As Time Goes By

The Long-Term Psychological Impact of either Regular Surveillance or Prophylactic Mastectomy in Women at Risk for Hereditary Breast Cancer

Mariska den Heijer

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Met het verstrijken van de tijd:

De lange termijn psychologische impact van ofwel regelmatige controles of profylactische mastectomie bij vrouwen met een risico op erfelijke borstkanker

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Voor mijn ouders

Joke en Rinus

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Chapter 1

General Introduction

INTRODUCTION

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death in women worldwide (1). In the Netherlands, approximately 13000 new breast cancer cases are diagnosed annually, mostly occurring in women older than 50 years. In total 12-13% (one in eight) of the women in the Netherlands will be diagnosed with breast cancer during lifetime, and population screening for breast cancer therefore is being offered to women as of 50 years of age. While the population risk of ovarian cancer is 1.5% in the Netherlands, population screening is not offered.

It is estimated that 5-10% of all cancer cases are due to a genetic predisposition (2). One of the first recognised entities was the clustering of breast and/or ovarian cancer in families. A strong family history of breast (and/or ovarian) cancer in combination with family members affected at a young age (below 50 years of age) may be suggestive of a cancer susceptibility gene in the family. As of the beginning of the nineteen nineties it became possible for women from families with clustering of breast (and/or ovarian) cancer cases to opt for genetic counselling and testing, and subsequently to receive a personal life time risk estimation. Depending on the risk estimation, decisions have to be made for either regular surveillance or prophylactic surgery. Both options are associated with pros and cons regarding on the one hand anxiety that cancer might develop or be detected (at an advanced stage) during surveillance versus on the other hand irreversible consequences after preventive surgery of either breasts and/or ovaries, potentially affecting physical and psychological functioning. As of the beginning of the availability of genetic testing, it became clear that more data on the (dis)advantages of the different strategies was needed. More knowledge about the psychosocial consequences of adhering to regular surveillance as well as prophylactic mastectomy and/or salpingo-ovariectomy was essential, in order to adequately inform and support women considering these options.

In 1999, two studies were initiated at the Erasmus University Medical Centre-Daniel den Hoed Cancer Centre, Rotterdam, evaluating the short-term psychological adjustment of women either adhering to regular breast cancer surveillance or opting for prophylactic surgery of the breasts and/or ovaries/fallopian tubes (MRISC-B study and PREVOM-B study, respectively) encompassing a time period of 12 months (see Figure 1). Later on, it became clear that data on the long term also were needed, and therefore, a long-term follow-up study was initiated aiming to explore long-term psychological adjustment in both cohorts of women and to identify risk factors of maladjustment through time.

'My mother died from breast cancer when she was 43 years of age. My grandmother and great-grandmother had also died from the disease, so my two sisters and I always felt that we were at high risk'.

1.1 HEREDITARY BREAST/OVARIAN CANCER

A major breakthrough in the field of breast cancer and oncogenetics was the cloning of the BReast CAncer susceptibility genes BRCA1 and BRCA2 in 1994 and 1995, respectively (3-4). Since then, it became possible to perform genetic testing, and identify individuals carrying a mutation in one of these genes. Women identified with a mutation in BRCA1 or BRCA2 have a cumulative life time risk (CLTR) for developing breast cancer of 43-87%. Most BRCA-associated breast cancers already occur before the age of 50 years (5-8), being younger than the age at which breast cancer population screening starts. Furthermore, it became clear that women with a BRCA1 or BRCA2 gene mutation have an increased lifetime risk for developing ovarian/fallopian tube cancer estimated to be 40-62% and 15-20%, respectively, which is much higher than the population risk of 1,5%. The inheritance pattern of a mutation in BRCA1/2 is autosomal dominant, irrespective of gender, and consequently each child of a male or female mutation carrier has a 50% chance of inheriting the mutation.

Unfortunately, genetic testing for a BRCA1/2 mutation only identifies a mutation in approximately 15-20% of the families with breast/ovarian cancer clustering (2), leaving the great majority of such families unidentified (= non-BRCA1/2). Inherently, it is not possible for a woman from a non-BRCA1/2 family to be tested for a specific mutation, while the presence of a genetic predisposition in the family and the respective woman also can not be ruled out. Women from these families, therefore, remain at increased risk for breast cancer compared to the general population, which is being estimated using pedigree data and genetic epidemiological tables, such as the risk tables developed by Claus et al (9).

1.2 MANAGEMENT OPTIONS FOR WOMEN AT RISK FOR HEREDITARY BREAST CANCER

Different options may be discussed with an individual woman to manage her estimated increased risk for hereditary breast/ovarian cancer, consisting of either regular surveillance of the breasts and/or ovaries or prophylactic surgery of the breasts (prophylactic mastectomy, PM) and/or the ovaries/fallopian tubes (prophylactic salpingo-oophorectomy, PSO). Over time, guidelines regarding both surveillance strategies and prophylactic surgeries for high-risk women have changed based on genetic testing techniques as well as progressing insights regarding the value of the respective surveillance and surgical options. As the scope of this thesis focuses on psychosocial aspects of the various procedures, only general information on the different risk management options is provided in the following paragraphs.

1.2.1 Regular surveillance

Regular surveillance of the breasts consisting of imaging examination(s), clinical breast examination (CBE), and breast self examination (BSE) aims to detect breast cancer at an as early stage as possible, but does not prevent breast cancer to develop, and therefore does not guarantee that breast cancer is detected before lymph node metastasis has occurred.

Research performed over the last decades in high-risk women and female BRCA mutation carriers, mostly being young women, has shown that mammography in this young group has a low sensitivity for detecting breast cancer, especially in BRCA1 mutation carriers. Furthermore, magnetic resonance imaging (MRI) of the breasts has been shown to be superior to mammography regarding the detection of breast tumours at an early (and prognostic favourable) stage (10-11) However, this comes at the expense of increased costs as well as false positive results, causing supplementary exams (and costs) and possibly increased anxiety for the respective woman.

The value of CBE by the physician at the clinic with respect to the early detection of breast cancer over and above mammography/MRI is thought to be limited (10, 12-13). However, the personal contact with the physician may benefit other purposes, for example enabling the update of the family history about the occurrence of breast and/or other cancers in relatives with potential consequences for additional genetic examinations and/or recommendations, discussing lifestyle factors, psychological support and identification of those individuals who may benefit from additional counselling and discuss new developments and studies.

The value of performing BSE remains a recurrent point of controversy, also for young high-risk women, and has led to various recommendations from key health organisations. BSE is not proven to be effective in reducing breast cancer mortality for the general population, and there are no data hereon yet for the high-risk women. A possible benefit of performing BSE on a regular basis is that women become more familiar with the structure of their breast tissue, and therefore will be more likely to detect early changes within the breast. Possible disadvantages associated with BSE include anxiety related to the findings after performing BSE, resulting in more contacts at the clinic for additional exams.

In the recently updated Dutch “Breast Cancer” guidelines (2011) including the issue breast cancer screening for high-risk women outside of population screening, which has been elaborated by a multidisciplinary working party, the following surveillance schedules for several risk subgroups are recommended:

BRCA1/2 mutation carriers and 50% risk carriers:
- annual imaging by MRI between 25-60 years
- annual imaging by mammography as of 30 years
- annual CBE as of 25 years

Women belonging to non-BRCA1/2 families with a CLTR between 30-50%:
- annual imaging by mammography and CBE between 35-60 years
- participation in the population screening programme between 60-75 years

Women belonging to non-BRCA1/2 families with a CLTR 20-30%:
- annual imaging by mammography through the general physician as of 40 years
- participation in the population screening programme as of 50 years of age

At the moment, regular surveillance of the ovaries/fallopian tubes still includes annual gynecological examination, transvaginal ultrasound and estimation of serum CA125, beginning at the age of 35 years onwards. Over time, however, gynecological screening has not proven to be effective in early detection of ovarian/fallopian tube cancer (14-16). The visit at the gynecological outpatient clinic to date mainly focuses on information about the lack of benefit regarding gynecological surveillance. Current guidelines in the Netherlands therefore recommend prophylactic removal of the ovaries and fallopian tubes (prophylactic salpingo-oophorectomy) as of the age of 35-40 for BRCA1 mutation carriers and 40-45 years for BRCA2 mutation carriers, and on indication for respective women from non-BRCA1/2 families with verified ovarian cancer in relative(s).

It is known that women at risk of developing hereditary breast cancer may experience elevated levels of psychological distress (17-20). Increased levels of breast cancer specific distress may be the consequence of having experienced the process of breast/ovarian cancer and/or death due to cancer in (close) relatives. Furthermore, women may worry about their own risk of developing breast/ovarian cancer. Given the rather large group of high-risk women being eligible for breast cancer surveillance outside of population screening, it is of clinical interest to identify at an early stage those women who may experience psychological problems during this programme.

1.2.2 Prophylactic mastectomy (PM)

Prophylactic mastectomy (PM) may be discussed as an alternative for breast cancer surveillance, and at the moment is the most effective method to reduce the life time risk of breast cancer. This radical procedure, however, implies preventive removal of all fibroglandular breast tissue, theoretically including the nipples. As the women deciding for this strategy are mainly young (<50 years), most women also opt for (immediate) breast reconstruction (BR) (21). In view of the drastic procedure with major impact on a woman's femininity, PM is only discussed as an option with mutation carriers, whereby the respective woman needs to make her personal decision. In the Netherlands, PM is not discussed with women from non-BRCA mutation families, as the lifetime breast cancer risk for these women does not exceed 50%, and there is uncertainty regarding the genetic status. PM is highly effective in reducing the risk of breast cancer, being approximately 90% or higher (21-25). However, the decision for PM is irreversible and the intervention has major implications, including the loss of healthy breasts and normal sensation (26), and the necessity to adapt to an altered body image being major as breasts are a crucial part of the woman's body. In addition, a substantial proportion of women opting for PM/BR experiences some form of complications following surgery and reconstruction, potentially leading to additional surgical intervention(s) and poor cosmetic outcomes (21, 27). Yet, psychological consequences must be considered such as the far-reaching impact on body image and sexual functioning. Balanced information regarding psychological outcomes is therefore eagerly needed, also to help in the counselling of women considering PM.

1.2.3 Prophylactic salpingo-oophorectomy (PSO)

Prophylactic (bilateral) salpingo-oophorectomy (PSO) is the most effective method for reducing the risk of ovarian/fallopian tube cancer, estimated to be as high as 80-95%, and implies the surgical removal of both ovaries and fallopian tubes (28-30). Adverse consequences of PSO include surgical complications and side effects associated with surgically induced early menopause, such as hot flashes, vaginal dryness, sexual dysfunction, sleep disturbances, emotional problems and cognitive changes, which all can significantly affect quality of life (31). Hormone replacement therapy (HRT) may be effective in alleviating the vasomotor symptoms (e.g. hot flushes, sweats) (32), however, it is insufficiently clear whether the administration of HRT is without any harm regarding the breast cancer risk in unaffected women. Moreover, in women with a history of breast cancer HRT is contraindicated (33).

1.3 PSYCHOLOGICAL IMPACT OF REGULAR SURVEILLANCE AND PROPHYLACTIC SURGERY

The psychological consequences of either adhering to regular breast cancer surveillance or having undergone prophylactic surgery for breast/ovarian cancer have been addressed in the context of the MRISC-B and PREVOM-B study, respectively, including high-risk women being seen at the family cancer clinic of the Erasmus University Medical Center-Daniel den Hoed.

1.3.1 Psychological impact of regular surveillance

The MRISC-B study aimed to evaluate the short-term psychological consequences of being at risk for hereditary breast cancer and adhering to regular surveillance (n=357), encompassing a study period of one year. Several subgroups of women being more vulnerable for psychological distress were identified including: young women performing excessive breast self-examination (BSE) (34), women overestimating their risk of developing breast cancer (35), and women with a sister affected with breast cancer (36). Importantly, it was also found that coping styles, representing cognitive and behavioural efforts to deal with stressful encounters, mattered (37-38). Several styles of coping may be distinguished, and depending on the duration and controllability of the stressor effects can differ (39). Problem-focused coping styles (i.e. acting out to confront or avoid the stressor) may be of significant impact when the stressor can be controlled and solved in some fashion, while emotion-focused coping styles (i.e. efforts to regulate the emotions associated with the stressor) may be particularly adequate in regulating the emotions associated with an uncontrollable stressor. In the MRISC-B cohort it was observed that seeking social support, expressing emotions and having comforting thoughts were significantly associated with lower levels of psychological distress. On the other hand, women using passive coping (i.e. feeling overwhelmed by the problem, isolating oneself from others, and escaping into fantasies while facing problems) and palliative coping styles (reducing arousal by distracting oneself from the problem) experienced increased levels of distress (40).

In view of the MRISC-B findings on the impact of coping styles on the short term, it would be of interest to investigate whether the impact of these coping styles persists through time, as it has been suggested that the effects of coping styles may be different over time (39). Coping styles being beneficial in early phases of acute stress may be less adaptive in the long-term (41), and coping styles contributing to increased distress on the short-term may be adaptive on the long-term (42). As there are no data on the long-term psychological adjustment of high-risk women adhering to breast cancer surveillance to date, the impact of coping styles in this group remains to be investigated.

Finally, the threat of developing breast (and/or ovarian) cancer may also be distressing for partners. Yet little research has focused on the psychological adjustment of partners of women at risk for hereditary breast cancer. Generally, the genetic testing process and, unfavourable test results in particular, may be distressing for some partners (43-46). Worries about the possibility that the partner will develop cancer and the risk for their children have indeed been found to be common concerns among partners (44). Of note, the mentioned studies all focused on the adjustment of partners after the disclosure of genetic test results, while there are currently no published prospective data on psychological outcomes among partners beyond six months after the genetic test result disclosure (47).

1.3.2 Psychosocial impact of prophylactic surgery

The PREVOM-B study aimed to evaluate the psychological consequences of prophylactic surgery, especially prophylactic mastectomy (PM), on women at risk for hereditary breast/ovarian cancer, and consisted of a retrospective and a prospective part.

In the retrospective part, satisfaction with breast reconstruction (BR) after PM was explored in 114 women. It was found that 60% of the women were satisfied with the results (48). Dissatisfaction was reported more often by women who felt insufficiently informed prior to PM/BR, women who experienced complications after surgery and/or ongoing complaints, and women who reported that their breasts did not feel 'like their own' after PM/BR. Women who reported adverse changes in their sexual relationship (44%) were more likely to report that they did not feel sufficiently informed about the procedure and its possible consequences, that surgery had not met their expectations, and that they were experiencing ongoing complaints and limitations in their daily life. Furthermore, adverse changes in the sexual relationship were associated with decreased feelings of femininity and perception of the partner's negative view on the sexual attractiveness of his wife. These findings suggested that the impact of PM/BR on the body image and quality of the sexual relationship should not be underestimated.

In the prospective part, covering a study period of one year after surgery, levels and courses of distress in women opting for PM/BR (n=52) and/or PSO (n=26) were explored (49). Anxiety and cancer related distress were significantly reduced at 12 months after PM/BR, being in accordance with findings from other studies (50-52). No significant changes in distress levels were observed before and after PSO. Furthermore, examining which factors were predictive of persistent increased distress at 6 and 12 months after prophylactic surgery, it was observed that high pre-surgery distress and being a mutation carrier were predictive for increased post-surgery distress, while coping by fostering comforting thoughts was predictive for decreased post-surgery distress (53). Finally, distress in partners (n=61) of high-risk women opting for prophylactic surgery also was examined (unpublished data). Intrusion gradually decreased over the first year after surgery, while there was no significant change in levels of avoidance, anxiety and depression. Factors associated with increased distress were fatherhood, high educational level, and having a wife with a history of cancer or a BRCA1/2 mutation.

Inherent to the nature of prophylactic surgery, especially PM/BR, one may expect changes in body image after this type of surgery. To date, there are however only few data from prospective studies examining the effects of PM/BR on body image (54).

One prospective qualitative study by Hatcher et al. found no evidence for body image problems 18 months after PM (51), while in two other prospective studies a substantial proportion of the women reported body image problems after one year (50, 52). A possible explanation for the discordant findings may be that a follow-up period of one year is too short to capture the assimilation of reconstructed breasts into a woman's body image. In addition, various breast reconstruction techniques may take different periods of time affecting the outcomes at a given time point. To our knowledge, the only data on body image on the long term have been reported by van Oostrom et al, describing that BRCA1/2 mutation carriers (n=23, 19 having opted for PM) experienced decreased satisfaction with body image at 5 years of follow-up (55). Therefore, more prospective data is needed on the psychological adjustment to PM/BR, especially regarding body image, in a sufficiently large sample size and longer follow-up period. In addition, the factors that are predisposing for poor body image after PM/BR also remain to be investigated.

1.4 CURRENT AVAILABLE DATA AND FURTHER RESEARCH QUESTIONS

Although the MRISC-B as well as the PREVOM-B studies identified several subgroups of women being more vulnerable for psychological distress, both studies, however, were limited by the short study period covering approximately 12 months, which is too short to draw definite conclusions. Unfortunately, prospective studies on the long-term psychological adjustment of women at risk for hereditary breast cancer are scarce, and results are inconsistent. One study conducted at our institute by van Oostrom et al. examined long-term psychological distress in high-risk women (n= 65) 5 years after genetic testing, and described that women reported an increase in anxiety and depression from one to 5 years follow-up (55). Reichelt et al. did not observe an increase in psychological distress at 18 months after the result of genetic testing in 68 unaffected BRCA1 mutation carriers (56).

Regarding the data on predictive factors for distress on the long term, Van Oostrom et al. found that women who experienced increased distress at 5 year follow-up were more likely to experience increased distress at baseline, to have children under the age of 15 years and to have lost a family member to breast/ovarian cancer. In addition, an open communication style within the family proved to be predictive of decreased psychological distress (55). Reichelt et al. also found that pre-test distress was the strongest predictor of distress at follow-up (56). Moreover, in an American study by Koehly et al. in high-risk women (n=65) it was suggested that social support is associated with long-term adjustment (57). Furthermore, Reichelt et al. observed that neuroticism contributed to distress, suggesting that personal resources may play a role in the psychological adjustment to being at risk for hereditary breast cancer.

Also, knowledge about an increased risk for hereditary breast cancer has the potential to impact on an individual's self-concept, including domains of self-perception of future health, self-worth, body image and identity (58-59). To date, research data on altered self-concept related to being at risk for hereditary breast cancer is limited. A recent report of the development an instrument designed to measure self-concept in BRCA1/2 mutation carriers addressed the specific impacts of being at risk for hereditary cancer on self-concept (60). Negative impacts on self-concept included a woman experiencing being 'stigmatized', 'labelled', 'different from others', and 'vulnerable'. However, feelings of mastery, resulting in increased hope for the future were observed to have a positive impact on the self-concept (60). Yet, in view of the small sample sizes included in the few available studies, the role of social resources to the psychological adjustment of being at risk for hereditary breast cancer certainly needs further investigation. Also, it is insufficiently known how changes in the particular self-concept aspects influence psychological adjustment in women at risk for hereditary breast cancer.

