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Cancer genetic risk assessment for individuals at risk of familial breast cancer (Review)

Hilgart JS, Coles B, Iredale R

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[Intervention Review]

Cancer genetic risk assessment for individuals at risk of familial breast cancer

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ABSTRACT

Background

The recognition of an inherited component to breast cancer has led to an increase in demand for information, reassurance, and genetic testing, which has resulted in the creation of genetic clinics for familial cancer. The first step for patients referred to a cancer genetic clinic is a risk assessment.

Objectives

To evaluate the impact of cancer genetic risk-assessment services on patients at risk of familial breast cancer.

Search methods

The specialised register maintained by the Cochrane Breast Cancer Group was searched on 16th February 2005. We also searched MEDLINE, EMBASE, CINAHL, PsycLIT, CENTRAL, DARE, ASSIA, Web of Science, SIGLE and LILACS. The original searches covered the period 1985 to February 2005. We also handsearched relevant journals. For this review update the search was repeated through to April 2011.

Selection criteria

We considered trials looking at interventions for cancer genetic risk-assessment services for familial breast cancer for inclusion. Trials assessed outcomes such as understanding of risk, satisfaction and psychological well-being. We excluded studies if they concerned cancers other than breast cancer or if participants were not at risk of inherited breast cancer. We also excluded trials concerning the provision of general cancer genetic information or education as this review was concerned with the delivery of genetic risk assessment. Participants could be individuals of any age or gender, with or without a known BRCA mutation, but without a previous history of breast cancer or any other serious illness.

Data collection and analysis

Two review authors independently assessed trial quality and extracted data. Additional information was sought from investigators as necessary. Due to the heterogeneity of both the interventions and outcomes, we reported data descriptively.

Main results

In this review update, we included five new trials, bringing the total number of included studies to eight. The included trials (pertaining to 10 papers), provided data on 1973 participants and assessed the impact of cancer genetic risk assessment on outcomes including perceived risk of inherited cancer, and psychological distress. This review suggests that cancer genetic risk-assessment services help to reduce distress, improve the accuracy of the perceived risk of breast cancer, and increase knowledge about breast cancer and genetics. The health professional delivering the risk assessment does not appear to have a significant impact on these outcomes.

Authors' conclusions

This review found favourable outcomes for patients after risk assessment for familial breast cancer. However, there were too few papers to make any significant conclusions about how best to deliver cancer genetic risk-assessment services. Further research is needed assessing the best means of delivering cancer risk assessment, by different health professionals, in different ways and in alternative locations.

PLAIN LANGUAGE SUMMARY

Cancer genetic risk assessment for individuals at risk of familial breast cancer

The recognition of an inherited component to breast cancer has led to an increase in demand for information, reassurance, and genetic testing, which resulted in the creation of genetic clinics for familial cancer. Cancer genetic services can involve extended counselling, specialist screening and genetic testing for mutations. Risk assessment is the first step in the process of providing information and support to patients and their families about their risk of inheriting cancer. Information on evidence-based methods of delivering cancer genetic risk-assessment services is, however, sparse. For this review a systematic search, review, and assessment of the literature on the delivery of cancer genetic risk-assessment services for individuals concerned with familial breast cancer was undertaken.

This review included eight trials (10 papers) which covered the process of risk assessment for familial breast cancer. These focused on the psychosocial impact on patients, as well as other outcomes and aspects of service delivery, and provided data on 1973 participants. Due to the limited number of trials, this review found insufficient evidence to make any firm conclusions about the best way to deliver risk-assessment services for individuals concerned about a family history of breast cancer. All eight included studies did, however, demonstrate improvements in psychological well-being and a decrease in the levels of cancer worry as a result of the risk-assessment service. Although limited, the findings of this review suggest that cancer genetic risk-assessment services can help to reduce distress, improve the accuracy of the individual's perceived risk of breast cancer, and increase knowledge about breast cancer and genetics. Existing evidence suggests that such services do not cause patients any harm and, in the short-term, can have a positive effect by helping to ease distress and decrease cancer worry. From this review, it does not appear that the health professional delivering the risk assessment has a significant impact on these outcomes.

SUMMARY OF FINDINGS

Summary of findings 1. Summary of findings for the main comparisons

Study	Intervention	Follow-up period and final sample size	Primary outcomes	Summary of findings
Bowen 2004	Group psychosocial versus individual genetic counselling compared with delayed counselling control group	6-month follow-up. Final sample n = 348; 117 genetic counselling, 110 psychosocial counselling, 121 control	Perceived risk: personal estimate of lifetime risk scale 0% to 100%; relative risk estimate. Anxiety and depression: shortened Hopkins symptom checklist; Cancer worry scale (Lerman 1991a). Reactions to counselling: perceived support from counsellor, enjoyment and perceived usefulness of counselling	Significantly lower perceived risk in intervention groups compared with control post-intervention (P < 0.01). Lower cancer worry in intervention groups compared with control post-intervention (P > 0.01). There were no effects of counselling type. Intervention groups reported lower levels of anxiety over time than control group. Significant difference in psychosocial group over time and a significant interaction between time and study arm (F = 3.0; df = 2344; P < 0.01). Non-significant reduction in depression scores over time for all groups. Satisfaction with counselling high in both intervention groups. More genetic counselling participants reported talking 'quite a bit' about concerns during counselling compared with psychosocial counselling (86% versus 72%) P < 0.05
Bowen 2006	Group psychosocial versus individual genetic counselling compared with delayed counselling control group for Ashkenazi Jewish women	6-month follow-up. 220 women randomised; 68 psychosocial counselling, 77 genetic counselling, 75 control group. 96% completed follow-up but numbers in each group not provided	Perceived risk: personal estimate of lifetime risk scale 0% to 100%. Cancer worry scale (Lerman 1991a). General anxiety: Brief Symptom Inventory (Derogatis 1983). Genetic testing beliefs, awareness and interest. Jewish identity: The Multigroup Ethnic Identity Measure (Phinney 1992)	Significant interactions of time and study group for all study variables, with women in the intervention groups changing more over time than women in the control group for perceived risk (F = 13.6; df = 2211; P < 0.001), cancer worry (F = 4.1; df = 2211; P < 0.001), awareness of genetic testing (F = 8.7; df = 2211; P < 0.001), and interest in genetic testing (F = 5.6; df = 2211; P < 0.01). There were no significant differences between the genetic counselling and psychosocial counselling groups. Participants with lower levels of identification with Jewish culture reported larger decreases in perceptions of their own risk (F = 6.2; df = 7138; P < 0.001). Endorsements of beliefs about stigma associated with genetic testing increased significantly in all groups between baseline and follow-up (F = 510; df = 2211; P < 0.0001), with no differences between intervention and control groups. Women in the control group increased their endorsement of beliefs about unrestricted access to genetic testing, whereas women in both counselling groups decreased their beliefs compared with the control group over time (P < 0.05). Participants with low levels of religious identity changed their interest in genetic testing less when compared with those with higher levels of religious identity (P < 0.001)

Brain 2000a	Surgical consultation with multidisciplinary genetic assessment (intervention) versus the standard surgical consultation without genetic assessment (control)	9-month follow-up. Final sample n = 545; 263 intervention group, 282 control. Brain 2002 report data on 653 women stratified into low- (n = 107), moderate- (n = 447) or high- (n = 99) risk categories.	Perceived risk of breast cancer. General anxiety: State-Trait Anxiety Inventory (Spielberger 1983). Breast cancer worry scale (Lerman 1991a). Knowledge of familial breast cancer. Satisfaction with Genetic Counseling Questionnaire (Shiloh 1990)	At both baseline and the first follow-up, participants' perceived risk was significantly higher in the high-risk group compared with the low- and moderate- risk groups. A significant reduction in perceived risk of breast cancer was found for those in both the intervention (mean = 7.29/6.44) and the control (mean = 7.33/6.62) groups (95% CI -0.21 to 0.08). Perceived risk from immediate post-clinic assessment to the follow-up at 9 months significantly increased; however the perceived risk at the 9-month follow-up was still significantly lower than at baseline, regardless of group allocation. Anxiety significantly decreased from baseline to assessment immediately after clinic (intervention: mean = 35.93/34.33; control: mean = 35.54/33.14; 95% CI -0.75 to 1.41), and then significantly increased at 9 months (intervention: mean = 36.38; control: mean = 35.18; 95% CI -0.85 to 1.98), although this increase did not exceed baseline levels. There was a significant decrease in cancer worry in both groups from baseline to post-clinic assessment (intervention: mean = 11.79/10.55; control: mean = 11.49/10.50; 95% CI -0.31 to 0.20) and from baseline to 9 months follow-up (intervention: mean = 10.55; control: mean = 10.63; 95% CI -0.59 to 0.05); the decrease from post-clinic assessment to 9-month follow-up was not significant. Cancer worry decreased significantly for those at low and moderate risk (low risk: $t(106) = 5.92$, $P < 0.001$; moderate risk: $t(443) = 12.13$, $P < 0.001$) but not for those at high risk ($t(98) = 1.67$, $P = 0.10$) (95% CI -0.88 to 2.35). High patient satisfaction with counselling was reported in both groups and the effect of study group on satisfaction was not statistically significant (intervention: mean = 42.82; control = 42.29; 95% CI -0.16 to 0.76). However, a significant main effect of risk classification was found. Those at high risk reported significantly lower instrumental satisfaction than those at low or moderate risk, with women at moderate risk reporting significantly lower satisfaction than women at low risk (F (2 to 593) = 13.80, $P < 0.001$). A statistically significant increase in knowledge was found in both the intervention (mean = 1.54/2.17) and control (mean = 1.45/1.89) groups where the degree of the increase was significantly greater for those in the intervention group (95% CI -0.001 to 0.27)
Braithwaite 2005	A computerized tool to support stratification of breast cancer genetic risk assessment in the clinical environment (GRACE) versus risk counselling by a clini-	3-month follow-up. Final sample n = 54 (follow-up analysis completed on n = 27 for GRACE group and n = 27 nurse counselling)	Risk perception on a 5-point scale. Risk accuracy: level of concordance between perceived risk estimate and those provided by GRACE or nurse specialist.	Increased accuracy in risk perceptions from baseline to follow-up, with no significant difference between groups. Significantly more women in the GRACE group than the nurse group who had initially accurate risk perceptions maintained accurate risk perceptions after the intervention ($P < 0.05$). No significant changes in comparative risk perceptions over time and no significant differences between groups. The interaction between study group and time approached statistical significance

	cal nurse specialist		Emotional outcomes: Anxiety and depression scale (HADS); General anxiety measured by the short version of the State-Trait Anxiety Inventory STAI ; Cancer worry scale (Lerman 1991a). Acceptability of the intervention: perceived benefits, perceptions of risk information, satisfaction and risk communication preferences	(P = 0.05), suggesting a greater reduction across time in elevated risk perceptions in the nurse group compared with the GRACE group. No significant between group differences in anxiety and depression scores at any time point. No significant changes in anxiety and depression scores across time and no interaction effects. For state anxiety there were significant changes across time (F = 41.20; P < 0.001) and a significant treatment effect (F = 8.81; P < 0.01). State anxiety levels increased from baseline to post-intervention in both groups with scores falling slightly at 3-month follow-up. However, state anxiety scores did not return to baseline levels. The increase in state anxiety from baseline to post-intervention was particularly prominent among women at increased risk, irrespective of treatment group. Cancer worry scores decreased significantly from baseline to follow up in both groups (P < 0.01) and there were no significant effects of study group or interaction effects. Satisfaction with the risk information was significantly higher for the nurse counselling compared with the GRACE (P < 0.01). Nurse counselling rated more positively than the GRACE in terms of addressing concerns (P < 0.01), being sensitive to these concerns (P < 0.01), and helping them make a good choice (P < 0.01)
Fry 2003	Novel (community-based) genetics service versus the standard regional service	6-month follow-up. Final sample size n = 244; 131 standard service (control), 113 novel service (intervention)	Subjective and objective understanding of breast cancer genetics. Perceived risk of breast cancer (perceive risk to be high, moderate or low). Psychological distress: GHQ-30 (Goldberg 1988). Cancer Worry Scale (Watson 1998)). Health behaviours	Improvement in subjective understanding of genetics and mammography across all participants. Significant improvement of subjective understanding of breast cancer genetic risk for participants in all risk categories (moderate/high risk: t = -13.70, df = 164, P = 0.000; low risk: t = -6.55, df = 66, P = 0.000) between baseline and 4 weeks; this improvement was significantly greater for those at moderate and high risk of breast cancer than for those at low risk (t = -2.51, df = 230, P = 0.013). Significant interaction found between the trial group, time and objective risk where differences between the risk groups were only statistically significant between baseline and 4-week follow-up (F(1, 226) = 5.27, P < 0.023). A significant improvement in subjective understanding for participants at moderate and high risk of breast cancer in the control group (t = -11.64, df = 98, P = 0.000), and participants in all risk categories in the novel service intervention (moderate/high risk: t = -7.58, df = 65, P < 0.000; low risk: t = -7.32, df = 41, P = 0.000) between assessment at baseline and 4-week follow-up. There were no significant differences in the extent to which subjective understanding had improved between the intervention groups, however those at low risk of breast cancer in the standard intervention showed an improvement in subjective understanding between baseline and 4-week follow-up. Subjective understanding improved in all participants; post-hoc tests showed scores to have significantly improved between assessment at baseline and 4 weeks only

