation testing through an affected proband or probands who have donated blood for mutation testing. With the permission of these individuals, family members who have already attended clinic are informed of the potential for a predictive test. The probands are encouraged verbally and in writing to disseminate information to other family members and often use their personal letters as a source of information. Other family members who attend for counselling are also encouraged to contact potentially eligible family members and transmission through males is emphasised. However, if the family make no further contact, no active measures are taken to chase up family communication. No specific information sheets were used during the time course of this study.

For the purposes of this study, eligible individuals were those who had been identified on the family pedigree in each vertical bloodline at high risk of inheriting the mutation, that is, those at 50% risk, or those at 25% (or 12.5%) risk where the intervening generation was unavailable for testing. We were reliant on the family members to inform us of the existence of such people, but family trees were purposefully extended as far as possible. Uptake was defined as the number of people tested divided by the number of people who could potentially be tested. For the purpose of this study, a predictive test was defined as a test for a known family mutation in an unaffected at-risk individual. We have therefore excluded individuals not fulfilling this criterion. Finally, any obligate carriers were said to be ineligible for inclusion in the denominator of the uptake calculation, as their status was in effect known by default.

Results

Manchester

As of 1st September 1999, 83 families had been informed of the presence of a *BRCA1/2* mutation and notified of the availability of presymptomatic testing in Manchester. The test result was initially conveyed to the affected proband and permission was asked to disseminate the information to family members already known to the clinic. We excluded eight families involved in previous proactive psychosocial studies examining uptake.[1,4] A large family containing 30 breast cancer affected individuals used in the isolation of *BRCA2*[5] was also excluded, as were a further 26 families where the majority of members lived outside the Manchester region. This left 51 families with a total of 299 (range 1–45) relatives eligible for testing. In all, 80 individuals (78 female) were informed directly as they were already known to the clinic and a further 55 either contacted the clinic directly or were referred by their GP after the family had been informed. The clinic has therefore had contact with 45% (135/299) of the individuals eligible for testing. This represented 68% (104/153) of females and 21% (31/146) of males. In all, 80% were eligible through an affected mother. Of these, 16 patients became eligible due to an unfavourable predictive test result in a parent.

As of 1st September 2002, 99 of the 299 (33%) eligible individuals have undertaken a presymptomatic genetic test, an uptake rate of 53% (81/153) in women and 12.3% (18/146) in men. The median time to testing was 0.8 years (mean 1.3, range 0.1–5.8) from the time the family were informed, but 27% (27/99, of whom 24 were women) did not undergo testing until 2 or more years after the family was first informed. Two further patients (one male and one female) had booked appointments for their final pretest counselling session more than 4 years after their families were first informed. One of the 16 individuals eligible due to a parent with an unfavourable predictive test result has herself now had a test.

Of those over 70 years, 40% (9/22) have undergone testing; 45% (5/11) of males in this age group have been tested.

Royal Marsden hospital

Uptake at RMH was much lower. Only 21% (18/85) of eligible individuals have opted for testing to date, between 0.1 and 4.1 years after their family was informed of the risk. The mean interval to testing was 1 year and 2/18 (11%) delayed more than 2 years. Uptake in women was 28%, while 11% of men took the test. However, the number of eligible second-degree relatives (SDR) and more distant relatives was very small (24/85 (28%)) compared to 159/299 (53%) in Manchester. The results are summarised in Table 1.

Table 1 Uptake of predictive genetic testing in Manchester and London in unaffected individuals

	N_a	C	A	U_i	U_c
Manchester					
Female	153	104	68%	81/104 (78%)	81/153 (53%)
Male	146	31	21%	18/31 (58%)	18/146 (12.3%)
FDR female	72	53	73.6%	38/53 (71%)	38/72 (52.8%)
FDR male	68	18	26.5%	10/18 (55%)	10/68 (14.7%)
SDR female	45	27	60%	21/27 (78%)	21/45 (46.7%)
SDR male	37	9	24.3%	6/9 (67%)	6/37 (16%)
DR female	36	24	66.7%	22/24 (92%)	22/36 (61%)
DR male	41	4	9.8%	2/4 (50%)	2/41 (4.9%)
Royal Marsden					
Female	49	24	48.9%	14/24 (58%)	14/49 (28.6%)
Male	36	5	13.9%	4/5 (80%)	4/36 (11.4%)
FDR female	34	16	47.1%	8/16 (50%)	8/34 (23.5%)
FDR male	27	3	11.1%	2/3 (67%)	2/27 (7.4%)
SDR female	4	1	25%	1/1 (100%)	1/4 (25%)
SDR male	6	0	0%	0	0/6 (0%)
DR female	11	7	64%	5/7 (71%)	5/11 (45%)
DR male	3	2	66%	2/3 (67%)	2/3 (66%)