In conclusion, while both the MRISC-B and the PREVOM-B study provided very relevant information on some aspects of psychological adjustment on the short term to either breast cancer surveillance of prophylactic mastectomy, several issues remained unanswered. Also, over time it became clear that data on the long-term adjustment was needed. Therefore, a follow-up study including both the MRISC-B and PREVOM-B cohorts was conducted at our institution, which is further addressed in Paragraph 1.5.

1.5 THIS THESIS

1.5.1 Aims and research questions

This follow-up study was set up as a longitudinal observational study on the long-term psychological adjustment to either regular breast cancer surveillance or prophylactic mastectomy in women at risk for hereditary breast cancer, and aimed to identify risk factors for maladjustment through time.

In the first part of this thesis (Chapters 2-4) we focused on the total group of women being at risk for hereditary breast cancer, and explored several characteristics potentially contributing to psychological adjustment. The research questions addressed were:

- What is the role of self-esteem and self-concept on the level of psychological distress? *(Chapter 2)*
- What is the role of family communication and perceived social support with respect to the level of psychological distress? *(Chapter 3)*

- What is the relative contribution of social and personal resources in the level of psychological distress? *(Chapter 4)*

In the second part of this thesis, we explored long-term psychological adjustment to either having undergone prophylactic mastectomy or adhering to regular breast cancer surveillance (Chapters 5-6). Furthermore, we examined psychological adjustment in partners of high-risk women adhering to regular surveillance (Chapter 7).

The explored research questions concerned:

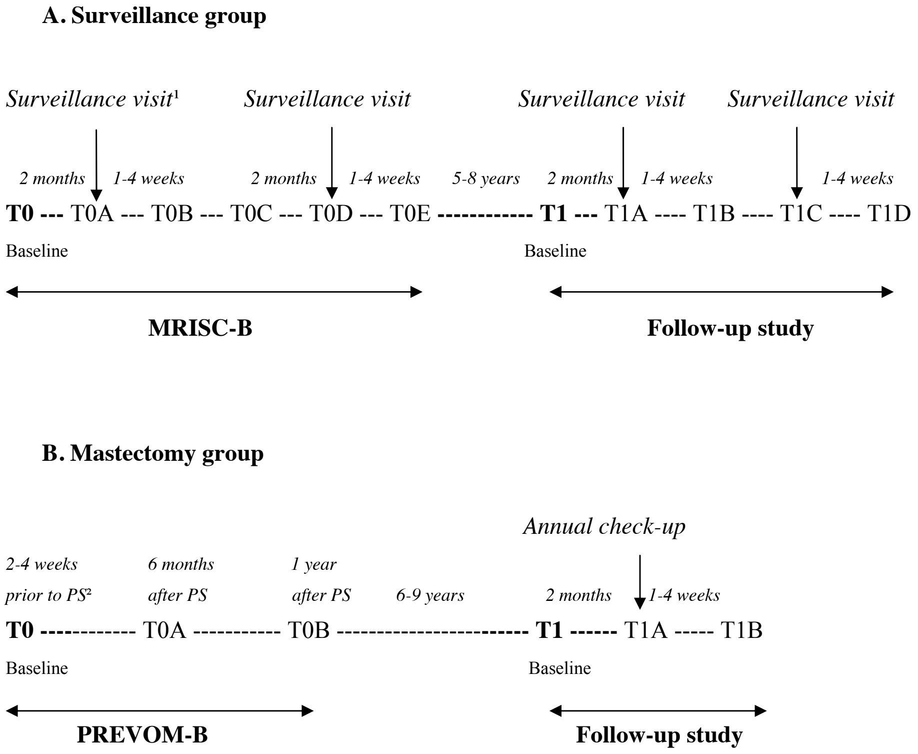
- What is the course of long term psychological distress and body image in high-risk women opting for prophylactic mastectomy, and what are predictors of long-term body image? *(Chapter 5)*
- What are the levels of long-term psychological distress in women adhering to regular surveillance, and which women are vulnerable for psychological distress through time? *(Chapter 6)*
- What are the levels of psychological distress in partners of high-risk women around the breast cancer surveillance appointment at the clinic, and which characteristics contribute to distress of partners? *(Chapter 7)*

1.5.2 Study procedures

Between 1999 and 2003, women at risk for hereditary breast/ovarian cancer adhering to breast cancer surveillance at the family cancer clinic of our institution were included in the MRISC-B study (n=357), addressing the psychological consequences of breast cancer surveillance over a period of 12 months, while women opting for either prophylactic mastectomy and/or salpingo-ovariectomy were included in the PREVOM-B study (n= 78) addressing the psychological consequences of prophylactic surgery over a period of 12 months. Detailed information on both studies has been described previously (19, 34, 49). In summary, the assessment points at which data collection has been performed in the context of both studies are shown in Figure 1.

In 2007, a follow-up study was initiated aiming to investigate the long-term psychological impact (i.e. between 5 and 9 years since enrollment in the MRISC-B and PREVOM-B studies) of either breast cancer surveillance or prophylactic surgery. Women were eligible if they had participated in the MRISC-B or PREVOM-B study, and still were under surveillance at the family cancer clinic of the Erasmus MC-Daniel den Hoed Cancer Centre. Women who had developed breast or ovarian cancer since enrollment in either study were not eligible for the follow-up study. Eligible women were sent an information letter regarding the follow-up study along with an informed consent form and a stamped envelope. All women had sufficient understanding of the Dutch language to fill in the questionnaires, and again gave informed consent. Approval was obtained from

Figure 1. Schematic representations of the study design



[1] Biannual surveillance visit

[2] Prophylactic surgery

the Medical Ethical Committee of the Erasmus Medical Center in Rotterdam. Assessment moments of the follow-up study are shown in Figure 1.

Data collection for the short term as well as the long term follow-up study was done by means of questionnaires at the respective assessment moments (Figure 1). Psychological adjustment was defined in terms of general distress (HADS) and breast cancer specific distress (IES). In the PM group, body image was added as a measure for psychological adjustment. Psychological adjustment measurements were completed at all assessment moments. The following predictive variables were included in the analyses performed: coping styles (UCL), family communication, social support, self-esteem, self-concept, breast self-examination frequency, breast cancer risk perception and the presence of relatives affected with breast cancer. The questionnaire contents and their psychometric properties are described in more detail in the following chapters.

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Chapter 2

The contribution of self-esteem and self-concept in psychological distress in women at risk for hereditary breast cancer

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ABSTRACT

Background: Clarification of the role of several aspects of self-concept regarding psychological distress in women at risk for hereditary breast cancer will help to target counseling and psychosocial interventions more appropriately. In the current study, we aimed (1) to examine the role of general self-esteem and specific aspects of self-concept (i.e. stigma, vulnerability, and mastery) in psychological distress in women at risk for hereditary breast cancer, and (2) to compare the relative importance of these self-concept aspects in psychological distress in women with low versus high self-esteem.

Methods: General and breast cancer specific distress, self-esteem, self-concept and demographics were assessed in 246 women being at risk for hereditary breast cancer, who opted either for regular breast surveillance or prophylactic surgery.

Results: In the total study group, self-esteem was negatively associated with general distress. Furthermore, feeling stigmatized was strongly associated with more breast cancer specific distress, and to a lesser degree with general distress. In women with low-self esteem, feelings of stigmatization were strongly associated with higher levels of both breast cancer specific and general distress, while a sense of mastery was associated with less general distress. For women with high self-esteem, feelings of both stigmatization and vulnerability were associated with more breast cancer specific distress, whereas there were no significant associations with general distress.

Discussion: Psychosocial interventions or support groups for women at risk for hereditary breast cancer should focus on self-esteem and feelings of stigmatization and isolation, and consequently tailor the interventions on specific items for respective women.

INTRODUCTION

Women identified with a mutation in BRCA1/2 have a significantly increased cumulative lifetime risk (i.e. up to the age of 70 years) for breast cancer of 40-85%, and for ovarian cancer of 11-65% (1-4). Women from families with a family history of breast cancer, but without an as yet identified BRCA1/2 mutation, are also at increased risk for breast cancer and in general are offered regular breast cancer surveillance. Although the initial short-term response to being at risk for breast cancer may include elevated levels of distress, the majority of women adjust well over time (5-7). Nevertheless, a subgroup of women may be at risk for experiencing elevated levels of psychological distress over time (8). Understanding positive adjustment to being at risk for hereditary breast cancer is an important aspect of research aiming at enhancing well-being for these women.

Psychological resources may play a crucial role in the adjustment to stressful life-events, as resources may buffer the negative impact of such an event (9). Self-esteem, for example, is strongly associated with psychological functioning, and has been shown to be associated with lower levels of depression and higher levels of well-being in cancer patients (10). Within current models of self-concept, self-esteem is considered as the generalized evaluation of the self, and is only one of the dimensions of the collection of cognitive representations included in the self-concept (11). Therefore, general self-esteem may not be the only aspect of self-concept which is relevant for well-being (12). With the increased emphasis on the multi-dimensionality of self-concept (13, 14), it is important that research addresses the specific aspects of self-concept being most vulnerable in women at risk for hereditary breast cancer.

Knowing that one is at increased risk for hereditary breast cancer may impact on an individual's self-concept (15). Currently, research data about alterations in self-concept related to being at risk for hereditary breast cancer is limited. Recently, the specific impact of being at risk for breast cancer on self-concept was addressed by Esplen et al.(16), reporting on the development of an instrument to measure self-concept in BRCA1/2 mutation carriers. Items having a negative impact on self-concept included a person feeling stigmatized, labelled, different from others and vulnerable. However, other items were observed to have a positive impact, such as feelings of mastery, resulting in increased hope for the future (16). These altered self-perceptions may play a role in psychological distress.

To date, there are no data available on how changes in these particular self-concept aspects influence psychological adjustment in women at risk for hereditary breast cancer. Clarification of the specific aspects of self-concept involved in the experience of psychological distress will help to target appropriate counselling and psychosocial interventions. Therefore, the current study focussed on the role of both general self-esteem and specific aspects of self-concept, as it has been reported that these constructs are neither equivalent, nor interchangeable, and that the relative importance should be compared (14). However, it has been reported that general self-esteem is relatively stable over time and that it is difficult to significantly improve self-esteem (17, 18). Therefore, targeting aspects of self-concept specifically related to the risk of developing hereditary breast cancer may be more effective. In this respect, it is of clinical relevance to identify aspects of self-concept that are important for the adjustment of women with low versus high self-esteem.

The objectives of the current study were (1) to examine the role of general self-esteem and specific aspects of self-concept in psychological distress in women at risk for hereditary breast cancer, and (2) to compare the relative importance of these self-concept aspects in psychological distress in women with low versus high self-esteem.

MATERIAL AND METHODS

Participants

Between 1999 and 2003, women at risk for hereditary breast cancer were included in either the MRISC-B study (addressing the psychological consequences of regular breast cancer surveillance) or the PREVOM-B study (addressing the psychological consequences of prophylactic surgery, either mastectomy and/or salpingo-oophorectomy). Women with a history of breast cancer were excluded from the MRISC-B study, whereas this was not an exclusion criterion for the PREVOM-B study. Detailed descriptions of the MRISC-B and PREVOM-B studies have been published elsewhere (19, 20).

In 2007, a follow-up study was activated investigating the long-term psychological impact of either regular surveillance or prophylactic surgery in women at risk for hereditary breast cancer. Women were eligible for the follow-up study if they participated in either MRISC-B or PREVOM-B. Women who developed breast or ovarian cancer since enrollment in these studies were not eligible for the follow-up study. The psychological follow-up study included a total of 248 women; 206 women from MRISC-B and 42 women from PREVOM-B. Women had sufficient understanding of the Dutch language to fill in the questionnaires and all gave informed consent. Approval was obtained from the Medical Ethical Committee of the Erasmus Medical Center in Rotterdam.

This study was set up as a longitudinal observational study on the long-term psychological impact (i.e. between 4 and 9 years since enrollment in the MRISC-B and PREVOM-B studies) of either regular breast cancer surveillance or prophylactic surgery in women at increased risk for hereditary breast cancer. The analysis for this article was carried out on the data obtained from the first assessment, performed two months prior to the women’s appointment at the clinic. The assessments took place between June 2007 and October 2009.

Procedure

Women having participated in the MRISC-B or PREVOM-B study, and still being under surveillance at the family cancer clinic of the Erasmus MC-Daniel den Hoed Cancer Centre, were sent an information letter regarding the psychological follow-up study along with an informed consent form and a prepaid envelope. After receipt of written informed consent, women were sent the first questionnaire of this follow-up study to their home two months prior to their next appointment at the family cancer clinic of the Erasmus MC-Daniel den Hoed Cancer Centre in Rotterdam.

Measures

Independent variables

Biographical and medical data

Data on age, having a partner, having children, educational level, carrier status, type of management option and cancer-related events in the family of origin were obtained by means of a questionnaire.

Self-concept

The BRCA Self-Concept Scale (16) is a 17-item scale with answers ranging from 1 ('strongly disagree) to 7 ('strongly agree'). The scale comprises three subscales for stigma, vulnerability and mastery. The scale was validated among a group of female BRCA1/2 carriers, revealing good internal consistency, with reported Cronbach's alphas of 0.90 for the total scale, 0.87 for stigma, 0.76 for vulnerability and 0.68 for mastery. In the current study the Cronbach's alpha coefficients were 0.87, 0.80, 0.71 and 0.63, respectively.

Self-esteem

Self-esteem was assessed with the Rosenberg Self-Esteem Scale (RSES) (21), a 10-item scale with response options ranging from 1 = "strongly agree" to 4 = "strongly disagree". In this study Cronbach's alpha was 0.92.

Dependent variables

Breast cancer specific distress

Intrusion and avoidance -two common responses to stressful situations- were assessed using the Impact of Events Scale (IES) (22). This questionnaire comprises 15 items and can be tailored to a specific event, namely 'breast cancer' in this study. Avoidance is measured in 8 items and intrusion in 7 items, and each item has four answer categories: not at all (score 0), seldom (score 1), sometimes (score 3), and often (score 5). The Dutch version of the IES has been subjected to reliability analysis, the avoidance subscale was found to have a Cronbach's alpha of 0.66 and the intrusion subscale of 0.72 (23).

General distress

The Hospital Anxiety and Depression Scale (HADS) is a 14-item questionnaire, measuring anxiety (7 items) and depression (7 items) (24). Every item has four response categories, anchored to that specific item. Each subscale has a score range from 0 to 21. A Dutch reliability study revealed a Cronbach's alpha of 0.84 for anxiety, 0.86 for depression and 0.90 for the entire scale (25).

Statistical analyses

Missing values on the items composing outcome variables were handled as follows: a total score corrected for the total number of questions of the subscale was calculated for participants who filled in more than 75% of the questions per subscale. No total score was calculated for participants who filled in less than 75% of the questions per subscale. Frequency analysis was used to describe the characteristics of the participants. To test whether there were differences between the three types of management options we used one-way analysis of variance for continuous data and chi-square test for ordinal data. The basic analyses were carried out using the SPSS 15.0 statistical package (SPSS Inc., Chicago).

The relationships between self-esteem and the three components of self-concept, being independent variables, and both types of distress, being outcome variables, were explored by means of the method of Structural Equation Modeling (SEM). SEM enables to identify, to test and to estimate the interrelationships of self-esteem and the self-concept components in relation to the psychological distress variables. Furthermore, it was explored whether the relationships between the three self-concept variables and the distress variables differed for women with low versus high self-esteem. Therefore, we dichotomized the self-esteem score at the median into low and high-self-esteem.

In general, modelling is aimed to identify the most plausible model. The maximum likelihood estimation method was used to identify the model and to estimate the parameters of the self-concept variables. SEM analyses were done with Mplus (Muthen & Muthen, 2004).

As measures of model performance, χ^{2}-tests were used for determining the adequacy of the model-fit. A non-significant *p*-value ($p > 0.05$) and the ratio of $\frac{\chi^2}{df} < 1.5$ would represent a good model-fit. Four other goodness-of-fit indices were also used: Comparative Fit Index ($CFI > 0.95$), Tucker-Lewis Index ($TLI > 0.95$), Root Mean Square Error of Approximation (RMSEA<0.05) and Square Root Mean Residuals (SRMR<0.05).

In this analysis age, education level, partner, having children, carrier status, type of management option and cancer-related events were considered as potential confounder variables. Standardized regression coefficients (β) were used as measures of relative importance of the self-concept variables. All statistical testing occurred at 0.05 level of significance (two-tailed).

RESULTS

Descriptive statistics

The background characteristics of the 246 participants are shown in Table 1. Most of the women had at least a middle level education (82%), were in a relationship (89%) and had one or more children (80%). The mean age of participating women was 47.4 years (range 29 – 69 years). Most of the participating women were adhering to regular surveillance (71%), while 13% had opted for salpingo-oophorectomy and 16% for prophylactic mastectomy. At the time of data collection for this follow-up study, there were no significant

Table 1. General characteristics of the study sample

Variable	Women (N=246)
Age; mean (sd)	47.4 (8.5)
Educational level[1]	
High	81 (33%)
Middle	122 (49%)
Low	35 (14%)
Having a partner	219 (89%)
Having children	197 (80%)
BRCA1/2 mutation carrier	72 (29%)
Type of risk management[2]	
Regular surveillance	175 (71%)
PSO	30 (12%)
PM	18 (7%)
PM + PSO	23 (9%)
Cancer related events	
Having a mother/sister diagnosed with breast/ovarian cancer	204 (83%)
Having a mother/sister died of breast/ovarian cancer	150 (61%)

[1] Percentages do not add up to 100% because of missing values

[2] PSO: prophylactic salpingo-oophorectomy; PM: prophylactic mastectomy

differences between the three management option groups on self-concept, self-esteem and both cancer specific and general distress variables (data not shown).

The mean values, the standard deviations and the inter-correlations of both the outcome and the independent variables are displayed in Table 2. All inter-correlations were significant at the 0.01 significance level (two-tailed).