				(genetics: t = -14.37, df = 232, P < 0.000; mammography: t = -5.56, df = 214, P < 0.000). Significantly fewer women in all risk categories perceived their risk as being low at 4-week follow-up when compared with baseline (P = 0.011). A significantly greater proportion of participants at low objective risk of breast cancer perceived their risk to be low at 4 weeks (X^2 = 19.94, df = 1, P < 0.000) and 6-month follow-ups (X^2 = 12.24, df = 1, P < 0.002) in comparison to those at moderate or high risk. There was a significant reduction in scores on the Cancer Worry Scale for all participants over time; with the greatest decrease between baseline and 4-week follow-up (t = 5.86, df = 239, P = 0.000). There was a smaller, yet still significant decrease in scores between assessments at 4 weeks and 6 months (t = 3.05, df = 238, P = 0.003). At 4-week follow-up proportionately more women in the control group reported examining their breasts on a monthly basis as recommended (32 versus 23%), and proportionately more women in the intervention group reported breast self-examination more frequently than once a month (11 versus 4%;X^2 = 9.86, df = 4, P = 0.043). There were no significant differences between the 2 groups in the extent to which they reported performing health behaviours prior to counselling or reported change in performing these behaviours after counselling. At 6-month follow-up there were no significant differences in the proportion of women who reported changing any health behaviours in the previous 6 months between the 2 groups
Helmes 2006	In-person versus telephone breast cancer risk genetic counselling by a certified genetic counsellor compared with a delayed counselling control group	3-month follow-up. Final sample n = 335; 102 in-person counselling, 119 telephone counselling, 114 control	Cancer worry scale (Lerman 1991a). A single-item measure of risk perception (on a scale 1-100). A single breast health intention scale assessed by averaging responses to 3 measures: Intentions to obtain mammograms, clinical breast examination and breast self-examination. Interest in genetic testing. Acceptability of counselling	Risk perceptions decreased in both counselling groups and increased in the control group from baseline to follow-up. Significant effect of risk perception at baseline to risk perception at follow-up (F = 188.92; df = 2331; P < 0.001) and significant effect of study group (F = 15.73; df = 2331; P < 0.001). There was a significant difference between the intervention groups and the control group (mean difference = 10.41; CI: 6.76 to 14.07; P < 0.001), but not between the 2 intervention groups (mean difference = 1.26; CI -3.02 to 5.53; P = 0.564). Cancer worry scores decreased over time for all participants. Significant effects were found on cancer worry at baseline to cancer worry at follow-up (F = 80.55; df = 1314; P < 0.001) and a significant effect of study group (F = 6.20; df =2341, P = 0.002). There were significant differences between intervention groups and the control group (mean difference = 0.43; CI 0.19 to 0.68; P < 0.001) but not between the 2 intervention groups (mean difference = 0.02; CI -0.27 to 0.30; P = 0.919). No significant difference between the groups at baseline or follow-up for breast health intentions. Genetic testing intention scores increased in the control group from 2.20 to 2.71. Scores in the in-

				person counselling group decreased from 2.23 to 1.62 and also decreased in the telephone counselling group from 2.24 to 1.72. There was a significant effect on intentions to pursue genetic testing at baseline to pursue genetic testing at follow-up (F = 209.98; df = 1330; P < 0.001). The effect of study group was also significant (F = 60.41; df = 2330; P < 0.001). There was a significant difference between the intervention groups and control group (mean difference = 0.52; CI 0.43 to 0.62; P < 0.001) but not between the 2 intervention groups (mean difference = 0.09; CI -0.02 to 0.20; P = 0.107). There were no significant differences between intervention groups in terms of satisfaction with counselling and support received
Matloff 2006	Two 60-minute genetic counselling sessions and risk assessment with a certified genetic counsellor compared with a delayed counselling control group	6-month follow-up. Final sample n = 48; 23 intervention, 25 control	Perceived lifetime risk of breast cancer, heart disease and osteoporosis (scale 0% to 100%); estimates of the lifetime risk of an average woman (scale 0% to 100%). Worry about breast cancer in past month measured with a single item. Decisional conflict regarding menopausal therapy decision making (Decisional Conflict Scale). Satisfaction with counselling intervention	No significant differences were found between the counselling group and the control group at baseline in terms of demographics, perceived risk of breast cancer, decisional intentions or decisional conflict about menopausal therapy. Participants perceived risk was significantly lower in the intervention group at 1-month follow-up (F(1, 44) = 14.08, P < 0.008) and at 6 months post-intervention (F(1, 44) = 8.48, P < 0.008). The intervention group was no less likely to rate their own risk for breast cancer as higher than that of the a vergae woman than the control group at 1 month (F(1, 43) = 7.52, P < 0.008) and 6 months (F(1, 43) = 4.43, P < 0.008). For participants in the intervention group, discrepancy between perceived risk and actual risk of breast cancer was significantly lower than baseline at 1 month (t(21) = 3.10, P < 0.008) and at 6 months (t(21) = 3.10, P < 0.008). However, some women continued to overestimate their risk level. There were no group differences at either follow-up point in the proportion taking hormone replacement therapy (Fisher's exact test, P = 0.98, P = 1.00). No participants were taking raloxifene or tamoxifen at any time point in the study. Participants reported high levels of satisfaction with the counselling session including the information received (M = 85.64, SD = 16.93), the support received (M = 80.13, SD = 21.87), and the time involved (M = 80.39, SD = 19.95), but less with the convenience of the session (M = 76.61, SD = 25.27)
Young 2006	Lower risk referrals to a breast cancer genetics centre received their genetic risk information in a personalised letter or attended the genetics department for an	3-month follow-up. Final sample n = 71; 37 interview group, 34 letter group	Breast cancer worry scale (Lerman 1991a; Lerman 1991b). Understanding of breast cancer risk (11 questions; 5 about perceptions of own risk, 2 about	No differences in cancer worry scores at 3-month follow-up between letter or interview group (t(69) = -0.636, P = 0.527). Significant between group differences found for personal breast cancer risk estimates. Those who received their risk assessment at interview (mean = 2.38) perceived their risk to be slightly higher than those who received their information by letter (mean = 2.0), t(69) = -2.246, P = 0.028).

	interview with a genetics associate or nurse specialist	perceptions of general population risk). Actions and experiences since receiving the risk assessment to assess adverse and positive effects on behaviour. General Health Questionnaire (Goldberg 1988). Experiences of and satisfaction with the intervention were assessed	No significant differences between groups for estimates of personal lifetime risk of breast cancer in the 2 items which measured risk estimates (t(64) =1.036, P = 0.304, and t(69) = -0.249, P = 0.804). Personal risk estimates were often inaccurate and there were poor correlations between estimates expressed in the different formats for the same respondent. As there were no baseline measures of any outcomes it is unknown whether cancer worry or risk perceptions changed after receiving genetic risk information. No reported differences between groups for actions since referral and for experiences since referral. There were also no differences between groups for concerns about personal breast cancer risk (t(69) = -0.705, P = 0.483). No significant differences were found between the letter and interview group for the subscores of the General Health Questionnaire. Mean satisfaction scores in the letter group ranged from 'quite satisfied' to 'very satisfied'. For 5 items the interview group expressed significantly higher levels of satisfaction than those who received their assessment via letter (P value range 0.020 to 0.001)

SD: standard deviation

BACKGROUND

Description of the condition

Advances in genetics have revealed that some cancers have a genetic component and can therefore, be inherited. It is estimated that between 5% and 10% of all incidents of breast cancer can be attributed to hereditary breast cancer susceptibility genes, including BRCA1 and BRCA2 (McPherson 2000; Rahman 1998).

Women who inherit a BRCA1/2 mutation have a 40% to 65% lifetime risk of breast cancer, and an 11% to 40% lifetime risk of ovarian cancer (Antoniou 2003; Chen 2007), with a typically young age of onset compared with sporadic cases of breast cancer. A mutation in the gene which causes a potentially high risk of cancer does not necessarily mean cancer will develop; nor does it predict at what age the cancer may appear. The development of the disease may also be affected by environmental factors and interactions with other genes (Begg 2008).

Recognition of the genetic component of breast cancer has led to greater public demand for information, reassurance, screening, and genetic testing, which has consequently led to significant increases in referrals to clinical genetic centres. The increase in referrals resulted in the development of a number of genetics clinics specifically dedicated to cancer. There has been little consensus about the delivery of cancer genetic services and differing arrangements exist, with wide variation in access and quality (Wonderling 2001). However, there has been research interest in examining how these services are organised and delivered (Elwyn 2002; Fry 1999; Iredale 2003) and the best ways to meet the needs of patients with a family history of breast cancer. Going through a cancer genetic service is a complex process for patients and their families, involving different stages, which can include the assessment of a patient's risk of developing cancer, extended counselling, specialist screening, and genetic testing for mutations. Therefore, to review cancer genetic service delivery in its entirety would be difficult. However, as the first stage in the cancer genetic journey is usually the assessment of risk of developing a particular cancer, it is vital to assess the impact this has on patients.

Description of the intervention

The first step in the risk-assessment process is usually to compile a detailed pedigree to assess whether cancers are more likely due to an inherited susceptibility rather than a sporadic occurrence. Although variations exist in different countries, patients at risk of breast cancer are typically assigned a category - average (or low), moderate or potentially high risk of inheriting cancer, and each category is managed differently according to service guidelines. Risk-assessment services can provide appropriate information and support to patients and their families, offer genetic counselling, and undertake genetic testing for those at increased risk of familial breast cancer. Patients offered a cancer genetic clinic appointment can normally expect to see either a geneticist or a genetic counsellor. A consultation in a cancer genetic clinic is significantly longer than a primary care consultation as issues such as reproductive decision-making, employment, insurance, the likelihood of having a gene mutation, and options for reducing the risk of breast cancer may be covered. This usually occurs regardless of how the patient is managed, or by whom, or whether the first contact with cancer genetic services necessitates a detailed risk assessment.

How the intervention might work

The benefits of risk-assessment services have been demonstrated by comparing anxiety rates of patients before and after the consultation (Julian-Reynier 2001). Studies suggest that while many patients do not experience increased distress as a result of the process, there are some who need additional psychological support (Hopwood 1998; Scott 2005; Van Roosmalen 2003; Watson 1998; Wood 2000) as a small but significant percentage of patients experience distress whilst waiting to learn their risk of breast cancer (Bennett 2007; Phelps 2010). Genetic counselling has also been found to lead to an increase in knowledge about breast cancer genetics but may not always improve accuracy of perceptions of risk (Brain 2000a; Braithwaite 2006; Meiser 2002; Roshanai 2009). Whilst much research has focused on the actual counselling process, less emphasis has been given towards the risk-assessment process that precedes this counselling.

It is possible for risk-assessment services to vary in a variety of ways and a number of pilot projects have explored alternative models of service delivery (see for example Coehlo 2005; Lea 2005; Tempest 2005). Studies have also focused on the experiences, expectations, and knowledge of referrers such as GPs, and the quality of their referrals (Elwyn 2002; Lucassen 2001; Watson 2001), and on computer-based risk-assessment tools (Braithwaite 2002; Emery 2007). Phelps 2004 compared the use of telephone calls and letters to transmit risk information to referred patients without bringing them to clinic. Alternatively, the risk assessment could be conducted via video-conferencing to provide cancer genetic services to rural populations (Gray 2000a; Meropol 2011).

Why it is important to do this review

Information on evidence-based methods of delivering cancer genetic risk-assessment services is sparse. Therefore, a systematic search, review, and assessment of the literature on the delivery of cancer genetic risk assessment for individuals concerned with familial breast cancer was undertaken, following the procedures of The Cochrane Collaboration. Although mutations in the BRCA1 and BRCA2 genes have also been found to be associated with an increased risk of ovarian cancer (e.g., Chen 2007; Easton 1995; Ford 1994; Ford 1998; Struewing 1997; Whittemore 1997; Wooster 1994); this review focuses solely on familial breast cancer.

OBJECTIVES

The objectives of this systematic review were to compare:

1. how different cancer genetic risk-assessment services can be delivered to individuals at risk of familial breast cancer;
2. the impact of different types of cancer genetic services for assessing risk on individuals with perceived risk of breast cancer; and
3. the impact of specialist cancer genetic services for assessing risk versus other non specialist services for individuals at risk of familial breast cancer.

METHODS

Criteria for considering studies for this review

Types of studies

We searched for randomised controlled trials (RCTs) and quasi-randomised trials in all languages.

Types of participants

Inclusion criteria

Participants could be individuals of any age or gender, concerned about their family history of breast cancer, with or without a known BRCA mutation, but without a previous history of breast cancer or any other serious illness.

Exclusion criteria

Studies of participants with a previous history of cancer were excluded as we were interested in the process of genetic risk assessment. Also, whilst we acknowledge that there is a link between breast and ovarian cancer studies, if ovarian cancer was the primary reason for a patient's referral these studies were excluded.

Types of interventions

Any intervention for delivering a cancer genetic risk assessment for familial breast cancer was considered and could include:

- type of counsellor;
- duration of counselling;
- where and how counselling takes place;
- ways of obtaining family history;
- how risk is presented;
- availability and types of support or aftercare or both;
- type of information available.

We excluded studies looking at ways of simply delivering information to women at high risk of familial breast cancer as this review was concerned with the delivery of cancer genetic risk assessments.

Types of outcome measures

Primary outcomes

Patient Centred

- Understanding of risk (objective and subjective)
- Patient satisfaction
- Anxiety
- Depression
- Quality of life
- Personal health care

There exist a number of validated measures of psychological morbidity, whilst measures of objective and subjective risk and patient satisfaction tend to vary widely. Measures used in the included studies are detailed in the Characteristics of included studies table.

Secondary outcomes

Patient Centred

- Perceptions of risks and benefits of genetic testing
- Perceptions of risks and benefits of screening surveillance
- Perceptions of risks and benefits of surgery
- Family members contacted
- Utilisation of genetic and other healthcare resources

Search methods for identification of studies

Electronic searches

For the first full version of this review (Sivell 2007), the specialised register maintained by the Cochrane Breast Cancer Group was searched on the 16th February 2005 (details of search strategies used by the group for the identification of studies and the procedure used to code references are outlined in the group's module http://www.mrw.interscience.wiley.com/cochrane/clabout/articles/BREASTCA/frame.html. Studies coded with the key words 'education', 'screen', 'psychosocial intervention/supportive care', 'prevent', 'diagnostic', 'genetic', 'high risk', as well as appropriate text words were extracted from the specialised register for consideration.

The search strategy used the recommended Cochrane search filter for RCTs to identify all relevant trials. This was adapted for the following electronic databases: MEDLINE, EMBASE, CINAHL, PsycLIT, CENTRAL, DARE, ASSIA, Web of Science, SIGLE and LILACS. The searches covered the period 1985 to February 2005 and included all languages. We did not search literature before 1985 as genes relating to breast cancer began to be discovered in the late 1980s (Hall 1990) leading to the development of cancer genetic clinics (Eeles 2004).