FDR = first-degree relative to the original proband informed of mutation identification; SDR = second-degree relative to proband; DR = distant relatives to proband.
N_a = the number of people in the bloodline who could be tested. This excludes those under the age of 18 years, obligate carriers, and those with mental health or learning difficulties. The level of risk must also be defined to reflect clinical practice, so that only those in each vertical bloodline at greatest risk (apart from healthy obligate carriers) are included.
C = the number of people eligible for testing under the criteria listed for A (the proportion of eligible family members who have attended for counselling N, who have attended clinic for counselling about the issues involved in testing.
U_i = the level of uptake among informed patients.
U_c = the combined uptake for all the families seen at a clinic.

Discussion

Late-onset disorders are unique in that the implications for the individual usually have priority over reproductive decisions. As a result, protocols for predictive testing for late-onset disorders have been developed using Huntington disease (HD) as a model. The anticipated rate of utilisation of a predictive test for HD was high (70+%; Schoenfeld *et al*[6]) when testing was hypothetical, but actual uptake is 10–20%.[7–9] This is probably related to the inevitability of the condition along with a lack of preventive/curative measures.

A Finnish study of uptake of predictive testing for hereditary nonpolyposis colorectal cancer (HNPCC) showed a rate of 88% of the study sample, qualified as 75% of the whole sample (including nonresponders) and redefined as 96% of those who attended for the first counselling session.[10] This involved one-to-one counselling, as opposed to the family group counselling offered in the Lerman *et al*[11] study, which reported a 43% uptake for HNPCC testing. It should be remembered that the prospects of colorectal cancer prevention in HNPCC are excellent without the necessity to have preventive surgery.

Evans *et al*[12] reported uptake for genetic testing for von Hippel–Lindau disease, familial adenomatous polyposis and neurofibromatosis type 2 (NF2), and demonstrated a high rate of uptake, with combined figures of 95% for children less than 16 years, 77% for adult males and 93% for adult females. This was a register-based study of three different conditions where there is some advantage to be conferred from early screening. Childhood testing is routinely offered and the high rates in under 16 years may represent parental influence.

In general, for late-onset conditions, the experience of presymptomatic genetic testing suggests that the better the prognosis and preventative measures, the higher the rate of uptake. However, if screening or preventative measures are unavailable, careful nondirective counselling often results in fewer family members taking the test.

Prior to the detailed characterisation of BRCA1 (and the discovery of BRCA2), a number of studies focused on individuals with a proven family history of breast and ovarian cancer. These studies suggested high reported rates of interest (definite or probable) between 76 and 95%.[13–16]

A number of reports that specifically deal with the rate of utilisation of *BRCA1/2* testing have arrived at a variety of different figures (Table 2), the lowest and highest quoted being 27 and 84%, respectively. Both these figures are from Julian-Reynier *et al*,[17] illustrating that these 'headline rates of uptake' can be very different, depending on the population included and the study protocol.

With active recruitment, it is easier to ensure that every eligible family member is aware of their personal risk and of the availability of a test. In these studies, the range of attendance is 39% (one family) to 70%. A recent update on a large kindred from Utah showed similar uptake in fully informed men of 52% compared to 55% for women.[18] In the studies of families where fewer informative interventions have been recorded, there is much greater agreement, with 32% attendance in France[17] and 34% in Israel.[19] This is comparable to our data, with our non-proactive approach resulting in 45 and 34% of unaffected relatives attending clinics in Manchester and London, respectively.

In general, therefore, it could be suggested that one-third to one-half of family members attend for counselling spontaneously; however, without a proactive approach, we cannot know for sure what proportion of family members are aware of the option of counselling. This then raises the issue of whether it is the clinician's responsibility to ensure that every family member is aware of their risk status. This important question merits further debate.

Once an individual has come forward for counselling, they are much more likely to proceed than to decline testing. Of the six reports[1,2,17,20–22] that discussed this, there was broad agreement that 78–99% of those attending clinic or research education sessions will proceed to testing. This compares to only 73% in Manchester and 62% in London in our clinic-based series. Overall, the method of initiating attendance appears not to impact on the rate of test utilisation. However, it must be remembered that those unwilling to undergo testing are more likely to refuse to participate in research or to not make contact spontaneously, and so will not attend.

