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ORIGINAL RESEARCH

Predictors of Cancer Worry in Unaffected Women from High Risk Breast Cancer Families: Risk Perception is not the Primary Issue

Melanie Anne Price · Phyllis Noami Butow · Sing Kai Lo · Judy Wilson · Kathleen Cuningham Consortium for Research into Familial Breast Cancer (kConFab) Psychosocial Group

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Abstract Some women at increased familial risk of breast cancer experience elevated levels of cancer-specific worry, which can possibly act as a barrier to screening, and may be a significant factor in decisions regarding risk-reducing surgery. The aim of this study was to comprehensively examine predictors of cancer-specific worry in high risk women and to test a model which proposes that perceived breast cancer risk mediates the impact of other factors on worry. 1,437 unaffected women from high risk breast cancer families completed questionnaires and interviews. Path analysis was used to test the model of potential predictors of cancer worry, including familial, personal and psychological variables, mediated via perceived cancer risk. Levels of cancer-specific worry were generally low despite an average perceived risk of 50.3%. The goodness-of-fit of the proposed model was poor, explaining only 9% of the variance for perceived risk and 10% of the variance for cancer specific worry. An alternative model of a direct relationship between all of the predictor variables and cancer worry, explained 24% of the variation in cancer worry. General anxiety, perceived risk, the stressful impact of recent cancer related events, a relative risk greater than 10, being closer in age to the youngest breast cancer diagnosis in family, and knowledge of personal mutation status, all independently contributed to cancer worry. Addressing general affective responses, experiences of recent cancer related events, in addition to education about personal risk, should be considered in counselling women with elevated cancer worry. Risk perception appears to act independently of other factors in its formulation and impact on cancer worry. Further research on the way in which women come to perceive their risk is indicated.

Keywords BRCA1 · BRAC2 · Cancer specific worry · Perceived risk · Life event stress · Social support

The kConFab Psychosocial Group are (in alphabetical order of institution): Brain and Mind Institute, University of Sydney, Australia (I Hickie) Department of Haematology and Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia (K-A Phillips) Department of Medical Oncology, Prince of Wales Hospital, Randwick, Australia (B Bennett, B Meiser, K Tucker) Department of Oncology, St Vincent's Hospital, Melbourne, Australia (S-A MaLachlan) Department of Psychological Medicine, Royal North Shore Hospital, St Leonards, Australia (C Tennant); Medical Psychology Research Unit, University of Sydney, Australia (P Butow, M Price).

M. A. Price (✉) · P. N. Butow · J. Wilson
Medical Psychology Research Unit, School of Psychology, Brennan MacCallum Building (A18), University of Sydney, Sydney, Australia
e-mail: melaniep@psych.usyd.edu.au

S. K. Lo
Faculty of Health, Medicine, Nursing & Behavioural Sciences, Deakin University, Geelong, Australia

Introduction

Women with a family history of breast cancer consistent with an hereditary breast cancer syndrome are at high risk of developing breast cancer. The cumulative risk of developing breast cancer to age 70 is estimated at between 44–78% for carriers of a BRCA1 mutation and between 31–56% for BRCA2 mutation carriers (Antoniou *et al.* 2003).

Despite the increased risk of developing cancer, the research evidence indicates that women from high risk breast cancer families do not have heightened levels of general psychological distress (Butow *et al.* 2005; Coyne *et al.* 2003). With respect to the impact of genetic counselling, education and clinical testing for mutation status, the evidence also indicates that for most, any increase in psychological distress associated with these interventions is modest and transient (Meiser 2005). However, some studies, although not all, have reported elevated levels of cancer specific anxiety or worry in women with a family history of breast cancer, including those from high risk families (Hay *et al.* 2005). While earlier studies indicated there may be a significant impact of cancer anxiety on daily life (Lerman *et al.* 1993; Lerman and Schwartz 1993), more recent studies indicate there is overall only modest elevations of cancer anxiety (Andersen *et al.* 2003; Schwartz *et al.* 2002).

