Randomized Trial of a Specialist Genetic Assessment Service for Familial Breast Cancer

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Background: Because of the growing demand for genetic assessment, there is an urgent need for information about what services are appropriate for women with a family history of breast cancer. Our purpose was to compare the psychologic impact and costs of a multidisciplinary genetic and surgical assessment service with those of current service provisions. Methods: We carried out a prospective randomized trial of surgical consultation with (the trial group) and without (the control group) genetic assessment in 1000 women with a family history of breast cancer. All P values are from two-sided tests. Results: Although statistically significantly greater improvement in knowledge about breast cancer was found in the trial group (P = .05), differences between groups in other psychologic outcomes were not statistically significant. Women in both groups experienced statistically significant reductions in anxiety and found attending the clinics to be highly satisfying. An initial specialist genetic assessment cost £14.27 (U.S. $22.55) more than a consultation with a breast surgeon. Counseling and genetic testing of affected relatives, plus subsequent testing of family members of affected relatives identified as mutation carriers, raised the total extra direct and indirect costs per woman in the trial group to £60.98 (U.S. $96.35) over costs for the control subjects. Conclusions: There may be little benefit in providing specialist genetics services to all women with a family history of breast cancer. Further investigation of factors that may mediate the impact of genetic assessment is in progress and may reveal subgroups of women who would benefit from specialist genetics services. [J Natl Cancer Inst 2000;92:1345–51]

Family history of breast cancer has long been recognized as an important risk factor in breast cancer (1,2). The recent identification of gene mutations that substantially increase the risk of breast cancer has enabled presymptomatic genetic testing in a small proportion of women (3–6). Consequently, there is a growing demand for genetic assessment services involving provision of genetic risk information and genetic counseling with possible presymptomatic testing (7–9). Concerns regarding potential adverse psychologic effects and high costs of genetics services mean that there is an urgent need for empirical evidence regarding appropriate service provision for at-risk women (10).

The TRACE project (Trial of Genetic Assessment in Breast Cancer) was conceived in recognition of the potential consequences of new genetics services proliferating throughout the U.K. National Health Service without systematic evaluation. A multidisciplinary genetics clinic, providing genetic assessment in addition to cancer surveillance and advice on risk management, was established for randomization and extra costs of the multidisciplinary genetics clinic. To our knowledge, this trial is the first to provide evidence on which to base future models of service delivery in the field of cancer genetics (11).

The aim of this study was to determine the psychologic benefits and costs of receiving genetic assessment. Beliefs about increased personal risk because of a family history of breast cancer play a large part in motivating women to seek advice from health-care providers (9,12–15). Studies (16,17) indicate that perceptions of high risk are related to increased levels of anxiety in at-risk women. As well as being inherently undesirable, excessive anxiety may impede understanding of genetic information (15) and threaten adherence to recommended cancer surveillance (18–21). Therefore, the goal of genetic assessment services is to communicate accurate genetic risk information without causing undue anxiety. The extent to which giving accurate information is counterbalanced with reassurance is an important factor influencing patient satisfaction and psychologic adjustment (12,22,23). Genetic assessment provides an opportunity for clinicians to moderate perceptions of cancer risk and associated anxiety, and studies indicate that there may indeed be psychologic benefits of receiving breast cancer risk information (24) and genetic testing (25).

This study reports prospective data regarding the impact of a multidisciplinary genetic assessment service on primary psychologic outcome relating to emotional well-being and perceived risk and secondary outcomes including knowledge and satisfaction. We predicted that the genetics intervention would lead to better outcomes relative to current service provision. Since it was not possible to specify any single outcome as being key (as would be required for a cost-effectiveness analysis), we used knowledge and satisfaction as key endpoints.

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analysis), the additional costs of providing the TRACE service model were assessed prospectively for consideration against multiple outcomes in the form of a cost and consequences analysis.