One of the interesting aspects about genetic testing is the length of time taken from the family receiving information about the availability of the test to an individual proceeding with testing. Meijers-Heijboer *et al*[23] demonstrated that the rate of uptake had stabilised in their study by 24 months. However, in this study, the mean follow-up time from identification of a family mutation was only 26 months. Anecdotal evidence suggests that some individuals will postpone testing for considerable periods. In our study, 20% of individuals who eventually undertook testing did so 2 years or more after the family was informed.

Different studies of uptake use differing eligibility criteria. These definitions range from being the first-degree relative (FDR) or SDR[17] of the affected proband (ie having a risk of inheriting the mutation of 50 or 25%) to a much looser definition such as 'being a member of the extended family'. This does then cause problems when comparing results between families. However, looking at studies confining eligibility to those at 50 or 25% risk,[17,19,23] 40–44% of counselees at 50% risk attended for counselling, with 36% proceeding to testing. The proportion of those at 25% risk seen/tested was considerably lower. This is somewhat different from our findings where degree of relationship did not matter for women, although there was some drop off in testing for men.

In general, women tend to proceed with predictive testing more often than men. Of all the studies measuring

Table 2 Results of studies in the context of the definitions they have used

	Author							
	Watson et al[1]		*Lerman et al*[2]		*Reichelt et al*[22]		*Smith et al*[21]	
Headline rate quoted	*41%*		*60 or 43% interviewees vs sample*		*78%*		*54%*	
	Definitions	*Results*	*Definitions*	*Results*	*Definitions*	*Results*	*Definitions*	*Results*
U_f at $t = X$ or U_c at t_{ave}	Uptake of linkage test, prior to cloning of the gene	41%	Uptake in registry families	43%	Uptake among persons already counselled and offered testing when it became available	All = 78% UF = 76%	Uptake in one large kindred	54% of SPs (92% of final analysis group) (= 35%[a] of EFMs)
No. of families		2 families		13 families		27 families		1 family
Time		1995		1996		1/5/99		1999
Delta $U_f \times$ delta t		(2 persons awaiting an appointment)	N/A	N/A		(6% undecided)	Offer of free testing restricted to study period	Not discussed
Time to report after offer of test		Unclear		Upto 17 months		Unclear		Unclear
U_i	Uptake amongst clinic attendees	13/15 = 87% Or 93[a]% after death	Uptake among attendees of	99% (SPs)[a]	Uptake in this sample	78%	Uptake among those who	91%
Attendance level	at time of report	47% - see below (One died sudden-ly before testing)	pretest education in the study Uptake in EFMs not calcuable	60% (SPs)		100% of sample	attended for counselling in the study	59.2% of SPs had counselling
A	Proportion of individuals entered into programme to have attended for pretest counselling	47% (or 52%[a] after those living out of area removed from calculation)	SPs attended for pretest education	60% (SPs)	Had earlier attended counselling sessions – offered testing when it became available	100%	Proportion attending for counselling	59.2% of SPs (= 39% of EFMs)
No. tested, breakdown by gender	Females Males	10 (59%[a]) 3 (20%)[a]	Females Males	SPs = 85 (66%[a]) SPs = 30 (48%[a])	Females Males	UF = 120 (76%) No further data given	Females Males (in final analysis)	(125) (87) No data on SPs not in final analysis
N	Age not specified	32 females = 17 (53%) Males = 15 (47%)	EFMs 18+(SPs)	279 EFMs (192 SPs Females = 129 (67% Males = 63 (31%))	Age not specified	232 females = 186 (80%) Males = 46 (20%)	EFMs 18+	759 EFMs (500 SPs, but only 212 used in final analysis Females = 125 (59%) Males = 87 (41%))
Cancer status	Unaffected only	Unaffected only	Unaffected and affected (some sporadic br./ov. or other sites)	38 (14%[a]) affected with cancer	Unaffected and affected.	AF = 30(13%) AM = 0 (0%) UF = 156 (67%) UM = 46 (20%)	Unaffected and affected	No breakdown given
No. tested, breakdown by cancer status	Unaffected only	13 (41%)	Unaffected Affected	87 (56%) 28 (74%)	Unaffected	UF = 120 (76%) No other data given	Unaffected Affected	No breakdown given
T	Not discussed	Not discussed	N/A – active approach with test offer	N/A	Not discussed	Not discussed	Not discussed	N/A – active offer in study context