Table 2. Intercorrelations[1], ranges and means of BRCA self-concept and self-esteem variables

Variable	1.	2.	3.	4.	5.	6.	Range[2]	M	SD
Self-concept							17-119	41.2	14.1
1. Stigma		.68**	.49**	-.40**	.60**	.42**	8-56	16.8	7.3
2. Vulnerability			.46**	-.28**	.48**	.28**	5-35	13.8	5.7
3. Mastery				-.41**	.33**	.37**	4-28	10.5	3.5
4. Rosenberg self-esteem					-.28**	-.57**	10-40	33.1	5.5
5. Breast cancer specific distress						.47**	0-75	7.51	11.3
6. General distress							0-42	7.21	7.8

[1] Pearson correlation coefficients
[2] Theoretical scale range
* p<0.05 (two-tailed)
** p<0.01 (two-tailed)

Psychological distress in relation to self-esteem and self-concept aspects

Data regarding the impact of self-esteem and self-concept aspects on breast cancer specific and general distress in the total study group are shown in Table 3. The performance of the model was good (χ^2 (20) = 25.04; p = 0.20). The other performance indices also indicated that this model was good (CFI = 0.98; TLI = 0.97; RMSEA = 0.03; SRMR = 0.02) Feelings of stigmatization were found to be significantly positively associated with both general distress and breast cancer specific distress (β = 0.20, p = 0.01 and β = 0.49, p = 0.01, respectively). Thus, women who feel more stigmatized reported more breast

Table 3. Impact of self-concept aspects and self-esteem on general distress and breast cancer specific distress in women at risk for hereditary breast cancer (N=246)

Variable	General distress		Breast cancer specific distress	
	β[1]	p	β	p
Self-concept				
Stigma	**0.20**	***0.01***	**0.49**	***0.01***
Vulnerability	-0.02	0.74	0.13	0.08
Mastery	0.10	0.12	-0.01	0.90
Rosenberg self-esteem	**-0.46**	***0.01***	-0.06	0.33

[1] Standardized regression coefficient as a measure of relative importance
Adjusted for age, education level, having a partner, having children, carrier status, type of management option and cancer-related events

cancer specific distress as well as general distress. Furthermore, there was a significant negative association between self-esteem and general distress ($\beta = -0.46$, $p = 0.01$).

Table 4 shows the results of the exploration on the impact of specific aspects of self-concept (i.e. stigma, vulnerability and mastery) in women with high versus low self-esteem. The performance of the model was good (χ^2 (33) = 40.00; p = 0.19). The other indices also indicated that this model was good (CFI = 0.95; TLI = 0.93; RMSEA = 0.04; SRMR = 0.03). In the group of women with low self-esteem, significant positive associations were found with general distress for stigma and mastery ($\beta = 0.34$, $p = 0.01$ and $\beta = 0.20$, $p = 0.04$, respectively) (Table 4). This means that women who feel more stigmatized and women with a reduced sense of mastery reported more general distress. Furthermore, feeling stigmatized was significantly associated with more breast cancer specific distress ($\beta = 0.55$, $p = 0.01$). In women with high self-esteem, positive associations were found with breast cancer specific distress for stigma and vulnerability ($\beta = 0.26$, $p = 0.02$ and $\beta = 0.28$, $p = 0.01$, respectively). In this group, no significant associations were found for any of the three self-concept variables with general distress.

Table 4. Impact of self-concept aspects on general distress and breast cancer specific distress in women with high and low self-esteem

	Variable	General distress		Breast cancer specific distress	
		β^1	p	β	p
Low self-esteem	Stigma	**0.34**	***0.01***	**0.55**	***0.01***
	Vulnerability	0.00	0.95	0.14	0.16
	Mastery	**0.20**	***0.04***	0.01	0.98
High self-esteem	Stigma	0.18	0.11	**0.26**	***0.02***
	Vulnerability	0.01	0.95	**0.28**	***0.01***
	Mastery	0.04	0.65	-0.12	0.20

[1] Standardized regression coefficient as a measure of relative importance
Adjusted for age, education level, having a partner, having children, carrier status, type of management option and cancer-related events

DISCUSSION

The current study is the first analysis into the impact of specific self-concept variables related to hereditary breast cancer in a group of women at risk for hereditary breast cancer, and demonstrates that both general self-esteem and feeling stigmatized were of significant impact on psychological distress.

Self-esteem was negatively associated with general distress, suggesting a buffering effect of self-esteem. This finding is consistent with data observed in cancer patients, indicating negative associations between self-esteem and depressive symptoms (10).

Possibly, a higher level of self-esteem is preceded by earlier experiences of successful coping, and accordingly women with high self-esteem are more likely to feel that they can manage stressful situations and are less likely to negatively attribute stressful life events to themselves (9, 26, 27). However, we did not find a significant relationship between self-esteem and breast cancer specific distress. While general self-esteem contributes to one's overall well-being, specific self-concept aspects being most vulnerable in women at risk for hereditary breast cancer may be more important for breast cancer specific distress.

A key finding of the current study was that stigma was strongly associated with increased levels of breast cancer specific distress, and to a lesser degree with general distress. Perceiving stigmatization implies feeling labelled, isolated and different from others (16). Women participating in this study may perceive themselves as different or labelled because of the increased risk of developing breast cancer or because of the physical deviance after prophylactic surgery. Noteworthy, we did not observe that women who opted for prophylactic surgery differed in the degree of feeling stigmatized from women who were adhering to regular breast cancer surveillance. Moreover, our findings indicate that the negative effect of stigmatization was most pronounced for women with low self-esteem. In the latter group, feeling stigmatized was strongly associated with breast cancer specific distress as well as with general distress. It is likely that perceiving one self as different or labelled is particularly distressing for women with low self-esteem, because these women are more sensitive to how others view them. In addition, a reduced sense of mastery was associated with a higher level of general distress in women with low self-esteem. Both self-esteem and mastery reflect a sense of resilience, and may buffer the stressful effects of being at risk for hereditary breast cancer. Having low levels of self-esteem and mastery may have a negative impact on general distress, through the related negative cognitions they entail (9). Also, women with low-levels of self-esteem and mastery may be less likely to use appropriate adaptive coping strategies (9, 27).

In women with high self-esteem, we observed that feeling stigmatized and vulnerable was associated with more breast cancer specific distress. The observation that negative alterations in the scores on these self-concept variables only affected breast cancer specific distress, whereas the level of general distress remained unaffected, may reflect greater resilience among women with high-self esteem as compared to women with low self-esteem.

Strengths of our study are the large sample size and the inclusion of both women adhering to regular surveillance and women having undergone prophylactic surgery (either prophylactic mastectomy and/or salpingo-oophorectomy), ensuring generalizability of the findings. Results of analysing the impact of self-concept in the subgroup of women adhering to regular surveillance indicated that the associations with psychological distress in the restricted group were comparable to the observations found for the total study population. Some limitations of the study, however, should be considered. First, as it is a cross-sectional study, the conclusions are limited to inferences regarding associations rather than cause and effect relationships. Second, we used the BRCA Self-Concept Scale to measure self-concept in a cohort of women at risk for hereditary breast cancer rather than solely BRCA mutation carriers. Esplen et al. (16) acknowledge that the scale may not be generalizable to women without a BRCA1/2 mutation. Nevertheless, we believe that the self-concept items are relevant for the whole population of women at risk for hereditary breast cancer. For example, women with a family history of breast cancer may feel vulnerable and different from others, regardless of whether one has undergone genetic testing or not. The Cronbach alpha's found in the current study were comparable to those reported in the study of Esplen et al (16), therefore the use of the BRCA Self-Concept Scale in this study cohort shows promise. Finally, it might be that variables of interest are not represented in this study. In this respect, it is of clinical interest to further explore the interrelationships between these psychological variables and social variables, such as social support and communication style. Esplen et al. (16) suggested that feeling stigmatized may play a role in obtaining support or the communication style with family members. Moreover, women with high self-esteem may have more social skills. Conversely, social support may also have positive effects on self-esteem and self-concept (27). Future research, therefore, should examine how psychological and social resources interrelate with respect to psychological distress, in order to further clarify whether these resources strengthen each other or can substitute for one another.

In the meanwhile, we recommend genetic counsellors and physicians involved in the care of women at risk of hereditary breast cancer to pay more attention to the self-perception of these women. Particularly, the assessment of self-concept aspects related to hereditary breast cancer (as described in this analysis) in addition to more general characteristics may provide clues for tailoring counselling and support. Supportive counselling interventions or support groups may be beneficial by reducing feelings of isolation or stigmatization (16). Finally, fostering feelings of mastery by identification of personal strengths from past accomplishments might promote the psychological adjustment of women at risk for hereditary breast cancer.

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Chapter 3

Psychological distress in women at risk for hereditary breast cancer: the role of family communication and perceived social support

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ABSTRACT

Background: Hereditary breast cancer has a profound impact on individual family members and on their mutual communication and interactions. The way at-risk women cope with the threat of hereditary breast cancer may depend on the quality of family communication about hereditary breast cancer and on the perceived social support from family and friends.

Objective: To examine the associations of family communication and social support with long-term psychological distress in a group of women at risk for hereditary breast cancer, who opted either for regular breast surveillance or prophylactic surgery.

Methods: The study cohort consisted of 222 women at risk for hereditary breast cancer, who previously participated in a study on the psychological consequences of either regular breast cancer surveillance or prophylactic surgery. General and breast cancer specific distress, hereditary cancer related family communication, perceived social support and demographics were assessed.

Results: Using structural equation modelling we found that open communication about hereditary cancer within the family was associated with less general and breast cancer specific distress. In addition, perceived support from family and friends was indirectly associated with less general and breast cancer specific distress through open communication within the family.

Discussion: These findings indicate that family communication and perceived social support from friends and family are of paramount importance in the long-term adaptation to being at risk for hereditary breast cancer. Attention for these issues needs to be incorporated in the care of women at risk for hereditary breast cancer.

INTRODUCTION

Women identified with a mutation in BRCA1 or BRCA2 have a significantly increased cumulative lifetime risk (i.e. up to the age of 70 years) for breast cancer of 40-85%, and for ovarian cancer of 11-65% (1-4). Women from families with a history of breast cancer but without an as yet identified BRCA1/2 mutation are also at increased risk for breast cancer compared to the general population. For both groups, management options include regular surveillance of the breast tissue and prophylactic surgery.

Hereditary breast cancer has a profound impact on individual family members and on their mutual communication and interactions (5-8). Therefore, family system characteristics may influence the way women cope with the threat of developing hereditary cancer. Family members may share appraisals of breast cancer threat (9). Most studies investigating the impact of family system characteristics have focused on psychological distress during and shortly after genetic testing. A family system characteristic that has been found to be of paramount importance is the quality of family communication. One study performed in women from identified BRCA1/2 families reported that open communication about hereditary cancer within the family during genetic testing had a positive effect on cancer related distress up to six months after test results (10). In that study, it was also found that social support during genetic testing- in particular of the partner- was an important buffer against psychological distress (10). The buffering effect of partner support has also been described in other studies (11-13).

Little research has been done on the psychological adjustment of women at increased risk for hereditary breast cancer on the long-term. One study conducted at our institute, examining psychological distress in at-risk women 5 years after genetic testing, showed that an open family communication style was associated with less psychological distress on the long-term (14). Low psychological distress may be considered as an indicator of positive psychological adjustment to the threat of having an increased risk of developing breast cancer. Furthermore, data from another study in at-risk women suggest that social support is associated with long-term adjustment (9). Yet, in view of the small sample sizes in these studies, this issue needs further investigation.

All of the above mentioned studies suggest positive effects on distress of an open family communication and social support. However, none of these studies examined the interrelationships between family communication and social support. Social support and family communication are likely to be related. Women who feel supported may feel less inhibited to talk in an open way about breast cancer. Also, it has been suggested that communicating about breast cancer is a means for eliciting social support (15). These interrelationships should be taken into account, in order to draw conclusions on the independent contribution of social support and family communication to psychological adjustment in at-risk women. Moreover, focusing on these interrelationships may provide insight into how family communication and social support affect psychological adjustment. As communication about breast cancer may be motivated by needs for social support, it is of interest to question whether the positive effects of talking about breast cancer are mediated by social support. Alternatively, women who feel supported may be more likely to talk in an open way about breast cancer, which in turn might account for less psychological distress.

The present study aimed to gain more insight into how family communication and social support jointly were related to long-term psychological distress in women at risk for hereditary breast cancer, who opted either for regular breast cancer surveillance or prophylactic surgery. It was examined whether both social support and family communication were directly associated with psychological distress, thus independently contributed to psychological distress. Furthermore it was examined whether (1) family communication was indirectly associated with psychological distress, through social support, and (2) social support was indirectly associated with psychological distress, through family communication. This analysis was performed in the context of a research project studying several aspects of long-term psychological adjustment in this patient group.

MATERIAL AND METHODS

Participants

The current analysis has been performed within the context of a follow-up study on two earlier projects – one on the psychological consequences of regular surveillance (MRISC-B) and the other on the psychological consequences of prophylactic surgery (mastectomy and/or oophorectomy) (PREVOM-B) in women at risk for hereditary breast cancer. Women with a history of breast cancer were excluded from the MRISC-B study, whereas this was not an exclusion criterion for the PREVOM-B study. Detailed descriptions of the MRISC-B and PREVOM-B studies have been published elsewhere (16, 17). Women were eligible for the follow-up study if they participated in either MRISC-B or PREVOM-B, and did not develop breast or ovarian cancer since enrollment in these studies. The psychological follow-up study included a total of 248 women; 206 women from MRISC-B and 42 women from PREVOM-B. For this analysis, only women having a partner were included because the study aimed at examining the effects of communication about hereditary cancer both within the nuclear family (partner, children) and the family of origin (parents, siblings). The total number of women included in the current analysis comprised 222, which is 90% of the total group. Women had sufficient understanding of the Dutch language to fill in the questionnaires and all gave informed consent. Approval was obtained from the Medical Ethical Committee of the Erasmus Medical Center in Rotterdam.

Procedure

Women previously participating in the MRISC-B or PREVOM-B study were sent a letter informing them about the follow-up study along with an informed consent form and a prepaid envelope. After written informed consent, women were sent the first questionnaire of this follow-up study to their home two months prior to their next appointment at the family cancer clinic of the Erasmus MC-Daniel den Hoed Cancer Centre in Rotterdam.

Design

This study was set up as a longitudinal observational study on the long-term psychological impact (i.e. between 4 and 9 years since enrollment in the MRISC-B and PREVOM-B studies) of either regular breast cancer surveillance or prophylactic surgery in women at risk for hereditary breast cancer. The cross-sectional analysis for this article was carried out on the data obtained from the first assessment, performed two months prior to the women's appointment at the clinic (M0). The assessments took place between June 2007 and October 2009.

Measures

Independent variables

Demographic data

Data on age, educational level, having children, history of breast cancer were obtained by means of a questionnaire.

Type of management option

Women were categorized into three groups: 1) women who opted for regular surveillance, 2) women who had undergone prophylactic oophorectomy, and 3) women who had undergone prophylactic mastectomy with or without prophylactic oophorectomy.

Cancer-related events in the family of origin

Information was gathered on whether or not the women had a mother or sister who had developed breast or ovarian cancer and whether a mother or sister had died of breast or ovarian cancer.

Family communication about hereditary cancer

The Openness to Discuss Cancer in the Family Scale (18) adapted to hereditary cancer (14) was used to measure openness of communication about hereditary cancer. The scale comprises 14 items on communication within the nuclear family (i.e. partner, children) and within the family of origin (i.e. parents, siblings) that have to be rated on a 5-point scale ranging from 1= "Yes!" to 5= "No!". The scale was validated in a group of women from families with a BRCA1/2 mutation, which revealed adequate reliability in the nuclear family (Cronbach's $\alpha = 0.78$) and in the family of origin (Cronbach's $\alpha = 0.82$) (14).

Social support

The Multidimensional Scale of Perceived Social Support (MSPSS) (19) is a 12-item scale that assesses perceived support. The scale yields three subscale scores for Family, Friends and Significant other. Each of the three subscales is measured with four items, with response options ranging from 1= "strongly disagree" to 7= "strongly agree". Previous research demonstrated good internal consistency for the Family, Friends and Significant other subscales (0.87, 0.85 and 0.91, respectively) (20, 21).

Dependent variables

Breast cancer specific distress

Intrusion and avoidance -two common responses to stressful situations- were assessed using the Impact of Events Scale (IES) (22). This questionnaire comprises 15 items and can be tailored to a specific event, namely 'breast cancer' in this study. Avoidance is measured in 8 items and intrusion in 7 items, and each item has four answer categories: not at all (score 0), seldom (score 1), sometimes (score 3), and often (score 5). The Dutch version of the IES has been subjected to reliability analysis, the avoidance subscale was found to have an internal consistency of 0.66 and the intrusion subscale of 0.72 (23).

General distress

The Hospital Anxiety and Depression Scale (HADS) is a 14-item questionnaire, measuring anxiety (7 items) and depression (7 items) (24). Every item has four response categories, anchored to that specific item. Each subscale has a score range from 0 to 21. A Dutch reliability study revealed an internal consistency of 0.84 for anxiety, 0.86 for depression and 0.90 for the entire scale (25).

Statistical analyses

Missing values on the items composing outcome variables were handled as follows: a total score corrected for the total number of questions of the subscale was calculated for participants who filled in more than 75% of the questions per subscale. No total score was calculated for participants who filled in less than 75% of the questions per subscale. The missing values of the independent variables resulted mainly from the fact that some women had no children, siblings or parent(s) at the time of the study, and were therefore not estimated. Frequency analysis was used to describe the characteristics of the participants. To test whether there were differences between the three management options we used one-way analysis of variance. The basic analyses were carried out using the SPSS 15.0 statistical package (SPSS Inc., Chicago).

To explore the relationship between communication within the family and social support as independent variables and psychological distress as outcome variables, Structural Equation Modelling (SEM) was applied. In general, modelling is aimed to identify the most plausible model. The maximum likelihood estimation method was used to identify the model and to estimate the parameters of the individual independent variables. SEM analyses were done with Mplus (Muthen & Muthen, 2004).

The plausibility of four models was tested, being: (1) whether family communication was indirectly related to the distress variables through social support; (2) whether family communication –in addition to its indirect relation- had a direct relation with the distress variables; (3) whether social support was indirectly related to the distress variables through social support; (4) whether social support -in addition to its indirect relation- had a direct relation with the distress variables.

As measures of model performance, χ^{2}-tests were used for determining the adequacy of the model-fit. A non-significant *p*-value (*p* >0.05) and the ratio of $\frac{\chi^2}{df}$ <1.5 would represent a good model-fit. Four other goodness-of-fit indices were also used: Comparative Fit Index (*CFI* >0.95), Tucker-Lewis Index (*TLI* >0.95), Root Mean Square Error of Approximation (RMSEA ≈0.05) and Square Root Mean Residuals (SRMR<0.05). As a measure of the individual performances of the independent variables we have used the standardized regression coefficient and the corresponding p-value.

In this study we considered age, education level, having children, cancer history, type of management option and cancer-related events as potential confounder variables. Standardized regression coefficients (β) were used as measures of relative importance. All statistical testing occurred at 0.05 level of significance (two-tailed).

RESULTS

Sample characteristics

The characteristics of the 222 women included in this analysis are shown in Table 1. The majority of the women had at least a middle level education (82%) and one or more children (84%). The mean age was 47.1 years (range 29 – 68 years). The three types of management options were not equally represented: 72% (n=159) of the women was adhering to regular breast cancer surveillance, 13% (n=28) had undergone prophylactic oophorectomy, and 15% (n=35) had undergone prophylactic mastectomy. At the time of data collection for this study, there were no significant differences between the three management options groups on family communication, social support and both breast cancer specific and general distress (data not shown).