Terminology for the MEDLINE strategy in the original review is presented in Appendix 1. The MEDLINE strategy was adapted for use in the other databases. The search strategies used for the updated search in April 2011 are shown in Appendices 2 to 8.

For this first review update, a search was carried out in the WHO International Clinical trials Registry Platform and the Cochrane Breast Cancer Group Specialised Register in April 2011. The following databases were searched between the 8th to 15th April 2011:

- Ovid MEDLINE (2005 - April 2011) Appendix 2
- Ovid EMBASE (2005 - April 2011) Appendix 3
- Ovid PsycINFO (2005 - April 2011) Appendix 4
- Cochrane Library (2005-April 2011) Appendix 5
- CINAHL (2005 - April 2011) Appendix 6
- ASSIA (2005 - April 2011) Appendix 7
- LILACS (2005 - April 2011) Appendix 8
- PreMEDLINE (searched 14th April 2011)
- SIGLE was not updated as it does not go beyond 2005

Searching other resources

We searched bibliographies of retrieved articles for additional references. We also handsearched the journals which published the most relevant articles to this review in order to identify additional studies.

Data collection and analysis

Selection of studies

We handsearched the abstracts of identified articles from the updated search for possible inclusion in the review. We rejected articles if the article was not a report of a randomised trial, if the trial included women who had a previous cancer diagnosis, and if the intervention did not involve the delivery of a cancer genetic risk assessment for familial breast cancer. Two review authors (JH and RI) independently carried out study selection to determine whether studies met the inclusion criteria. Any disagreement about a particular study was resolved by discussion. We sought missing information from investigators as necessary.

Data extraction and management

Two review authors (JH and RI) independently extracted data from each included study using a data extraction sheet. Data extracted concerned participant characteristics, trial inclusion and exclusion criteria, intervention type, settings, and the nature of the outcome measured. Clinical differences between studies were explored. We discussed any differences in opinion and, if necessary, a third person arbitrated before consensus was reached. We contacted authors if relevant data were missing from the study.

Assessment of risk of bias in included studies

For the update of this review, two review authors (JH and BC) assessed each included study independently using The Cochrane Collaboration tool for assessing risk of bias (Higgins 2008). This tool addresses six specific domains, namely, sequence generation; allocation concealment; blinding of participants, personnel or assessors; incomplete outcome data; selective outcome reporting and other issues (e.g. extreme baseline imbalance). Due to the nature of the trials included in this review, it would have been impossible for the trials to have been fully blinded and hence we did not assess blinding of participants, personnel or assessors. We completed a 'Risk of bias' table for each eligible study. Any disagreement amongst authors was discussed to achieve a consensus. We presented an assessment of risk of bias using a 'Risk of bias' summary figure (see Figure 1 and Figure 2), which presents all of the judgments in a cross-tabulation of study by entry. Evaluating the validity of each study may assist the reader in interpreting and making conclusions about the study.

Figure 1. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

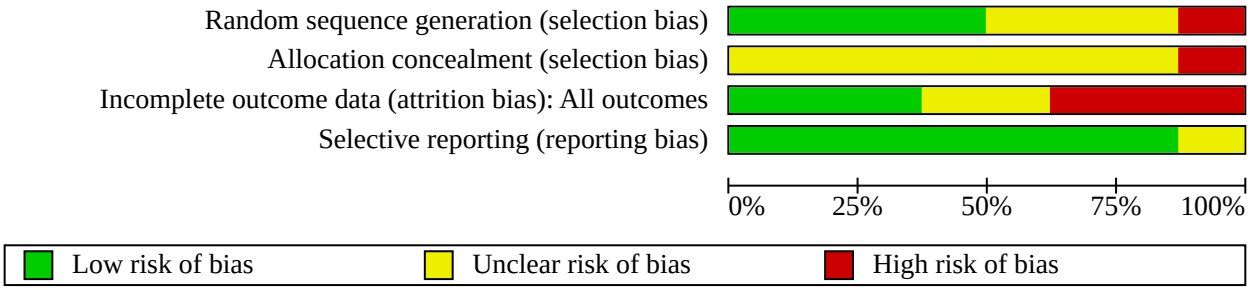
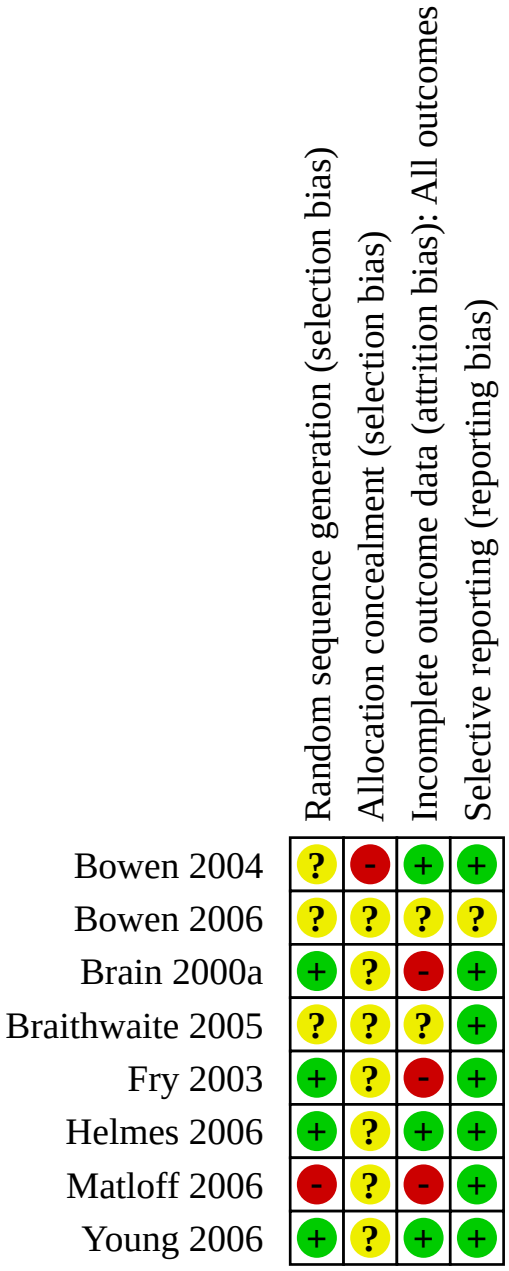


Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Assessment of heterogeneity

Considerable heterogeneity was identified in the included studies in terms of the populations, settings, interventions, and outcome measures. We did not find homogeneity across any of the study populations, settings or interventions and therefore, did not undertake a formal assessment of statistical heterogeneity using the I^2 statistic. We did not undertake a meta-analysis of the data but present a narrative synthesis of the included studies.

Assessment of reporting biases

As few studies were identified and had diverse interventions, we decided that an assessment of reporting bias would not be suitable.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of ongoing studies; Summary of findings 1.

Results of the search

In the original search and review, fifty-eight records were identified as being relevant to the review, out of which 51 were RCTs and therefore considered in detail. Out of the 51 papers considered in detail, we excluded 46, leaving five papers to be included in the review.

Our updated search (to April 2011) yielded 1466 titles. However, we found that the majority were irrelevant during the initial stage of screening the study titles and abstracts. We retrieved 54 full-text articles for further assessment. Thirty-two articles were found to present data from randomised trials and were screened for inclusion. We excluded 27 articles, leaving five studies to be included in this review update.

Included studies

Five papers presenting data from three trials were included in the original review (Bowen 2002; Brain 1999; Brain 2000b; Cohen 2004; Campbell 2003). However, all publications additional to the main trial papers were excluded with the exception of the Bowen 2004 and Brain 2000a trials, which presented further data of interest to this review in an additional paper for each. Fry 2003 looked at where and how counselling takes place. Fry 2003 examined ways of obtaining a family history, as did Brain 2000a. Brain 2000a also looked at the availability and type of support and after-care. An additional five studies were identified by the updated search and met the inclusion criteria (Bowen 2006Braithwaite 2005Helmes 2006Matloff 2006Young 2006). Further details on each of these studies can be found in the 'Characteristics of included studies' table.

Both Bowen 2004 and Bowen 2006 reported on a RCT comparing individual genetic counselling and group psychosocial counselling with a delayed counselling control group. Both studies recruited women from the greater Seattle area, USA. In Bowen 2006, only Ashkenazi Jewish women were recruited. In Bowen 2004, the genetic counselling intervention comprised a single two-hour session with a genetic counsellor focusing on the patient's family history and each participant was provided with information regarding her own personal risk for breast cancer. The genetic counsellor provided information about breast cancer screening and participants were encouraged to discuss any concerns. Participants randomised to receive group psychosocial counselling met in groups of four to six participants for four, two-hour sessions. A trained health counsellor led each group covering four main topics: risk assessment and perception, screening, stress management and problem solving, and social support. Each participant received an individual risk-assessment sheet, which personalised the group discussion to her own risk status. The interventions used in Bowen 2006 were similar except that genetic issues specific to Ashkenazi Jewish women and breast cancer were also discussed during the counselling sessions. Also, the individual genetic counselling session in Bowen 2006 was one hour in duration compared with two hours in Bowen 2004.

The effects of different models of risk counselling for breast cancer were also examined in Helmes 2006, where in-person counselling and telephone counselling were compared with a delayed counselling control group. Women were recruited from a healthcare database in Washington state, USA. A family history of breast cancer was not required to take part in the study. In both counselling groups, participants reviewed their family history of breast cancer with a genetic counsellor and were provided with their individual breast cancer risk. Information about screening and breast cancer genes was given and genetic testing was discussed where appropriate, although genetic testing was not offered as part of this study.

In Braithwaite 2005, 72 women with a family history of breast cancer were randomised to either undergo risk counselling by a nurse specialist or to use a computerised tool that supports stratification of breast cancer risk, genetic risk assessment in the clinical environment (GRACE). Following completion of their family pedigree in GRACE, the GRACE software calculated and presented participants' breast cancer risk as either low, moderate or high. Participants received a personal risk report containing pedigree printouts, specific advice according to risk level, and recommendations about breast screening and genetic testing. In the nurse specialist group, pedigree information was gathered and the nurse assessed women's risk as low, moderate or high, based on the same guideline as that used in the GRACE. Participants were sent a letter summarising the content of the consultation.

Brain 2000a reported the results of a RCT comparing surgical consultations, with and without, genetic assessment for women with a family history of breast cancer, to determine the psychological impact of receiving genetic assessment. The standard service involved clinical input from specialist surgical staff. Participants received information on breast cancer surveillance and advice on risk management, surgical assessment of their risk of breast cancer, the option to enter the UK Tamoxifen Prevention Trial, and annual surgical review involving appropriate breast cancer surveillance and advice. Women were informed of their breast cancer risk based on nongenetic information including age, reproductive history, and minimal family history of breast cancer. In the intervention group, women received a multi-disciplinary genetic assessment service, including a specialist genetic consultation with a clinical geneticist and a genetic nurse specialist. The consultation focused on education about breast cancer genetics, assessment for breast cancer risk, and, where applicable, presymptomatic testing for the BRCA1 and BRCA2 genes. Two of the papers publishing data from this trial have been included in this review. Brain 2000a presented data from 545 participants, analysed at all levels of risk at three time points. Secondary analyses of the same data were presented in an additional paper (Brain 2002). The two study groups are compared at baseline and follow-up immediately after attending the clinic. In Brain 2002, 653 participants were stratified into low-, moderate- or high-risk categories on the following outcomes: anxiety, worry, perceived risk and satisfaction.

Fry 2003 reported a clustered RCT where 170 GP practices in the UK were randomised to either a novel community-based service (intervention) held in GP practices by a genetic nurse specialist or the existing multidisciplinary specialist service (control). In both groups, cancer genetic risk level was assessed based on family history of breast cancer. In the control group, women assessed

as being at moderate or high risk were offered appointments at a familial breast cancer clinic where they discussed risk status with a genetic consultant and risk management with a specialist breast surgeon. In the novel service intervention group, women at increased risk (moderate and high) were offered an appointment at a regional centre with a geneticist and genetic nurse specialist.

Matloff 2006 investigated the effects of a personalised risk assessment and genetic counselling intervention compared with a delayed intervention control group. Participants were at least 40 years of age, with at least one first-degree relative with breast cancer and had gone through natural menopause. Women with a greater than 10% risk of carrying a BRCA1/2 mutation were excluded. The intervention included two 60-minute sessions with a genetic counsellor. Information was given to participants about the risks and benefits of menopausal therapy and the factors that influenced disease risk assessments. Womens' 10-year and lifetime risk of breast cancer was calculated and presented to women at the second visit. Participants also received a personalised risk assessment for endometrial cancer, heart disease and osteoporosis. After the risk-counselling sessions, each participant received a letter summarising her risk data.

Only women at low or average risk of familial breast cancer were included in the study by Young 2006. This study examined the method of communicating risk information for lower risk referrals to a familial breast cancer clinic in Scotland, UK. Eligible women were randomised to receive their risk assessment via letter or were invited to an interview with a genetic specialist or nurse. The interview was followed up with a personal letter summarising the discussion. All letters included information that despite being below the threshold for inclusion in a regular surveillance programme, risk of breast cancer was still real. Women were instructed to remain breast aware, report breast symptoms to their GP, and notify the familial breast cancer clinic of any change in their family history of breast or ovarian cancer.

Excluded studies

In the original review, 51 studies presented data from RCTs and therefore were considered for inclusion in greater detail. We excluded 32 papers reporting data from 19 different RCTs because they related to the provision of information and education and not the overall delivery of service (Appleton 2004b; Bluman 1999; Butow 1998; Cameron 2001; Cull 1998; Daly 1998; Green 2001 (two papers); Green 2004; Halverson 2000; Helgeson 2001; Hurt 2001; Jibaja 2000; Lerman 1994; Lerman 1995; Lerman 1996; Lerman 1997; Lerman 1999; Lobb 2002a; Lobb 2002b; Miedzybrodzka 2001; Miron 2000; Schwartz 1998; Schwartz 1999; Schwartz 2001; Skinner 2002; Van Roosmalen 2004a; Van Roosmalen 2004b; Wade-Walsh 2001; Watson 1996; Watson 1998; Watson 2001).