Of clinical concern is the research indicating that higher levels of cancer anxiety or worry, rather than objective risk, is associated with uptake of prophylactic surgery and adherence to screening programs (Andersen *et al.* 2003; Hurley *et al.* 2001; Meiser *et al.* 2000; Stefanek *et al.* 1995; Schwartz *et al.* 1999; Schwartz *et al.* 2005). Thus even if there is a relatively low prevalence of significant cancer worry overall, it is important to understand the factors that effect cancer specific worry in order to design appropriate interventions to target these factors in the promotion of psychological wellbeing and adherence to recommended screening guidelines, and in counselling women regarding the pros and cons of prophylactic surgery. However, very few studies have been conducted exploring predictors of cancer worry.

Most of what is known about the correlates of cancer anxiety and worry comes from studies of risk perception and screening behaviour. Perceived, rather than objective risk, has been found to be positively associated with cancer anxiety, while age and optimism are reported to be negatively associated with cancer anxiety (McGregor *et al.* 2004). There is some evidence to suggest that the experiences associated with having a family history of breast cancer (such as a bereavement), in addition to the more objective risk associated with family history, are both likely to contribute to cancer anxiety (Rees *et al.* 2001). Having a mother die from breast cancer during childhood or adolescence (Erblich *et al.* 2000), being directly involved in the care of a mother (Erblich *et al.* 2000) or sister (van Dooren *et al.* 2005) with breast cancer and a recent diagnosis of breast cancer within the family (van Dooren *et al.* 2005), all make the threat of cancer more tangible and real, and have also been associated with increased cancer specific anxiety. Indeed, many women from high risk breast families report an elevated risk perception which is very hard to shift, even after genetic counselling (Cull *et al.* 1999).

A number of theories have been developed to explain the relationship between risk perception, emotions such as anxiety and worry, and behaviour. Protection Motivation Theory (PMT) is particularly relevant. PMT posits that change in behaviour is motivated by fear, which is mediated through perception of threat, or risk (Rogers 1983). A key goal of genetic counselling is to provide information in order to improve the accuracy of risk perception and reduce distress, and indeed the majority of studies suggest that it often achieves that goal (Cull *et al.* 1999). Informal social support has also been shown to be effective in many areas of health in reducing distress and promoting adjustment (Cohen and Wills 1985). However, no study has comprehensively explored demographic, family history, psychological and social factors associated with cancer worry within a conceptual framework. Furthermore, the relative importance of these factors has not been empirically examined.

On the basis of the PMT and existing literature, a model of cancer worry has been constructed (Fig. 1). This model proposes that a number of factors contribute to a woman's perceived risk, which in turn influences breast cancer worry. This relationship is moderated by the social support a woman receives as well as the experience of genetic counselling which may provide information and reassurance.

The aims of this study were to:

(1) examine levels of cancer worry in unaffected women from high risk breast cancer families;
(2) identify predictors of cancer worry and their relative importance;
(3) test a model of cancer worry, where the predictors of cancer worry, such as family history, biological and psychological factors, are mediated by perceived breast cancer risk.

The hypotheses were that:

(1) a combination of family history, genetic and biological variables and psychosocial variables (perceived breast

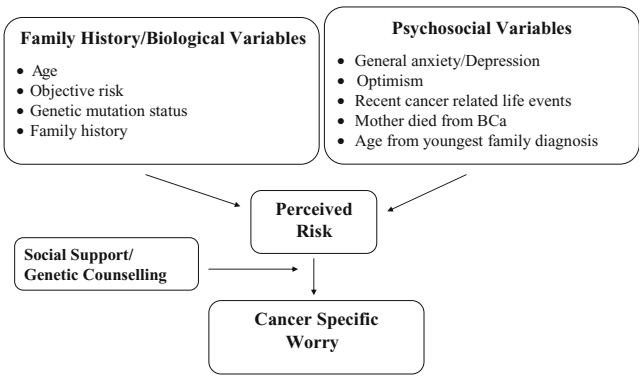

Fig. 1 Proposed model of predicting cancer specific worry mediated via perceived risk

cancer risk, recent family cancer related stress, general anxiety, optimism) would be related to cancer worry in unaffected high risk women;
(2) perceived breast cancer risk would mediate the relationship between this combination of variables and cancer worry; and
(3) genetic counselling and level of social support may moderate the relationship between perceived breast cancer risk and cancer worry.