Table 1. General characteristics of the study sample

Variable	Total (N=222)
Age; mean (sd)	47.1 (8.3)
Educational level[1]	
High	72 (32%)
Middle	111 (50%)
Low	33 (15%)
Having children	186 (84%)
BRCA1/2 mutation carrier	66 (30%)
Type of risk management[2]	
Regular surveillance	159 (72%)
PSO	28 (13%)
PM	14 (6%)
PM + PSO	21 (9%)
Cancer related events	
Having a mother/sister diagnosed with breast/ ovarian cancer	186 (84%)
Having a mother/sister died of breast/ovarian cancer	130 (60%)

[1] Percentages do not add up to 100% because of missing values

[2] PSO: prophylactic salpingo-oophorectomy; PM: prophylactic mastectomy

Intercorrelations between family communication, social support and distress variables

Intercorrelations and mean values of family communication, social support and psychological distress variables are displayed in Table 2. The mean value on general distress of the women in this analysis was 7.2, which was significantly lower than the mean value of 8.4 found in a general Dutch population sample (p = 0.01) (25).

Table 2. Intercorrelations[1], ranges and means of family communication and social support variables

Variable	1.	2.	3.	4.	5.	6.	7.	Scale range[2]	M	SD
Open communication										
1. Nuclear family		.36**	.20*	.32**	.39**	-.28**	-.30**	7-35	28.3	6.2
2. Family of origin			.13	.31**	.21*	-.31**	-.29**	7-35	27.6	7.9
Social support										
3. Significant other				.41**	.52**	.03	-.21**	4-28	24.9	5.0
4. Family					.40**	-.08	-.25**	4-28	22.2	5.9
5. Friends						.04	-.23**	4-28	23.1	4.6
Psychological distress										
6. Breast cancer specific distress							.50**		7.8	11.5
7. General distress									7.2	6.8

[1] Pearson correlation coefficients
[2] Theoretical scale range
* $p<0.05$ (two-tailed)
** $p<0.01$ (two-tailed)

Psychological distress related to family communication and social support

The results of testing the plausibility of four models, on whether family communication and social support had indirect and/or direct associations with both types of distress, are shown in Table 3. The most plausible model was model 4 (χ^2 (18) = 20.90; $p = 0.28$), which is visualized in Figure 1.

In this model, social support had an indirect association with both types of distress, mediated by family communication. Support from the family had a significant positive association with both open communication within the nuclear family and open communication within the family of origin ($\beta = 0.20$, $p = 0.02$ and $\beta = 0.27$, $p = 0.01$, respectively). Also, support from friends was significantly associated with more open communication within the nuclear family ($\beta = 0.28$, $p = 0.01$). Open family communication, in turn, was directly related to less breast cancer specific and general distress. Both open communication within the nuclear family and open communication within the family of origin were associated with less breast cancer specific distress ($\beta = -0.27$, $p = 0.01$ and $\beta = -0.23$, $p = 0.01$, respectively). Furthermore, a significant association was found for open communication within the family of origin with general distress ($\beta = -0.18$, $p = 0.05$). There was a negative association between open communication within the nuclear family and general distress, although this was not significant ($\beta = -0.17$, $p = 0.06$).

Furthermore, this model implied that social support had a direct association with both types of distress. Although the association of family support with general distress was not significant ($\beta = -0.13$, $p = 0.09$), this model had a better fit than model 3, which was the same as model 4 except that it did not allow a direct association between social support and both types of distress.

Table 3. Plausibility of four models regarding distress variables in relation to family communication and social support

Model[1]	Indirect effect family communication[2]	Direct effect family communication	Indirect effect social support[3]	Direct effect social support	χ^2	df	χ^2/df	p-value	CFI	TLI	RMSEA	SRMR
1	+	-	-	+	23.70	4	5.93	0.00	0.93	0.07	0.15	0.04
2	+	+	-	+	55.43	21	2.94	0.00	0.88	0.69	0.09	0.06
3	-	+	+	-	18.75	6	3.13	0.00	0.92	0.35	0.10	0.02
4	**-**	**+**	**+**	**+**	**20.90**	**18**	**1.16**	**0.28**	**0.98**	**0.94**	**0.03**	**0.05**

[1] A non-significant p-value (p >0.05) and the ratio of $\frac{\chi^2}{df}$<1.5would represent a good model-fit.

[2] Indirect association of family communication with both types of distress mediated by social support

[3] Indirect association of social support with both types of distress mediated by family communication

+ = Levels of distress were indirect/direct related to family communication and social support, respectively

- = Levels of distress were not indirect/direct related to family communication and social support, respectively

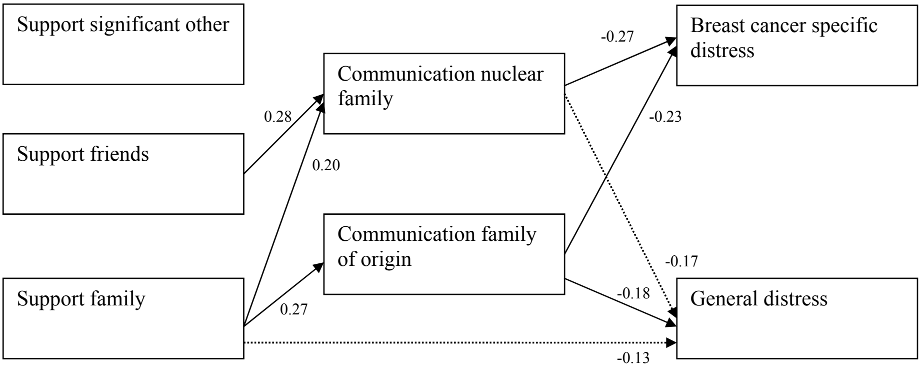
CFI = Comparative Fit Index

TLI = Tucker-Lewis Index

RMSEA = Root Mean Square Error of Approximation

SRMR = Standardizes Root Mean Square residual

Figure 1. Association between social support, family communication and psychological distress variables[1]



[1] Marked pathways represent significant regression weights between the variables ($p \leq 0.05$).

Dotted pathways represent a trend ($p \leq 0.1$).

DISCUSSION

The results of the current report on the long-term psychological outcomes of women at risk for hereditary breast cancer suggest that family communication about hereditary cancer and social support are of paramount importance in the long-term adaptation to being at risk for hereditary breast cancer.

A key finding was that family communication about hereditary cancer is important for long-term adjustment. Women who were communicating in an open way about their thoughts and feelings regarding hereditary cancer with family members reported less breast cancer specific distress and general distress. Similar findings hereon have been reported when studying women from BRCA1/2 mutation families at six months (10) as well as at five years after genetic testing (14). If communication about hereditary cancer is hampered, the woman may remain alone with her worries and emotions, and feel isolated. It has been suggested that talking about one's feelings might promote psychological adjustment by eliciting social support (15). The results of our study, however, indicate that the positive effect of open family communication on psychological distress is direct, and not mediated by social support. Furthermore, it has been shown that individuals who perceived the communication about hereditary cancer as less open reported more intimate relational difficulties after genetic testing (5). So, couples who are encouraged to talk in an open way about their emotions related to hereditary cancer might enrich their relationship and enhance feelings of intimacy. Besides the interpersonal mechanism, there might be an intrapsychic mechanism by which communication about hereditary cancer reduces distress. Talking about feelings and thoughts about hereditary cancer may facilitate insight (15). Attempting to verbalize the feelings regarding hereditary cancer can help people to understand their feelings more clearly. Talking with others about hereditary cancer can also lead to new perceptions and a broader perspective on the hereditary cancer related worries.

Another main finding was that there was an indirect positive effect of perceived support from family and friends on psychological distress, which was mediated by family communication about hereditary cancer. Furthermore, there was a weak direct association between family support and general distress, although this was not significant. The positive effect of support from the family during and shortly after genetic testing has been demonstrated in a previous study (10). In that study, social support was measured with two items tailored to measure family support regarding hereditary cancer. A possible explanation for the lack of significant associations between social support and psychological distress in the current study is that the Multidimensional Scale of Perceived Social Support measures the general support a woman perceives. It may be that a more cancer-specific measure of social support would reveal direct associations with psychological distress. The finding of the current study that the effects of social support on psychological distress is mediated by open family communication, implies that the process of translating social support into coping may involve talking in an open way about breast cancer. Women who feel supported by their immediate environment are more likely to communicate in an open way about hereditary cancer with their close relatives (i.e. partner, children, parents and siblings), which may in turn promote individual psychological adjustment. These findings underscore that attempts to be supportive may not always have a beneficial effect. It seems that providing support by talking about feelings regarding hereditary cancer provides the most benefit. As a consequence, not talking about hereditary cancer in order not to upset and burden the respective person, also called 'protective buffering'(26), however well-intended, might not be helpful in this patient group.

It is noteworthy that we did not find any association between support from a significant other person and psychological distress. We speculate that it was not clear for participants who to consider as a significant other. Hence, it is difficult to comment further on these data. More research hereon therefore should be performed.

To our knowledge, this is the first study to examine the role of family communication about hereditary cancer and social support in psychological distress on the long term in women at risk for hereditary breast cancer. A particular strength of the study is the large sample size. On the other hand, our study sample consisted only of women having a partner. Women without a partner were excluded for statistical reasons. However, it is possible that the effects of social support and communication within the family on psychological distress are different for women without a partner. We speculate that support from friends may be more important for these women. Future research is warranted to examine the effects of family communication and social support on psychological distress in women without a partner.

Our findings underscore that the quality of family communication and support from family and friends is important for women at risk for hereditary breast cancer, also for long-term adjustment. An elaboration on approaches that can be applied to the clinical setting is beyond the scope of the article. However, in general, exploration of the dynamics in family interaction and communication might provide a starting point for facilitation of open family communication. A couple-focused approach may be beneficial if communication about hereditary cancer with the partner is impeded, which has been shown to be efficacious for breast cancer patients (27, 28).

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Chapter 4

The impact of social and personal resources on psychological distress in women at risk for hereditary breast cancer

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ABSTRACT

Objective: The objectives of the present study were (1) to evaluate whether social and personal resources were independently related to psychological distress, and (2) to examine the interrelationships of social and personal resources in women at risk for hereditary breast cancer.

Methods: General and breast cancer specific distress, family communication regarding hereditary breast cancer, perceived social support, self-esteem, self-concept and demographics were assessed in 222 high-risk women, having opted either for regular surveillance or prophylactic surgery.

Results: Structural equation modelling showed that (1) both personal and social resources were independently associated with psychological distress, and (2) the associations between social resources and psychological distress were partially mediated by personal resources. Support from family and friends was associated with a higher level of self-esteem, which in turn was associated with less general distress. Furthermore, communication regarding cancer within the nuclear family was associated with decreased feelings of stigmatization, which in turn was associated with less general and breast cancer specific distress. Moreover, open communication within the family was associated with a reduced sense of vulnerability.

Conclusion: Health workers involved in the care of high-risk women should carefully monitor women's personal and social resources, and if compromised refer them for appropriate support.

INTRODUCTION

It is estimated that approximately 5-10% of all breast cancer cases are due to a genetic predisposition. By means of genetic testing, a mutation in the breast cancer susceptibility genes BRCA1 or BRCA2 can be identified in approximately 15-20% of the suspected families (1). Women identified with a mutation in BRCA1/2 have a significantly increased cumulative lifetime risk of developing breast cancer (40-85%) and/or ovarian cancer (11-65%) (2-5). Women from families with a clustering of breast/ovarian cancer, but without an as yet identified BRCA1/2 mutation, remain at increased risk for breast cancer and in general are offered regular breast cancer surveillance. Although the initial short-term response to being at increased risk for hereditary/familial breast cancer may include elevated levels of distress, the majority of women adjust well over time (6-8). Nevertheless, a subgroup of women is at risk for experiencing elevated levels of psychological distress over time (9).

Social and personal resources may play an important role in the adjustment to being at risk for hereditary breast cancer. Self-esteem is an important personal resource and may buffer the effects of cancer-related stressors (10-11). In line with this, a positive impact of self-esteem on general distress was observed in a previous analysis of our group examining the roles of multiple aspects of the self-concept regarding psychological distress in women at risk for hereditary breast cancer (12). In addition, we found that feeling stigmatized was important, in that women who felt stigmatized (e.g. felt labeled, isolated and different than others (13)) because of the hereditary breast cancer risk experienced increased levels of psychological distress.

With regard to social resources, studies have shown a positive impact of social support – in particular from the partner- on psychological distress (14-16). Little research, however, has been done on how and why social support influences psychological distress. In order to arrive at a better understanding of how social resources influence well-being, mediational models need to be tested. Previously, we found that more open communication about hereditary cancer is one way by which social support may buffer psychological distress (17). Women who felt supported by their close environment (e.g. family and friends) were more likely to talk in an open manner about hereditary breast cancer within the family, which, in turn, had a beneficial effect on psychological distress.

In sum, several studies on psychological distress in women at risk for hereditary breast cancer so far have shown significant effects of social and personal resources. To date, no data is available evaluating the impact of social and personal resources simultaneously. However, it is likely that personal and social resources affect each other (11). For instance, women with high self-esteem may have greater social skills, and consequently receive more social support (18). Conversely, social support may strengthen a woman's self-esteem. Indeed, several studies have shown that social support effects were (partially) mediated by self-esteem, suggesting that the process of translating social support into coping may involve personality factors (19-22). Focusing on intervening mechanisms will enrich our understanding on how the various resources available to a person influence psychological well-being.

In the current analysis it was examined how social and personal resources are interrelated in their effects on psychological distress in women at risk for hereditary breast cancer. One aim was to evaluate whether social and personal resources were independently related to psychological distress. The second aim was to determine whether (1) personal resources mediated the relationships between social resources and psychological distress; or (2) social resources mediated the relationships between personal resources and psychological distress. We hypothesized that personal resources would mediate the relationships between social resources and psychological distress. That is, it was hypothesized that social resources would strengthen personal resources, which in turn would be related to less psychological distress.

MATERIAL AND METHODS

Participants

Between 1999 and 2003, women at risk for hereditary breast/ovarian cancer were included in either the MRISC-B study (addressing the psychological consequences of regular breast cancer surveillance) or the PREVOM-B study (addressing the psychological consequences of prophylactic mastectomy and/or salpingo-ovariectomy). Women with a history of breast cancer were excluded from the MRISC-B study, whereas this was not an exclusion criterion for the PREVOM-B study. Detailed descriptions of the MRISC-B and PREVOM-B studies have been published elsewhere (23-24).

In 2007, a follow-up study was activated investigating the long-term psychological impact (i.e. between 4 and 9 years since enrollment in the MRISC-B and PREVOM-B studies) of either regular surveillance or prophylactic surgery in women at risk for hereditary breast cancer. Women were eligible for the follow-up study if they had participated in either MRISC-B or PREVOM-B. Women who developed breast or ovarian cancer since enrollment in these studies were not eligible for the follow-up study. Eligible women had sufficient understanding of the Dutch language to fill in the questionnaires and all gave informed consent for the follow-up study. Approval was obtained from the Medical Ethical Committee of the Erasmus Medical Center in Rotterdam.

This study was set up as a longitudinal observational study on the long-term psychological impact (i.e. between 4 and 9 years since enrollment in the MRISC-B and PREVOM-B studies) of either regular breast cancer surveillance or prophylactic surgery in women at increased risk for hereditary breast cancer. The assessments took place between June 2007 and October 2009.

The psychological follow-up study included a total of 248 women; 206 women from MRISC-B and 42 women from PREVOM-B. For the current analysis, only women having a partner were included because the study aimed at examining the effects of communication about hereditary cancer both within the nuclear family (partner, children) and the family of origin (parents, siblings). The total number of women included in the current analysis comprised 222, which is 90% of the total group. The analyses for the current article were carried out on the data obtained from the first assessment, performed two months prior to the women's appointment at the clinic.

Procedure

Women having participated in the MRISC-B or PREVOM-B study, and still being under surveillance at the family cancer clinic (FCC) of the Erasmus MC-Daniel den Hoed Cancer Centre, were sent an information letter regarding the psychological follow-up study along with an informed consent form and a prepaid envelope. After receipt of written informed consent, women were sent the first questionnaire of this follow-up study to their home two months prior to their next appointment at the family cancer clinic of the Erasmus MC-Daniel den Hoed Cancer Centre in Rotterdam.

Measures

Biographical and medical data

Data on age, having a partner, having children, educational level, type of management option and cancer-related events in the family of origin were obtained by means of a questionnaire.

Outcome variables

Breast cancer specific distress

Intrusion and avoidance -two common responses to stressful situations- were assessed using the Impact of Events Scale (IES) (25). This questionnaire comprises 15 items and can be tailored to a specific event, namely 'breast cancer' in this study. Avoidance is measured in eight items and intrusion in seven items, and each item has four answer categories: not at all (score 0), seldom (score 1), sometimes (score 3), and often (score 5). The Dutch version of the IES has been subjected to reliability analysis, the avoidance subscale was found to have a Cronbach's alpha of 0.66 and the intrusion subscale of 0.72 (26).

General distress

The Hospital Anxiety and Depression Scale (HADS) is a 14-item questionnaire, measuring anxiety (7 items) and depression (7 items) (27). Every item has four response categories, anchored to that specific item. Each subscale has a score range from 0 to 21. A Dutch reliability study revealed a Cronbach's alpha of 0.84 for anxiety, 0.86 for depression and 0.90 for the whole scale (28).

Personal variables

Self-concept

The BRCA Self-Concept Scale (13) is a 17-item scale with answers ranging from 1 ('strongly disagree) to 7 ('strongly agree'). The scale comprises three subscales for stigma, vulnerability and mastery. The scale was validated among a group of female BRCA1/2 carriers, revealing good internal consistency, with reported Cronbach's alphas of 0.90 for the total scale, 0.87 for stigma, 0.76 for vulnerability and 0.68 for mastery. The original BRCA-Self Concept Scale was translated into Dutch by a translation agency, and formulations were adjusted by psychologists (J. V., A. T.) to cover the content of the items better. This scale was used in a pilot study (J. Vos et al, 2008), which lead to several small changes in formulations. The final version was back-translated into English, and no significant differences were found with the original scale.

Self-esteem

Self-esteem was assessed with the Rosenberg Self-Esteem Scale (RSES) (29), a 10-item scale with response options ranging from 1 = "strongly agree" to 4 = "strongly disagree". In this study Cronbach's alpha was 0.92.

Social variables

Family communication about hereditary cancer

The Openness to Discuss Cancer in the Family Scale (30) adapted to hereditary cancer (31) was used to measure openness of communication about hereditary cancer. The scale comprises 14 items on communication within the nuclear family (i.e. partner, children) and within the family of origin (i.e. parents, siblings) that have to be rated on a 5-point scale ranging from 1= "Yes!" to 5= "No!". The scale was validated in a group of women from families with a BRCA1/2 mutation, which revealed adequate reliability in the nuclear family (Cronbach's α = 0.78) and in the family of origin (Cronbach's α = 0.82) (31).

