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Risk-reducing surgery in women with familial susceptibility for breast and/or ovarian cancer

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ABSTRACT

This multicentre study examined uptake of bilateral risk-reducing mastectomy (BRRM) and bilateral risk-reducing oophorectomy (BRRO) in women at increased risk for breast and/or ovarian cancer who had attended a familial cancer clinic (FCC) between January 1999 and June 2000. Eligible women ($N = 396$), were mailed a questionnaire assessing: BRRM and BRRO details; risk perception; and anxiety. Family history, genetic testing and risk assessment were abstracted from medical records. Surgery was cross-tabulated with demographics, risk perception and anxiety with either Fisher's exact test or the exact form of the Mantel–Haenszel test (for ordinal factors) used to investigate for associations. Ordinal logistic regression was used with continuous-scale covariates. In total, 130 women were lost to follow-up leaving 266; of these 182 (68.4%) responded. Mean follow-up time was 3.73 years. The BRRM rate was 4.4%; with no difference found between moderate and high-risk groups. BRRM was associated with increasing numbers of affected relatives ($P = 0.025$). BRRO was undertaken by 17.3%, more commonly in women older than 40 years of age ($P = 0.023$) and with a *BRCA1/2* mutation ($P = 0.017$). Women who underwent BRRM ($P = 0.052$) or BRRO ($P < 0.001$) had a lower post-procedure risk perception than those who did not. During the timeframe of this study, risk-reducing surgery was undertaken by a small percentage of Australian women at increased risk for breast and/or ovarian cancer who attended FCCs. Family cancer history and mutation status were associated with uptake.

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1. Introduction

In westernized countries, breast cancer affects between one in nine and one in eleven women, and ovarian cancer affects one in 100 by 75 years.[1,2] Women who have a strong family history of these diseases and/or carry a mutation in a breast and ovarian cancer predisposition gene (*BRCA1* or *BRCA2*) have a much higher risk for one or both cancers.[3] In such

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women, bilateral risk-reducing mastectomy (BRRM) reduces the risk of breast cancer by up to 95%.[4–6] In women who carry a mutation in *BRCA1* or *BRCA2*, bilateral risk-reducing salpingo-oophorectomy (BRRO) reduces the risk of a BRCA-associated gynaecological cancer (ovarian, fallopian tube and primary peritoneal) by up to 95%.[7,8] Salpingo-oophorectomy also reduces the risk of breast cancer in mutation carriers by approximately 50%.[7–9]

The uptake of BRRO, as a risk management strategy, is extremely varied, with reported rates of between 13% and 78%.[5,7,10–12] Most reports, to date, reflect single institution experience in closely followed cohorts[5,7,10,11] and also include women with a previous history of breast cancer.[7,11] The acceptability of BRRM as a strategy for breast cancer risk management appears culturally varied[13–16] with reports of uptake ranging from 0% in an extended (predominantly Mormon) North American kindred [11] to 55% of Dutch women.[5]

Consultation in Family Cancer clinics (FCCs) enables women to discuss risk management strategies, such as risk-reducing surgery, chemoprevention and cancer screening. While the addition of breast magnetic resonance imaging to mammography may improve the efficacy of breast screening, if mortality reduction is used as the endpoint, the efficacy of breast and ovarian cancer screening remains to be proven as beneficial in this high-risk group.[17–21] Tamoxifen is not approved by the Australian Therapeutic Goods Association for chemoprevention and is infrequently prescribed to Australian women for chemoprevention, apart from in the limited setting of the IBIS (International Breast Cancer Intervention Study) I trial.[22] Thus, it is important to know the uptake rates for risk-reducing surgery in women attending FCCs, as currently this is the major strategy proven to reduce the morbidity and possibly mortality of breast and ovarian cancer. This study examined the rate of uptake and consideration of BRRM and BRRO in women assessed as being at moderate or high-risk for breast and/or ovarian cancer development on the basis of their family history. Potential influencing factors for uptake and consideration of future uptake were examined, together with a comparison of anxiety and risk perception between those who chose surgery and those who did not.