We excluded a further five papers because they were either testing the feasibility of an RCT, rather than being an RCT per se (Hoskins 2001), were looking at pre-screening education for pregnancy (Ormond 1996), concerned education promoting breast cancer screening (Street 1998), were a meta-analysis of randomised trials (Stoddard 2002), or looked at other cancers as well as breast cancer (Hopwood 2004). Four trials (Eeles; Murday; Steel; Wilson) from the literature searches of the original review (Sivell 2007) were placed in Ongoing studies as these trials had no results at that time. However, we have been unable to find further details, published or unpublished of these trials and they have been removed from Ongoing studies. The remaining 10 papers reported data from the three included trials, of which five papers were excluded as they did not present data on outcomes of interest to this review (Bowen 2002; Brain 1999; Brain 2000b; Cohen 2004; Campbell 2003).

In the updated search, we identified 32 potential studies, of which we excluded 27. In 16 studies, participants included women with a previous or current cancer diagnosis (Armstrong 2005; Calzone 2005; Charles 2006; Green 2005; Halbert 2010; Hall 2009; Miller 2005; Rahm 2007; Roshanai 2009; Roussi 2010; Torrance 2006; Wakefield 2008a; Wakefield 2008b; Wang 2005; Wevers 2011; Wilson 2005). Five studies were not related to the provision of cancer genetic risk assessment for familial breast cancer (Barcenas 2006; Bellcross 2009; Emery 2007; Gray 2009; Venne 2007). One paper was a review of risk-assessment models (Amir 2010), two reported no patient outcomes (Hoskins 2001; Wilson 2006), one paper included other cancers than breast cancer (Ramirez 2008), and one reported on a decision aid for known BRCA carriers (Schwartz 2009). One further study referred to a trial protocol. The results of the trial could potentially be included in a future review update and has therefore been classified as an ongoing study (Ockhuysen-Vermey 2008).

Details of individual studies can be found in the 'Characteristics of excluded studies' table.

Risk of bias in included studies

Allocation

All the included trials reported that the trials were randomised but two did not provide any details of the sequence generation method (Bowen 2006; Braithwaite 2005). In Brain 2000a, Helmes 2006 and Young 2006, randomisation was based on a computer-generated sequence of random numbers. In Bowen 2004, randomisation was carried out through assigning a randomisation number to each participant. In Fry 2003, the GP practices were randomly assigned through the use of a minimisation technique (Pocock 1983) to ensure that the study groups were balanced for size of practice, historical referral rate, and social deprivation index. Quasi-randomisation was used in Matloff 2006, where every other patient was randomised into the intervention or control arm of the trial.

Many studies did not clearly state the method of allocation concealment (Bowen 2006; Braithwaite 2005; Fry 2003; Helmes 2006; Matloff 2006; Young 2006). In Brain 2000a, allocation concealment was deemed to be adequate. In Bowen 2004, randomisation was carried out in a "blinded fashion" where each randomisation number had been pre-assigned to one of the three study conditions without bias. However, Bowen 2004 also stated that women were informed of their randomised study arm over the telephone.

Due to the nature of the trials examined, it would have been impossible for the trials to have been fully blinded and hence we did not feel that 'inadequate' blinding would detract from the quality of the included studies. For many trials of cancer genetic risk assessment, participants and staff were aware to which study group they had been assigned (Bowen 2004; Bowen 2006; Brain 2000a; Helmes 2006; Matloff 2006). It is unclear whether the participants were blinded to their treatment allocation in Young 2006. Participants and clinical staff were blind to the treatment allocation until just prior to the appointment in Braithwaite 2005. In Fry 2003, the GP practices were not blinded to their randomisation as this would have been impossible.

Incomplete outcome data

In total, 2248 women were randomised across the eight trials, and the data of 1973 were analysed. Four studies included women at all risk levels for familial breast cancer (average, moderate and high) (Brain 2000a; Braithwaite 2005; Fry 2003; Helmes 2006). Although in Helmes 2006, the Gail score of the sample was 9.5%, which is the risk level of the general population. Women at high risk of familial breast cancer were not included in three studies (Bowen 2004; Bowen 2006; Matloff 2006). In Young 2006, only those assessed as being at 'low' risk and therefore not eligible for increased surveillance were included in the study. In all studies, both the inclusion and exclusion criteria and the outcome measures used were clearly defined. Where appropriate, the validity of measures had been reported and hence were deemed adequate. The assessment of these outcome measures was only conducted in the short-term; no study looked at the long-term implications for these outcomes. Braithwaite 2005, Helmes 2006, and Young 2006 followed up participants three months after the intervention. Bowen 2004, Bowen 2006, Fry 2003, and Matloff 2006 conducted a six-month follow-up. Brain 2000a followed up participants at nine months.

The intervention and control groups were comparable at baseline in all of the studies. Only in Bowen 2004, Bowen 2006, and Helmes 2006 were the withdrawals or loss to follow up less than 10% of the study population. Withdrawals in Bowen 2004 were 2.3% with no differences found between all participants who were randomised and only those who completed the follow-up survey. In Bowen 2006, the follow-up response rate was 96%. In Brain 2000a, approximately a quarter of those randomised (26.35%) were withdrawn from the trial; five participants were excluded due to non-attendance in the surgical aspect of the multidisciplinary trial clinic and 190 were lost to follow up. In Fry 2003, there were a total of 129 withdrawals, 34.6% of the total number of patients randomised to the trial. Reasons given for the withdrawals were: lost to follow up (n = 19), not returning the baseline questionnaire (n = 65), withdrew from the study (n = 8), clinical reasons (n = 9), administration reasons (n = 27) and returning a blank questionnaire (n = 1). In Braithwaite 2005, 14 participants (22%) were lost to follow up three months after the intervention. Reasons for loss to follow up are not reported. Only 1.5% of participants did not return their three-month follow-up survey in Helmes 2006. In Matloff 2006, analyses were confined to the 48 participants who completed all three assessments (75% of randomised participants) and those with missing data were excluded. Reasons for withdrawal are stated in Young 2006 where only data from the 71 participants who returned their three-month follow-up questionnaire were analysed. There are no data on the differences between responders and non-responders.

Selective reporting

All studies reported on the pre-specified outcomes. Bowen 2006 reported measuring general anxiety in the methods section but there are no data on this measure in the results. Therefore, all studies except Bowen 2006 have been graded as low risk of selective outcome reporting.

Effects of interventions

See: **Summary of findings 1** Summary of findings for the main comparisons

Due to the heterogeneity in both the interventions and outcomes across all the included studies, we were unable to combine the data for statistical analysis as it would not have been possible to interpret the results. Therefore, a narrative synthesis of the studies is presented. Refer to the Summary of findings 1.

In Bowen 2004, few significant differences were found between the intervention groups (genetic counselling and psychosocial counselling) at the two assessment points (baseline and six months). At follow-up and in comparison to the control group, both counselling interventions showed significantly lower perceived risk of breast cancer ($P < 0.01$) and cancer-specific worry ($P < 0.01$) with no differential effects of counselling type. In comparison to those in the control group, participants in both counselling interventions decreased their cancer-specific worry; the interaction between time and study group was found to be statistically significant ($F = 4.2$; degrees of freedom (df) = 2344; $P < 0.01$). Participants in the counselling interventions reported slightly lower levels of anxiety over time in comparison to the control group, with only a significant difference shown in participants in the psychosocial group. The interaction between time and counselling intervention was statistically significant ($F = 3.0$; df = 2344; $P < 0.01$). A non-statistically significant decrease in depressive symptoms over time in both the intervention and control groups was also observed. Overall, there was a positive reaction to the counselling with almost all participants in both counselling interventions completing their counselling protocols (98% for genetic counselling, 96% for psychosocial counselling). The majority of participants reported that they liked the counselling activities "very much" (82% for genetic counselling, 71% for psychosocial counselling) although only one-third of participants read all of the written materials they received in either intervention group. Participants rated highly both the support they received from the counsellors and the experience of talking about their concerns during their counselling sessions. Eighty-six percent of participants in the genetic counselling group and 72% in the psychosocial group reported talking "quite a bit" about their concerns during counselling, which was found to be statistically significant ($P < 0.05$). In both interventions, over half the participants reported counselling to be "very useful" (65% for genetic counselling and 59% for psychosocial counselling).

In Bowen 2006, there were no differences at baseline for any of the variables among the study arms. Perceived risk and cancer-specific worry decreased over time (from baseline to six month follow-up) in both intervention groups. Cancer worry increased slightly in the control group. Awareness of genetic testing increased in all study groups, and interest in genetic testing and candidacy judgements decreased over time. There were significant interactions of time and study group for all study variables, with women in the intervention groups changing more over time than women in the control group for perceived risk ($F = 13.6$; df = 2211; $P < 0.001$), cancer worry ($F = 4.1$; df = 2211; $P < 0.001$), awareness of genetic testing ($F = 8.7$; df = 2211; $P < 0.001$), and interest in genetic testing ($F = 5.6$; df = 2211; $P < 0.01$). There were no significant differences between the genetic counselling and psychosocial counselling groups; all significant differences were between women in the control group and the two intervention groups. Multiple regression analyses showed that the only significant predictor of change in perceived risk in the counselling groups was level of baseline Jewish cultural identity ($F = 6.2$; df = 7138; $P < 0.001$). Participants with lower levels of identification with Jewish culture reported larger decreases in perceptions of their own risk. Bowen 2006

also examined beliefs about genetic testing. Endorsements of beliefs about stigma associated with genetic testing increased significantly in all groups between baseline and follow-up (F = 510; df = 2211; P < 0.0001), with no differences between intervention and control groups. Women in the control group increased their endorsement of beliefs about unrestricted access to genetic testing, whereas women in both counselling groups decreased their beliefs compared with the control group over time (P < 0.05). Participants with low levels of religious identity changed their interest in genetic testing less than those with higher levels of religious identity (P < 0.001).

In Brain 2000a, those who dropped out at baseline reported statistically significantly higher trait anxiety (mean = (study drop-outs) 43.07/ (participants) 39.67; standard deviation (SD) 11.12/10.37; P = 0.008), state anxiety (mean = 40.61/36.63; SD 10.40/11.33; P = 0.004) and lower personal risk (mean = 6.95/7.37; SD 1.49/1.24; P = 0.006) than participants who remained in the trial. Brain 2000a also reported that the mean trait anxiety score of those who dropped out of the study was higher than population norms. At the first assessment after clinic, drop-outs were found to be significantly younger (mean = 37.85 versus 41.90) and were reporting higher baseline cancer worry than those who remained in the study (mean = 13.33/11.72; SD 4.01/3.13; P = 0.001). At the nine-month follow-up point, those who dropped out of the study were again significantly younger than those who remained in the study (mean = 37.15 versus 42.59), and were found to be reporting significantly higher baseline state anxiety (mean = 40.17/36.05; SD 13.10/11.07; P = 0.007), cancer worry (mean = 12.68/11.62; SD 2.84/3.16; P = 0.01), and perceived risk (mean = 7.82/7.31; SD 1.26/1.20; P = 0.002). Brain 2000a reported some evidence of differential drop-out between the study groups themselves; participants in the control group were significantly less likely to return the questionnaire immediately after clinic (X^2 (1) = 7.86; P = 0.005).

Few significant differences were found between the intervention (multidisciplinary genetic assessment service) and the control (standard service with input from specialist surgical staff) groups at the three assessment points (baseline, immediately after clinic and nine months); however, some significant differences were found between the different risk categories.

Some statistically significant differences were found between risk categories, between and within study groups for perceived risk, cancer worry and patient satisfaction reported in the subsequent publication. Significant differences in perceived risk were found between risk groups at both baseline (F(2, 637) = 17.48, P < 0.001) and at the first follow-up (F(2, 640) = 128.56, P < 0.001). At both baseline and the first follow-up, participants' perceived risk was significantly higher in the high-risk group compared with the low and moderate risk groups. A significant reduction in perceived risk of breast cancer from baseline to assessment immediately after the clinic was found for those in both the intervention (mean = 7.29/6.44) and the control (mean = 7.33/6.62) groups (95% CI -0.21 to 0.08). Perceived risk from immediate post-clinic assessment to the follow-up at nine months significantly increased; however the perceived risk at the nine-month follow-up was still significantly lower than at baseline, regardless of group allocation. On looking at differences across risk classification, a significant decrease in perceived risk was found for those at low and moderate risk from baseline to the first follow-up point (low risk: t(101) = 10.78, P < 0.001; moderate risk: t(431) = 13.27, P < 0.001), with no significant change found in those at high risk (t(96) = 0.00, P = 1.00). Within the intervention group, perceived risk decreased significantly for those at low (t(49) = 6.90, P < 0.001) and moderate (t(221) = 11.83, P < 0.001) risk, whereas for those at high risk in the intervention group, there was a marginal significant increase (t(53) = -1.72, P = 0.09). Within the control group, perceived risk decreased significantly for low (t(51) = 8.35, P < 0.001) and moderate (t(209) = 7.03, P < 0.001) risk women, with no difference for those at high risk (t(42) = 1.83, P = 0.07).

Anxiety levels remained within the normal range both before and after the study intervention, and the effect of study group or risk classification on anxiety was not significant. Anxiety significantly decreased from baseline to assessment immediately after clinic (intervention: mean = 35.93/34.33; control: mean = 35.54/33.14; 95% CI -0.75 to 1.41), and then significantly increased at nine months (intervention: mean = 36.38; control: mean = 35.18; 95% CI -0.85 to 1.98), although this increase did not exceed baseline levels. There was a significant decrease in cancer worry in both groups from baseline to post-clinic assessment (intervention: mean = 11.79/10.55; control: mean = 11.49/10.50; 95% CI -0.31 to 0.20) and from baseline to nine-month follow-up (intervention: mean = 10.55; control: mean = 10.63; 95% CI -0.59 to 0.05); the decrease from post-clinic assessment to nine-month follow-up was not significant. Cancer worry decreased significantly for those at low and moderate risk (low risk: t(106) = 5.92, P < 0.001; moderate risk: t(443) = 12.13, P < 0.001) but not for those at high risk (t(98) = 1.67, P = 0.10) (95% CI -0.88 to 2.35).