C	Number to have attended pretest counselling	15 (47%)	Number of SPs who attended for pretest education	116 (60% of SPs)	Had earlier attended counselling sessions	232 (100%)	Number of SPs to have completed first genetic counselling session	296/500 SPs (59%) (296/759 EFMs (39%))
	Biesecker et al[20]		*Hagoel et al*[18]		*Julian-Reynier et al*[17]		*Meijers-Heijboer et al*[23]	
	55 and 78% EFMs vs SPs		*34% had counselling*		*26.7 and 84.2% F/SDRs vs attendees*		*38%*	
	Definitions	*Results*	*Definitions*	*Results*	*Definitions*	*Results*	*Definitions*	*Results*
U_f at $t = X$ or U_c at t_{ave}	Uptake in NCI study families	EFMs = 55% SPs = 78%	N/A – focus of paper is on uptake of counselling, not of testing	N/A (34% had counselling)	Uptake in families with ⩾1 FDR or SDR: information from 36 clinics & checked with other clinics In the process of testing (completed tests)	0 in 14.7% of families AF = 69% UF = 31% UM = 13% (56%: 23%: 7%) Total = 27% (19%)	Uptake in family members at 50% risk: series of consecutive families attending Rotterdam clinic	EFMs = 38% UF = 57% (at 50% risk) UM = 22% (at 50% risk)
No. of families		11 families		67 families		37 families		53 families
Time		2000		2000		8+ months after family informed		24 m after mutation found
Delta $U_f \times$ delta t	Not discussed	Not discussed	N/A	N/A (change in attendance rate over time not discussed)	Data includes those still in the process of testing	Data broken down – above (is assumption safe that all will receive a result?)	Graph used to show proportion not had DNA test *vs* time since genetic diagnosis (9, 12, 24 months)	UF (9:12:24/12) = 51%: 54%: 58% UM (9:12:24/12) = 19%: 19%: 24%
Time to report after offer of test						Upto 35 months		Mean follow-up = 26 m (range: 16–62 months)
U_l	Uptake amongst education & counselling attendees	78%	N/A – focus of paper is on uptake of counselling, not of testing	N/A	Uptake among attendees, including those still in the process	84% (59% had actually had a result[a])	Not discussed	Not discussed
Attendance level		70.5%[a]		34%		32%		
A	Proportion participating in education & counselling sessions	70.5%	Proportion of those at risk family members to attend clinic on invitation from the AP	34% (Only 1 EFM in 27 families gave possible attendance of 0% or 100%)	Proportion of FDRs and SDRs attending clinic after the AP had received her result	FDR AF: UF: UM = 96%: 60%: 25% total = 34% SDR AF: UF: UM = 58%: 21%: 10% total = 18% All total = 32%	Not discussed	Not discussed
No. tested, breakdown by gender	Females Males	87 (66%[a]) 48 (43%[a])	Females Males	(No breakdown given)	Females Males (tested+in process)	67+23 (37% total) 12+10 (13% total)	Females Males	198 (48%) 59 (22%)
N	Aged ⩾18 years	244 females = 132 (54%) Males = 112 (46%)	Aged ⩾22 years	371 EFMs females = 244 (66.1%) (actually its 65.8%!) Males = 127 (34.2%)	Aged 18+	419 females = 244 (58.2%) Males = 175 (41.8%)	Aged 20+ years	682 females = 411 (60.2%) Males = 271 (39.7%)

Table 2 (*Continued*)