**METHODS**

**Participants**

Ethical approval for the study was obtained from local research ethics committees. Participants were drawn from women residents throughout Wales who were referred by their general practitioner to a breast surgeon at the district general hospital because of a family history of breast cancer. These women constituted around 10% of the referrals to breast clinics for all breast disorders. Information about the study was circulated to all general practitioners in Wales (total, 1700 practitioners) advising that women who fulfilled the study entry criteria could be referred to local breast surgeons. Eligibility required having a family history of breast cancer, no personal history of breast cancer, no prior genetic counseling, and being a resident of Wales. A family history of breast cancer was defined as having a first-degree female relative diagnosed with breast cancer before 50 years of age, a first-degree female relative with bilateral breast cancer at any age, two or more first-degree relatives with breast cancer, or a first- and second-degree relative with breast cancer. Written informed consent was obtained from each participant. Further details of the referral procedure (11) and referral patterns (9) were reported elsewhere.

Fig. 1 shows the progress of patients through the prospective randomized trial. During an 18-month recruitment period, 1172 women were referred to the trial and were sent a baseline questionnaire. Since a power calculation had indicated that data from 1000 women would yield 89% power to detect a statistically significant difference between groups at the 5% level, data from the first 1000 referrals were sufficient for the purposes of the psychosocial evaluation. Seven hundred forty women were randomly allocated to attend the trial or control clinic. Of the 260 women who were not randomly assigned, 167 had not returned the baseline questionnaire and 93 had returned the questionnaire but declined to enter the study (n = 75), did not attend their scheduled appointment on two or more occasions and were returned to the care of their local breast surgeon (n = 11), or were found to be ineligible (n = 5). Two women died before attending the clinic. Of those participants who were randomly assigned, five women had been allocated to the trial group but were excluded from the research study because of nonattendance at the surgical component of the multidisciplinary trial clinic. The remaining 735 randomly assigned participants in both study groups were asked to complete further questionnaires to assess psychologic outcomes at two follow-up points: immediately and 9 months after the clinic. Participants who did not complete both follow-up questionnaires were not included in the main comparative analyses. The final sample consisted of 545 women, giving an overall participation rate of 55% (263 in the trial group and 282 in the control group).

The costing exercise made use of the total referral sample of 1172 women (11). Costs are, therefore, based on 824 women who attended for initial consultation (412 in the trial group and 412 in the control group).

**Study Design and Procedures**

Random assignment of an individual to the trial clinic or control clinic was contingent on returning a completed baseline questionnaire (26). There was no reference to group allocation either in the baseline questionnaire or in the initial appointment letter. Two clinic venues were chosen for the study: the Breast Test Wales Screening Centre and the Family History Clinic at the University Hospital of Wales, both in Cardiff. The Breast Test Wales Screening Centre is primarily a well-woman setting that provides breast screening as part of the U.K. national program, and the Family History Clinic at the University Hospital of Wales is based in a unit seeing many symptomatic women. To control for differences between the two venues, a four-way randomization was conducted, representing each combination of clinic type (trial and control) and clinic venue (the Breast Test Wales Screening Centre and the Family History Clinic at the University Hospital of Wales). The randomization procedure was based on a computer-generated sequence of random numbers.

**Control group.** Women who were randomly assigned to the control group received clinical input from the specialist surgical staff, including a breast surgeon and breast care nurse. The breast surgeon adhered to a standard protocol that included the following components: 1) appropriate breast cancer surveillance (systematic clinical breast examination and, for women >35 years of age, a mammogram) and advice on risk management, 2) surgical assessment of individual breast cancer risk, 3) the option of entering the U.K. Tamoxifen Prevention Trial, and 4) annual surgical review involving appropriate breast cancer surveillance and advice. Referral for genetic counseling or presymptomatic genetic testing was not offered. Surgical assessment of individual breast cancer risk was based on nongenetic information collected by the surgeon, including age, reproductive history, and minimal family history of breast cancer. This information was presented to the women by the breast surgeon in descriptive terms and was stratified by the surgeon into one of the following three categories: low risk, moderate risk, or high risk.

**Trial group.** Women randomly assigned to the trial group received a newly developed multidisciplinary genetic assessment service. This service combined clinical input from the surgical staff (components 1, 3, and 4 of the control intervention) with a specialist genetics consultation provided by a clinical geneticist and genetic nurse specialist. The genetics consultation involved education about breast cancer genetics, genetic assessment of individual breast cancer risk, and, in women identified as high risk, possible presymptomatic testing for the BRCA1 and/or the BRCA2 gene. Assessment of individual genetic risk was based on detailed family pedigree data that were collected and analyzed by the geneticist with the use of the model developed by Claus et al. (27). The geneticist presented this information to the women as a residual lifetime risk