Materials and Methods

Participants

Women participating in the *K*athleen Cuningham *Con*sortium for Research into *Fa*milial *B*reast Cancer (kConFab), aged between 18–75 years, with adequate English language skills, and with no personal history of cancer (apart from non-melanoma skin cancer or in situ carcinoma of the cervix), were invited to participate in the kConFab Psychosocial Study. The aim of this study is to examine the role of psychosocial factors in the development of breast cancer and to examine psychosocial predictors and outcomes related to being at high risk. The study commenced in August 2001 and is ongoing. Ethics approval for the study has been granted from the following sites in Australia: In New South Wales, the University of Sydney, Hunter New England Area Health Service, St Vincent's Hospital, Sydney West Area Health Service, South Eastern Sydney/Illawarra Area Health Service —both the Eastern and Southern Sections; In Victoria, the Peter MacCallum Cancer Centre, Monash Medical Centre, Royal Children's Hospital, Royal Melbourne Hospital in Victoria; in Queensland, Royal Brisbane Hospital; in South Australia, the Women's and Children's Hospital; in Western Australia, the King Edward Memorial Hospital; in Tasmania, the Southern Tasmania Health and Medical Human Research Ethics Committee. In New Zealand, the Health and Disability, Multi-region ethics committee.

KConFab was established in 1995 to co-ordinate the collection of genetic, epidemiological and clinical data in Australian and New Zealand families with a family history consistent with a dominantly inherited predisposition to breast cancer (Mann *et al.* 2006). Eligibility criteria for families are complex and details can be found at http://www.kconfab.org. Essentially, families require either a dense family history of breast and/or ovarian cancer, or a documented BRCA1/2 mutation. Within each eligible family all those with breast or ovarian cancer, their spouses and first degree relatives older than 18 years are eligible. While recruitment into kConFab requires a family member to attend a Familial Cancer Clinic to be eligible, other recruits from that family do not have to attend a clinic. Epidemiological data are collected at enrolment and blood is collected for BRCA1/2 mutation analysis and is stored for future research. The Clinical Follow-Up Study contacts participants at three yearly intervals, updating epidemiological and clinical data, documenting new cancer diagnoses, genetic mutation testing results and screening behavior (Phillips *et al.* 2005). When a BRCA1/2 mutation is identified by kConFab, all consenting members of that family are informed that a mutation in the family has been found. They are encouraged to attend a Genetic Counselling Centre so as to make an informed decision about being individually tested, and to receive advice about managing their risk; however this is in no way obligatory.

Design and Procedure

Prospective assessment of psychosocial variables, including life event stress, social support, psychological distress, depression, general anxiety, cancer-specific worry, dispositional optimism, perceived risk of developing breast cancer, attitudes toward and uptake of genetic testing and risk-reducing surgery, are undertaken at three yearly intervals. Participation involves completing a questionnaire booklet and a telephone interview at baseline, 3 and 6 years. KConFab and the Clinical Follow-Up Study undertake consent for participants to be contacted by the Psychosocial Study (Butow *et al.* 2005; Phillips *et al.* 2005). Women are mailed a letter of invitation, an information sheet, consent form, the questionnaire booklet, and a reply paid envelope. Telephone interviews are conducted 2–3 weeks after the questionnaires to reduce participant fatigue, while ensuring that measures are sufficiently proximal to be comparable.

Measures

Primary Outcome Variable

Cancer specific worry was assessed using the seven item Intrusive Thoughts subscale of the Impact of Event Scale (IES) (Horowitz *et al.* 1979). Participants were asked about the frequency and severity of intrusive thoughts about being at risk of developing breast cancer/ovarian in the past week, ranging from 'Not at all' to 'Often.' Scores range from 0–35, with a score of 20 or higher considered clinically significant intrusive thoughts (Cella *et al.* 1990). Internal consistency in this sample was 0.92.

Primary Explanatory Variable

Perceived life time risk of developing breast cancer was assessed by asking participants to indicate their perceived

risk on a numerical differential scale ranging from 0 ('No chance') to 100 ('Definitely') (Meiser *et al.* 1999).

Hypothesized Predictors of Perceived Life Time Risk

Demographics Age, educational and marital status were assessed at interview.