2. Patients and methods

2.1. Subjects

Subjects were a consecutive sample of women, who attended one of six FCCs in New South Wales and Victoria, Australia between January 1999 and June 2000. The consultation included both risk assessment and risk management components and all eligible women were assessed as being at either moderate (estimated lifetime risk 12.5–25%) or high-risk (estimated lifetime risk 25–85%) for hereditary breast cancer.[23] A woman is assessed as at high-risk for breast cancer development if she has: (1) breast or ovarian cancer diagnosed in three or more first- or second-degree relatives on the same side of the family; or (2) two or more first- or second-degree relatives on the same side of the family with at least one high-risk feature (bilateral breast cancer, onset of breast cancer before age 40 years, breast or ovarian cancer in one individual, Jewish ancestry, breast cancer in a male relative), or; (3) a demonstrated germline mutation in a high-risk breast cancer predisposition gene (*BRCA1*, *BRCA2*). A woman is considered at moderate risk for breast cancer if she has either: (1) one or two first-degree relatives on the same side of the family diagnosed with breast cancer before the age of 50 years (without any additional high-risk features) or; (2) two first- or second-degree relatives on the same side of the family, diagnosed with breast or ovarian cancer (without any additional high-risk features). Women were assessed as at high-risk for ovarian cancer if the estimated lifetime risk was greater than 5%.[23] These estimates are based on a woman fulfilling the following risk-assessment criteria: (1) one first degree relative diagnosed with epithelial ovarian cancer in a family of Ashkenazi Jewish ancestry; or (2) two first or second-degree relatives on the same side of the family diagnosed with breast or ovarian cancer, especially if one or more of the above mentioned high-risk features occurs on the same side of the family or; (3) a member of a family in which the presence of a high-risk ovarian cancer gene such as *BRCA1*, *BRCA2* has been demonstrated.

Women were ineligible if they had a personal history of invasive cancer (excluding non-melanomatous skin cancer), if they were enrolled in either the IBIS I breast cancer prevention trial[24] or a national study of high-risk hereditary breast and ovarian cancer families (kConfab) (as kConFab participants complete similar questionnaires on a regular basis as part of longitudinal follow up, it was felt by the investigators that this study would potentially over burden these women);[25] were non-English speaking (as the study required completion of a detailed questionnaire), or had intellectual or psychiatric disabilities preventing informed consent. Study participants provided written informed consent and the study protocol was approved by ethics committees at all participating sites.

2.2. Data collection

Data were obtained by postal self-report questionnaire and abstraction of some data from medical records. A package containing a covering letter, participant information and consent form, questionnaire and stamped, addressed return envelope was mailed to eligible women between March and September 2003. For individuals from whom a completed questionnaire had not been received after four weeks, a reminder letter and second copy of the questionnaire were mailed. To determine which individuals never received the package due to incorrect current address details; the reminder package was sent via registered mail, allowing an automatic return of undeliverable questionnaires for half the centres and follow-up phone calls attempting to confirm whether the participant was still living at that address for the remaining centres.

2.3. Measures

2.3.1. Demographic information

Demographic information collected by self-report included: age, employment status, household income, level of education, marital status, ethnicity, and number of offspring. Med-

ical records were abstracted for: genetic testing, assessment of risk for breast and ovarian cancer and family history of breast and ovarian cancer.

2.3.2. *Risk-reducing surgery*

Women were asked to provide details about any mastectomy or oophorectomy for either therapeutic or risk-reducing indications. Information about whether family members had also undergone risk-reducing surgery was obtained. Women who had not already had risk-reducing surgery were asked to indicate whether they would consider such surgery in the future.

2.3.3. *Risk perception*

Women were asked to estimate the risk for developing breast cancer in a woman of population risk and then by comparison, were asked to estimate their own risk using the same scale. The scale was developed and validated for assessment of breast cancer risk perception in a high-risk population[26] and adapted for the purposes of this study, by the investigators, to assess ovarian cancer risk perception.

2.3.4. *Impact of events*

The intrusion subscale of the Impact of Events Scale, developed by Horowitz and colleagues for the assessment of current subjective distress about a given stressor,[27] was used to assess psychological distress. The specific stressors, in this study, were development of breast and/or ovarian cancer. Scores were added with higher scores indicating greater levels of anxiety.