![Registered or Eligible Patients (N = 1000)](https://academic.oup.com/jnci/article-abstract/92/16/1345/2905925)

![Not Randomized (n = 260)](https://academic.oup.com/jnci/article-abstract/92/16/1345/2905925)

![Randomization (N = 740)](https://academic.oup.com/jnci/article-abstract/92/16/1345/2905925)

![Received Standard Intervention as Allocated (n = 369)](https://academic.oup.com/jnci/article-abstract/92/16/1345/2905925)

![Did not Receive Standard Intervention as Allocated (n = 0)](https://academic.oup.com/jnci/article-abstract/92/16/1345/2905925)

![Immediate follow-up (n = 317)](https://academic.oup.com/jnci/article-abstract/92/16/1345/2905925)

![Withdrawn (n = 52)](https://academic.oup.com/jnci/article-abstract/92/16/1345/2905925)

![Lost to Follow-up (n = 52)](https://academic.oup.com/jnci/article-abstract/92/16/1345/2905925)

![Other (n = 0)](https://academic.oup.com/jnci/article-abstract/92/16/1345/2905925)

![Nine months follow-up (n = 282)](https://academic.oup.com/jnci/article-abstract/92/16/1345/2905925)

![Withdrawn (n = 35)](https://academic.oup.com/jnci/article-abstract/92/16/1345/2905925)

![Lost to Follow-up (n = 35)](https://academic.oup.com/jnci/article-abstract/92/16/1345/2905925)

![Other (n = 0)](https://academic.oup.com/jnci/article-abstract/92/16/1345/2905925)

![Completed Trial (n = 282)](https://academic.oup.com/jnci/article-abstract/92/16/1345/2905925)

![Received Trial Intervention as Allocated (n = 366)](https://academic.oup.com/jnci/article-abstract/92/16/1345/2905925)

![Did not Receive Trial Intervention as Allocated (n = 5)](https://academic.oup.com/jnci/article-abstract/92/16/1345/2905925)

![Immediate follow-up (n = 338)](https://academic.oup.com/jnci/article-abstract/92/16/1345/2905925)

![Withdrawn (n = 28)](https://academic.oup.com/jnci/article-abstract/92/16/1345/2905925)

![Lost to Follow-up (n = 28)](https://academic.oup.com/jnci/article-abstract/92/16/1345/2905925)

![Other (n = 0)](https://academic.oup.com/jnci/article-abstract/92/16/1345/2905925)

![Nine months follow-up (n = 263)](https://academic.oup.com/jnci/article-abstract/92/16/1345/2905925)

![Withdrawn (n = 75)](https://academic.oup.com/jnci/article-abstract/92/16/1345/2905925)

![Lost to Follow-up (n = 75)](https://academic.oup.com/jnci/article-abstract/92/16/1345/2905925)

![Other (n = 0)](https://academic.oup.com/jnci/article-abstract/92/16/1345/2905925)

![Completed Trial (n = 263)](https://academic.oup.com/jnci/article-abstract/92/16/1345/2905925)

Fig. 1. CONSORT (progress of patients through the trial) diagram.
of breast cancer expressed in percentage terms. Women were categorized by the geneticist as low risk if they had a lifetime risk of less than 10% and were at no appreciably increased risk of breast cancer, as moderate risk if they had a risk between 10% and 24%, and as high risk if they had a risk of 25% or more. Genetic testing was available to those women who had a risk of 25% or more and a living affected relative (n = 24 of 263). Of these women, four went on to receive genetic test results. To determine the effect of the treatment intervention apart from the impact of receiving test results, we excluded these participants from the impact analyses. This did not change the pattern of findings. Further details of the study protocol are reported elsewhere (11). A chi-square analysis was used to compare the number of participants stratified as low, moderate, or high risk in each study group. This indicated equivalence across study groups in the outcomes of risk assessment \( \chi^2 (2) = 2.58; P = .28 \).

**Psychologic Measures**

**Demographic characteristics.** Age, marital status, ethnicity, educational level, and family history (the number of first- and second-degree relatives with breast cancer) were assessed at baseline.