Family History/Biological Variables Family history and personal data were obtained from kConFab, including: number of first and second degree relatives diagnosed with breast cancer and who died from breast cancer; whether their mother has ever been diagnosed with breast cancer; absolute age difference of participant from youngest family breast cancer diagnosis; relative risk of breast cancer (calculated using Tyrer-Cuzick algorithm) (Tyrer *et al.* 2004); whether there was a BRCA1/2 mutation in family; personal BRCA1/2 mutation status.

Participants' knowledge (or understanding) of their BRCA1/2 mutation status was determined during the psychosocial interview. Knowledge was critical, since worry could only be affected by mutation status if the participant knew their status. Two summary knowledge variables were calculated. The first was: *correct knowledge of mutation result or not* (participants who could correctly identify their mutation status as positive or negative or no familial mutation identified were classified as correctly knowing their status; participants who thought they were positive and were negative and vice versa were classified as incorrectly knowing; participants who thought they were positive and no familial mutation had been identified were classified as incorrectly knowing). The second summary variable was: *knowing negative mutation status or not* (participants who believed their mutation status was negative, whether or not this was correct, were classified as knowing negative status; those who believed they were positive or did not know their mutation status were classified as not knowing negative status). This variable was considered important because negative mutation status could truly provide participants with the reassurance that their risk was at population levels and was not elevated.

Psychosocial Variables

1. Cancer related life event stress and non-cancer related life event stress during the past three years were assessed using the Life Event and Difficulties Schedule (Brown and Harris 1978), a comprehensive and widely accepted method of objectively assessing the severity of acute and chronic stressor exposure. The semi-structured format utilises qualitative probes to document the context, details, personal meaning, and timing of stressors. Stressors are independently rated for severity of threat (inherent loss experienced in a stressor), without reference to the emotional content of the interview, that potentially introduces bias. Stressors are also coded for dependence on or independence from familial or personal cancer risk. Total 'stress' scores for cancer related and non-cancer-related stressors are calculated by summing the stressors' threat ratings within each category, to reflect both intensity and cumulative impact of stressors (Price *et al.* 2001).
2. General anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (Zigmond and Snaith 1983), which consists of two, seven-item subscales measuring anxiety and depression. High scores indicate greater morbidity. Internal consistency of subscales were 0.86 for anxiety and 0.80 for depression for this sample.
3. Dispositional optimism is measured using the Life Orientation Test, a widely used questionnaire with well-documented psychometric properties (Scheier and Carver 1985). High scores indicate greater optimism. Internal consistency in this sample was 0.81.

Moderating (or Buffer) Variables

1. Social support was assessed using the Duke-UNC Functional Social Support Questionnaire (Broadhead *et al.* 1988), a validated measure of the degree of satisfaction with available support. High scores indicate greater satisfaction with support. Internal consistency in this sample was 0.91.
2. Attendance at genetic counseling was identified by participant self-report.

Approach to Data Analysis

1. Identify predictors of cancer worry and their relative importance;
2. Test a model of cancer worry, where the predictors of cancer worry, such as family history, biological and psychological factors, are mediated by perceived breast cancer risk.

Descriptive statistics was used to describe the prevalence of cancer worry in this sample of unaffected women from high risk breast cancer families (aim 1). In order to achieve aim 2, firstly univariate and bivariate correlation analyses were used to identify individual demographic, family history, biological and psychosocial variables associated with either perceived breast cancer risk or cancer specific

worry, and to assess the degree of association between variables measuring similar constructs. Secondly, variables which were correlated ($p<0.05$) with either breast cancer worry or perceived risk, were entered into a backward stepwise regression analysis (SPSS version 12, SPSS Inc.) with cancer worry as the outcome. Where similar variables were highly correlated, the variable most highly correlated with the outcome variable was included in the backward stepwise regression analysis. In order to achieve aim 3, path analyses were used to test the proposed model of cancer worry, using Amos (version 5). In this analysis, the recursive model was used to depict the relationships shown in Fig. 1.

Results

Sample Demographics

Of 2,107 women eligible for this study, 1,744 (82.8%) returned completed questionnaires and 1,578 (74.9%) completed the life event stress interview. Both baseline questionnaire and interview data were available from 1,437 (68.2%) women and these data were included in the current analyses. Participants were aged between 18–74 years, with a mean age of 44.5 years (SD=12.8). Most were currently married or living as married (76.5%) and over half (52.7%) had post school qualifications (Table I).