2.4. *Statistical analysis*

Fisher's exact test was used to check for differences in the response status groups (respondents, non-respondents and lost-to-follow-ups). The association of response status group with age at first consultation was tested using a one-way analysis of variance and pairwise *t*-tests of the group means. Only women at increased risk for ovarian cancer or those for whom oophorectomy might be recommended to reduce breast cancer risk (i.e. those with a family history of ovarian cancer and or those with a known mutation in *BRCA1* or *BRCA2*) were included in analyses for oophorectomy. Women were only included in the analysis of consideration of risk-reducing mastectomy or oophorectomy if the subject had at least one breast and one ovary, respectively.

The incidence of BRRM and BRRO were cross-tabulated with demographic factors, risk perception scores and the intrusion of events subscale for psychological distress. Fisher's exact test was used to investigate associations between risk-reducing surgery binary outcome variables and each factor. When the factor was ordinal, the Mantel–Haenszel χ^2 test was used to investigate associations between risk-reducing surgery and the ordinal factor – an exact test was used but *P*-values were sometimes estimated via Monte Carlo estimation. The association between the intrusion of events subscale, which has possible values from 7 to 28 in increments of one, and potential uptake of risk-reducing surgery, was also investigated via the ordinal logistic regression of the potential for uptake of risk-reducing surgery on the values of the subscale (a discrete-valued covariate). Intentions for future BRRM and BRRO were also cross-tabulated with the same factors and associations investigated with Fisher's exact test with the methods described above.

3. Results

3.1. *Subjects*

Four hundred and forty-two women were seen in one of six participating FCCs for an initial risk assessment appointment between January 1999 and June 2000 (inclusive). Forty-six women were ineligible for the study: participation in alternate study,[36] assessed as low-risk for breast and ovarian cancer,[7] non-English speaking,[1] and failed attendance for risk management consultation.[2] Of the remaining 396 women, 130 were lost to follow-up (due to changed address details). Of the 266 women who received the study package 182 (68.4%) responded to the self-report questionnaire. The mean duration of follow-up was 3.73 years (SD ± 0.65 years).

The mean age at time of first risk management consultation was significantly older in the respondent group (42.5 years) than the lost to follow-up group (37.6 years) ($P < 0.001$) with no significant difference between the means of the other two groups (data not shown). No significant associations between risk category: access to genetic testing at the time of risk management assessment (women with no living or willing affected relatives available to pursue mutation detection and those who had a family member who had received an uninformative result, were generally not offered genetic testing in Australia at the time of the study); results of genetic testing; numbers of first and second-degree relatives with histories of breast or ovarian cancer; and response status were found (data not shown). Characteristics of respondents are outlined in Table 1. Among responders, 61 were at moderate-risk and 121 at high-risk for breast cancer development while 52 were assessed as being high-risk for ovarian cancer. For demographic measures other than mutation status, there were no significant differences found between women at moderate and those at high-risk. For the 14 women who had a mutation in either *BRCA1* or *BRCA2,* 12 recalled having had a positive test result, one did not recall any abnormal gene being found while a further subject did not recall genetic testing ever having been performed.

3.2. *Risk-reducing mastectomy*

A total of 180 of the 182 respondents were assessable for BRRM with missing data for both breasts for two women. A further four women completed details for only one breast, but as all four indicated they had not undertaken a risk-reducing mastectomy on the side they completed details for, they have been included in the analysis for uptake of '*bilateral*' mastectomy. Eight women reported having had bilateral mastectomies, seven for risk-reducing purposes and the eighth for "therapeutic reasons" (multiple biopsies for benign fibrocystic breast disease). As the indication for removal of her breast tissue was not for carcinoma, for the purposes of this study, this subject has been recorded as having had a BRRM. Three women reported the date of their surgery was prior to their risk assessment and management consulta-