**General anxiety.** The State–Trait Anxiety Inventario (STAI) (28) was used to measure general anxiety. The Trait Anxiety scale (included at baseline assessment) asks respondents to indicate how they generally feel regarding 20 statements, and the State Anxiety scale (included at all three assessment points) asks respondents to describe how they feel currently regarding the same 20 statements. Extensive normative data are available in the STAI manual (28). In this study, high internal consistency was found for both scales (Cronbach’s alpha = .92 for trait scale; alpha = .93 for state scale; scale range = 20–80).

**Breast cancer worry.** The Breast Cancer Worries scale (19,20) was used at all three assessments to measure frequency of concerns about breast cancer and their impact on mood and daily functioning. In previous studies (18,19), higher levels of cancer worry have been associated with nonadherence to recommended cancer surveillance in at-risk women. The scale demonstrated good internal consistency (alpha = .86; scale range = 6–24).

**Perceived risk of breast cancer.** Perceived risk was measured at all three assessment points by use of two items derived from previous research (19,29–32). These items were as follows: 1) What level of risk do you personally think you face? 2) In your opinion, what are your chances of getting breast cancer compared with the average woman? These items were rated on a 5-point scale and summed to create a composite scale with adequate internal consistency (alpha = .71; scale range = 2–10).

**Knowledge of familial breast cancer.** Four true/ false items were used at baseline and immediately after the clinic to assess knowledge, including topics relating to causative heterogeneity and incomplete penetrance of breast cancer gene mutations. Two items were true statements, and two were false statements. One point was given for each correct answer, and items were summed to create a knowledge score (range = 0–4).

**Patient satisfaction.** The 12-Item Satisfaction With Genetic Counseling Questionnaire (22) was used immediately after the clinic (33,34). The scale assesses the following three dimensions of patient satisfaction: 1) instrumental (satisfaction with the doctor’s competence), 2) affective (satisfaction with the doctor’s personal qualities), and 3) procedural (satisfaction with administrative procedures, such as waiting time and staff conduct) (35,36). Items were summed to create a total satisfaction score (alpha = .85; scale range = 12–48).

**Costs**

It should be stressed that reported costs relate to the TRACE model. Different models of service provision—and they exist (11)—would mean costs that were different from those reported herein. We focused on the marginal cost of sending a woman to a special genetics service rather than a normal practice of referral to a breast-care surgeon at the local District General Hospital. All costs that remained the same, whatever the service attended (e.g., mammography), were thus ignored. A social welfare approach was adopted that included costs borne by patients and relatives as well as National Health Service resource use. Health professional time was valued at gross employment costs by grade, travel time of patients/relatives was determined by survey, and travel time of professionals included direct costs and the opportunity cost of time spent traveling. All costs are in 1997/1998 prices. Conversion to U.S. dollars was at the rate of £1 = $1.58.

Within the TRACE model, genetic testing included three tests on all samples of extracted DNA: heteroduplex analysis (37), protein truncation test (38), and single-stranded conformational polymorphism (39). All detected mutations were subject to sequencing of a smaller part of the exon to locate the precise point of the change and confirm that it was a disease-causing mutation. If a mutation was confirmed, then the presenting woman and her relatives were offered testing with additional counseling before and after testing. The cost of testing these latter individuals for the presence of the same mutation (cascade testing) is markedly lower than that for the original test because the test focused only on the prespecified location. The costs of mutation testing are thus highly dependent on the ratio of first-to-cascade tests undertaken, and different protocols for determining eligibility for testing can have marked effects on costs, as can different combinations of tests used.

**Statistical Methods**

All statistical analyses were carried out by use of a Statistical Package for Social Sciences for Windows, version 6.0. Chicago, IL. Before analysis, data were screened for accuracy, and assumptions of linearity and normality were tested. The analysis was conducted in two stages.

First, participation bias was examined by comparing study participants with those who dropped out at each of the three assessment points on baseline demographic and psychologic variables. Ethnic background was not included in the analysis because of low variation. Although data were not available for women who were referred to the study but refused participation, we examined participation bias at baseline by comparing participants who attended the clinic (n = 735) with those who completed the baseline questionnaires but subsequently declined the study (n = 75). Attrition bias after a visit to the clinic was tested first by comparing participants who completed the questionnaire immediately after the clinic (n = 655) with those who did not complete this questionnaire (n = 80) on study group allocation and baseline variables. Participants who completed the 9-month follow-up questionnaire (n = 545) and those who did not (n = 62) were compared similarly. Chi-square tests of association were conducted for categorical variables, and independent Student’s t-tests (two-tailed) were conducted for continuous variables. When using t tests, Levene’s test for equality of variances was examined to account for the possibility of unequal variance of samples. In cases where F values were statistically significant at P <.01, separate variance estimates are reported. All P values are from two-sided tests. Descriptive statistics were then used to examine the characteristics of the final sample (n = 545 participants who attended the clinic and completed both follow-up questionnaires).