Biological and Family History Variables

Breast Cancer Susceptibility Genetic Testing

BRCA1/2 mutation testing was undertaken for all participants as part of the kConFab research program. These were research testing results, rather than personal clinical results and therefore not all women were aware of their results. Only 339 (23.6%) of the sample had a BRCA1/2 mutation identified within the family (Table I). For a personal result to be disclosed, individuals needed to undergo clinical genetic counselling and testing. Of the 339 women identified as having a BRCA1/2 mutation within the family, 156 (46%) were aware of their personal mutation result.

Objective Breast Cancer Risk

Objective breast cancer risk, calculated using the Tyrer-Cuzick algorithm (Tyrer *et al.* 2004) was available from kConFab (Mann *et al.* 2006). These estimates incorporate BRCA1/2 mutation status, family history data and personal epidemiological risk factor data. The median relative risk was 2.7, and given these data were skewed, relative risk was treated as categorical in all analyses (see Table I). As only the highest objective risk category was associated with cancer worry, objective risk was collapsed into two categories for multivariate analyses (less than 10 versus 10+).

Family History

Family history data are summarised in Table I. The average number of first and second degree relatives with breast cancer was 4.1 (SD 2.1) and ranged between 0–15. Six women had confirmed BRCA1/2 mutations within the family but no verified breast cancer cases. The average age of the youngest breast cancer diagnosis in the family was 37.6 years. Nineteen percent of the sample had a mother who had died from breast cancer.

Psychosocial and Risk Perception Variables

Table II provides a descriptive summary of psychosocial and risk perception variables. Overall, levels of cancer worry were low, with a sample mean of 5.5 (SD=7.1) on a scale of 0–35. Surprisingly, 36.2% scored zero (i.e., no intrusive thoughts about being at high risk of breast cancer within the last week), while 5.2% scored within the clinically significant range (above 20). Cancer related life event stress scores for the previous three years ranged between 0–16, with a mean of 1.8 (SD=2.8). The mean perceived life time risk of developing breast cancer was 50.3%, with the full range of 0–100 nominated.

Predictors of Cancer Specific Worry

Table III shows correlations between potential predictor variables, and cancer worry and perceived risk. Where variables were inter-correlated, such as those related to family history and genetic testing, those with the strongest correlation with cancer worry or perceived risk were considered for inclusion. The 16 variables included in regression analysis were: perceived risk, age, education, marital status, number of relatives diagnosed with breast cancer, objective risk of breast cancer (<10.0 versus 10.0+), absolute age difference from the youngest family diagnosis, correctly knowing genetic mutation result, knowing negative mutation status or not, degree of recent cancer related life event stress, degree of non-cancer related life event stress, have attended genetic counselling or not, general anxiety, depression, optimism, and social support. Manual backward stepwise regression was conducted (criteria for variable removal was $p<0.1$), the final model including eight variables (Table IV). The overall goodness-of-fit of this model was 0.273 (adjusted $R^2=0.268$), indicating the model explained 26.8% of the variance in cancer worry.

Table I Descriptives of Demographic, Family History, Genetic and Biological Variables with Cancer Specific Worry (N=1,437)[a]