Social support

The Multidimensional Scale of Perceived Social Support (MSPSS) (32) is a 12-item scale that assesses perceived support. The scale yields three subscale scores for Family, Friends and Significant other. Each of the three subscales is measured with four items, with response options ranging from 1= "strongly disagree" to 7= "strongly agree". The MSPSS has demonstrated good psychometric properties (33-34).

Statistical analyses

For participants who filled in more than 75% of the questions per subscale, a total score corrected for the total number of questions of the subscale was calculated, whereas no total score was calculated for participants who filled in less than 75% of the questions per subscale. The missing values of the independent variables mainly resulted from the fact that some women had no children, siblings or parent(s) at the time of the study assessment, and were therefore not estimated. Frequency analysis was used to describe the characteristics of the participants. To test whether there were differences between the three management option groups we used the method of one-way analysis of variance in the case of continuous data and the method of chi-square in the case of ordinal data. The basic analyses were carried out using the SPSS 15.0 statistical package (SPSS Inc., Chicago).

The relationships between the distress variables, being outcome variables, and the personal and social variables, being independent variables, were explored by means of the method of Structural Equation Modeling (SEM). SEM enables one to identify, to test and to estimate the interrelationships of these variables. The maximum likelihood estimation method was used to evaluate the models and to estimate the parameters of the individual independent variables. SEM analyses were done with Mplus (Muthen & Muthen, 2004).

In order to obtain information on how psychological and social resources are interrelated in their impact on psychological distress, two models were tested. Both models assume that psychological and social variables are directly associated with distress variables, and that support variables have an effect on communication variables, as this was found in previous analyses (17). The models differ with regard to the character of the relationship between personal and social variables. According to model 1, personal variables would (partially) mediate the relationships between social and distress variables. Model 2, on the contrary, proposes that social variables would (partially) mediate the relationships between personal and distress variables.

As measures of model performance, χ^{2}-tests were used for determining the adequacy of the model-fit. A non-significant *p*-value ($p > 0.05$) and the ratio of $\frac{\chi^2}{df} < 1.5$ would represent a good model-fit. Also, four other goodness-of-fit indices were also used: Comparative Fit Index (*CFI* >0.95), Tucker-Lewis Index (*TLI* >0.95), Root Mean Square Error of Approximation (RMSEA <0.05) and Square Root Mean Residuals (SRMR<0.05). As a measure of the individual performances of the independent variables we have used the standardized regression coefficient and the corresponding p-value.

Age, education level, having children, carrier status, type of management option and cancer-related events were considered as potential confounder variables. Standardized regression coefficients (β) were used as measures of relative importance. All statistical testing occurred at 0.05 level of significance (two-tailed).

RESULTS

Background characteristics

The characteristics of the 222 women included in this analysis are shown in Table 1. Most of the women had at least a middle level education (82%) and one or more children (84%). The mean age of the women was 47.1 years (ranging from 29 to 68 years). Most of the participants were adhering to regular surveillance (72%), while 13% had opted for salpingo-oophorectomy and 15% for prophylactic mastectomy. Of note, at the time of data collection for the current analysis, there were no significant differences between

Table 1. General characteristics of the study sample

Variable	Total (N=222)
Age; mean (sd)	47.1 (8.3)
Educational level[1]	
High	72 (32%)
Middle	111 (50%)
Low	33 (15%)
Having children	186 (84%)
BRCA1/2 mutation carrier	66 (30%)
Type of risk management[2]	
Regular surveillance	159 (72%)
PSO	28 (13%)
PM	14 (6%)
PM + PSO	21 (9%)
Cancer related events	
Having a mother/sister diagnosed with breast/ovarian cancer	186 (84%)
Having a mother/sister died of breast/ovarian cancer	130 (60%)

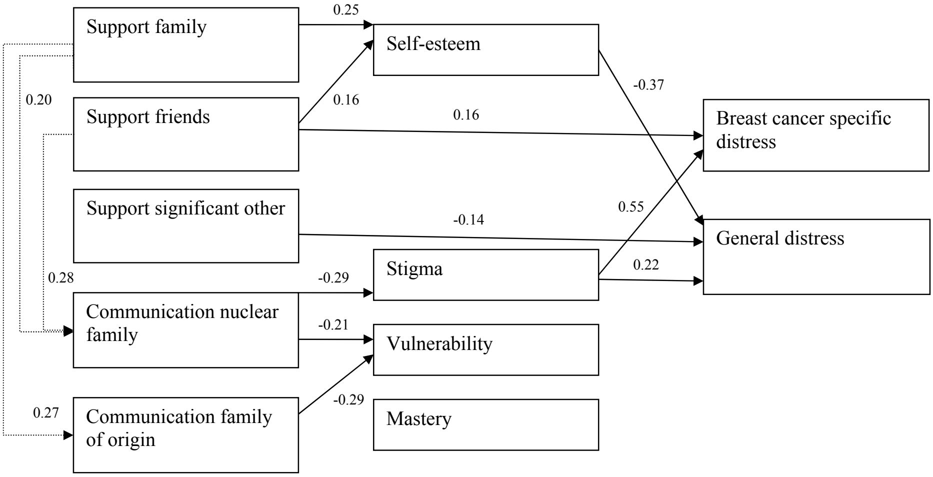
[1] Percentages do not add up to 100% because of missing values

[2] PSO: prophylactic salpingo-oophorectomy; PM: prophylactic mastectomy

the three management options groups regarding personal, social and distress variables (data not shown).

The interrelationships between personal and social variables were examined by evaluating two models. The Chi square fit-index of model 1 was good (χ^2 (48) = 59.53; p = 0.12). The other performance indices also indicated that this model was good (CFI = 0.98; TLI = 0.96; RMSEA = 0.03; SRMR = 0.05). The Chi square fit-index of model 2 was moderate although significant (χ^2 (64) = 100.84; p = 0.01). The other indices also indicated a moderate performance (CFI = 0.95; TLI = 0.90; RMSEA = 0.05; SRMR = 0.06). Accordingly, model 1 (visualized in Figure 1) fitted the data best, which implied that personal variables mediated the relationships between social and distress variables.

Figure 1. Interrelationships between the social, psychological an distress variables



Associations between social variables and personal variables

Table 2 shows the impact of social variables on personal variables. Support from both family and friends was associated with higher self-esteem (β = 0.25, p = 0.01 and β = 0.16, p = 0.03, respectively). Furthermore, open communication within the nuclear family was associated with feeling less stigmatized (β = -0.29, p = 0.01). Open communication both within the nuclear family and the family of origin was associated with feeling less vulnerable (β = -0.21, p = 0.02 and β = -0.29, p = 0.01, respectively).

Psychological distress related to personal and social variables

Data on the exploration of the direct associations between personal and relational variables on the one hand and distress as outcome variables on the other hand, is shown in

Table 2. Impact of social variables on personal variables

	Personal variables							
	Rosenberg self-esteem		Stigma		Vulnerability		Mastery	
Social variables	β[1]	p	β	p	β	p	β	p
Open communication								
Nuclear family	0.12	0.18	**-0.29**	***0.01***	**-0.21**	***0.02***	-0.12	0.17
Family of origin	0.12	0.17	-0.13	0.14	**-0.29**	***0.01***	-0.13	0.14
Social support								
Significant other	-0.05	0.56	0.12	0.11	0.08	0.31	0.00	0.98
Family	**0.25**	***0.01***	0.02	0.81	0.03	0.73	-0.03	0.66
Friends	**0.16**	***0.03***	-0.01	0.88	0.01	0.93	0.06	0.47

[1] Standardized regression coefficient as a measure of relative importance
Adjusted for age, education level, having a partner, having children, carrier status, type of management option and cancer-related events

Table 3. Feeling stigmatized was associated with more breast cancer specific and general distress (β = 0.55, p = 0.01 and β = 0.22, p = 0.01, respectively). High self-esteem was associated with less general distress (β = -0.37, p = 0.01). Support from friends was associated with more breast cancer specific distress (β = 0.16, p = 0.02), whereas support from a special person was associated with less general distress (β = -0.14, p = 0.03).

Table 3. Impact of personal and social variables on distress variables

Variable	General distress		Breast cancer specific distress	
	β[1]	p	β	p
Self-concept				
Stigma	**0.22**	***0.01***	**0.55**	***0.01***
Vulnerability	-0.04	0.61	0.03	0.74
Mastery	0.11	0.11	0.05	0.48
Rosenberg self-esteem	**-0.37**	***0.01***	0.02	0.73
Open communication				
Nuclear family	-0.05	0.53	-0.08	0.28
Family of origin	-0.11	0.19	-0.15	0.06
Social support				
Significant other	**-0.14**	***0.03***	-0.02	0.77
Family	0.00	0.99	0.03	0.63
Friends	0.09	0.21	**0.16**	***0.02***

[1] Standardized regression coefficient as a measure of relative importance
Adjusted for age, education level, having a partner, having children, carrier status, type of management option and cancer-related events

DISCUSSION

The present study aimed at gaining insight into how social and personal resources affect psychological distress in women at risk for hereditary breast cancer. It was observed that both personal and social resources play a role in the psychological adjustment of high-risk women. Moreover, our findings suggest that strengthening personal resources is one way by which social resources may affect psychological distress.

In the current analysis, it was found that self-esteem was associated with less general distress, whereas feeling stigmatized (e.g. feeling labeled, isolated and different than others (13)) was associated with both more breast cancer specific distress and general distress. The data, therefore, are in line with previous observations, as the importance of feeling stigmatized and self-esteem regarding psychological distress in women at risk for hereditary breast cancer has also been found in a previous study of our group (12). The current study extended the previous findings by examining personal and social resources simultaneously, while the concordant findings increase our confidence in the importance of self-esteem and feelings of stigmatization. Moreover, to our knowledge, the current study is the first to demonstrate that self-esteem and feelings of stigmatization at least partially mediated the relationships between social resources and psychological distress, thereby providing us new insights regarding the possible mechanisms by which social resources affect psychological distress.

Self-esteem mediated the relationships between social support from friends and family and general distress. Support from friends and family was positively associated with self-esteem, which in turn was inversely related to general distress. The finding that social support effects were mediated by self-esteem has previously been described for various populations (19-22). Support from family and friends conveys the idea that one is loved and valued, which may promote positive feelings toward the self. However, it should be emphasized that strengthening self-esteem is only one potential mechanism by which social support may buffer psychological distress. In fact, we previously reported that social support may also affect psychological distress in a positive way by increasing family communication about hereditary breast cancer (12).

Moreover, the current findings indicated that one way by which open communication within the nuclear family affects psychological distress is by decreasing feelings of isolation and stigmatization. Women who talk in an open manner about hereditary breast cancer with the partner were less likely to feel stigmatized, which, in turn, was associated with less psychological distress. These findings underline the importance of couple interactions with respect to reducing the feelings of stigmatization and isolation.

Furthermore, it was found that open communication regarding hereditary cancer within both the nuclear family and the family of origin was associated with a reduced sense of vulnerability. This finding is of clinical interest, as a greater sense of vulnerability may affect behavioral outcomes, such as the uptake of breast cancer surveillance (35-36).

Of the social resources, support from a significant other was directly associated with less general distress. This finding indicates that support of at least one significant person independently contributed to less general distress over and above the contribution of personal resources. Noteworthy, support from friends was associated with more breast cancer specific distress. At first sight this finding may seem inconsistent, since support from friends had indirect positive effects on psychological distress by bolstering self-esteem and promoting communication about hereditary breast cancer. Several explanations are possible. First, women who have friends whom they can share their worries about breast cancer with may be more aware of these worries and/or be more comfortable reporting them. Second, having easily available friends to discuss breast cancer worries with may be, at least for some women, associated with dwelling and focusing on these worries. While constructive expression of one's thoughts and feelings about breast cancer is most likely to be beneficial, dwelling on the negative aspects of one's situation or complaining may be unproductive (37). Alternatively, those women who experienced most distress may have received or sought more social support from friends. Most probably, support and distress are related in a bidirectional fashion across time. It is warranted that in future studies these issues should be investigated further.

Overall, attachment theory may provide a useful perspective in considering our findings. Attachment theory assumes that support that matters most is support provided by attachment relationships, in our study the significant other. Moreover, attachment theory denies that support from friends and relatives can compensate for the loss of support from an attachment figure (38). Consistent with this overall line of thinking, our findings point to the particular importance of support from a significant other who is close to the woman, i.e. attachment figure. Furthermore, one might hypothesize that secure attached women had higher self-esteem, and felt more competent in recruiting social support and to make use of that support. On the other hand, women with an insecure attachment -which is associated with worries about abandonment and about not being loved, as well as difficulties becoming close to others- may have lower self-esteem and increased distress (39). In a previous study of our group focusing on attachment in families with Huntington's disease, we have emphasized the relevance of attachment for psychological well-being in families with genetic disorders (40). Future studies should investigate the association between attachment style and adjustment of women at risk for hereditary breast cancer.

Some limitations in the current study should be acknowledged when interpreting the results. Our study sample was restricted to women having a partner, to ensure relative homogeneity with respect to social resources. This implies that the results can only be generalized to women with a partner. Future research is warranted to examine the effects of social and personal resources on psychological distress in women without a partner. Furthermore, as it was a cross-sectional study, the conclusions are limited to inferences regarding relations rather than cause and effect relationships. As mentioned above, many of these relations are probably reciprocal over time.

Nevertheless, the present study has several strengths and extends prior research data in several ways. First, the study sample consisted of a relatively large group of women adhering to regular surveillance or having undergone prophylactic surgery (either prophylactic mastectomy and/or salpingo-oophorectomy), not always being the case in other studies on this subject. Second, the inclusion of both personal and social resources enabled us to take the interrelationships between these resources into account when examining their independent associations with psychological distress. Third, both personal and social resources were examined as mediators. Previous research in which self-esteem mediation models were tested, did not examine the alternative interpretation that self-esteem effects are mediated by social support (22). Fourth, the inclusion of various personal resource types enabled us to detect differences in how specific personal resources functioned as a mediator for social resources. In sum, the inclusion of both personal and social resources has been valuable and generated extra information. Future studies should focus on combinations of these and other resources, in order to obtain an even more complete understanding of the roles of different resources available to high-risk women.

Overall, the results of the current analysis demonstrate that social and personal resources play a role in the adjustment of women at risk for hereditary breast cancer. Health workers involved in the care of these women, therefore, should carefully monitor women's personal and social resources, and if compromised refer particular women for additional support. Information on the role of personal and social resources and suggestions for enhancement of a woman's own resources may help to improve the management of the psychological consequences of being at risk for hereditary breast cancer. Interestingly, interventions aimed at increasing support and communication may also have a positive effect on a woman's self view.

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Chapter 5

Body image and psychological distress after prophylactic mastectomy and breast reconstruction in genetically predisposed women: a prospective long-term follow-up study

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ABSTRACT

Purpose: To explore the course of psychological distress and body image at long-term follow-up (6-9 years) after prophylactic mastectomy and breast reconstruction (PM/BR) in women at risk for hereditary breast cancer, and to identify pre-PM risk factors for poor body image on the long-term.

Methods: Psychological distress (general and breast cancer specific) and body image (general and breast specific) were assessed in 36 high-risk women before PM (T0), at 6 months (T1) and 6-9 years (T2) after PM/BR. Investigated predictive variables (assessed at T0) for long-term body image (assessed at T2) included psychological distress, body image and coping styles.

Results: Breast cancer specific and general distress significantly decreased from T0 to T1 as well as from T1 to T2. Problems regarding breast related and general body image were significantly higher at T1 than at T0. Subsequently, breast related body image scores significantly decreased from T1 to T2, while the decrease in general body image scores was not significant. Active coping and seeking social support were predictive of lower scores (i.e. less problems) on breast related and general body image at long-term follow-up. Furthermore, higher scores on general body image before PM/BR were predictive for increased general body image scores at long-term follow-up.

Conclusion: Our findings indicate that psychological distress is decreased after PM/BR, at the cost of persistent problems regarding body image. Exploration of coping styles and body image perception before PM/BR may help to identify vulnerable women who may benefit from additional support.

INTRODUCTION

At this moment, bilateral or contralateral prophylactic mastectomy with or without breast reconstruction (PM/BR) is the most effective, although radical, strategy to reduce the risk of breast cancer in high-risk women (1-3). As DNA-testing becomes more readily available and cosmetic results of reconstruction techniques are improving, PM has become an important and recognized option for women at risk for hereditary breast cancer. Balanced information regarding long-term psychological outcomes therefore is eagerly needed in order to enable adequate counselling of women considering PM/BR.

Overall, women at risk for hereditary breast cancer who have undergone PM are satisfied with their decision (4-6). Several studies concluded that PM may have psychological benefits in terms of reduced anxiety and worries about developing cancer (5, 7-10). Nevertheless, many women included in the studies reported negative effects of PM(/BR) on body image (5-6, 10-11). However, as most of these observations were obtained from retrospective studies, information on women's body image prior to PM is not available, and consequently changes in body image specifically as a result of PM/BR could not be assessed.

So far, prospective studies examining the effects of PM on psychological variables and body image have been scarce (11). One prospective, qualitative study reported reduced anxiety 18 months after PM, while no evidence was found for body image problems (8). In two other prospective studies with a follow-up of one year, reduced anxiety in women after PM was confirmed, while, in contrast, a substantial proportion of the women reported body image problems after one year (10, 12). However, it may be that a follow-up period of one year was too short to capture the assimilation of reconstructed breasts into a woman's body image, especially in view of the fact that the breast reconstruction period (depending on the reconstruction technique) may encompass several months. Therefore, longer follow-up data is needed on the psychological adjustment to PM/BR, especially regarding body image. Furthermore, no data is available on factors that are predictive of poor body image after PM/BR. Knowledge about these factors is important in order to enable early identification of women who may be vulnerable, and might benefit from additional support.

In the present prospective study, we aimed (1) to explore the course of psychological distress and problems regarding body image before PM and at long-term follow-up (6-9 years) after PM/BR in women at risk for hereditary breast cancer, and (2) to identify pre-PM variables being predictive of poor body image in the long term.

PATIENTS AND METHODS

Participants

Between 1999 and 2003, women at risk for hereditary breast/ovarian cancer who decided to undergo prophylactic mastectomy (PM) with/without BR or bilateral salpingo-ovariectomy (BPSO) at the Family Cancer Clinic of the Erasmus MC- Daniel den Hoed Cancer Centre were invited to participate in a study on the psychological impact of prophylactic surgery (PREVOM-B study). A history of breast or ovarian cancer was not an exclusion criterion, but women with (suspicion of) new or recurrent cancer were not eligible. Detailed descriptions of the PREVOM-B study have been published elsewhere (7, 13).