Second, the effect of genetic assessment on psychologic outcomes was analyzed by use of repeated-measures or general factorial analysis of variance (ANOVA), as appropriate. Effect sizes were calculated with the use of the \( \eta^2 \) statistic (a value of .01 represents a weak effect, .06 represents a moderate effect, and .14 represents a strong effect). Statistically significant main effects of ANOVA were followed up with post hoc unrelated or related t tests. Before ANOVA, the extent to which the data met the assumption of multivariate homogeneity of variance was assessed with a Box’s M test. A more conservative statistical significance level (probability of type I error = .025) was used when this assumption was not met to compensate for a potentially more liberal F test (40). For repeated-measures ANOVA that had more than two levels of the within-subjects factor, the assumption of sphericity was tested by use of the Huynh-Feldt epsilon statistic (41). The potential impact of the clinic venue on outcomes of genetic assessment was examined by the use of a general factorial ANOVA and is reported where statistically significant effects were found.

**RESULTS**

**Participation Bias**

As shown in Table 1, those who dropped out at baseline reported statistically significantly higher trait and state anxiety and lower personal risk than participants. Mean trait anxiety scores of dropouts were higher than population norms (28). At the first assessment after the clinic, dropouts were significantly younger and reported higher baseline cancer worry. At the 9-month assessment, dropouts were significantly younger and reported higher baseline state anxiety, cancer worry, and perceived risk.

There was some evidence of differential dropout between study groups, with control group participants significantly less likely to return the questionnaire immediately after the clinic \( \chi^2 (1) = 7.86; P = .005 \). We tested the equivalence of study groups on demographics and base-
Sample Characteristics

The final sample consisted of 545 women who had a mean age of 42.59 years (standard deviation [SD] = 9.57; range = 19–73) and an average of two relatives affected with breast cancer (range = 1–9). The sample was predominantly white (99%), married or cohabiting (82%), and educated to at least the secondary level (69%).

Psychologic Outcomes of Genetic Assessment

Table 2 shows mean scores for each study group on psychologic outcome measures. Table 3 shows the results of repeated-measures ANOVA.

General anxiety remained within the normal range before and after the study intervention. While the effect of the study group on state anxiety was not statistically significant, there was a significant, weak-to-moderate main effect of time. Post hoc tests of the effect of time indicated a significant overall reduction in state anxiety from baseline to assessment immediately after the clinic \[t(501) = 5.08; \ P < .001\]. By the 9-month assessment, there was a significant increase in state anxiety \[t(501) = −4.60; \ P < .001\] that did not exceed baseline levels \[t(501) = −.05; \ P > .96\]. The group × time interaction was not significant (i.e., the magnitude of change in state anxiety scores did not differ between the study groups).

There was a large, significant main effect of time on breast cancer worry, with a reduction in worry from baseline to immediate postclinic assessment \[t(538) = −0.31 to 0.20\].