High patient satisfaction with counselling was reported in both groups and the effect of study group on satisfaction was not statistically significant (intervention: mean = 42.82; control = 42.29; 95% CI -0.16 to 0.76). However, a significant main effect of risk classification was found. Those at high risk reported significantly lower instrumental satisfaction than those at low or moderate risk, with women at moderate risk reporting significantly lower satisfaction than women at low risk (F(2 to 593) = 13.80, P < 0.001). A small significant main effect of clinic venue was also found; participants seen at the well-woman clinic setting reported greater satisfaction than those seen in a hospital-based setting (mean = 42.96/41.95; SD 4.97/4.79; t(450) = 2.11; P = 0.04). A statistically significant increase in knowledge was found in both the intervention (mean = 1.54/2.17) and control (mean = 1.45/1.89) groups, where the degree of the increase was significantly greater for those in the intervention group (95% CI -0.001 to 0.27).

In Fry 2003, it was evident that only the characteristics of those who returned the baseline questionnaire were available so the authors looked for evidence of participation bias by comparing those participants who only returned the baseline questionnaire (n = 97) and those who completed the follow-up at four weeks (n = 276). A significantly greater number of the 'baseline only' group had been randomised to the intervention arm of the trial (61 versus 39%; X^2 = 5.70, df = 1, P = 0.018) and were categorised as being at 'low risk' (54 versus 32%; X^2 = 14.01, df = 1, P = 0.000). This group was also found to be suffering 'case-level' distress at baseline (43 versus 31%; X^2 = 4.53, df = 1, P = 0.043) and scored significantly higher on the Cancer Worry Scale (mean = 12.18/11.10; SD = 3.29/2.98; t = 2.97, df = 367, P = 0.003) which may have had an impact on the results of the trial. Fry 2003 found no significant differences

between these two groups on any other psychological or socio-demographic variables.

No significant differences were found between the two trial arms (community-based and multidisciplinary services) on any of the variables at the three assessment points (baseline, four weeks and six months).

There was an improvement in objective understanding of genetics and mammography across all groups and participants of all risk categories during the study; post-hoc tests showed scores to have significantly improved between assessment at baseline and four weeks only (genetics: t = -14.37, df = 232, P < 0.000; mammography: t = -5.56, df = 214, P < 0.000). An overall significant improvement in subjective understanding of breast cancer genetic risk over time was found, where statistically significant improvement was only found between baseline and follow-up at four weeks (t = -14.97, df = 231, P < 0.000). Participants at moderate and high risk of breast cancer scored significantly higher than those at low risk at both the four weeks (t = -2.69, df = 235, P = 0.008) and six months follow-up (t = -2.46, df = 109.214, P = 0.015). There was a significant improvement of subjective understanding of breast cancer genetic risk for participants in all risk categories (moderate/high risk: t = -13.70, df = 164, P = 0.000; low risk: t = -6.55, df = 66, P = 0.000) between assessment at baseline and follow-up at four weeks; this improvement was significantly greater for those at moderate and high risk of breast cancer than for those at low risk (t = -2.51, df = 230, P = 0.013). A significant interaction was found between the trial group, time and objective risk where differences between the risk groups were only statistically significant between baseline and four weeks follow-up (F(1, 226) = 5.27, P < 0.023). A significant improvement in subjective understanding took place for participants at moderate and high risk of breast cancer in the control group (t = -11.64, df = 98, P = 0.000), and participants in all risk categories in the novel service intervention (moderate/high risk: t = -7.58, df = 65, P < 0.000; low risk: t = -7.32, df = 41, P = 0.000) between assessment at baseline and four-week follow-up. There were no significant differences in the extent to which subjective understanding had improved between the intervention groups, however those at low risk of breast cancer in the standard intervention showed an improvement in subjective understanding between baseline and four-week follow-up.

Significantly fewer women in all risk categories perceived their risk as being low at four-week follow-up when compared with baseline (P = 0.011). A significantly greater proportion of participants at low objective risk of breast cancer perceived their risk to be low at the four-week (X^2 = 19.94, df = 1, P < 0.000) and six-month follow-ups (X^2 = 12.24, df = 1, P < 0.002) in comparison to those at moderate or high risk. There was a significant reduction in scores on the Cancer Worry Scale for all participants over time with the greatest decrease between baseline and four-week follow-up (t = 5.86, df = 239, P = 0.000). There was a smaller, yet still significant decrease in scores between assessments at four weeks and six months (t = 3.05, df = 238, P = 0.003). There was also a decrease in the proportion of participants suffering 'case-level' psychological distress, which was found to be significant between baseline and four-week follow-up (t = 8.27, df = 1, P < 0.004). There were no significant differences found in the proportion of women suffering 'case-level' distress between the groups or risk categories at the three assessment points. Fry 2003 also examined the impact of attending genetics services on health behaviours and found that at four-week follow-up proportionately more women in the control group reported examining their breasts on a monthly basis as had been recommended (32% versus 23%), and proportionately more women in the intervention group reported breast self-examination more frequently than once a month (11% versus 4%; X^2 = 9.86, df = 4, P = 0.043). There were no significant differences between the two groups in the extent to which they reported performing health behaviours prior to counselling or reported change in performing these behaviours after counselling. At the six-month follow-up, there were no significant differences in the proportion of women who reported changing any health behaviours in the previous six months between the two groups.

In Braithwaite 2005, both participants who used the GRACE tool and received risk counselling by a nurse specialist increased accuracy in risk perceptions from baseline to three-month follow-up, with no significant difference between the groups. Significantly more women in the GRACE group than the specialist nurse group who had initially accurate risk perceptions maintained accurate risk perceptions after the intervention (P < 0.05). There were no significant changes in comparative risk perceptions over time and no significant differences between groups. The interaction between study group and time approached statistical significance (P = 0.05), suggesting a greater reduction across time in elevated risk perceptions in the nurse counselling group compared with the GRACE group.

There were no significant between-group differences in anxiety and depression scores at any time point. Anxiety scores as measured by HADS (Hospital Anxiety and Depression Scale) decreased over time in both groups although this was not statistically significant. HADS depression scores decreased between baseline and three-month follow-up in the GRACE group and increased slightly in the counselling group. However, there were no significant changes in anxiety and depression scores across time and no interaction effects. There were significant changes across time (F = 41.20; P < 0.001) and a significant treatment effect (F = 8.81; P < 0.01) for state anxiety scores. State anxiety levels increased from baseline to post-intervention in both groups with scores falling slightly at three-month follow-up. However, state anxiety scores did not return to baseline levels. The increase in state anxiety from baseline to post-intervention was particularly prominent among women at increased risk, irrespective of treatment group. Cancer worry scores decreased significantly from baseline to follow up in both groups (P < 0.01) and there were no significant effects of study group or interaction effects.

Satisfaction with the risk information was significantly higher for the nurse counselling compared with the GRACE (P < 0.01). Perceptions of risk information in terms of credibility (P < 0.01), trustworthiness (P < 0.01), accuracy (P < 0.05), clarity (P < 0.01) and helpfulness (P < 0.05) were significantly higher for the nurse counselling than the GRACE. Participants also rated more positively nurse counselling than the GRACE in terms of addressing concerns (P < 0.01), being sensitive to these concerns (P < 0.01), and helping them make a good choice (P < 0.01).

In Helmes 2006, there were no baseline differences in demographic or background variables among any of the groups. Risk perceptions decreased in both counselling groups (in-person and telephone counselling) and increased in the control group from baseline to three-month follow-up. There was a significant effect of risk

perception at baseline to risk perception at follow-up (F = 188.92; df = 2331; P < 0.001). The effect of study group was also significant (F = 15.73; df = 2331; P < 0.001). There was a significant difference between the intervention groups and the control group (mean difference = 10.41; CI 6.76 to 14.07; P < 0.001), but not between the two intervention groups (mean difference = 1.26; CI -3.02 to 5.53; P = 0.564).

Cancer worry scores in all groups decreased over time. Significant effects were found on cancer worry at baseline to cancer worry at follow-up (F = 80.55; df = 1314; P < 0.001) and a significant effect of study group (F = 6.20; df =2341; P = 0.002). There were significant differences between intervention groups and the control group (mean difference = 0.43; CI 0.19 to 0.68; P < 0.001) but not between the two intervention groups (mean difference = 0.02; CI -0.27 to 0.30; P = 0.919).

With regards to breast health intentions, there were no significant differences between the groups at baseline or follow-up. Genetic testing intention scores increased in the control group from 2.20 to 2.71. Scores in the in-person counselling group decreased from 2.23 to 1.62 and also decreased in the telephone counselling group from 2.24 to 1.72. There was a significant effect of intentions to pursue genetic testing at baseline to pursue genetic testing at follow-up (F = 209.98; df = 1330; P < 0.001). The effect of study group was also significant (F = 60.41; df = 2330; P < 0.001). There was a significant difference between the intervention groups and control group (mean difference = 0.52; CI 0.43 to 0.62; P < 0.001) but not between the two intervention groups (mean difference = 0.09; CI -0.02 to 0.20; P = 0.107).

There were no significant differences between intervention groups in terms of satisfaction with counselling and support received. However, 77.4% of women in the in-person counselling group felt that they were able to talk more about their concerns compared with 67.3% in the telephone counselling group (P < 0.05).

In Matloff 2006, no significant differences were found between the genetic risk-counselling group and the control group at baseline in terms of demographics, perceived risk of breast cancer, decisional intentions or decisional conflict about menopausal therapy. Participants' perceived risk was significantly lower in the intervention group at one-month follow-up (F(1, 44) = 14.08, P < 0.008) and at six months post-intervention (F(1, 44) = 8.48, P < 0.008). The intervention group was no less likely to rate their own risk for breast cancer as higher than that of the average woman than the control group at one month (F(1, 43) = 7.52, P < 0.008) and six months (F(1, 43) = 4.43, P < 0.008). For participants in the intervention group, discrepancy between perceived risk and actual risk of breast cancer was significantly lower than baseline at one month (t(21) = 3.10, P < 0.008) and at six months (t(21) = 3.10, P < 0.008). However, some women continued to overestimate their risk level after counselling.

With regards to medication usage, there were no group differences at either follow-up point in the proportion taking hormone replacement therapy (Fisher's exact test, P = 0.98, P = 1.00). No participants were taking raloxifene or tamoxifen at any time point in the study.

Participants reported high levels of satisfaction with the counselling session including the information received (M = 85.64, SD = 16.93), the support received (M = 80.13, SD = 21.87), and the time involved (M = 80.39, SD=19.95), but less with the convenience of the session (M = 76.61, SD = 25.27).

Young 2006 found no differences in cancer worry scores at three-month follow-up between those who received their risk assessment by letter or those who received their risk assessment face-to-face (t(69) = -0.636, P = 0.527). Significant between-group differences were reported for personal breast cancer risk estimates. Those who received their risk assessment during an interview (mean = 2.38) perceived their risk to be slightly higher than those who received their information by letter (mean = 2.0, t(69) = -2.246, P = 0.028). Young 2006 reported no significant differences between groups for estimates of personal lifetime risk of breast cancer in the two items which measured risk estimates (t(64) =1.036, P = 0.304, and t(69) = -0.249, P = 0.804).The authors noted that personal risk estimates were often inaccurate and there were poor correlations between estimates expressed in the different formats for the same respondent. As there were no baseline measures of any outcomes it is unknown whether cancer worry or risk perceptions changed after receiving genetic risk information. There were no reported differences between groups for actions since referral and for experiences since referral. There were also no differences between groups for concerns about personal breast cancer risk (t(69) = -0.705, P = 0.483). No significant differences were found between the 'letter' and 'interview' group for the subscores of the General Health Questionnaire.

In terms of satisfaction with the risk communication process, the mean scores in the letter group ranged from 'quite satisfied' to 'very satisfied'. Although for five items the group who received their assessment face-to-face expressed significantly higher levels of satisfaction than those who received their assessment via letter (P value range 0.020 to 0.001).

DISCUSSION

Summary of main results

All eight studies involved the process of risk assessment for familial breast cancer focusing on the psychosocial impact on patients, as well as looking at other outcomes and aspects of service delivery. Improvements in psychological well-being and a decrease in the levels of cancer worry were found in most studies. Bowen 2004 and Brain 2000a reported an overall decrease in anxiety and Fry 2003 demonstrated a decrease in the proportion of patients suffering case-level psychological distress. Bowen 2004 also reported a decrease in depressive symptoms over-time. Braithwaite 2005 reported a small non-significant decrease in anxiety as measured by the HADS. However, state anxiety levels increased in both groups from baseline to post-intervention and had not returned to baseline levels at the three-month follow-up. It is important to note that the higher levels of psychological distress in the participants who withdrew from the Brain 2000a and Fry 2003 trials compared with those who remained in the trial, may have had an impact on the results. Young 2006 only reported outcomes at one time point, three months after participants had received their 'lower risk' information via letter or in a face-to-face interview. There were no significant differences between groups in terms of cancer worry, adverse and positive effects of receiving risk information, concerns about breast cancer risk and general psychological health. However, it is unknown whether there were any changes in any of the outcomes over time due to the lack of baseline data.