Table 1 – Demographic features of respondents by risk category and in total

Demographic feature	Mod risk[a] (Group total = 61)		High risk[a] (Group total = 121)		Total (Group total = 182)	
	n	%	*n*	%	*n*	%
Age (years) at time of questionnaire completion						
Median	48		44		45	
Range	23–73		22–74		22–74	
<30	3	5.0	11	9.2	14	7.8
30–39	12	120.0	29	24.4	41	22.9
40–49	17	28.3	39	32.8	56	31.3
50–59	20	33.3	27	22.7	47	26.3
60+	8	13.3	13	10.9	21	11.7
Employment						
No	11	19.0	33	28.0	44	25.0
Full-time	28	48.3	46	39.0	74	42.0
Part-time	19	32.8	39	33.1	58	33.0
Annual Family Income ($AUD)						
<20000	4	7.0	16	13.9	20	11.6
20000–40000	9	16.0	23	20.0	32	18.6
40000–60000	19	33.3	23	20.0	42	24.4
>60000	25	44.0	53	46.1	78	45.3
Education						
Partial secondary school or less	10	16.9	23	19.5	33	18.6
Completed secondary school	7	12.0	23	19.5	30	16.9
Vocational training/ partial degree	18	30.5	30	25.4	48	27.1
Tertiary	24	41.0	42	36.0	66	37.3
Marital status						
Never married	4	6.8	13	11.0	17	9.6
Married	41	69.5	81	68.6	122	68.9
Living as married	7	12.0	9	7.6	16	9.0
Separated	2	3.4	1	0.8	3	1.7
Divorced	5	8.4	11	9.3	16	9.0
Widow	0	0	3	2.5	3	2
Offspring						
0	16	27.1	22	18.8	38	21.5
1	12	20.3	17	14.5	29	16.5
2	15	25.4	39	33.3	54	30.7
3	12	20.3	32	27.4	44	25.0
⩾4	4	6.8	7	6.0	11	6.3
Offspring living at home						
0	16	37.2	21	22.6	37	27.2
⩾1	27	62.8	72	77.4	99	72.8
Genetic testing – subject interpretation						
Unsure if testing performed	6	9.8	9	7.7	15	8.3
Testing not performed	52	85.2	74	62.2	126	70.0
Testing performed	3	4.9	36	30.3	39	21.7
Unsure if abnormal gene found	0	0	6	17.6	6	16.7
No abnormal gene found	2	100	12	35.3	14	38.9
Abnormal gene found	0	0	16	47.1	16	44.4
Genetic testing – centre results						
No genetic testing possible[b]	59	96.7	73	60.8	132	72.9
Genetic testing possible	2	3.2	47	39.2	49	27.1
Result not known to the patient	0	0	15	34.9	15	33.3
Negative result known to patient	2	100	14	32.6	16	35.6
Positive result known to patient	0	0	14	32.6	14	31.1

Mod, moderate; AUD, Australian dollars; *n*, number.

a Percentages are based on the number of women per risk category who completed the specific question and are rounded to one decimal place.

b In Australia genetic testing is generally not available to moderate risk women or those from families where there is no living affected family member to test.

tions while the other five took place afterwards. The mean time from first risk management consultation to surgery was −4.28 years and the median time was 0.57 years (range −24.25 years to +3.14 years). The rate of mastectomy (for all reasons) was estimated to be 4.4% (95% CI 1.9–8.3) of all women with no significant difference in the rate between moderate (2 of 61) and high-risk (6 of 119) women ($P = 0.718$). The uptake appeared to vary between centres, from 9.4% (5 of 53) in one centre to 0% in 2 centres (0 of 31 and 0 of 17) with one subject from each remaining centre, however this was not statistically significant. All but one of the women were over 40 years old at the time of their BRRM (median age 46 years, range 28–50 years).

A significant association was seen between uptake of BRRM (0%, 3% and 13%) and number of first-degree relatives affected by breast cancer (0, 1, 2 or more) ($P = 0.025$) however no association was seen between uptake of BRRM and number of relatives who had died from breast cancer. Women who reported BRRM tended to give lower estimations of their own cancer risk than those who had not undertaken the procedure ($P = 0.052$) (5/8 women who had undertaken BRRM indicated their cancer risk was 1/10 or lower compared with 44/165 women who had not undergone BRRM).

3.3. *Risk-reducing oophorectomy*

Of the 182 questionnaire respondents, 52 had a family history of ovarian cancer or a known *BRCA1* or *BRCA2* mutation and were therefore eligible for assessment of uptake of BRRO. Of these, 12 (23%) reported having had both ovaries removed, nine (17.3% of the subgroup) for a risk-reducing rather than therapeutic indication (95% CI 9.1–29.6) with two reporting having had both ovaries removed before their first risk management consultation. The mean time from first risk management consultation to surgery was 0.28 years and the median time was 1.07 years (range −5.64 years to +3.27 years). The median age at oophorectomy was 44 years (range 37–52 years).