Table 1. Comparison of study participants (top line of each comparison) and dropouts (bottom line) on baseline variables*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Stage of study dropout</th>
<th>Baseline Mean</th>
<th>Baseline SD</th>
<th>Immediately after clinic Mean</th>
<th>Immediately after clinic SD</th>
<th>9 mo after clinic Mean</th>
<th>9 mo after clinic SD</th>
<th>P†</th>
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<tbody>
<tr>
<td>Age, y</td>
<td>Baseline</td>
<td>41.45</td>
<td>9.79</td>
<td>41.90</td>
<td>9.80</td>
<td>42.59</td>
<td>9.57</td>
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<td></td>
<td>Immediately after clinic</td>
<td>40.58</td>
<td>10.31</td>
<td>37.85</td>
<td>8.10</td>
<td>37.15</td>
<td>7.98</td>
<td>.00</td>
</tr>
<tr>
<td>Family history, No. of relatives with breast cancer</td>
<td>Baseline</td>
<td>2.40</td>
<td>1.28</td>
<td>2.40</td>
<td>1.28</td>
<td>2.39</td>
<td>1.27</td>
<td>.81</td>
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<tr>
<td></td>
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<td>2.21</td>
<td>1.14</td>
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<td>1.30</td>
<td>2.44</td>
<td>1.34</td>
<td>.76</td>
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<td>Trait anxiety, score</td>
<td>Baseline</td>
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<td>10.37</td>
<td>39.49</td>
<td>10.22</td>
<td>39.25</td>
<td>10.28</td>
<td>.08</td>
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<td></td>
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<td>43.07</td>
<td>11.12</td>
<td>41.19</td>
<td>11.57</td>
<td>41.47</td>
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<td>State anxiety, score</td>
<td>Baseline</td>
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<td>11.33</td>
<td>36.43</td>
<td>11.19</td>
<td>36.05</td>
<td>11.07</td>
<td>.04</td>
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<td></td>
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<td>40.61</td>
<td>10.40</td>
<td>38.28</td>
<td>12.42</td>
<td>40.17</td>
<td>13.10</td>
<td>.98</td>
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<tr>
<td>Breast cancer worry, score</td>
<td>Baseline</td>
<td>11.89</td>
<td>3.27</td>
<td>11.72</td>
<td>3.13</td>
<td>11.62</td>
<td>3.16</td>
<td>.01</td>
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<td></td>
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<td>11.85</td>
<td>3.25</td>
<td>13.33</td>
<td>4.01</td>
<td>12.68</td>
<td>2.84</td>
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<td>Baseline</td>
<td>7.37</td>
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<td>7.31</td>
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<td>6.95</td>
<td>1.49</td>
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<td>1.38</td>
<td>7.82</td>
<td>1.26</td>
<td>.14</td>
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<td>Knowledge, score</td>
<td>Baseline</td>
<td>1.50</td>
<td>1.06</td>
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<td>1.49</td>
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<td>.55</td>
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<td></td>
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<td>1.32</td>
<td>1.04</td>
<td>1.59</td>
<td>1.05</td>
<td>1.58</td>
<td>1.10</td>
<td>.98</td>
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<tr>
<td>Marital status, % married or cohabiting</td>
<td>Baseline</td>
<td>82</td>
<td>.20</td>
<td>83</td>
<td>.16</td>
<td>82</td>
<td>.98</td>
<td>.16</td>
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<tr>
<td>Education, % secondary level or more</td>
<td>Baseline</td>
<td>70</td>
<td>.13</td>
<td>70</td>
<td>.65</td>
<td>69</td>
<td>.39</td>
<td>.00</td>
</tr>
<tr>
<td></td>
<td>Immediately after clinic</td>
<td>61</td>
<td>.67</td>
<td>67</td>
<td>.74</td>
<td>67</td>
<td>.74</td>
<td>.00</td>
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</table>

*Study participants were compared with dropouts at each of the three assessment points on baseline demographic and psychologic variables. Independent Student′s t tests were conducted for continuous variables, and chi-square tests of association were conducted for categorical variables. SD = standard deviation. †All \( P \) values are from two-sided tests.

Table 2. Mean scores (standard deviations) of study groups (n = 545) on baseline and follow-up values of outcome variables