Variables	*n* (valid %)	
Age (years)		
<30	172 (12.0)	
30–39	374 (26.0)	
40–49	397 (27.6)	
50–59	279 (19.4)	
60–69	175 (12.2)	
70+	40 (2.8)	
Marital Status		
Not Married	332 (23.1)	
Married/Defacto	1,099 (75.5)	
Education		
< 9 years	64 (4.5)	
9–10 years	358 (24.9)	
11–12 years	257 (17.9)	
Technical/College	453 (31.5)	
University	305 (21.2)	
Research genetic mutation result		
BRCA1/2 mutation positive	120 (8.4%)	
BRCA1/2 mutation negative	219 (15.2%)	
No mutation identified in family	1,098 (76.4%)	
Knowledge of mutation result		
Individual tested and knows mutation positive	70 (4.9%)	
Individual tested and knows mutation negative	86 (6.0%)	
BRCA1/2 in family, but individual not tested so does not know result	183 (12.7%)	
No BRCA1/2 mutation identified in family, but Reported 'knowing' result	78 (5.4)	
No BRCA1/2 mutation identified in family/Not tested[b]	1,020 (71.0%)	
Relative Risk (Breast Cancer)		
< 1.0	113 (8.2%)	
1.0–1.9	258 (18.7%)	
2.0–2.9	439 (31.8%)	
3.0–9.9	403 (29.2%)	
10.0+	166 (12.0%)	
Mother died from Breast Cancer		
Yes	271 (18.9%)	
No	1,166 (81.1%)	
Perceived Risk Breast Cancer		
0–20	301 (20.9)	
21–40	169 (11.8)	
41–60	492 (34.2)	
61–80	339 (23.6)	
81–100	123 (8.6)	
	Mean (SD)	Range
Number of 1st and 2nd degree relatives ever diagnosed with breast cancer[b]	4.1 (2.1)	0–15
Youngest age family member diagnosed[c] in years	37.6 (8.1)	15–68
Age (in years) difference from youngest family breast cancer diagnosis[c]	7.1 (15.3)	−28 to +57

[a] Due to missing values, the percentages do not always reflect the total
[b] 6 women (0.4%) had confirmed BRCA1/2 mutations within the family, but no verified breast cancer cases
[c] Women with no breast cancer cases in family not included

Model Testing

Variables identified as significant predictors of cancer worry in the regression analysis were included in a recursive path analysis, to test the hypothesised model (Fig. 1). As shown in Fig. 2, the goodness-of-fit of this model was poor, explaining only 9% of the variance for perceived risk and 10% of the variance for cancer specific

Table II Descriptive Statistics of Psychosocial and Risk Perception Variables (N=1,437)

Variable	Mean (SD)	Range
Cancer specific worry (intrusive thoughts)	5.5 (7.1)	0–35
Perceived breast cancer risk (lifetime)	50.3 (26.1)	0–100
General anxiety	6.6 (4.1)	0–20
Depression	3.8 (3.2)	0–18
Disposition optimism	20.1 (5.5)	0–32
Cancer related life event scores (past 3 years)	1.8 (2.8)	0–16
Non cancer related life event scores (past 3 years)	5.8 (5.6)	0–46
Social support	30.7 (7.5)	8–40

worry. However, the percentage of total variation explained by the model was far less than the regression model reported above. Hence, we used path analysis that tested the model of a direct relationship between all of the predictor variables and cancer worry, which explained 24% of the variation in cancer worry (see Fig. 3).

Discussion

The levels of cancer specific worry in unaffected high risk women was in general low, despite women reporting their perceived average lifetime chance of developing breast cancer as 50%. In this study, only about 5% of women reported clinical levels of cancer worry, comparable to those previously reported by Schwartz *et al.* (1999) and Isaacs *et al.* (2002) in unaffected women from high risk breast cancer families.

Although perceived risk and cancer worry were correlated, there is no evidence to support the hypothesis that perceived risk mediates the impact of other predictor variables on cancer worry.

This is in contrast to the premise of Protection Motivation Theory, which suggests that worry and anxiety is primarily mediated by perception of threat or risk. This is, however, consistent with models of adaptation to illness (or in this case risk of illness), such as the self regulation model of Leventhal *et al.* (1984), which proposes that adjustment is not only the result of a person's cognitive assessment of a health threat, but also the emotional response to that threat. Thus the experience of family history is likely to impact on women's emotional response, perhaps independently of their perceived risk.

Our results suggest that women's anxiety or worry about breast cancer is influenced by a range of factors, including risk perception, and that these experiences have an independent affect on worry, over and above a woman's sense of her risk. Thus even if a woman is able to quote her risk accurately and understands that she is in no way certain of developing cancer, if she has had very difficult experiences in her family with cancer, or is in general, a "worrier," then her breast cancer worry might be elevated.