In 2007, a follow-up study was activated investigating the long-term psychological impact (i.e. between 6-9 years since enrollment in the PREVOM-B study) of prophylactic surgery in high-risk women. Women were eligible for the follow-up study if they had participated in PREVOM-B, had not developed a new cancer or recurrent cancer since enrollment in the PREVOM-B study, and still were in follow-up at the family cancer clinic of the Erasmus MC. Women had sufficient understanding of the Dutch language to fill in the questionnaires and all gave informed consent for the follow-up study. Approval for the follow-up study was obtained from the Medical Ethics Committee of the Erasmus Medical Center in Rotterdam.

Procedure

Women having participated in the PREVOM-B study and having undergone PM/BR were sent an information letter regarding the psychological follow-up study along with an informed consent form and a prepaid envelope. After receipt of written informed consent, women were sent the first questionnaire of this follow-up study to their home address two months prior to the next appointment at the family cancer clinic. The analyses for the current report were carried out on the data obtained from the following assessment moments: 2-4 weeks before PM/BR (T0), at 6 months after (T1) and 6-9 years after (T2) PM/BR.

Measurements

Biographical and medical data

Data on age, having a partner, having children, educational level, carrier status and breast cancer history were obtained by means of a questionnaire completed at both T0 and T2.

Coping

Coping was assessed at T0 with the Utrecht Coping List (UCL) (14). The UCL is a 48-item questionnaire, measuring 7 coping styles: Active Approach, Palliative Reaction, Avoidance, Seeking Social support, Passive Coping, Emotional Expression and Comforting Thoughts. Previous studies revealed satisfying validity and reliability measures of the UCL (15-16).

Psychological distress

At all assessment moments (T0, T1 and T2) women completed the Impact of Events Scale (IES) (17) and the Hospital Anxiety and Depression Scale (HADS) (18), measuring breast cancer specific distress and general distress, respectively. Both scales have been described in detail elsewhere (19).

Body image

Body image was assessed at T0, T1 and T2 by the Body Image Scale (10), which was constructed following recommendations made by Hopwood (20). The scale comprises two subscales, one for general body image (score range 5-25) and one for breast related body image (score range 2-10). General body image measures satisfaction with appearance both when dressed and when naked, feelings of femininity and feelings of sexual attractiveness. Breast related body image measures satisfaction with the way the breasts feel and with their appearance. A higher score indicates increased problems with body image. Cronbach's alphas at long-term follow-up assessment were 0.84 for general body image and 0.69 for breast related body image.

Statistical analyses

Longitudinal analyses were performed using mixed modelling. Dependent variables were general body image, breast related body image, general distress and breast cancer specific distress.

Linear regression analysis was conducted to identify potential prognostic variables that enabled predicting general and breast related body image measured at long-term follow-up. The following baseline variables were tested for their predictive quality: general body image, breast related body image, general and breast cancer specific distress, coping styles, having children, educational level and carrier status. All potential prognostic variables were entered individually into the regression analysis, adjusted for age, having a partner and breast cancer history. All statistical testing took place at 0.05 level of significance (two-sided). The data were analyzed using the SPSS 17.0 statistical package (SPSS Inc., Chicago).

RESULTS

The characteristics of the 36 women included in the current analyses are shown in Table 1. Comparison of the characteristics of these women and of the 16 eligible PREVOM-B women not included in the current analyses showed that in the latter group significantly less women had a partner, while more women had children ($\chi^2 = 4.10$, $p = 0.04$ and $\chi^2 = 6.20$, $p = 0.01$, data not shown). Reasons for non-inclusion were: not being under surveillance at the family cancer clinic anymore, having had complications after surgery leading to removal of the prostheses, diagnosis of ovarian cancer in between, and finding the questionnaire too burdensome.

All 36 women underwent PM with BR, mainly by means of silicone prosthesis (94%). The mean age at PM/BR was 40.1 years, and the majority of the women had a partner, children and at least a middle level education. After a median follow-up of 7 years, significantly less women had a partner ($p = 0.02$), whereas more women had children ($p = 0.01$). Most women were proven mutation carriers both at baseline (75%) and at long-term follow-up (78%). At baseline, 33% of the participants had a history of breast cancer, while one woman a history of ovarian cancer.

Table 1. General characteristics of the study population (N=36)

Variable	Baseline assessment (T0)	Long-term follow-up assessment (T2)
Follow-up time; median	7 years (range 6-9)	
Demographic and medical variables		
Age; mean (sd)	40.1 (7.7)	47.0 (8.0) **
Having a relationship	34 (94%)	31 (86%) **
Having children	25 (69%)	28 (78%) **
Educational level		
High	14 (39%)	
Middle	17 (47%)	
Low	5 (14%)	
BRCA1/2 mutation carrier	27 (75%)	28 (78%)
Cancer history		
Breast cancer history	12 (33%)	
Ovarian cancer history	1 (3%)	
P(B)SO	17 (47%)	22 (61%) *
Reconstruction technique		
Immediate silicone prosthetic implant	34 (94%)	
Autologous tissue reconstruction	2 (6%)	

* $p<0.05$ (two-tailed); ** $p<0.01$ (two-tailed)

Courses of psychological distress and body image

The estimated scores for psychological distress and body image variables before PM (T0), at 6 months after PM (T1), and at long-term follow up (T2) are shown in Table 2, and graphically shown in Figure 1. Both breast cancer specific distress and general distress scores significantly decreased from T0 to T1 as well as from T1 to T2. In contrast, the scores for breast related body image significantly increased from T0 to T1 (i.e. more problems), and subsequently significantly decreased from T1 to T2. Also, scores on

Figure 1. Psychological distress and body image scores in high-risk women prior to (T0), and at 6 months after (T1) and 6-9 years after (T2) prophylactic mastectomy (figure 1 continued on next page)

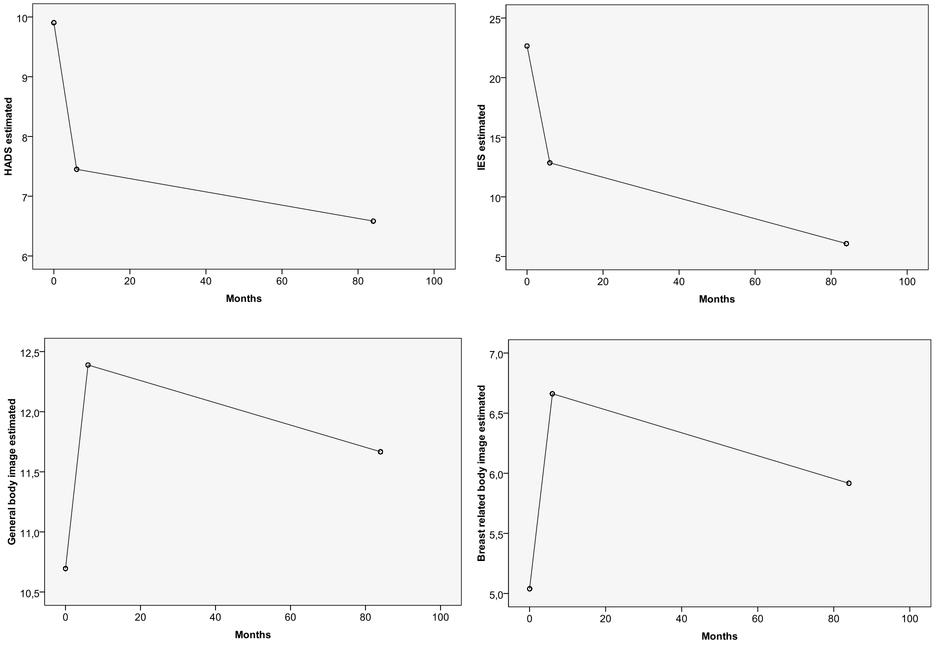

Table 2. Psychological distress and body image scores in high-risk women prior to

	T0	T1	T2	T0-T1		T1-T2	
	Mean (SD)	Mean (d^1)	Mean (d)	T $_{(df)}$	P	T $_{(df)}$	P
General distress	9.91 (5.98)	7.45 (- 0.41)	6.58 (- 0.15)	2.3 $_{(69)}$	0.03	3.1 $_{(69)}$	0.01
Breast cancer specific distress	22.7 (11.6)	12.9 (- 0.85)	6.1 (-0.58)	4.3 $_{(69)}$	0.01	7.4 $_{(70)}$	0.01
General body image^2	10.7 (4.3)	12.4 (0.40)	11.7 (- 0.17)	2.4 $_{(72)}$	0.02	1.4 $_{(72)}$	0.18
Breast related body image^2	5.0 (2.1)	6.7 (0.78)	5.9 (- 0.17)	4.1 $_{(71)}$	0.01	2.2 $_{(70)}$	0.03

(T0), and at 6 months after (T1) and 6-9 years after (T2) prophylactic mastectomy

1 Effect size, Cohen's d

^{2} A higher score indicates more problems general body image significantly increased from T0 to T1, and decreased from T1 to T2, but the decrease did not reach statistical significance.

Predictive factors for body image at long term follow-up

Table 3 presents predictors of general and breast related body image problems at long-term follow-up. Active coping and coping through seeking social support were predictive for decreased scores (i.e. less problems) on both general and breast related body image (at T2). General body image scores at T0 were significantly and positively related to general body image scores on the long term (at T2). No significant associations were found between breast related body image scores at T0 and breast related or general body image scores at T2.

Table 3. Predictors for long-term general and breast related body image (after median follow-up of 7 years)

Predictors (T0)	**General body image [2] (T2)**		**Breast related body image[2] (T2)**	
	β[1]	p-value	β	p-value
General body image	**0.49**	***0.01***	0.17	*0.38*
Breast related body image	0.16	*0.42*	0.18	*0.37*
Active coping	**-0.54**	***0.01***	**-0.49**	***0.02***
Seeking social support	**-0.41**	***0.02***	**-0.37**	<***0.05***

[1] Standardized regression coefficient as a measure of relative importance
Adjusted for age, partner and breast cancer history
[2] A higher score indicates more problems

DISCUSSION

To our knowledge, this is the first prospective study on long term psychological distress and body image after PM/BR in women at risk for hereditary breast cancer, mainly being BRCA mutation carriers. After a median follow-up period of 7 years, a significant decrease in breast cancer specific as well as general distress was observed over time. This is extending on and in accordance with the findings of previous studies concerning a one year follow-up period (7, 10), and most probably indicate relief from fear of developing breast cancer.

In contrast, in the first six months following PM/BR women reported a significant increase in problems with breast related and general body image. These findings are in line with the findings of a prospective one-year follow-up study (12), and most likely represent the difficulties women experience in adjusting to the loss of their breasts and the new proportions of their body. It is the question whether, despite extensive pre-surgery information on the possibilities and limitations of breast ablation and reconstruction, women have carefully thought through what the reconstructed breasts will feel and look like, while the urge to reduce the breast cancer risk predominates before surgery. Furthermore, body image problems at six months after PM/BR potentially reflect that the breast reconstruction is not yet definite potentially requiring additional interventions (for example nipple reconstruction). Moreover, body image problems may be a consequence of complications following surgery, possibly leading to loss of the implants (9). For the included cohort, complications following PM/BR were experienced by 14 women (39%).

The findings that problems with breast related body image decrease between 6 months and 7 years after PM/BR suggest that women adapt to the look and feeling of the reconstructed breasts, also potentially due to additional cosmetic interventions. In our cohort, 11 women (31%) indeed underwent additional surgeries after the primary PM/BR. Nevertheless, of importance is the observation that the body image scores at long-term follow-up remained higher (i.e. more problems) than the pre-PM level, suggesting persisting feelings of decreased femininity and sexual attractiveness after PM/BR.

Overall, the findings of the current analyses are very relevant and underscore the importance of appropriately informing the women about the problems which may be experienced after PM/BR, both on the short and the long term. Furthermore, the data indicate that for future studies on the outcomes of PM/BR the assessment moments should be planned after a longer period of time, i.e. more than 6-12 months after PM/BR.

We found that general body image prior to PM was predictive for general body image on the long-term after PM/BR. Women with a low general body image (high score) before PM/BR were more vulnerable for low body image at long term follow-up. This finding suggests that PM/BR may alter general body image temporarily, but that other factors determine satisfaction with body image over time. Interestingly, women's breast related body image before PM did not predict for breast related body image after PM/BR. We hypothesize that adverse cosmetic outcomes of the reconstructed breasts, such as visible scars, unnatural look, hardening and altered sensitivity of the reconstructed breasts may play a role in the decreased satisfaction of the women about their breasts. Conversely, it may be that women who were dissatisfied with the look of their breasts pre-PM/BR accepted their reconstructed breasts more favourably, focussing on the benefits of the new proportions of their body (21).

Our results indicated that seeking social support was a beneficial coping strategy, in that it was predictive for increased satisfaction with both general and breast related body image on the long-term. It is known from interview studies that most women experience feelings of loneliness and isolation post-surgery, which may be counterbalanced by the process of sharing the effects of surgery and showing others (21-22). Partners in particular are an important source of support for women (21). Several studies have indicated that PM could result in adverse effects on the sexual relationship and decreased feelings of femininity (4-5, 10, 23). Partner's acceptance of a changed appearance of the woman's body and his reassurance of her desirability may help to maintain a sense of attractiveness. Furthermore, women opting for PM while not having a partner (yet) may be more reluctant to get involved in future intimate relationships because of the fear to show the reconstructed breasts, and the subsequent risk of rejection or adverse reactions (23). Such anticipatory fear might affect their breast specific body image.

Another important predictor of increased satisfaction with body image was an active coping style. Women with an active coping style may have sought extensive information about the potential consequences of PM/BR prior to surgery, such as the likely appearance of the reconstructed breasts. These women may have considered in advance the possibilities of coping with the consequences of PM/BR, thereby anticipating on a new body image. In this respect, it is important to note that before PM women may not feel able to thoroughly contemplate possible adverse consequences of PM/BR on body image, while the urge to reduce breast cancer risk prevails.

Strengths of our study are the prospective study design and the long-term follow-up. Some limitations should be considered as well. First, it is possible that variables not included in the current analyses may be of relevance when considering the abovementioned findings. More specifically, we speculate that self-esteem could have influenced both coping strategies as well as body image. Future research is indicated to examine the associations between self-esteem prior to PM/BR and body image after PM. Second, the small sample size disabled the performance of additional multiple regression analyses. However, despite the small sample size some significant associations between pre-PM variables and body image were observed, which has not previously been reported.

In conclusion, psychological distress decreased on the long-term after PM/BR, at the cost of persistent body image problems. The potentially negative consequences of PM/BR on a woman's body image on the short- and long-term should be incorporated in the information given to a woman considering PM/BR. Also, it is essential to thoroughly explore prior to surgery the way the woman experiences her body as well as the potential consequences of PM/BR hereon. Additionally, evaluation of the coping styles of the woman (and her partner) may provide valuable information for the determination of strengths and weaknesses of the individual. We suggest that a consultation with a psychologist or social worker is warranted as standard of care in the counseling of women considering PM/BR. In case vulnerability is identified, it is worthwhile to offer extra counseling sessions. Finally, we plan to develop a group intervention for women who have undergone PM/BR, focusing on issues such as body image, changes in sexuality and communication with the partner.

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Chapter 6

Long-term psychological distress in women at risk for hereditary breast cancer adhering to regular surveillance: a risk profile

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ABSTRACT

Purpose: Some women at risk for hereditary breast cancer are at increased risk of psychological distress. In order to tailor support for individual women, the availability of a tool enabling the identification of psychologically vulnerable women at an early stage is warranted. The objectives of this study were (1) to explore long-term psychological distress in women at risk for hereditary breast cancer adhering to regular surveillance, and (2) to identify women being vulnerable for long-term psychological distress, defined in terms of a multifactorial risk profile.

Methods: General distress and cancer related distress were assessed at baseline (T0) and after 5-8 years (T1) in 197 high-risk women adhering to breast cancer surveillance. Coping styles, occurrence of breast cancer in the family of origin, breast cancer risk perception and frequency of breast self-examination, as assessed at T0, were examined as predictor variables for long-term distress (T1).

Results: Across time, women reported a significant reduction in intrusion and avoidance, whereas no significant changes in anxiety and depression were observed. Predictors of increased long-term distress were passive and palliative coping styles, excessive breast self examination and overestimation of breast cancer risk. On the other hand, coping through fostering reassuring thoughts was predictive for decreased long-term distress.

Conclusion: On the basis of the identified risk profile it is possible to identify vulnerable women at an early stage, who then may be offered additional and individually tailored support.

INTRODUCTION

It is estimated that approximately 5-10% of all breast cancer cases are due to a genetic predisposition. Women identified with a mutation in BRCA1 or BRCA2 have a significantly increased cumulative lifetime risk (CLTR) of developing breast cancer (40-85%) and/or ovarian cancer (11-65%) (1-4). At this moment, genetic testing allows for the identification of a BRCA1/2 mutation in only approximately 15-20% of the suspected families (5).Women from families with a clustering of breast/ovarian cancer, but without an as yet identified BRCA1/2 mutation, remain at increased risk for breast cancer compared to the general population. Options for women at increased risk of hereditary breast cancer are either regular surveillance or prophylactic mastectomy. In general, the latter is discussed as the most effective risk reducing strategy with identified BRCA1/2 mutation carriers, while regular surveillance by means of mammography with or without magnetic resonance imaging (MRI) is another option aiming at early detection. At the Rotterdam Family Cancer Clinic, 35-51% of the women carrying a BRCA1/2 mutation opt for prophylactic mastectomy (6-7), which leaves a large group of mutation carriers eligible for regular surveillance. Also, breast cancer surveillance outside of population screening is offered to women belonging to a breast/ovarian cancer family in which genetic testing did not identify a BRCA mutation (non-BRCA1/2 family), being the most extensive group.

Some women at increased risk of developing breast cancer may experience elevated levels of psychological distress (8-10). Given the rather large group of high-risk women adhering to breast cancer surveillance outside of population screening, it is of clinical interest to be able to identify at an early stage those women who may experience psychological problems (somewhere) during the surveillance programme. In a previous study of our group (the MRISC-B study), which aimed to explore the short-term psychological adjustment of adherence to breast cancer surveillance in high-risk women, several subgroups of vulnerable women were identified including: young women performing excessive breast self-examination (BSE) (11); women overestimating their risk of developing breast cancer (12); and women with a sister affected with breast cancer (13). In this group it was also found that coping styles mattered. (14). Coping strategies represent cognitive and behavioural efforts to deal with stressful encounters (15-16). Several styles of coping may be distinguished, and depending on the duration and controllability of the stressor effects can differ (17). Problem focused coping styles (i.e. acting out to confront or avoid the stressor) may be of significant impact when the stressor can be controlled and solved in some fashion. Emotion focussed coping styles (i.e. efforts to regulate the emotions associated with the stressor) may be particularly adequate in regulating the emotions associated with an uncontrollable stressor.