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Time</th>
<th>Trial group</th>
<th>Control group</th>
<th>Adjusted differences and 95% confidence intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td>State anxiety</td>
<td>Baseline</td>
<td>35.93 (11.11)</td>
<td>35.54 (10.87)</td>
<td>−0.75 to 1.41</td>
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<tr>
<td></td>
<td>Immediately after the clinic</td>
<td>34.33 (10.79)</td>
<td>33.14 (10.11)</td>
<td>−0.85 to 1.98</td>
</tr>
<tr>
<td></td>
<td>9 mo after the clinic</td>
<td>36.38 (12.34)</td>
<td>35.18 (11.75)</td>
<td>−0.21 to 0.78</td>
</tr>
<tr>
<td>Breast cancer worry</td>
<td>Baseline</td>
<td>11.79 (3.37)</td>
<td>11.49 (2.97)</td>
<td>−0.31 to 0.20</td>
</tr>
<tr>
<td></td>
<td>Immediately after the clinic</td>
<td>10.55 (2.91)</td>
<td>10.50 (2.70)</td>
<td>−0.59 to 0.05</td>
</tr>
<tr>
<td></td>
<td>9 mo after the clinic</td>
<td>10.55 (3.21)</td>
<td>10.63 (2.90)</td>
<td>−0.24 to 0.07</td>
</tr>
<tr>
<td>Perceived risk</td>
<td>Baseline</td>
<td>7.29 (1.24)</td>
<td>7.33 (1.17)</td>
<td>−0.21 to 0.08</td>
</tr>
<tr>
<td></td>
<td>Immediately after the clinic</td>
<td>6.44 (1.30)</td>
<td>6.62 (1.14)</td>
<td>−0.02 to 0.08</td>
</tr>
<tr>
<td></td>
<td>9 mo after the clinic</td>
<td>6.74 (1.30)</td>
<td>6.90 (1.25)</td>
<td>−0.24 to 0.07</td>
</tr>
<tr>
<td>Knowledge</td>
<td>Baseline</td>
<td>1.54 (1.09)</td>
<td>1.45 (1.06)</td>
<td>−0.001 to 0.27</td>
</tr>
<tr>
<td></td>
<td>Immediately after the clinic</td>
<td>2.17 (1.08)</td>
<td>1.89 (1.08)</td>
<td>−0.16 to 0.76</td>
</tr>
<tr>
<td>Patient satisfaction</td>
<td>Baseline</td>
<td>42.82 (5.23)</td>
<td>42.29 (4.57)</td>
<td>−0.16 to 0.76</td>
</tr>
</tbody>
</table>
and from baseline to assessment at 9 months $t(538) = 8.97; P<.001$. The change in cancer worry from immediate postclinic assessment to assessment at 9 months was not significant $t(538) = -6.86; P = .50$.

Again, there was a statistically significant, strong main effect of time on perceived breast cancer risk, with an overall reduction in perceived risk from baseline to assessment immediately after the clinic $t(520) = 14.02; P<.001$. Although there was a significant increase in perceived risk from the immediate postclinic assessment to the 9-month assessment $t(520) = -5.17; P<.001$, perceived risk at 9 months was significantly lower than baseline levels $t(520) = 8.71; P<.001$.

There were significant main and interaction effects of study group and time on knowledge. Although the difference between groups was not statistically significant at baseline $t(522) = 93; P = .35$, the trial group had significantly higher knowledge scores immediately after the clinic $t(522) = 2.92; P = .004$. There was a statistically significant increase in knowledge in both the trial group $t(247) = -8.68; P<.001$ and the control group $t(275) = -6.78; P<.001$, but the magnitude of the increase was significantly greater in the trial group $t(522) = -1.95; P = .05$.

Mean satisfaction scores were high in both groups. General factorial ANOVA indicated that, although the effect of study group on satisfaction was not statistically significant $F(1, 448) = 1.66; P = .20$, there was a small significant main effect of the clinic venue $F(1, 448) = 4.45; P = .04$. There was no significant interaction effect $F(1, 448) = .81; P = .37$. Participants seen at Breast Test Wales Screening Centre (mean = 42.96; SD = 4.97) reported significantly greater satisfaction than those seen at the University Hospital of Wales (mean = 41.98; SD = 4.79) $t(450) = 2.11; P = .04$.

### DISCUSSION

Current pressure placed on cancer genetics services has led to an urgent need for development and evaluation of appropriate models of service provision for women with a family history of breast cancer. To our knowledge, this study is the first to address this issue by examining the impact of a multidisciplinary genetics service on psychologic outcomes and costs.

These findings indicate that the concerns of at-risk women may be alleviated in the short-term by consulting a genetic or surgical specialist for advice in relation to a family history of breast cancer. Regardless of their study group allocation, women’s levels of anxiety, worry, and perceived risk were reduced after attending the clinic, and satisfaction with the service that they received was high. Although some of the women’s concerns may have begun to resurface at longer term follow-up, this may have been an effect of awaiting cancer screening at annual review (42). It was not possible to test this potential effect within this study.