Bowen 2004, Bowen 2006, and Matloff 2006 reported an overall reduction in participants' perceived risk of breast cancer. Similarly Brain 2000a reported an overall reduction in perceived risk; however Brain 2002 did report significant differences across the differing risk categories. Overall, those at high risk had a slightly higher perceived risk than those at low and moderate risk, and while levels of risk perception for those at low and moderate risk decreased over time, no changes in perceived risk were observed among high-risk participants. In both the intervention and control study groups, risk perceptions of those at low and moderate risk again decreased over time. However, risk perceptions of those at high risk in the intervention group increased over time whereas risk perceptions of those at high risk in the control group marginally decreased over time. Braithwaite 2005 reported increased accuracy of breast cancer risk in both groups. Whereas in Helmes 2006, participants' risk perceptions decreased in both counselling groups and increased in the control group from baseline to follow-up. Fry 2003 reported an overall improvement in subjective understanding of breast cancer genetic risk. Brain 2000a looked at changes in participants' knowledge of hereditary breast cancer, reporting a significant increase over-time. Fry 2003 reported an improvement in objective understanding of breast cancer and mammography across all groups and all risk categories. Young 2006 found that women who received their low-risk information face-to-face perceived their risk to be slightly higher than those who were informed by a letter only. Both groups appeared to be uncertain of their risk level at the three-month follow-up in terms of lifetime risk estimates of breast cancer but there were no significant differences between the two groups.

In terms of health behaviours, Fry 2003 found proportionately more patients in the control group examining their breasts on a monthly basis, and proportionately more women in the intervention group examining their breasts more than once a month. In contrast, Helmes 2006 found no differences between groups in terms of breast health intentions. Matloff 2006 found no differences between groups in menopausal therapy decisions or use of menopausal therapy. Genetic testing beliefs and intentions were explored in Bowen 2006 and Helmes 2006. Awareness of and interest in genetic testing increased more in the intervention group than the control group in Bowen 2006. In Helmes 2006, genetic testing intention scores increased in the control group and decreased in both counselling groups.

Positive reactions to counselling and high satisfaction with the service were found in many studies (Bowen 2004; Brain 2000a; Braithwaite 2005; Helmes 2006; Matloff 2006; Young 2006). Brain 2000a found that those at high risk reported less instrumental satisfaction than those at moderate and low risk, and those at moderate risk were less satisfied than those at low risk. Participants in the study by Braithwaite 2005 were significantly more satisfied with the nurse counselling than the GRACE computerised risk assessment. There also appeared to be no differences in satisfaction between telephone and in-person risk counselling, except women in the in-person counselling group felt more able to talk about their concerns (Helmes 2006). In Young 2006, participants in the face-to-face interview group expressed significantly higher levels of satisfaction with the process of receiving their risk information for five out of the twelve items than those who received their risk information via letter. However, mean satisfaction scores in the letter group indicated that they were satisfied with the process.

Overall completeness and applicability of evidence

This review suggests that there are benefits to receiving a specialist cancer genetic risk assessment in that it can help to reduce psychological distress and worry about breast cancer, and improve the accuracy of perceived risk about breast cancer, while helping to increase knowledge of breast cancer and genetics. Although there is some fluctuation in these outcomes among individuals when measured at different time points, this review found no evidence to suggest that undergoing cancer genetic risk assessment for breast cancer causes any harm to the psychological well-being of patients, although this was not followed up for any longer than nine months. Further longitudinal research is needed to assess long-term effects, particularly since the cancer genetics journey can involve many genetic counselling sessions and a protracted period of waiting for the results of genetic testing. Some of the included studies in this review only explored the impact of cancer genetic risk assessment on women at average or moderate risk of breast cancer. As those at high risk of cancer were sometimes shown to have different outcomes to those at lower risk (Brain 2000a; Fry 2003), some caution is warranted when generalising the conclusions of this review to high-risk groups. This review also indicates that patients are generally satisfied with genetic counselling with the type of health professional delivering the risk assessment, having minimal impact on the observed outcomes. High patient satisfaction was reported in all included studies. It is worth noting that Brain 2000a found a small significant effect related to venue with those participants seen outside the traditional hospital setting reporting greater satisfaction than those seen in a hospital-based setting. This suggests that further research as to the best location of cancer genetic service delivery is warranted. Also this review suggests that patients report slightly higher levels of satisfaction with face-to-face communication of genetic risk compared with a computer programme, telephone counselling or receiving risk assessment via a letter.

Demand for cancer genetic services is likely to increase particularly in light of the discovery of new cancer predisposing genes and greater public and media awareness. Consequently cancer genetic services will experience increases in referrals from people concerned about their family history of breast cancer. Escalating demand, coupled with limited resources, make it important for cancer genetic clinics to deliver a consistently high quality service for every new patient referred. This updated review only identified three studies that compared alternative means of service delivery over face-to-face contact (Braithwaite 2006; Helmes 2006; Young 2006). This review found no randomised trials assessing the impact of genetic consultations via telemedicine, which studies show could help meet the increasing demand for specialist genetic services and be a cost-effective alternative to consultations in clinic (Lea 2005; Meropol 2011). Those studies that do exist focus on establishing the validity of services through pilot projects and feasibility studies rather than comparing alternative means of delivery. This review found no RCTs that compared the duration or frequency of counselling sessions for breast cancer. Also interventions did not include any substitution of place, person or procedure at the time of the review. This review also highlights the need for trials of cancer genetic risk assessment to examine decision-making about cancer screening behaviours and genetic testing at all risk levels as additional outcome measures.

Quality of the evidence

For cancer genetic risk assessment it is not possible to blind participants and clinicians to the treatment arm. Randomisation was generally adequate, although methods of allocation concealment were often not specified in the studies included in this review. Many of the included trials did not report on the characteristics of participants drop-outs or state reasons for withdrawal. As shown in Brain 2000a, participants who decline from cancer genetic risk assessment may have high levels of anxiety and therefore attrition bias should be assessed where possible in similar trials.

Potential biases in the review process

We did not identify any sources of potential bias in the review process.

Agreements and disagreements with other studies or reviews

Results from this review are similar to that of a review of cancer genetic counselling (Braithwaite 2004), which showed improvements in cancer knowledge after genetic counselling but no long-term increases in anxiety, cancer worry or depression. The impact of genetic counselling on risk perception was less clear, with some studies reporting no change in risk perception while others report significant differences before and after counselling. Other studies have also reported patient high satisfaction with genetic counselling (Bober 2007) and satisfaction is generally comparable for face-to-face counselling and remote counselling via telephone or videoconferencing (Coehlo 2005; Gray 2000a). However, these reviews and studies tend to focus on the psychological impact of genetic counselling and, to our knowledge, there are no other reviews of the impact of cancer genetic risk assessment for familial breast cancer.

AUTHORS' CONCLUSIONS

Implications for practice

This review suggests that cancer genetic risk assessment is beneficial for patients at risk of familial breast cancer. However, more studies are required to assess the best means of delivering these services by different health professionals and in alternative locations, through a variety of interventions. We acknowledge that cancer genetic services are delivered differently within different healthcare systems, with varying ways for patients to access those services. In some cases, patients may have previously purchased additional services, such as genetic tests, which may further affect how services are delivered. This however does not negate the fact that risk-assessment services delivered to patients can be examined in standardised ways through the use of rigorous methods such as RCTs.

This review suggests that many patients are satisfied with the existence of cancer genetic risk-assessment services. Nevertheless, as cancer genetics has become more common and the inherited components of other diseases are elucidated, evaluation rigour will have to improve and pilot studies and exploratory projects will no longer be sufficient. The challenge for cancer genetic services is to develop services that adequately reassure inappropriately worried individuals (who are still at average risk) and to identify those at moderate and potentially high risk who require further information, management and support. Involving patients in these processes will be crucial.

Implications for research

Despite the differences in the provision of cancer genetic services in different countries, more research is needed into the effectiveness and efficiency of these services. There is much more to cancer genetic services than simply assessing patients' risk for a genetic predisposition to developing familial cancer. Therefore, the full scope of cancer genetic services and patient journeys through these services needs to be examined, including decisions to undertake predictive genetic testing and the impact on other decision-making such as the uptake of preventive measures such as prophylactic surgery. More research is also needed looking at how risk is presented (i.e. verbal, numerical, graphical), the duration of, where and how risk assessment takes place (e.g. face-to-face or videoconferencing), the availability of, and types of support or after care, or both, and the type of information which is available to patients. However as the full range of services is unlikely to be examined in one RCT, this will require a meta-analysis of prospective studies. In the current review, many studies only included patients at average or moderate risk of breast cancer. The impact of cancer genetic risk assessment for those at high risk is an important area for further research, as these women are generally eligible for genetic testing and may have the option for increased screening or prophylactic surgery, or both. Patient preferences, as well as the psychological impact of all aspects of cancer genetic services on patients should be measured, as should the acceptability of these services to healthcare professionals. A genetic predisposition is something that an individual carries for the duration of their lifetime; hence there is a need for longitudinal studies to reflect this.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Bowen 2004

Study characteristics	
Methods	RCT
Participants	354 women aged between 18 and 74 were randomised. Patients with a family history of breast cancer but with no personal history of breast/ovarian cancer or BRCA1/2 mutation. The Gail lifetime score for the sample as a whole was 12%, which is close to population lifetime risk of breast cancer. Women living within a 60-mile radius of the research centre were eligible to participate
Interventions	Individual genetic counselling versus group psychosocial counselling compared with a no-counselling comparison group
Outcomes	Perceived risk (4 items developed by research team measuring beliefs about perceived personal breast cancer risk: personal estimate of lifetime risk on scale from 0% to 100%; personal estimate of risk relative to average woman rated on 8-point scale; personal estimate of risk relative to own age group rated on 8-point scale; personal risk without referrant using categories of 'very high', 'high', 'low', and 'very low') Actual breast cancer risk information (patients provided information on their family history of breast cancer, current age and reproductive and breast health risk factors. Risk estimates were calculated) Emotional reactions (measured in two ways: brief symptom inventory measuring general anxiety and depression - shortened version of Hopkins symptom checklist - 49 items on 5-point Likert scales; Cancer worry scale (Lerman 1991a) Reactions to counselling (brief survey focusing on use of written educational materials, enjoyment and perceived usefulness of counselling, perceived support from counsellor, comfort of talking during counselling)
Notes	Parts of methodology not fully explained but explained in earlier papers (Bowen 1999; Bowen 2002). High-risk patients not included in study. Blinding in the randomisation process was not possible.

Bowen 2004 *(Continued)*

Bowen 1999 was not excluded from the study however, it is the data from Bowen 2004 which are presented as the main trial paper.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Randomization was conducted by assigning a randomization number to each participant in a blinded fashion. Each randomization number was pre-assigned to one of three study conditions without bias" Comment: Method of randomisation not reported
Allocation concealment (selection bias)	High risk	"Those women who completed the baseline were randomized into the study and informed of their randomized study arm over the telephone" Comment: No allocation concealment
Incomplete outcome data (attrition bias) All outcomes	Low risk	354 participants randomised. 346 (98%) completed the 6-month follow-up. Final analyses performed on those who completed follow-up and baseline assessment (n = 348).
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes reported

Bowen 2006

Study characteristics

Methods	RCT
Participants	220 Ashkenazi Jewish women aged between 18 and 74 years were randomised. Participants had no personal history of breast or ovarian cancer and did not have a family history consistent with a BRCA1/2 mutation. The samples risk level was close to that of the general population lifetime risk. Participants living within 60 miles of Seattle were eligible to participate
Interventions	Group psychosocial counselling versus individual genetic counselling compared with a delayed counselling control group.
Outcomes	Perceived risk of breast cancer (personal estimate of lifetime risk on a continuous scale from 0% to 100%) Cancer worry (Cancer worry scale (Lerman 1991a)). General anxiety (measured with the 49-item Brief Symptom Inventory (Derogatis 1983) on 5-point Likert scales) Genetic testing beliefs (measured using three scales with 4-point responses: fear of stigma; access to genetic testing; information flow about test results) Genetic testing awareness, interest and candidacy (measured with three single items) Jewish identity (measured using the 14-item Multigroup Ethnic Identity Measure (Phinney 1992))
Notes	High-risk patients not included in study. Blinding in the randomisation process was not possible.

Bowen 2006 *(Continued)*

	Two counselling protocols based on previous study (Bowen 2004)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Participants were randomly assigned to one of three study groups" Comment: Method of randomisation not reported
Allocation concealment (selection bias)	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	220 women randomised. Overall follow-up rate 96% (77% returned 6-month follow-up questionnaire and 19% completed follow-up telephone call). Reasons for attrition not reported. No differences among arms in follow-up rates and no differences in baseline demographic data between women who did and did not provide follow-up data. No data are available about the number of participants who provided follow-up data from each group
Selective reporting (reporting bias)	Unclear risk	All pre-specified outcomes reported except measure of general anxiety reported in methods section but not in results

Brain 2000a

Study characteristics

Methods	Prospective RCT
Participants	735 women aged between 19 and 73 were randomised. The final sample consisted of 545 women in Brain 2000a. In Brain 2002, 653 participants were compared at baseline and follow-up immediately after attending clinic. Patients with a family history of breast cancer, who had no personal history of breast cancer, no prior counselling and were resident in Wales were eligible to participate. The data reported in Brain 2002 state that of the 653 women who received risk information and completed the immediate follow-up questionnaire, 107 were at low risk of cancer, 447 were at moderate risk and 99 were at high risk. A four-way randomisation was carried out to control for differences between two venues (Breast Test Wales Screening Centre and the Family History Clinic at the University Hospital of Wales)
Interventions	Surgical consultation with genetic assessment versus the standard surgical consultation without genetic assessment
Outcomes	Primary outcomes: Emotional well-being (2 measures: general anxiety measured by the State-Trait Anxiety Inventory STAI (Spielberger 1983); breast cancer worry measured by the Breast Cancer Worries Scale (Lerman 1991a; Lerman 1991b)) Perceived risk of breast cancer (2 items derived from previous research (Lerman 1991a; Lerman 1993; Champion 1984)) Secondary outcomes: Knowledge of familial breast cancer (4 true / false items to make knowledge score) Patient satisfaction (12-Item Satisfaction with Genetic Counseling Questionnaire (Shiloh 1990)) Costs were also compared with current service provision

Brain 2000a *(Continued)*

Notes	Secondary analyses of the data are presented in Brain 2002. The 2 study groups are compared at baseline and follow-up immediately after attending the clinic of 653 participants stratified into low, moderate or high-risk categories on the following outcomes: anxiety; worry; perceived risk; satisfaction