Investigation of the impact of coping styles on psychological distress in the cohort of high-risk women adhering to regular surveillance revealed that seeking social support, expressing emotions and having comforting thoughts were significantly associated with lower levels of psychological distress. On the other hand, women using passive coping (i.e. feeling overwhelmed by the problem, isolating oneself from others, and escaping into fantasies while facing problems) and palliative coping styles (reducing arousal by distracting oneself from the problem) experienced increased levels of distress (14).

The effects of coping styles may be different over time (17). Coping styles being beneficial in early phases of acute stress may be less adaptive in the long-term (18). In the same way, coping styles contributing to increased distress on the short-term may be adaptive on the long-term (19). To our knowledge, there are no data yet on the long-term psychological adjustment of high-risk women adhering to breast cancer surveillance. Consequently, it is not possible to identify those women being vulnerable for psychological distress on the long term at an early stage. The availability of known risk factors or a risk profile of psychologically vulnerable women would provide a valuable instrument for health care workers. Vulnerable high-risk women may be identified and offered additional counselling and support tailored to their individual features.

In the current study, we explored long-term psychological distress in women adhering to breast cancer surveillance and compared this with short-term psychological distress. The second study aim was to identify women being vulnerable to long-term psychological distress, defined in terms of a multifactorial risk profile.

METHODS

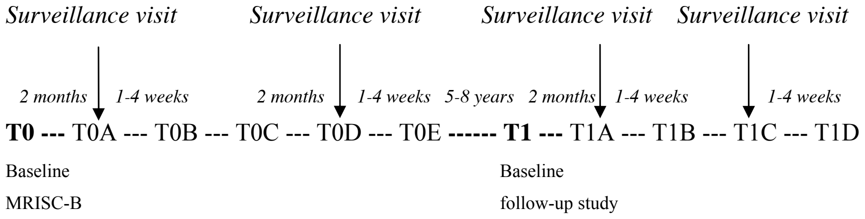
Participants

Between 2000 and 2003, women at increased risk of hereditary breast cancer adhering to regular surveillance were recruited into the MRISC-B study, aiming at evaluating the short-term psychological consequences of a breast cancer surveillance programme. Eligibility criteria were: no history of breast cancer and having a CLTR of developing breast cancer of at least 15%, based on the risk tables by Claus et al (20). A detailed description of the MRISC-B study has previously been published (11-13). In short, 6 assessments were performed around two consecutive biannual surveillance appointments at the clinic during a screening programme, scheduled on the following moments: two months prior to a surveillance visit, the day of the surveillance visit and one to four weeks after the surveillance visit (Figure 1).

In a follow-up study, activated in 2007, we aimed to investigate the psychological impact of regular surveillance on the long-term (i.e. 5-8 years since enrollment in the MRISC-B study) in women at risk for hereditary breast cancer. Women were eligible for the follow-up study if they had participated in the MRISC-B study, had not developed breast and/or ovarian cancer during the surveillance programme, had remaining breast tissue at risk (i.e. had not opted for prophylactic mastectomy meanwhile) and had sufficient understanding of the Dutch language. The follow-up study was set up as a longitudinal observational study consisting of 5 assessments around two consecutive biannual surveillance appointments (Figure 1), being performed between June 2007 and October 2009.

Approval was obtained from the Medical Ethical Committee of the Erasmus Medical Center in Rotterdam.

Figure 1. Time points of the different assessments during the surveillance programme



Procedure and design

Women having participated in the MRISC-B study, and still being under surveillance at the Family Cancer Clinic of the Erasmus MC-Daniel den Hoed Cancer Centre, were sent an information letter regarding the psychological follow-up study along with an informed consent form and a prepaid envelope. After receipt of written informed consent, women were sent the first questionnaire to their home address two months prior to their next appointment at the clinic (T1).

For the current analyses the results obtained at two assessment moments were used, namely: the baseline assessment of the MRISC-B study (T0) and the first assessment of the follow-up study (T1), both scheduled two months prior to an appointment at the clinic. Of the 351 MRISC-B study participants, a total of 207 women were included in the psychological follow-up study. Due to missing values in the questionnaires, data of 197 women were included in the current analyses.

Measures

Independent variables

Biographical and medical variables

Data on age, having a partner, having children, educational level and carrier status were obtained at baseline of both the MRISC-B (T0) and the follow-up study (T1) by means of a questionnaire.

Frequency of breast self-examination (BSE)

BSE frequency was measured on T0 and T1 with the question: Do you perform breast self-examination regularly in order to detect possible anomalies? The six answer possibilities were recoded into three categories: (1) never, once every 3, 6 or 12 months, (2) once a month, and (3) at least once a week.

Breast cancer risk perception

Cognitive risk perception was measured at baseline in the two studies, on T0 and T1 respectively, asking for the women's perception of her own risk estimate of developing breast cancer during life in terms of '1 in x' in combination with percentages. The answer to this question was compared to the objective risk status and recoded into underestimation, accurate estimation and overestimation. For risk category 1, the answer: greater than 1 in 2 was considered as an accurate answer; for risk category 2, the answers: about 1 in 2 and about 1 in 3 were both considered as an accurate answer; and for risk category 3, the answers: about 1 in 4 and about 1 in 7 were both considered as accurate answers.

Breast cancer in the family of origin

Status on having a sister and/or mother affected with breast cancer was obtained on T0 and T1. The answers were dichotomized into "yes' and 'no'.

Coping styles

Coping was assessed on T0 and T1 by means of the Utrecht Coping List (UCL) (21), a Dutch questionnaire used for measuring general coping styles. The UCL measures coping as a personal disposition. The respondent is asked to imagine 'problems in general'. The UCL comprises 47 items in seven scales, that represent different coping styles in problematic situations: Active Approach (i.e. taking action to solve a problem); Palliative Reaction (i.e. distracting one's attention from the problems, decrease pressure by smoking and drinking); Avoidance (i.e. avoiding difficult situations, letting things go); Seeking Social support (i.e. discussing the problem with friends and family); Passive Coping (i.e. rumination, not taking or feeling able to take action, isolating oneself from others);

Emotional Expression (i.e. showing anger or annoyance); and Comforting Thoughts (i.e. imagining that things could be worse). Its validity has been established in several populations (Cronbach's alpha was 0.67–0.84 in a random selection of Dutch cancer patients) (17, 22-23).

Outcome variables

The assessed psychological distress measures included: intrusion, avoidance, anxiety and depression. Intrusion and avoidance were measured with the Impact of Events Scale (IES) (24), anxiety and depression with the Hospital Anxiety and Depression Scale (HADS) (25). Both scales have been described in more detail elsewhere (11-13). Distress measurements were completed on T0 and T1.

Statistical analyses

Significant differences on general characteristics between T0 (baseline MRISC-B) and T1 (long-term follow-up) were analyzed using Wilcoxon tests for continuous variables and McNemar's tests for binomial data. The method of analysis of variance for repeated measurements was performed to test for differences in the levels of distress at T0 and T1 and between the groups of women who lost and who did not lose a first degree relative to breast cancer. As the dependent variables were skewed, these were transformed (logarithmic for intrusion, anxiety and depression, inverse for avoidance). The skewness of the transformed variables did not differ significantly from a normal distribution (26).

To examine whether the distress variables measured at long-term follow-up (T1) were predicted by variables assessed at baseline (T0), the method of multiple linear regression analysis was used including the following variables: biographical and medical variables, BSE frequency, risk perception, breast cancer in family of origin, coping styles and baseline distress. As we expected that baseline distress would be dependent on the other baseline variable included as potential predictors, we partialled these effects out, and included the residuals of the baseline distress variables (the proportion of baseline distress not predicted by any of these variables) in the regression analyses.

First, all the candidate predictive variables were entered in the regression model. We eliminated in a backward procedure the insignificant predictor variables (p-out > 0.25 for removal). Second, a regression model with a forced entry of the significant predictor variables was postulated. By this procedure cases with missing values on the excluded predictor variables can be retained in the analyses. In all analyses educational level, age and years of follow-up were adjusted for. The standardized regression coefficients of the individual predictive variables were presented as a measure of performance. The probability level for statistical significance was set at .05 (two-tailed). The data were analyzed using the SPSS 15.0 statistical package (SPSS Inc., Chicago, Illinois, USA).

RESULTS

Sample characteristics

The baseline characteristics of the 197 women included in the current analyses, as obtained at T0 and T1, are shown in Table 1. Comparing the characteristics of the 197 participants and the 154 MRISC-B women not included in the current analyses, it was observed that in the latter group significantly less women had a partner ($\chi = 5.48$, $p = 0.02$, data not shown).

At T1, the mean age of the women was 47.3 years (ranging from 29 to 69 years). The majority of the women had a partner, had children and at least had a middle level education. Compared with the data obtained at T0, there was a significantly increased proportion of women at T1 who underestimated their breast cancer risk ($p = 0.01$), who

Table 1. General characteristics of the included high-risk women (N=197)

Variable	T0	T1
Demographic and medical variables		
Age; mean (sd)	40.9 (8.4)	47.3 (8.4)
BRCA1/2 mutation carrier	25 (13%)	28 (14%)
Having a relationship	180 (91%)	178 (90%)
Having children	158 (80%)	160 (81%)
Educational level		
High	56 (20%)	
Middle	102 (52%)	
Low	39 (28%)	
Breast cancer risk estimation		
Overestimation	38 (19%)	35 (18%)
Accurate estimation	79 (41%)	60 (31%)
Underestimation	77 (40%)	99 (51%) **
Breast self examination frequency		
Underperformance (never/once every 3/6/12 months)	60 (31%)	63 (33%)
Once a month	109 (55%)	103 (52%)
Overperformance (≥ once a week)	26 (13%)	29 (15%)
Breast cancer in family of origin		
Mother affected with breast cancer	138 (70%)	152 (77%) **
Sister affected with breast cancer	59 (30%)	74 (38%) **

$p<0.05$ (two-tailed); ** $p<0.01$ (two-tailed)
T0: Baseline MRISC-B study, two months prior to clinic appointment
T1: Baseline follow-up study (5-8 years follow-up), two months prior to clinic appointment

had a sister affected with breast cancer (p = 0.01), and a mother affected with breast cancer (p = 0.01).

Table 2 displays the mean scores and standard deviations of the coping styles obtained at the two assessment moments by means of the UCL. Of note, while the mean scores of most coping styles were not different over time, coping through reassuring thoughts increased from T0 to T1 (Z = -2.69, p = 0.01), whereas passive coping decreased over time (Z = -2.18, p = 0.03).

Table 2. Coping styles of the study population (N=197)
* p<0.05 (two-tailed); ** p<0.01 (two-tailed)

Variable	T0	T1
Coping styles		
Active approach	18.95 (3.50)	19.21 (3.46)
Palliative reaction pattern	17.77 (3.34)	18.13 (3.22)
Avoidance	15.25 (3.20)	15.60 (3.27)
Seeking social support	14.35 (3.49)	14.57 (3.60)
Passive coping	11.21 (2.72)	10.86 (2.92)*
Expressing emotions	6.19 (1.67)	6.05 (1.54)
Fostering reassuring thoughts	12.75 (2.64)	13.18 (2.48) **

Levels of distress

Table 3 presents the mean scores per psychological distress outcome variable at each measurement moment in women who lost and women who did not lose a first degree relative to breast cancer. Compared to the scores obtained at T0, women showed a significant decrease in levels of intrusion and avoidance on T1 (F = 16.79, p = 0.01 and F = 5.35, p = 0.02). The mean scores of anxiety and depression remained similar over time. Furthermore, women who lost a first degree relative to breast cancer experienced

Table 3. Psychological distress subscale scores on the two measurement moments for women who lost and women who did not lose a first degree relative to breast cancer.

Outcome variable	Lost a first degree relative to breast cancer		Did not lose a first degree relative to breast cancer		Time	Group
	T0 Mean (sd)	T1 Mean (sd)	T0 Mean (sd)	T1 Mean (sd)	P-value	P-value
Intrusion	6.46 (7.85)	4.77 (6.46)	4.58 (6.12)	2.75 (4.58)	*0.001*	*0.02*
Avoidance	4.26 (6.99)	3.47 (6.44)	4.07 (6.01)	3.34 (6.41)	*0.02*	*0.84*
Anxiety	5.22 (3.88)	5.07 (4.16)	4.87 (3.36)	4.91 (3.95)	*0.17*	*0.69*
Depression	2.79 (3.42)	2.71 (3.55)	2.47 (3.60)	2.64 (3.38)	*0.69*	*0.67*

higher levels of intrusion than women who did not lose a first degree relative to breast cancer (F = 5.55, p = 0.02).

Predictive factors for distress

Table 4 shows the relevance of the predictive variables (as assessed on T0) for long term distress (T1) regarding intrusion, avoidance, anxiety and depression, respectively. All distress measures on T1 were significantly predicted by their corresponding baseline-score, intrusion (β = 0.32, p = 0.01), avoidance (β =0.30, p = 0.01), anxiety (β = 0.44, p = 0.01) and depression (β =0.32, p = 0.01), respectively.

In addition, passive coping at T0 predicted for higher levels of all distress measures, intrusion (β = 0.23, p = 0.01), avoidance (β =0.26, p = 0.01), anxiety (β = 0.51, p = 0.01) and depression (β =0.49, p = 0.01), respectively. Furthermore, variables that also significantly predicted levels of intrusion and avoidance on T1 were: coping through palliative reaction (β = 0.21, p = 0.01 and β = 0.18, p = 0.02), coping through fostering reassuring thoughts (β = -0.26, p = 0.01 and β = -0.24, p = 0.01) and overestimation of breast cancer

Table 4. Predictive factors (assessed at T0) for long-term distress (assessed at T1)

	Predictive factors	β^1	p-value	R^2
Intrusion				.44
	Baseline	0.32	*0.01*	
	Palliative reaction	0.21	*0.01*	
	Passive coping	0.23	*0.01*	
	Reassuring thoughts	-0.26	*0.01*	
	Risk overestimation	0.14	*0.04*	
Avoidance				.34
	Baseline	0.30	*0.01*	
	Palliative reaction	0.18	*0.02*	
	Passive coping	0.26	*0.01*	
	Reassuring thoughts	-0.24	*0.01*	
	Risk overestimation	0.15	*0.03*	
Anxiety				.46
	Baseline	0.44	*0.01*	
	Passive coping	0.51	*0.01*	
	BSE at least once a week	0.15	*0.03*	
Depression				.36
	Baseline	0.32	*0.01*	
	Passive coping	0.49	*0.01*	
	Having a partner	-0.16	*0.02*	

[1] Standardized regression coefficient as a measure of relative importance

Adjusted for educational level, age and years of follow-up risk ($\beta = 0.14$, $p = 0.04$ and $\beta = 0.15$, $p = 0.03$). Additionally, we found that excessive breast self examination at T0 predicted for increased anxiety at T1 ($\beta = 0.15$, $p = 0.03$), while having a partner was associated with decreased levels of depression ($\beta = -0.16$, $p = 0.02$).

DISCUSSION

To our knowledge, this is the first study on long-term psychological adjustment in women at risk for hereditary breast cancer adhering to regular surveillance, and reassuringly shows that distress levels on the long term (after 5-8 years) are either lower or similar compared to baseline. Also, we found that passive and palliative coping styles, as well as excessive breast examination and breast cancer risk overestimation were predictors for higher long term distress. On the other hand, coping through fostering reassuring thoughts was predictive for decreased long-term distress.

The observation that intrusion and avoidance levels were significantly decreased on the long-term, as compared to the short-term assessment, suggests that the worries provoked by the actual threat that an abnormality or breast cancer might be diagnosed diminished across time. There may be several explanations for this observation. First, some degree of habituation may have occurred as a consequence of repeatedly undergoing the breast cancer surveillance process. Second, women in our study did not have a history of breast cancer, and thus repeatedly had received favourable results at breast cancer screening, potentially providing reassurance for future control visits. Moreover, as the proportion of women underestimating their breast cancer risk increased over time, it is possible that decreased breast cancer specific distress on the long term was a consequence of underestimating one's breast cancer risk.

Importantly, women who had lost a first degree relative to breast cancer reported a higher level of intrusion than those who did not. This finding is in accordance with previous research findings and may reflect unresolved grief (9, 27-28). Unresolved loss has been reported to be one of the main reasons to refer high-risk women for psychological support (29). Furthermore, it may be that women who had an affected mother or sister perceived higher breast cancer risks through identification with the lost relative.

Levels of anxiety and depression did not change over time and were comparable to distress levels reported in studies on the short-term psychological impact of genetic testing for hereditary breast and ovarian cancer (30-31). Furthermore, additional analyses showed that 6-10% scored above the clinical cut-ff score (>8) on depression and 16-18% scored above the clinical cut-off score (>8) on anxiety, which is comparable to the non-clinical population (32). A possible explanation for low distress in our study population may be selection bias. It is possible that women who experienced increased levels of depression were less likely to participate in the study. In addition, we found that a higher proportion of included women had a partner as compared women not included in the MRISC-B study. Our results indicated that having a partner was predictive for decreased levels of depression. Notwithstanding this potential limitation, it is important to identify those women who are vulnerable for increased distress, while these women may benefit from additional psychological support.

All long-term distress measures (i.e. intrusion, avoidance, anxiety, and depression) were significantly predicted by their corresponding baseline-scores. Women with higher levels of distress in the short-term remained more vulnerable for distress on the long-term. This finding may reflect that specific personal characteristics are responsible for increased levels of distress, and underlines the importance of identifying vulnerable women at an early stage.

One of the most powerful predictors of long-term distress was the type of coping strategies of high-risk women. Passive coping was an unbeneficial coping style overall, such that it was associated with increased levels of all distress measures. Another adverse coping style was a palliative reaction pattern (seeking distraction of problems at hand), which was found to be predictive for increased levels of intrusion and avoidance. In contrast, coping through having reassuring thoughts was predictive for less intrusive thoughts and avoidance, and could therefore be considered as beneficial coping style. Presumably, both passive and palliative coping styles impede cognitive restructuring, which may be particularly important when dealing with the emotional distress associated with an uncontrollable stressor. On the other hand, women coping through having reassuring thought may be more apt to positively reframe the situation. Interestingly, passive coping (unbeneficial) decreased over time, while coping through having reassuring thoughts (beneficial) increased over time. These changes in coping in certain women over time argue against considering coping styles as stable and trait-like behaviour, and opens up possibilities to be addressed during psychological interventions. Exploring whether a woman's use of a certain coping strategy is associated with the presence of specific stressful conditions, lack of social support (partner) or personal dispositions (low self-confidence) might provide a starting point for interventions aimed at enhancing adequate coping strategies (34). Clinicians may help women who feel unable to deal with hereditary breast cancer risk by stimulating active coping strategies aimed at regulating emotions, such as mobilizing support and appraisal focused coping. Cognitive emotional regulation based interventions focusing on positive reappraisal may help to reframe the situation. A woman may conclude that indeed breast cancer worries diminish, that the risk is not as dire as originally conceived and that through adhering to regular surveillance an eventual breast tumour will be detected at an early stage.