An additional finding was that women who received genetic assessment demonstrated slightly greater improvements in knowledge compared with those who received standard assessment; however, their knowledge was not optimal. The type of information that is communicated in genetic counseling is complex, and difficulties in understanding risk information (13,43) and genetic explanations of disease (44) have been observed previously in at-risk samples. The development of educational interventions to improve comprehension of genetic information remains a challenge for genetics services.

These findings must be interpreted in light of possible sample selection bias, as well as differential dropout between study groups, which may affect the ability to apply our results to other populations. At baseline, the small number of women who declined were more anxious by disposition, yet they perceived lower personal risk than those who attended the clinic. A similar pattern of findings has emerged from previous studies (45–47), suggesting that there may be a small group of highly...

### Table 3. Analysis of variance for repeated-measures study group × time on psychologic outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Effect</th>
<th>F</th>
<th>df</th>
<th>P*</th>
<th>$\eta^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>State anxiety</td>
<td>Study group</td>
<td>1.20</td>
<td>1, 500</td>
<td>.27</td>
<td>.002</td>
</tr>
<tr>
<td></td>
<td>Time</td>
<td>13.29</td>
<td>2, 1000</td>
<td>.00</td>
<td>.03</td>
</tr>
<tr>
<td></td>
<td>Group × time</td>
<td>.52</td>
<td>2, 1000</td>
<td>.60</td>
<td>.001</td>
</tr>
<tr>
<td>Breast cancer worry</td>
<td>Study group</td>
<td>.15</td>
<td>1, 537</td>
<td>.70</td>
<td>.000</td>
</tr>
<tr>
<td></td>
<td>Time</td>
<td>70.46</td>
<td>2, 1074</td>
<td>.00</td>
<td>.12</td>
</tr>
<tr>
<td></td>
<td>Group × time</td>
<td>1.70</td>
<td>2, 1074</td>
<td>.18</td>
<td>.003</td>
</tr>
<tr>
<td>Perceived risk</td>
<td>Study group</td>
<td>2.06</td>
<td>1, 519</td>
<td>.15</td>
<td>.004</td>
</tr>
<tr>
<td></td>
<td>Time</td>
<td>106.62</td>
<td>2, 1038</td>
<td>.00</td>
<td>.17</td>
</tr>
<tr>
<td></td>
<td>Group × time</td>
<td>.99</td>
<td>2, 1038</td>
<td>.37</td>
<td>.002</td>
</tr>
<tr>
<td>Knowledge</td>
<td>Study group</td>
<td>5.03</td>
<td>1, 522</td>
<td>.03</td>
<td>.01</td>
</tr>
<tr>
<td></td>
<td>Time</td>
<td>121.50</td>
<td>1, 522</td>
<td>.00</td>
<td>.19</td>
</tr>
<tr>
<td></td>
<td>Group × time</td>
<td>3.79</td>
<td>1, 522</td>
<td>.05</td>
<td>.01</td>
</tr>
</tbody>
</table>

*All $P$ values are from two-sided tests.
anxious individuals who cope with their distress by avoiding genetic information. Furthermore, women lost to follow-up evaluation were more anxious than those who remained in the study. Additional psychologic support and possible referral to specialist services may be required to manage distress in the subset of at-risk women who are psychologically vulnerable.

Contrary to our predictions, the current pattern of findings suggests that consulting with a genetic or surgical specialist may be equally reassuring for at-risk women. Although receiving genetics input may lead to slightly greater improvement in knowledge, this should be weighed against the extra cost of providing specialist genetic assessment. We acknowledge the difficulties associated with accepting the null hypothesis. The observed lack of differences may be attributed to reduced statistical power as a consequence of study dropout, or the two groups may have been functionally equivalent in terms of providing individualized risk information. Despite these limitations, the current findings suggest that there may be little benefit in providing genetics services to all women with a family history of breast cancer. Further examination of the factors that mediate the impact of genetic assessment may reveal subgroups of women who are more likely to experience adverse psychologic effects and others who improve or remain unchanged. Comparison of psychologic outcomes in women at various levels of risk for breast cancer is in preparation and should provide further evidence regarding appropriate service provision (10). Targeting specialist genetic assessment would have marked effects on the cost-effectiveness of such services.

REFERENCES


(38) Lancaster JM, Cochran CJ, Brownlee HA, Evans AC, Berchuck A, Futreal PA, et al. Detection of BRCA1 mutations in women with early-onset ovarian cancer by use of the protein


NOTES

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