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"The randomization procedure was based on a computer-generated sequence of random numbers"
Allocation concealment (selection bias)	Unclear risk	Randomisation is likely to have been concealed although this is not stated
Incomplete outcome data (attrition bias) All outcomes	High risk	26.35% of randomised participants were withdrawn from the trial; five participants were excluded due to non-attendance in the surgical aspect of the multidisciplinary trial clinic and 190 (87 control group, 103 intervention group) were lost to follow-up. "Those who dropped out at baseline reported statistically significantly higher trait and state anxiety and lower personal risk than participants." At the first assessment and at 9-month assessment, drop-outs were significantly younger and reported higher baseline cancer worry. Those in the control group were less likely to return the questionnaire immediately after the clinic. "Participants who did not complete both follow-up questionnaires were not included in the main comparative analyses."
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes reported

Braithwaite 2005

Study characteristics

Methods	Randomised trial
Participants	72 women over the age of 18 were randomised. Women had at least one first or second degree relative affected with breast cancer but no personal history of breast cancer. 35 (50.7%) participants were found to be at average risk, 16 (23.2%) at moderate risk and 18 (26.1%) at high risk. Participants were recruited from the Greater London area in the UK
Interventions	A computerised tool to support stratification of breast cancer genetic risk assessment in the clinical environment (GRACE) versus risk counselling by a clinical nurse specialist. Intervention lasted for one session only
Outcomes	Acceptability of the intervention (attitudes towards GRACE or consultation, perceived benefits, perceptions of risk information (credibility, trustworthiness, accuracy, clarity and helpfulness), satisfaction and risk communication preferences) Cognitive outcomes: comparative risk perception (measured with a single-item on a 5-point scale); risk accuracy (measured by assessing level of concordance between the women's perceived risk estimate and those provided by GRACE or nurse specialist) Emotional outcomes: Anxiety and depression scale (HADS); General anxiety (measured by the short version of the State-Trait Anxiety Inventory STAI); Cancer worry scale [(Lerman 1991a)

Braithwaite 2005 *(Continued)*

Notes	Women were relatively young (62% aged between 18-34 years) and a majority reported being computer literate

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"...those found to be eligible were emailed further information about the study and randomized to one of the study conditions" Comment: Method of randomisation not reported
Allocation concealment (selection bias)	Unclear risk	"Both the clinical nurse specialist and the participants were blinded to the treatment arm until just prior to their appointment" Comment: Allocation concealment not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	72 participants randomised and provided data immediately post-clinic. 54 women provided 3-month follow-up data. Reasons for attrition not reported. No comparison between respondents and non-respondents in terms of risk perception or psychological variables
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes reported

Fry 2003

Study characteristics

Methods	Cluster randomised trial
Participants	373 women referred from participating GP practices to regional clinical genetics departments in south east Scotland participated in this study. Those who were symptomatic or had a breast/ovarian cancer diagnosis or those who had previously consulted another clinic about a family history of cancer were excluded from the trial. 31% of the sample were at low risk of cancer, 69% were at moderate/high risk
Interventions	Novel (community-based) service versus the standard regional service
Outcomes	Subjective understanding (4-point scale rating how well understand 4 issues relevant to breast cancer genetic risk to give composite score) Objective understanding (true/false to 10 factual statements about breast cancer genetics - give total scores for genetics understanding and mammography understanding) Perceived risk of breast cancer (one item for analysis - perceive risk to be high, moderate or low) Psychological distress (2 measures: GHQ-30 (Goldberg 1988); Cancer Worry Scale (Watson 1998)) Health behaviours (rate whether frequency of certain behaviours had changed since baseline)
Notes	GP practices randomly assigned using a minimisation technique and was not possible to blind assignment status

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Practices were randomly assigned to either arm of the trial using a minimisation technique (Pocock 1983, pp 84-86)"

Fry 2003 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	High risk	All reasons/numbers for attrition stated. 373 participants were randomised. Main analyses were performed on data from 244 (65%) participants who completed all three follow-up assessments. "Women who dropped out of the trial tended to be in the novel service arm of the trial or at low risk of breast cancer." Women who dropped out also had significantly higher baseline cancer worry scores
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes reported

Helmes 2006

Study characteristics	
Methods	RCT
Participants	340 women from a healthcare network in Washington state, USA were randomised. Women were aged 18-64, with no personal history of breast/ovarian cancer, who had not previously received genetic counselling or genetic testing. Other eligibility criteria included living within 60 miles of the research centre, ability to speak and write in English, having a telephone at home and being covered by health insurance. The sample was at population risk of cancer
Interventions	In-person versus telephone breast cancer risk genetic counselling by a certified genetic counsellor compared with a delayed counselling control group
Outcomes	Cancer worry (measured by the cancer worry scale (Lerman 1991a)) Risk perception (single-item measure on a scale of 1-100) Breast health intention scale assessed by averaging responses to three measures: Intentions to obtain mammograms; clinical breast examination; breast self-examination Interest in genetic testing (measured using 4 items, from which a single testing intention score was calculated) Acceptability of counselling assessed with intervention participants
Notes	Recruitment described further in Helmes 2000. The same counsellor was used for the entire study

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Participants were randomised using a computer-generated list of numbers Comment: Information from personal communication with author
Allocation concealment (selection bias)	Unclear risk	Not stated

Helmes 2006 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	98.5% of randomised participants completed 3-month follow-up assessment. "We analyzed the data using the intention to treat principle, including all randomized women."
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes reported

Matloff 2006

Study characteristics	
Methods	RCT
Participants	64 participants randomised, of whom 48 completed both questionnaires and received the intervention. Women were aged 40 years or over, had at least one first degree relative with breast cancer, had gone through natural menopause and were not currently taking menopausal therapy. Women were excluded if they had a personal cancer history, were a known BRCA1/2 mutation or had heart disease. Trial setting in Connecticut, USA
Interventions	Two 60-minute genetic counselling sessions and risk assessment with a certified genetic counsellor. Individuals' risk for breast and endometrial cancer, heart disease, and osteoporosis were calculated based on family history and personal health data and were presented to the participant at the second visit, which was held 3-4 weeks after the first session. Control participants were offered the counselling intervention after the trial data collection finished
Outcomes	Perceived lifetime risk of breast cancer, heart disease and osteoporosis (scale 0% to 100%), estimates of the lifetime risk of an average woman (scale 0% to 100%). Worry about breast cancer in past month measured with a single item (1 = not at all, 4 = almost all of the time). Decisional conflict regarding menopausal therapy decision making assessed with the Decisional Conflict Scale (5-point scale). Satisfaction with counselling intervention in terms of information received, support received, amount of time involved and convenience of counselling session. Accuracy of knowledge about menopause assessed using a 30-item true/false questionnaire
Notes	High-risk patients not included in study

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	"randomized to either an intervention or control arm upon recruitment (every other patient)" Comment: Quasi-randomisation
Allocation concealment (selection bias)	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	High risk	64 participants randomised. 57 completed baseline questionnaire and received the intervention (n = 29) or in control group (n = 28). "Analyses are confined to the 48 participants who completed assessments at all three time points (23 in the intervention group and 25 in the control group). "Participants

Matloff 2006 *(Continued)*

		were excluded from the analyses for which they had missing data, and no imputations were conducted." No reasons for attrition reported
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes reported

Young 2006

Study characteristics	
Methods	Randomised trial
Participants	90 women were randomised, of whom 3 were subsequently withdrawn. Women who were referred to the Tayside Familial Breast Cancer Service in Scotland, UK and whose risk of breast cancer was assessed as being at below the threshold for inclusion in a regular surveillance program were eligible for inclusion. All participants were therefore at low or average risk
Interventions	Women were randomised to receive their genetic risk information in a personalised letter or to attend the genetics department for an interview with a genetics associate or nurse specialist. This gave the opportunity for questions to be asked and answered but did not include breast examination or mammography. The interview was followed up by a personal letter summarising the discussion
Outcomes	Three months after the intervention, all participants were asked to complete a patient satisfaction questionnaire based on the instrument used in Brain 2000a. Breast cancer worry measured by the cancer worry scale (Lerman 1991a; Lerman 1991b). Understanding of breast cancer risk (11 questions: 5 about perceptions of own risk, 2 about perceptions of general population risk). Actions and experiences since receiving the risk assessment (12 items about possible adverse effects on behaviour, 10 items about possible positive effects on behaviour). Experiences of and satisfaction with the interview or written communication. General Health Questionnaire (Goldberg 1988)
Notes	No baseline measures on any of the outcomes. Also no details of participant characteristics such as age and educational level

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"Randomised by a genetics associate (using computer-generated random numbers)"
Allocation concealment (selection bias)	Unclear risk	Allocation is likely to be concealed although this is not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	87 participants randomised after 3 exclusions. 81.6% completed 3-month follow-up. Reasons for exclusion and drop-out reported. No data on differences between responders and non-responders
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes reported

RCT: randomised controlled trial
Due to the nature of the interventions, it would not always be possible for participants and treatment providers to be blind to assignment status once assigned therefore excluded from assessment of quality of allocation concealment

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Amir 2010	Article is a review of risk-assessment models
Appleton 2004b	Relating to the provision of information and education
Armstrong 2005	Includes participants with a previous or current cancer diagnosis
Barcenas 2006	Relating to a risk-assessment model rather than the provision of genetic risk assessment
Bellcross 2009	Relating to a genetics referral screening tool, not the provision of a genetic risk assessment
Bluman 1999	Survey of baseline data - not the full trial. Also, relating to the provision of information and education
Bowen 2002	Same trial as Bowen 2004 and Bowen 1999 but focusing on interest in genetic testing
Brain 1999	Data from same trial reported in Brain 2000a, Brain 2000b and Brain 2002 but outcome is breast self-examination measured at baseline, prior to genetic counselling
Brain 2000b	Data from same trial reported in Brain 1999, Brain 2000a and Brain 2002 looking at reasons for attending clinics
Butow 1998	Relating to the provision of information and education. Also from the same trial as Lobb 2002a and Lobb 2002b
Calzone 2005	Includes participants with a previous or current cancer diagnosis
Cameron 2001	Data from the same trial reported in Campbell 2003 and Fry 2003 but looking at GP referral rates
Campbell 2003	Data from the same trial reported in Fry 2003
Charles 2006	Includes participants with a previous or current cancer diagnosis
Cohen 2004	Data from same trial reported in Brain 1999; Brain 2000a; Brain 2002 but concerning health economics
Cull 1998	Comparing methods of delivering education
Daly 1998	Relating to the provision of information and education
Emery 2007	Relating to primary care support for GP referrals to clinical genetics, includes breast and colorectal cancer
Gray 2009	Relating to the provision of information and education. Includes women with a previous or current cancer diagnosis
Green 2001	Relating to the provision of information and education. Also from the same trial as Green 2004
Green 2004	Relating to the provision of information and education. Also from the same trial as Green 2001

Study	Reason for exclusion
Green 2005	Includes participants with a previous or current cancer diagnosis
Halbert 2010	Includes participants with a previous or current cancer diagnosis
Hall 2009	Includes participants with a previous or current cancer diagnosis
Halverson 2000	Relating to the provision of information and education. Also, participants are staff not patients
Helgeson 2001	Relating to the provision of information and education
Hopwood 2004	Not just looking at breast cancer - includes bowel and ovarian cancer also
Hoskins 2001	Testing the feasibility of a RCT, not an RCT per se
Hoskins 2006	Relating to a pedigree assessment tool. No patient outcomes
Hurt 2001	Relating to the provision of information and education
Jibaja 2000	Relating to the provision of information and education
Lerman 1994	Relating to the provision of information and education. Also from the same trial as Lerman 1995 and Schwartz 1999
Lerman 1995	Relating to the provision of information and education. Also from the same trial as Lerman 1994, Lerman 1996 and Schwartz 1999
Lerman 1996	Relating to the provision of information and education. Same trial as Lerman 1994, Lerman 1995 and Schwartz 1999
Lerman 1997	Relating to the provision of information and education
Lerman 1999	Data taken from same trial as Lerman 1997 but only looking at racial differences excluding the control group
Lobb 2002a	Relating to the provision of information and education. Also from the same trial as Lobb 2002b
Lobb 2002b	Relating to the provision of information and education. Also from the same trial as Lobb 2002a
Miedzybrodzka 2001	Relating to the provision of information and education. Also, participants are students
Miller 2005	Includes participants with a previous or current cancer diagnosis
Miron 2000	Relating to the provision of information and education
Ormond 1996	Looking at pre-screening education for pregnancy
Rahm 2007	Includes participants with a previous or current cancer diagnosis
Ramirez 2008	Relating to method of referral to genetics clinic. Also includes men and women and other cancers apart from breast cancer
Roshanai 2009	Includes participants with a previous or current cancer diagnosis
Roussi 2010	Includes participants with a previous or current cancer diagnosis

Study	Reason for exclusion
Schwartz 1998	Relating to the provision of information and education
Schwartz 1999	Relating to the provision of information and education
Schwartz 2001	Relating to the provision of information and education
Schwartz 2009	Relating to a decision aid for BRCA1/2 carriers rather than the provision of genetic risk information
Skinner 2002	Relating to the provision of information and education
Stoddard 2002	Meta-analysis of randomised trials looking at mammography, not genetics
Street 1998	Education promoting breast cancer screening
Torrance 2006	Same trial as Wilson 2005. Includes participants with a previous or current cancer diagnosis
Van Roosmalen 2004a	Focusing on decision aid for genetic testing rather than on service delivery - also same trial as Van Roosmalen 2004b
Van Roosmalen 2004b	Focusing on decision aid for genetic testing rather than on service delivery - also same trial as Van Roosmalen 2004a
Venne 2007	Relating to the provision of information and education
Wade-Walsh 2001	Relating to the provision of information and education. Also from the same trial as Watson 1996 and Watson 1998
Wakefield 2008a	Refers to the use of a decision aid for genetic testing. Includes participants with a previous or current cancer diagnosis
Wakefield 2008b	Refers to the use of a decision aid for genetic testing. Includes participants with a previous or current cancer diagnosis
Wang 2005	Includes participants with a previous or current cancer diagnosis
Watson 1996	Relating to the provision of information and education. Also from the same trial as Wade-Walsh 2001 and Watson 1998
Watson 1998	Relating to the provision of information and education. Also from the same trial as Wade-Walsh 2001 and Watson 1996
Watson 2001	Relating to the provision of information and education. Also, participants are GPs
Wevers 2011	Includes participants with a previous or current cancer diagnosis
Wilson 2005	Same trial as Torrance 2006. Includes participants with a previous or current cancer diagnosis
Wilson 2006	No patient outcomes. Participants are GPs