BRRO was more likely to have been performed in women over 40 years ($P = 0.023$) and in women who had a mutation in either *BRCA1* or *BRCA2* ($P = 0.017$). The perceived risk for ovarian cancer (post-procedure) was lower in those who had undergone BRRO than in those who had not ($P < 0.001$) with 89% rating their risk as 1 in 20 or lower. In comparison, 63.4% (26 of 41) of women who had not undergone BRRO reported their risk as 1 in 6 or higher. As for BRRM, there appeared to be a difference in uptake of BRRO between centres with 41% (7/17) from one centre and another 16% (1/6) and 12% (1/8) in a further two centres, however this did not reach significance ($P = 0.415$). No significant association was found with other measured factors (employment, family income, education, presence or absence of a partner, presence or absence of cohabiting children, number of first-degree relatives with a history of ovarian cancer, and anxiety).

3.4. *Consideration of future BRRM*

This analysis included 168 women (8 women who had previously had a BRRM were excluded and a further 6 subjects did not complete the questions). Twenty-seven women (16.1%) reported that they would consider BRRM in the future (Table 2) with no significant difference between likelihood of consideration of BRRM and risk category ($P = 0.145$).

Women who definitely would consider future BRRM were more likely to have higher scores for cancer specific anxiety ($P < 0.001$) than women who would not or were undecided as to whether they would undergo the procedure. Women who definitely would not consider mastectomy were more likely to rate their own risk lower than those who indicated they would consider future BRRM ($P = 0.035$).

3.5. *Consideration of risk-reducing oophorectomy*

Thirty-nine of the 52 women at high-risk for ovarian cancer were included in this analysis (12 excluded for previous bilateral oophorectomy, missing data for one woman). Eleven (28.2%) women reported that they would consider BRRO, with 3 (7.7%) indicating they would not consider this procedure (Table 2). There were no significant associations between measured factors and consideration of oophorectomy.

Table 2 – Consideration given to future risk-reducing mastectomy and oophorectomy by risk group

	Mod risk		High risk		Total[a]	
	n	%	*n*	%	*n*	%
BRRM						
Yes	11	18.6	16	14.7	27	16.1
Perhaps	8	13.6	30	27.5	38	22.6
Unsure	19	32.2	24	22.0	43	25.6
No	21	35.6	39	35.8	60	35.7
Total	59		109		168[a]	
BRRO						
Yes	–	–	11	28.2	11	28.2
Perhaps	–	–	14	35.9	14	35.9
Unsure	–	–	11	28.2	11	28.2
No	–	–	3	7.7	3	7.7
Total			39		39[a]	

Abbreviations as in Table 1.
a Total reflects all subjects for whom there was interpretable data available.

4. Discussion

During the timeframe of this study, a minority of Australian women assessed in a FCC as being at increased risk for breast and/or ovarian cancer elected to undergo risk-reducing surgery. In keeping with most other studies, we found a low rate (4.4%) of uptake of BRRM.[10,11,28,29] Much higher rates (approximately 55%) have been reported among women with a known deleterious mutation from the Netherlands[5,30] and in two of four centres in the UK.[12] Differences in physician recommendations between institutions may be one factor influencing uptake.[31] Watson and colleagues[12] found considerable variation in the percentage of women from different centres electing to undertake BRRM, with reports of 42% from one site to 13% or less from the other participating sites. All other studies published to date reflect single institution experience of BRRM.[5,11,28,30] In our multicentre study, the proportions of women undergoing BRRM were not significantly different between centres, but the power to detect a difference was low due to the small number of BRRMs in the study.

While the risk reduction associated with a BRRM is well documented, views on the appropriateness of such surgery have been divided among the medical community.[14] It is likely that in such a specialized population (women at increased genetic risk for breast cancer) that all women within each centre will receive similar advice regarding risk management. One report of audio taped genetic counselling sessions in Australian FCCs found that BRRM was discussed in only 24% of consultations.[32] 'Non-discussion' of mastectomy as a management strategy may be interpreted by women as an indirect recommendation against surgery in favour of surveillance.[33] As part of the study protocol, BRRM was discussed with all women in the two Dutch studies and in the study reported by Scheuer and colleagues,[5,28,30] for the remaining published studies the specifics of the discussion with individuals are not clear.[10–12] No study, to date, has examined patient interpretation of recommendations received, which would provide an indication of the impact physician attitude might have on decision-making.