In fact, the strongest predictor of cancer worry was higher general anxiety. General anxiety was significantly

Table III Selected Correlation Matrix for Cancer Specific Worry, Perceived Breast Cancer Risk and Potential Predictor Variables

	Cancer Worry	Perceived Risk
Cancer specific worry	1	
Perceived breast cancer risk	0.28 (p<0.001)	1
Age	−0.11 (p<0.001)	−0.30 (p<0.001)
Education	−0.08 (p=0.003)	0.06 (p=0.03)
Marital status	−0.01 (p=0.70)	0.02 (p=0.36)
Objective risk >10[a]	0.17 (p<0.001)	0.11 (p<0.001)
No. first degree relatives with breast cancer	0.03 (p=0.24)	−0.07(p=0.005)
No. first and second degree relatives with breast cancer	0.02 (p=0.44)	−0.02 (p=0.51)
Knows BRCA1/2 result[a]	0.01 (p=0.68)	−0.07 (p=0.006)
BRCA1/2 positive[a]	0.04 (p=0.14)	0.04 (p=0.18)
BRCA1/2 negative[a]	−0.01 (p=0.64)	−0.09 (p=0.001)
Age difference from youngest diagnosis in family	−0.001 (p=0.98)	−0.25 (p<0.001)
Cancer related stress	0.20 (p<0.001)	0.05 (p=0.08)
Non cancer related stress	0.02 (p=0.40)	0.06 (p=0.02)
General anxiety	0.44 (p<0.001)	0.20 (p<0.001)
Depression	0.28 (p<0.001)	0.19 (p<0.001)
Optimism	−0.29 (p<0.001)	−0.25 (p<0.001)
Social support	−0.24 (p<0.001)	−0.16 (p<0.001)

[a] Categorical variable—nonparametric correlation coefficient reported

Table IV Multivariate Step-wise Regression Model[a]

Predictors of Cancer Specific Worry	B	SE	Partial correlation	*P*
General anxiety	0.65	0.05	0.40	<0.001
Perceived breast cancer risk (lifetime)	0.05	0.01	0.21	<0.001
Cancer related life event scores (past 3 years)	0.45	0.07	0.19	<0.001
Objective risk >10	2.59	0.58	0.13	<0.001
Closer age to youngest BCa diagnosis in family	0.04	0.01	0.09	0.001
Correctly knows personal BRCA1/2 mutation result	1.75	0.57	0.09	0.003
Correctly knows BRCA1/2 negative	2. 15	0.69	0.09	0.002
Marital status	0.89	0.43	0.06	0.040

[a] Only variables significant in the regression were left in the model, all non-significant variables had been removed in earlier steps

correlated with other predictors of cancer worry, including perceived risk (r=0.20), recent non-cancer related life event stress (r=0.23), and to a lesser extent cancer related life event stress (r=0.08). This suggests that women who respond generally to life with anxiety are also likely to respond to other stresses, such as being at risk of familial breast cancer, with anxiety.

As hypothesised, the impact of experiences related to familial breast cancer within the last three years, contributed significantly to cancer worry. The measure of cancer related life event stress included a weighting according to the ongoing impact of these cancer events, such as involvement in decision-making, treatment or provision of care. This is consistent with recent studies of women with a family history of breast cancer (van Dooren *et al.* 2005) and is the first report of the comparative importance of personal experiences and the family history of events. The implication is that mere counting of cancer related events, or reporting of family history, will not sufficiently reflect the impact of these events on the individual.

Interestingly, being closer in age to the age of the youngest family diagnosis was also predictive, suggesting that people interpret their own place within the family history and possibly alter their perceptions of their immediate risk, and therefore worry, accordingly. As the gap between this first diagnosis and their own age widens, they feel less vulnerable. This result is consistent with findings by Gerend *et al.* (2004), who reported that women who perceived themselves' to be dissimilar to women with breast cancer perceived themselves to be less vulnerable.

Consistent with previous studies, perceived risk and objective risk were both independent predictors of cancer worry. Objective risk, calculated using the Tyrer-Cuzick algorithm, was based on mutation status, family history and epidemiological risk factors. Only women with an objective risk of greater than ten experienced higher breast cancer worry. Of note, all women in this study were from high risk families, with 73% having an objective relative risk greater than two. The proportion of women with lower levels of objective risk was small, and this may limit the predictive power of this variable.