RCT: randomised controlled trial

Characteristics of ongoing studies *[ordered by study ID]*

Ockhuysen-Vermey 2008

Study name	Design of the BRISC study: a multi-centre controlled clinical trial to optimise the communication of breast cancer risks in genetic counselling
Methods	The BRISC study is designed as a pre-post-test controlled group intervention trial with repeated measurements using questionnaires
Participants	Women with a family history of breast cancer who are first-time attendees applying for breast cancer counselling are invited to participate in the study. A family history of breast cancer is defined as having or having had at least one first-degree- and/or paternal second-degree family member with breast cancer. Women are considered ineligible if they are under 18 years of age, have evident psychiatric illness or terminal disease, and are unable to read and write Dutch. Women with a personal history of breast or ovarian cancer are also excluded
Interventions	One additional consultation by a trained "risk counsellor" immediately after a standard genetic counselling session. During the additional consultation, risks are communicated in one of five ways (conditions): 1) lifetime breast cancer risk in numerical format (in natural frequencies, i.e. X out of 100), 2) lifetime breast cancer risk in both numerical format and graphical format (i.e. population figures in 10 rows of 10) 3) lifetime breast cancer risk and age-related breast cancer risk in numerical format, 4) lifetime breast cancer risk and age-related breast cancer risk in both numerical format and graphical format, and 5) lifetime breast cancer risk in percentages
Outcomes	Cognitive outcomes, psychological well-being, decision-making, evaluation of the intervention
Starting date	Protocol approved in 2005
Contact information	Caroline F Ockhuysen-Vermey: karen.ockhuysen@hotmail.com
Notes	

APPENDICES

Appendix 1. MEDLINE Search Strategy (1985-2005)

1 exp Breast Neoplasms/
2 exp "Neoplasms, Ductal, Lobular, and Medullary"/
3 exp breast/
4 exp neoplasms/
5 3 and 4
6 (breast$ adj5 (neoplasm$ or cancer$ or tumo?r$ or carcinoma$ or adenocarcinoma$ or sarcoma$ or dcis or ductal or infiltrat$ or intraductal$ or lobular or medullary)).mp.
7 exp mammary neoplasms/
8 (mammar$ adj5 (neoplasm$ or cancer$ or tumo?r$ or carcinoma$ or adenocarcinoma$ or sarcoma$ or dcis or ductal or infiltrat$ or intraductal$ or lobular or medullary)).mp.
9 or/1-2,5-8
10 exp Genetic Predisposition to Disease/
11 exp Neoplastic Syndromes, Hereditary/
12 exp Genetics/
13 (familial or inherit$ or heredit$ or predispos$ or susceptib$).mp.
14 exp risk factors/ and ge.fs.
15 genes, BRCA1/
16 genes, BRCA2/
17 or/10-16
18 9 and 17
19 exp genetic services/

20 exp Genetic Counseling/
21 exp Counseling/
22 health facilities/
23 exp "health services administration"/
24 exp "health care quality, access and evaluation"/
25 exp "health care economics and organizations"/
26 exp health services/
27 ((cancer$ or oncolog$ or genetic$) adj5 (service$ or inform$ or counsel$ or test$)).mp. (35094)
28 or/19-27
29 18 and 28
30 randomized controlled trial.pt.
31 controlled clinical trial.pt.
32 exp randomized controlled trials/
33 exp random allocation/
34 exp double blind method/
35 exp single-blind method/
36 or/30-35
37 animal/ not human/
38 36 not 37
39 clinical trial.pt.
40 exp clinical trials/
41 (clin$ adj25 trial$).tw.
42 ((singl$ or doubl$ or tripl$ or trebl$) adj25 (blind$ or mask$)).tw.
43 exp placebos/
44 placebo$.tw.
45 random$.tw.
46 exp research design/
47 or/39-46
48 47 not 37
49 48 not 38
50 exp Comparative Study/
51 exp evaluation studies/
52 exp follow up studies/
53 exp prospective studies/
54 (control$ or prospectiv$ or volunteer$).tw.
55 or/50-54
56 55 not 37
57 55 not (38 or 49)
58 38 or 49 or 57
59 29 and 58

Appendix 2. MEDLINE search strategy (Ovid version) 2005-April 2011

Medline (OVID version)

1. exp Breast Neoplasms/

2. exp "Neoplasms, Ductal, Lobular, and Medullary"/

3. exp breast/

4. exp neoplasms/

5. 3 and 4

6. (breast$ adj5 (neoplasm$ or cancer$ or tumo?r$ or carcinoma$ or adenocarcinoma$ or sarcoma$ or dcis or ductal or infiltrat$ or intraductal$ or lobular or medullary)).mp.

7. exp mammary neoplasms/

8. (mammar$ adj5 (neoplasm$ or cancer$ or tumo?r$ or carcinoma$ or adenocarcinoma$ or sarcoma$ or dcis or ductal or infiltrat$ or intraductal$ or lobular or medullary)).mp.

9. or/1-2,5-8

10. exp Genetic Predisposition to Disease/

11. exp Neoplastic Syndromes, Hereditary/

12. exp Genetics/

13. (familial or inherit$ or heredit$ or predispos$ or susceptib$).mp.

14. exp risk factors/ and ge.fs.

15. genes, BRCA1/

16. genes, BRCA2/

17. or/10-16

18. 9 and 17

19. exp genetic services/

20. exp Genetic Counseling/

21. exp Counseling/

22. health facilities/

23. exp "health services administration"/

24. exp "health care quality, access and evaluation"/

25. exp "health care economics and organizations"/

26. exp health services/

27. ((breast$ or genetic$) adj2 (service$ or counsel$)).mp.

28. or/19-27

29. 18 and 28

30. randomized controlled trial.pt.

31. controlled clinical trial.pt.

32. randomized.ab.

33. placebo.ab.

34. drug therapy.fs.

35. randomly.ab.

36. trial.ab.

37. groups.ab.

38. or/30-37

39. humans.sh.

40. 38 and 39

41. 29 and 40

42. limit 41 to yr="2005 -Current"

Appendix 3. EMBASE search strategy (Ovid version) 2005-April 2011

Embase (OVID version)

1. exp Breast Tumor/

2. exp breast cancer/

3. exp breast/ and exp neoplasm/

4. (breast$ adj5 (neoplasm$ or cancer$ or carcinoma$ or tumo?r$ or adenocarcinoma$ or sarcoma$ or dcis or ductal$ or infiltrat$ or intraductal$ or lobular or medullary)).mp.

5. (mammar$ adj5 (neoplasm$ or cancer$ or carcinoma$ or tumo?r$ or adenocarcinoma$ or sarcoma$ or dcis or ductal$ or infiltrat$ or intraductal$ or lobular or medullary)).mp.

6. or/1-5

7. exp genetic predisposition/

8. exp familial cancer/

9. exp cancer family/

10. exp cancer genetics/

11. exp heredity/

12. exp high risk population/

13. exp genetic risk/

14. exp cancer risk/ and exp genetics/

15. exp risk assessment/ and exp genetics/

16. (familial or inherit$ or heredit$ or predispos$ or susceptib).mp.

17. or/7-16

18. exp Genetic Counseling/

19. exp "health care facilities and services"/

20. health care delivery/

21. health economics/

22. exp health education/

23. exp patient referral/

24. exp consultation/

25. ((cancer$ or oncolog$ or genetic$) adj5 (service$ or inform$ or counsel$)).mp.

26. or/18-25

27. 6 and 17 and 26

28. Crossover Procedure/

29. double-blind procedure/

30. randomized controlled trial/

31. single-blind procedure/

32. (random$ or factorial$ or crossover$ or cross over$ or placebo$ or assign$ or allocat$ or volunteer$).mp.

33. ((doubl$ or singl$) adj blind$).mp.

34. or/28-33

35. 27 and 34

36. limit 35 to yr="2005 -Current"

Appendix 4. PsycInfo (Ovid Version) 2005 - April 2011

Psycinfo (OVID version)

1. exp Breast Neoplasms/

2. exp Counseling/

3. exp GENETICS/

4. ((breast$ or mammar$) adj3 (carcinoma$ or neoplasm$ or cancer$ or tumo?r$ or adenocarcinoma$ or sarcoma$ or dcis or ductal$ or infiltrat$ or intraductal$ or lobular or medullary)).mp.

5. exp Family Background/

6. exp "SUSCEPTIBILITY (DISORDERS)"/

7. (familial or inherit$ or heredit$ or predispos$ or susceptib$).mp.

8. ((cancer$ or oncolog$ or genetic$) adj5 (service$ or inform$ or counsel$)).mp.

9. 1 or 4

10. or/3,5-7

11. 2 or 8

12. 9 and 10 and 11

13. limit 12 to yr="2005 -Current"

Appendix 5. *The Cochrane Library* search strategy 2005 - April 2011

***The Cochrane Library*(Wiley)**

ID	Search
#1	MeSH descriptor Breast Neoplasms explode all trees
#2	breast:ti,ab,kw NEAR/3 (cancer* or carcinoma* or neoplasm* or tumor* or tumour*)
#3	(#1 OR #2)
#4	MeSH descriptor Genetic Predisposition to Disease explode all trees
#5	MeSH descriptor Neoplastic Syndromes, Hereditary explode all trees
#6	(familial or inherit* or heredit* or predispos* or susceptib*):ti,ab,kw
#7	(#4 OR #5 OR #6)
#8	(#3 AND #7)
#9	MeSH descriptor Genetic Services explode all trees
#10	MeSH descriptor Genetic Counseling explode all trees
#11	MeSH descriptor Genetic Counseling explode all trees
#12	(breast* or genetic*):ti,ab,kw NEAR/2 (service* or counsel*):ti,ab,kw
#13	(#9 OR #10 OR (#11 AND or#12))

#14 (#8 AND #13)

Appendix 6. CINAHL search strategy April 2005-2011

S19. S12 and S17 and S18

S18. S15 or S16

S17. S13 or S14

S16. TX ((genetic n3 counsel*) or (counsel* n3 service*))

S19	
S18	S15 or S16
S17	S13 or S14
S16	TX ((genetic n3 counsel*) or (counsel* n3 service*))
S15	(MH "Genetic Counseling")
S14	TX ((breast n3 cancer*) or (breast n3 neoplasm*) or (breast n3 tumo?r*) or (breast n3 carcinoma*))
S13	(MH "Breast Neoplasms+")
S12	S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11
S11	TX allocat* random*
S10	(MH "Quantitative Studies")
S9	(MH "Placebos")
S8	TX random* allocat*
S7	(MH "Random Assignment")
S6	TX randomi* control* trial*
S5	TX ((singl* n1 blind*) or (singl* n1 mask*)) or TX ((doubl* n1 blind*) or (doubl* n1 mask*)) or TX ((tripl* n1 blind*) or (tripl* n1 mask*)) or TX ((trebl* n1 blind*) or (trebl* n1 mask*))
S4	TX clinic* n1 trial*
S3	TX clini* n1 trial*
S2	PT clinical trial
S1	(MH "Clinical Trials+")

Appendix 7. ASSIA search strategy April 2005 - 2011

(DE=("breast cancer") or KW=((Breast within 3 cancer) or (breast within3 (tumour* or tumor*)) or (breast within3 neoplasm*))) and((DE=(genetic counselling) or DE=(genetic services) or DE=(counselling services)) or(KW=(genetic within 3 (service* or counsel*))))

Appendix 8. LILACS search strategy April 2005 - 2011

(breast or mammary or mama) and (cancer or neoplasm$ or carcinoma$) [Words] and genetic$ [Words] and Counsel$ or Consejo or Asesoramiento or Aconselhamento or Conselho [Words]

WHAT'S NEW

Date	Event	Description
20 December 2021	Amended	Topic is no longer being updated.
20 December 2021	Review declared as stable	The delivery of cancer genetic risk assessment has evolved since the publication of the review. Validated risk assessment models are available and genetic testing results may influence cancer treatment as well as family management. Reviews of this area are likely to have more focused clinical questions, therefore this review topic will no longer be updated.

HISTORY

Protocol first published: Issue 3, 2002
Review first published: Issue 2, 2007

Date	Event	Description
17 October 2011	New citation required but conclusions have not changed	Five new studies included, adding 722 participants. Conclusions remain unchanged.
8 April 2011	New search has been performed	Performed search for new studies on 8 April 2011.
14 August 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

RI and JG contributed to the design and development of the original review. The search strategy was carried out by BC. Articles to be included in the review, data extraction, assessment of methodological quality and interpretation of the findings was carried out by SS and RI in the original review and by JH and RI in the review update. JG acted as arbiter. SS led on the drafting of the original review with RI along with contributions from JG. JH led on the review update.

DECLARATIONS OF INTEREST

Jonathon Gray was part of the team which published as Brain 2000a.

SOURCES OF SUPPORT

Internal sources

- Institute of Medical Genetics, School of Medicine, Cardiff University, UK

External sources

- Tenovus the Cancer Charity, UK

NOTES

While it was our original intention - as stated in the protocol - to evaluate all aspects of cancer genetic service delivery, we soon discovered it was beyond the scope of this review to look at more than one aspect of cancer genetic service delivery. As each stage brings with it a potentially unique set of issues and concerns, we have chosen to focus just on genetic risk assessment.

INDEX TERMS

Medical Subject Headings (MeSH)

Breast Neoplasms [*genetics] [psychology]; *Family Health; Genetic Counseling [psychology]; Genetic Predisposition to Disease [genetics] [psychology]; Genetic Services [organization & administration]; Randomized Controlled Trials as Topic; Risk Assessment; Stress, Psychological [psychology]

MeSH check words

Female; Humans