	Biesecker et al[20]		*Hagoel et al*[18]		*Julian-Reynier et al*[17]		*Meijers-Heijboer et al*[23]	
	55 and 78% EFMs vs SPs		*34% had counselling*		*26.7 and 84.2% F/SDRs vs attendees*		*38%*	
	Definitions	*Results*	*Definitions*	*Results*	*Definitions*	*Results*	*Definitions*	*Results*
Cancer status	Unaffected and affected	Affected = 14 (8%)	Unaffected and affected	Affected (br./ov. ca.) = 54 (14.5%) Affected (other ca.) = 14 (3.8%) No cancer = 303 (81.7%)	Unaffected and affected (affected men excluded)	AF = 36 (8.6%) UF = 208 (49.6%) UM = 175 (41.8%)	Unaffected only	Unaffected only
No. tested, breakdown by cancer status	Unaffected Affected	UF SPs = 76 (79%) AF SPs = 11 (79%) Not possible to analyse by risk status	Unaffected Affected % Break-down by risk status (counselled)	(76 (25%) counselled) (49 (72%) counselled) FDR of cancer pt = 40% Not FDR of a cancer pt = 21%	Unaffected (tested+in process) Affected % Breakdown by risk status	59+28 (23% total) 20+5 (69% total) FDRs = 36% (= 51% UF, 18% UM) SDRs = 14% (= 18% UF, 9% UM)	Unaffected only % Break-down by risk status	UF 50% risk = 158 (57%) UF 25% risk = 40 (29%) UM = 59 (22%) Total = 38% Total at 50% risk = 36% UF at 25% risk = 29%
t	Not discussed	Not discussed	Not discussed	Not discussed	Time from AP being informed of mutation detection to firsst result in relation	In 24 families: Mean = 6.5 m Median = 4 m Range = 0–35 months Subsequent cutoff at 75th centile = 8 months	Time from mutation identification	9, 12 and 24 months
C	Number to have attended pretest education & counseling	172 (70.5%)	Number to have accepted invitation to participate in counselling	(34%)		All total = 133 (32%)	Not discussed	Not discussed

AF = affected female; AM = affected male; UF = unaffected female ;UM = unaffected male; FDR = first-degree relative; SDR = second-degree relative; AP = affected proband in whom mutation identified; SPs = study participants (where uptake measured in a wider, for example, psychosocial study); EFMs = eligible family members; N/A = not applicable.
[a]Some figures calculated from the data given for this table, not supplied in the original paper; A+proportion of eligible family members who have attended for counselling; U_c = combined uptake for all families at clinic.

uptake, overall the ratio of women to men tested appears to be approximately 3:1. It is difficult to be more precise than this because of the varying study methodologies. This is not surprising given the differing health implications of carrying a BRCA mutation between males and females. Our own figures would support these levels of uptake. Our previous study of five families showed a 40% uptake in males compared to 60% in women.[4] This dropped in this current study to an uptake of only 11–12% in men as compared to 30–50% in women. What is not so clear is whether the poor attendance rates for men is due to disinterest, the perception that the test is irrelevant or poor communication within the family. The high uptake in fully informed men from the Utah study[18] would suggest that communication or the lack of it may be the cause.

While nonparticipants can be identified within research projects and study families, this is not possible in clinical practice. Without records linked between regional centres, it is difficult to ensure that every individual is aware of their risk or the opportunity to attend counselling. In all, 14% of breast cancer patients in a survey[15] refused to contact their relatives. In this study, it is then impossible to say if patients have not come forward for testing because they actively have declined testing or because they are unaware of the availability of the test. A few previous studies have been able to obtain useful data about the nonattenders. Smith *et al*[21] report that nonparticipants are younger (<35) when the risk may not seem as important personally. It may be that at this stage the impact on children is not perceived to be as great.

It is striking that there is such a difference in the uptake in this study between the two centres, with uptake for women in Manchester at 53% as compared to 29% in London. The higher uptake of testing in Manchester may reflect a more coherent family structure in the North West where many women in each family support each other through the process. The small numbers for the London families, particularly of more distant relatives, possibly reflect the more dispersed nature of family members. This may then have an impact upon family communication. Anecdotally from the North West of England, it does appear that family members like to communicate 'bad' or upsetting news face-to-face, which is potentially more problematic if families are geographically spread. Manchester offers a regional genetic register to stay in contact with families (both tested and untested individuals) and this may prompt more family communication, as consenting individuals are written to on an annual basis. However, no active measures are taken to approach individuals not known to the clinic. We have not attempted to compare results in this paper with those from centres offering mutation screening to unaffected relatives where there is no known family mutation, as the denominator for attendance is not known, and because of the uncertainty of a negative test result.[24]

The trends indicated above reflect the current experience, with the range of surveillance options that are open to today's patient. These may change and therefore increase or decrease levels of uptake particularly in women. The much lower uptake of presymptomatic testing in men is replicated by our study, but is even lower than would be expected from comparisons with studies with direct approaches. Use of family information leaflets has recently been welcomed by patients and may result in more relatives coming forward for information, if not genetic testing. Finally, many individuals wait 2 or more years before undertaking predictive tests, which is longer than previously suggested. This will obviously impact upon long-term planning for services.

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