When compared to uptake of BRRM, a greater number of women elect to undergo BRRO,[11,12,28,30] indicating that oophorectomy may be a more acceptable risk management strategy. In this study 17.3% of women at increased risk for ovarian cancer had undergone oophorectomy, considerably lower than most other reports.[7,11,12,28,30] This may be explained, in part, by the characteristics of our study sample in that all other studies included a much greater percentage of women with known deleterious mutations in *BRCA1* and *BRCA2*, a known mutation being associated with uptake of oophorectomy in this study ($P = 0.017$). For many women, genetic testing is not helpful in assisting decision-making regarding risk-reducing surgery, either because genetic testing has not been possible (in Australia mutation detection is usually restricted to families that have a living affected individual) or because testing has been uninformative. The lower rate may reflect that for women where genetic testing has not been useful, oophorectomy is less likely to be an acceptable strategy for risk management.

We found that women were more likely to undergo BRRO after age 40 years than opt for surveillance ($P = 0.023$), as has been previously reported by others.[12,28] Guidelines for ovarian cancer surveillance recommend a combination of transvaginal ultrasonography with serum CA-125.[18,34] To date, the results of studies examining the efficacy of ovarian screening have been disappointing.[18] Clinicians may therefore have a bias when relaying potential risk management strategies to women at risk, with an emphasis toward BRRO rather than surveillance.

The experience of seeing other family members affected by cancer is likely to contribute to an individual's perceptions of risk and cancer specific anxiety.[35,36] In keeping with this, there are reports that women who elect to undergo risk-reducing surgery (mastectomy or oophorectomy) have greater numbers of affected first and second-degree relatives with breast or ovarian cancer than women who elect to maintain high-risk surveillance.[28,29,37] We too found that women who underwent mastectomy ($P = 0.025$) had a greater number of affected family members than women who elected to undergo surveillance. Almost all the women assessed as being at risk for ovarian cancer had at least one first-degree relative with a history of ovarian cancer and therefore similar analyses were not meaningful for oophorectomy. We also found that those women with greater levels of cancer specific anxiety were more likely to indicate that BRRM would be something they would consider in the future ($P < 0.001$). Similarly women with a low perception of their breast cancer risk were more likely indicate that they would not consider mastectomy as a risk management strategy ($P = 0.035$). In contrast, like others,[6] we did not find that BRRM was associated with objective breast cancer risk; with moderate-risk women just as likely to undergo the procedure as high-risk women. These results thus support the theory that personal experiences of cancer are likely to affect the choice of strategies undertaken to manage ongoing cancer risk more profoundly than communication of an objective risk level.

In women at high-risk for breast cancer development who have elected to undertake BRRM, perceived level of breast cancer risk has been reported as being significantly reduced following surgery.[38,39] Consistent with those results we found that for women who had previously undergone either a BRRM or BRRO, current perceived cancer risk was significantly lower than for the women who had not undergone the procedure ($P = 0.052$, $P < 0.001$, respectively).

The limitations of this study include the possibility that our results may over- or under-estimate uptake of risk-reducing surgery, as we were unable to determine either in the non-responding group. The response rate however, was reasonably high (68.4% when those lost to follow up were excluded) and no significant demographic differences were found between responders and non-responders. While the number of women with a known deleterious mutation in this study is relatively low (11.6% of high-risk women); this is likely to be representative of the proportion of women attending FCCs who are ultimately documented to have pathogenic mutations in *BRCA1* or *BRCA2*.

Currently, surgical prophylaxis is the major method of risk reduction for women at increased genetic risk for both ovarian and breast cancer and yet it would appear from the

results of this and other studies that both BRRO and BRRM are acceptable as a means of risk reduction to only a small percentage of women. The way in which women are counselled about risk-reducing surgery together with clinician driven preferences are likely to weight pressure in decision-making; however this is almost certainly combined with individual influences such as previous cancer experiences. While it would appear that in the short-term, women who choose to undertake risk reduction surgery have reduced cancer related psycho-morbidity, further research is required to establish whether this is maintained in the long-term. More importantly however, as surgical strategies are the choice of the minority of women, further research is required into alternative non-operative risk management strategies, such as chemoprevention and screening.

Conflict of interest statement

None declared. Associate Professor Judy Kirk has had an advisory role for the National Breast Cancer Centre however this does not constitute a conflict of interest.

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