Knowledge of mutation status revealed itself to be a complex construct with a number of important associated issues. Overall, those who knew they were either BRCA1/2 mutation positive or negative reported lower cancer worry compared with the rest of the sample who did not know their result (including women where no familial mutation had been identified). In fact, women who knew they were mutation positive reported similar levels of cancer worry to those where a familial mutation had not been identified. This supports previous findings which have shown the highest levels of distress in those who chose not to know their mutation status (decliners) (Lerman *et al.* 1996). Lerman *et al.* posited that learning one's mutation status may reduce prolonged uncertainty and thereby enhance quality of life. This may

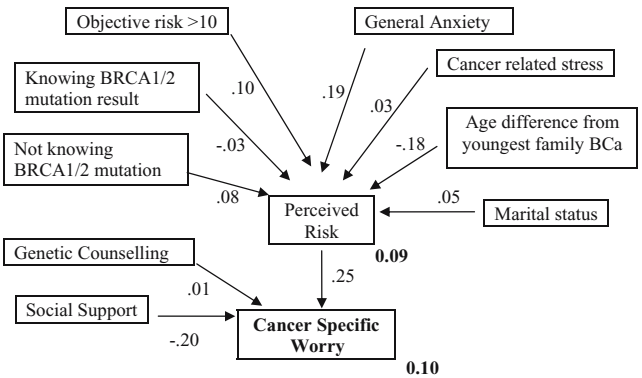

Fig. 2 Path analysis of predictors of cancer specific worry mediated via perceived risk

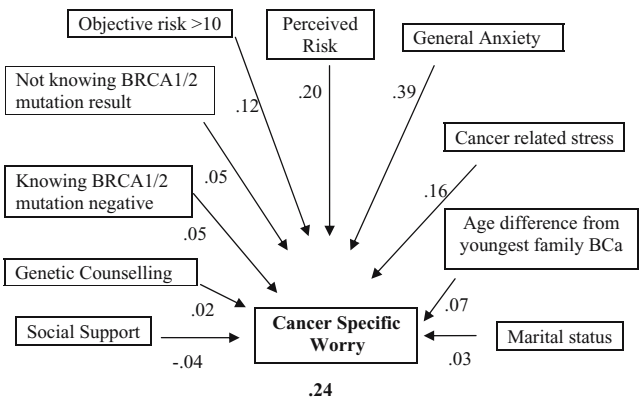

Fig. 3 Path analysis of predictors of cancer specific worry

be true even when the result reveals a risk-conferring mutation. Decliners avoid knowledge but face ongoing uncertainty while those who cannot be tested because a family mutation has not been found are denied certainty.

Not having the support of a close family relationship was a significant predictor of cancer worry, supporting our hypothesis that social support may act as a buffer against the anxiety associated with being at high risk. Genetic counselling did not emerge as a predictive variable. However, this should not be interpreted as meaning that genetic counselling cannot reduce cancer worry; rather that in the current study genetic counselling was correlated with receiving a mutation result, therefore reducing its independent explanatory power in our model.

One of the strengths of this study of women at high risk of breast cancer lies in the study population. While not truly a population based sample, the utilisation of kConFab as the source of recruitment minimised the self-selecting clinic attendee biases of other studies. The distribution of education level of the current sample approximates that of the wider Australian community. However, some limitations should be noted. Firstly, the intrusive thoughts subscale of the Impact of Events Scale, used to assess cancer worry, targets a particular form of cancer related anxiety and such anxiety may manifest in different ways from intrusive thoughts. The inclusion of other measures may have improved sensitivity. Secondly, the primary aim of the study was to identify the relative importance of predictors of cancer worry and to test the model of a mediating role for perceived risk. Therefore, some issues, such as the individuals' understanding of their mutation results and the relationship to genetic counselling, have not been fully examined here.

The study findings have clinically significant implications. Firstly, a number of variables, other than perceived risk, independently impact on level of cancer worry and may be useful to identify those at risk of elevated levels of cancer worry, to guide the development of appropriate interventions, and to inform the counseling process related to screening and prophylactic surgery decisions. Secondly, these results suggest that interventions targeted toward reducing cancer worry should incorporate strategies which target emotional responses, as well as support, education and information about hereditary breast-ovarian cancer risk.

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