The finding that breast cancer risk overestimation was predictive for increased intrusion and avoidance on the long-term is in accordance with the adverse effect of risk overestimation observed in studies with a short-term follow-up (12, 35-36). Furthermore, our findings indicate that inaccurate risk perception was not corrected over time. More specifically, the proportion of women who overestimated their risk did not change, while the proportion of women who underestimated their risk increased over time. While our sample consisted of women who did not have a history of breast cancer, we hypothesize that the increase in risk underestimation is associated with getting older without developing breast cancer. Furthermore, risk underestimation may reflect minimisation of their elevated risk, in order to protect themselves again worries. However these women, in spite of their underestimation as a possible way of self-protection, continued to adhere to the regular surveillance programme, otherwise they were not included in this psychological follow-up study. It is well known that women may have difficulty understanding probabilities of risk and risk-related information. Therefore, the clinician should pay careful attention to the way women process information about their given risk estimation. Since women underestimating their breast cancer risk continued to adhere to regular surveillance, it may be that they are adequately protecting themselves from (unnecessary) worries. The question then is how much effort should be put into improving the risk perception of these women. On the other hand, women overestimating their breast cancer risk may benefit from additional psychological support to gain insight in factors that contribute to persistent risk overestimation and to eventually address these factors, since they experienced increased levels of distress.

Furthermore, excessive breast self examination was predictive for increased anxiety, being in accordance with cross-sectional data on the association between BSE performance and distress (11, 37-38). For some high-risk women, preoccupation with breast cancer may lead them to excessive practicing of BSE. A vicious cycle may develop in which BSE performance causes increased distress, which, in turn, results in a need to examine the breasts as often to get momentary reassurance (38). Excessive BSE may reflect an underlying personal vulnerability factor, such as neuroticism, which may be related to greater anxiety reporting. Dependent on the etiology of the excessive BSE, clinicians can help women by giving information about appropriate frequency, technique and timing (in premenopausal women) of performing BSE or discuss referral for psychosocial diagnosis and subsequent treatment. It is beyond the scope of this article to discuss in detail the psychological treatment options. However, in order to offer tailor-made treatment, unresolved loss, partner-relation and family dynamics, coping strategies, and the introspective potential of the woman concerned needs to be explored. Psychological treatment options may vary from psycho-education, counselling or psychotherapy at an individual, marital, family or group level, and using cognitive-behavioural, client-centered or psychodynamic approaches.

Besides the fact that this is the first study of psychological adjustment on the long term in high-risk women adhering to a breast cancer surveillance program, other strengths of our study are the prospective study design and the large sample size. On the other hand, our study exclusively assessed a group of self-selected women adhering to breast cancer surveillance.

In conclusion, mean distress levels on the long-term do not exceed levels of clinically relevant psychological distress. On the other hand, we found several risk factors enabling the early identification of women vulnerable to increased psychological distress. The subset of women that is in need for additional psychological support has to be identified correctly. We recommend clinicians to pay attention to women's handling of loss experiences in the family, coping styles, current distress, breast cancer risk perception and frequency of breast self-examination. On the basis of the identified risk profile, we plan to develop a user-friendly one-page questionnaire. This questionnaire should be used and evaluated in the family cancer clinic as a screening tool allowing identifying psychologically vulnerable women. Women who are found to be vulnerable may benefit from and should therefore be offered additional support, focusing on the particular stressors of a specific woman.

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Chapter 7

Distress in partners of high-risk women undergoing breast cancer surveillance

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ABSTRACT

Background: Partners are an importance source of support for women at risk for hereditary breast cancer. The impact of regular breast cancer surveillance in at-risk women on psychological distress in the partners of these women is unknown. This study aimed to (1) examine the levels and courses of psychological distress of partners and high-risk women around breast cancer surveillance appointments at the clinic, (2) to explore the relationship between partners' and women's distress, and (3) to identify factors that were associated with distress in partners.

Methods: Partners of 77 high-risk women adhering to breast cancer surveillance and participating in a psychological follow-up study, completed questionnaires measuring psychological distress 2 months before (T0), on the day of (T1) and 1 to 4 weeks after (T2) two consecutive biannual appointments of the women at the clinic.

Results: Partners' breast cancer specific distress was positively related to the women's cancer specific distress prior to breast cancer surveillance. Fatherhood and affective risk perception were positively associated with distress in partners.

Conclusions: Our findings indicate that the psychological distress associated with stressful waiting for the breast cancer surveillance appointment, and -after the appointment- for the results, is an interpersonal experience, which is shared within the couple. These findings underscore the importance of involving partners in the clinical interventions for high-risk women. Clinicians should address the affective risk perception of partners, i.e. how they experience the increased breast cancer risk of the woman.

INTRODUCTION

Breast cancer is the most common type of cancer affecting women in Western countries, where approximately one in every nine or ten women will develop the disease during the course of her life. A hereditary origin is estimated to be present in 5-10% of all breast cancer cases [1]. Two breast cancer susceptibility genes, BRCA1 and BRCA2, have been identified in 1994 and 1995, respectively [2, 3]. Healthy female carriers of a mutation in one of these genes have a significantly increased cumulative lifetime risk for breast cancer of 39-85%, and for ovarian cancer of 11-63% [4-6]. Women from families with a family history of breast cancer but without an as yet identified mutation in a BRCA1/2 gene are also at increased risk for breast cancer. Currently, available management options for these women include prophylactic surgery and regular surveillance. Regular breast cancer surveillance aims at early detection, and generally consists of annual imaging by means of mammography and/or magnetic resonance imaging (MRI) scan, biannual clinical breast examination and recommended monthly breast self examination [7].

It is known that women at high-risk who adhere to regular surveillance may experience increased levels of both general and breast cancer specific distress [8-11]. So far, research has mainly focused on identifying those women who are most vulnerable to psychological distress [9-16]. Excessive breast self-examination while being younger than 40 years, heightened risk perception and having a passive coping strategy were reported to be associated with elevated levels of psychological distress [13-15].

Partners are an important source of support for women facing the threat of hereditary breast cancer [17, 18]. Yet little research has focused on the psychological adjustment of partners of women at risk for hereditary breast cancer. It has been shown that the genetic testing process and, unfavorable test results in particular, are distressing for some partners [17, 19, 20]. Worries about the possibility of the woman developing cancer and the risk for their children have been found to be common concerns among partners [17]. Furthermore, it has been reported that women's distress is positively associated with distress experienced by the partner [21]. Moreover, a study among breast cancer patients approached for genetic counseling indicated that highly distressed women with highly distressed partners were more likely to experience high levels of distress in the long term [22].

The studies mentioned above all focus on the adjustment of partners after the disclosure of genetic test results. Currently, there are no prospective data on psychological outcomes among partners beyond six months after test result disclosure [23].

As part of the Dutch national MRISC-study (Magnetic Resonance Imaging Screening, MRISC-A), which evaluated the efficacy of MRI as compared to mammography in women at increased risk of hereditary breast cancer (i.e. at least 15% lifetime risk), the psychological sub-study (MRISC-B) aimed to evaluate the psychological impact of breast cancer surveillance. Within the context of this prospective study, the partners of the high-risk women were also included. This partner sub-study aimed to (1) examine the levels and courses of psychological distress of partners and high-risk women around breast cancer surveillance appointments at the clinic, (2) to explore the relationship between the distress experienced by partners and their wives, and (3) to identify factors that were associated with distress in partners. In this report, we describe the findings of this study, which, to our knowledge, is the first prospective study regarding distress in partners of high-risk women adhering to surveillance.

MATERIAL AND METHODS

Participants

Of the 351 women enrolled in the MRISC-B study, 154 were randomly selected and contacted to obtain consent to approach their partners for the purpose of this partner sub-study. Of these, sixteen women did not have a partner. Of the remaining 138 eligible women, 17 women did not respond and 44 partners declined participation. Hence, data were collected from a total of 77 couples (77 women and 77 partners), resulting in a participation rate of 55.8%. No differences regarding sociodemographic characteristics and distress levels were found between women included in the current study (n = 77) and women whose partners declined participation (n = 44).

At entry, the women did not have a history of breast cancer, and had a cumulative life time risk for breast cancer of at least 15%, based on the risk tables by Claus et al. [24]. Both women and partners had sufficient understanding of the Dutch language to fill in the questionnaires and all signed informed consent. Approval was obtained from the Medical Ethical Committee of the Erasmus MC in Rotterdam.

Procedure

The enrolment-procedure of the women in the MRISC-B study has been described in detail elsewhere [13-15]. Women consenting to participate in the MRISC-B study received the baseline questionnaire at their home address two months prior to their next surveillance appointment at the family cancer clinic. Along with this questionnaire, the randomly selected subgroup of women received a letter explaining the purpose of involving partners in the study. The women were asked to return a form including the question if she was currently involved in a spousal relationship and, if confirmative, whether her partner was interested in and consented to participate in the study. Partners who agreed to participate were sent a package including an information booklet, informed consent form, the first questionnaire, and a prepaid envelope. The questionnaires for the subsequent measurement moments were sent in separate envelopes to the women and their partners.

Design

The partner-study consisted of 6 assessments performed around two consecutive biannual surveillance appointments of the high-risk women at the family cancer clinic during a breast cancer surveillance programme. The assessments were performed on the following moments: two months prior to a surveillance visit (twice: T0 and T3), the day of the surveillance visit (twice: T1 and T4) and one to four weeks after the surveillance visit (twice: T2 and T5). The assessments T2 and T5 were planned one week after the clinic visit in case of physical examination only, and four weeks after an appointment consisting of physical examination in combination with imaging examinations (mammography and MRI). The six measurement moments were aggregated to three measurement moments: (T0) two months prior to the surveillance appointment, (T1) the day of the surveillance appointment, and (T2) one to four weeks after the appointment.

Measures

Demographic characteristics

Age and the duration of adherence to regular surveillance were measured in years. Educational level was divided into three categories, i.e. low, medium and high. Marital status and having children were dichotomized into 'yes' and 'no'.

Risk perception

Risk perception was measured by two questions. The first one measured knowledge about women's personal risk estimate of developing breast cancer in terms of '1 in x' in combination with percentages (cognitive). The second question assessed risk perception in terms of feelings about women's chance of developing breast cancer with answer-categories in words (affective).

Breast cancer specific distress

Intrusion and avoidance, two common responses to stressful situations, were assessed using the Impact of Events Scale (IES). This questionnaire developed by Horowitz et al. [25] comprises 15 items and can be tailored to a specific event, namely 'breast cancer' in this study. Avoidance is measured in 8 items and intrusion in 7 items, and each item has four answer categories: not at all (score 0), seldom (score 1), sometimes (score 3), and often (score 5). The Dutch version of the IES has been subjected to reliability analysis, the avoidance subscale had an internal consistency of 0.66 and the intrusion subscale of 0.72 [26].

Statistical analyses

Missing values on the items composing outcome variables were handled as follows: for participants who filled in more than 75% of the questions per subscale a total score was computed, corrected for the total number of questions of the subscale. For participants who filled in less than 75% of the questions per subscale no total score was computed.

Differences in characteristics between women at risk and partners were determined by means of the chi-square-test for categorical data, and in case of continuous data by paired *t* test.

Paired differences between women and partners in the levels and courses of breast cancer specific distress (IES) were analyzed using ANOVA for doubly repeated measurements, with time and women/partner as factors. The distress variables were negatively skewed and were, therefore, subjected to square root transformation to normalize the data. In the results section, we presented the raw data.

Spearman's rank correlations were calculated between partners' and women's breast cancer specific distress.

Finally, the method of multiple linear regression analysis was performed with partners' breast cancer specific distress as dependent variable. Independent variables included demographic variables (age, educational level, having children), risk perception (cognitive and affective) and women's cancer specific distress. All statistical testing took place at 0.05 level of significance (two-sided). Analyses were carried out using the SPSS 15.0 statistical package (SPSS Inc., Chicago).

RESULTS

Descriptive statistics

Sample characteristics of the partners and high-risk women are shown in Table 1. The mean age of the partners at the time of the baseline measurement was 41.8 years and of the women 40.1 years. The majority of the partners and women had at least a middle level education. Further, most of the couples were married and had children.

Levels and courses of breast cancer specific distress

The mean scores on the IES of the partners and women at the different time points during the surveillance programme are presented in Table 2.

Partners reported significantly lower levels of intrusion than the women at all measurement moments ($F(1,73) = 8.71$, $P = 0.001$). Levels of avoidance were not significantly different between partners and women ($F(1,73) = 1.87$, $P = 0.18$).

Table 1. General characteristics of the study sample[1]

Variable	Partners (n=77)	Women (n=77)
Years of adherence; Mean (Std. Dev.)	Na[1]	4.7 (+3.79)
Age; Mean (Std. Dev.)	41.8 (+9.03)	40.1 (+9.23)
Educational level[2]		
High	26 (33.8%)	21 (27.2%)
Middle	36 (46.7%)	45 (58.4%)
Low	14 (18.2%)	9 (11.7%)
Married	63 (81.8%)	
Having children	54 (70.1%)	

[1] Not applicable

[2] Percentages do not add up to 100% because of missing values

Table 2. Breast cancer specific distress in high-risk women and their partners

	Time	Partners		Women	
		N=77		N=77	
		Mean	Std. Dev.	Mean	Std. Dev.
Intrusion	T0	2.30	3.34	4.23	5.73
	T1	2.82	4.10	4.34	5.45
	T2	2.30	3.70	3.71	5.21
Avoidance	T0	1.85	2.93	2.92	5.41
	T1	2.36	3.86	3.61	5.69
	T2	1.95	3.25	2.72	5.06

Both partners and women showed an increase in intrusion and avoidance levels on the day of the surveillance visit (T1), which was quadratically significant (F(1,72) = 7.30, *P* = 0.01; and F(1,72) = 9.46, *P* = 0.001), respectively).

No significant differences in the courses of intrusion and avoidance were found for partners and women (F(2,72) = 0.18, *P* = 0.84; and F(2,72) = 0.74, *P* = 0.48, respectively).

Associations between partners' and women's breast cancer specific distress

There was a significant positive correlation between partners' and women's levels of intrusion at all time points (Table 3). Furthermore, partners' and women's levels of avoidance were significantly correlated at T0 and T1, but not at T2.

Factors associated with breast cancer specific distress in partners

Having children was significantly and positively associated with breast cancer specific distress in partners (Table 4). Additionally, we found that partners with a higher affective risk perception reported higher levels of cancer specific distress.

Table 3. Correlations between partners' and women's breast cancer specific distress[1]

	Time	Intrusion partner	Avoidance partner
Intrusion woman	T0	0.43**	0.44**
	T1	0.52**	0.44**
	T2	0.28*	0.16
Avoidance woman	T0	0.13	0.25*
	T1	0.39*	0.27*
	T2	0.21	0.16

[1] Spearman's rank correlations between women's and partners' IES scores
* p<0.05 (two-tailed)
** p<0.01 (two-tailed)

DISCUSSION

The current report describes the results of the first prospective study beyond six months after genetic test disclosure on distress in partners of women at risk for hereditary breast cancer adhering to regular breast cancer surveillance. We investigated the distress levels of the partners and women around breast cancer surveillance appointments at the clinic, and the relationship between their distress. Partners reported lower levels of cancer specific distress as compared to the women, which is congruent with other studies [19, 21], whereas courses of psychological distress around a surveillance appointment appeared to be similar. For both partners and women, levels of distress were highest on the day of the surveillance appointment. Most probably, this increase is due to the threat that an abnormality or breast cancer will be detected.

Table 4. Factors associated with distress in partners of at-risk women adhering to regular breast cancer surveillance

Partner variable	Breast cancer specific distress partner	
	β[1]	p-value
Age	-0.05	0.76
Education	-0.02	0.89
Having children	**0.31**	***0.04***
Cognitive risk perception	-0.29	0.13
Affective risk perception	**0.53**	***0.01***
Breast cancer specific distress woman	0.23	0.13

[1] Standardized regression coefficient

We found that partners' breast cancer specific distress was positively related to women's cancer specific distress. It seems that women with a highly distressed partner are more likely to experience high levels of cancer specific distress themselves, and vice versa. This is in line with the results of a previous study [21]. That study, however, focused on the adjustment of partners after genetic testing, and was cross-sectional of character. As we adopted a prospective design, it enabled us to investigate the relation between the partners' and the women's distress on the long term, around breast surveillance appointments at the clinic.

A consistent relationship between the breast cancer specific distress of partners and women was only found prior to the breast surveillance appointment. This suggests that facing a threatening event, such as the surveillance appointment or the results, may be seen as an interpersonal experience that is shared by women and their partners. However, we did not find a consistent relationship after good results of examination have been disclosed. It seems that the relief from distress after the good news, i.e. 'no cancer', is associated with a more individual emotional experience of dealing with the increased breast cancer risk. Moreover, the distress of partners at pre-surveillance moments might be at least partly ego oriented. Partners might be concerned about what the consequences are of detection of cancer in their wives for themselves as husband and father. This needs to be further studied. In our study, the variables of the Impact of Events Scale, which was used to assess distress, were anchored to 'breast cancer' for both women and partners. We suggest considering the use of other anchors for partners, which may better suit the content of their thoughts and feelings, such as 'cancer in your wife' or 'impact of wife's cancer for yourself".

The relation between the distress of partners and the distress of their wives may reflect the strain breast cancer surveillance puts on the couple relationship. Both women and partners need to manage their own distress and may therefore be less available for their partner, which may explain the positive relationship between distress in high-risk women and their partners. Furthermore, partners who are distressed may be less able to support their wife to cope with the increased risk of breast cancer and the burden of surveillance [17, 18]. As a consequence, the woman who is already distressed may become more anxious. The causal mechanism behind the positive relationship between women's distress and distress in partners warrant further investigation. The factors that contributed to elevated levels of distress in the partners were fatherhood and affective risk perception. Fatherhood was associated with higher cancer-related distress in partners, which is in accordance with other studies on partners of high-risk women [17, 20]. This is thought to be due to worries about future development of cancer in one's children as well as fear of losing the mother of one's children to breast or ovarian cancer. Our results suggest that the distress related to worries about one's children is long-lasting. This finding supports the suggestion to adjust anchoring the IES in partner studies to cancer-related themes that affect partners. With regard to risk perception, only partners' affective risk perception was significantly associated with cancer specific distress. A positive association between partners' perceived cancer risk and distress was also suggested by Mireskandari et al [21]. However, they did not make a distinction between cognitive and affective risk perception. Our findings underscore the importance of partners' affective risk perception and the lesser relevance of cognitive risk perception with regard to distress. This effect has also been reported in a previous study conducted at our institute on the role of risk perception in distress of high-risk women adhering to regular surveillance [14]. A limitation of the current study concerns the relatively low participation rate of the partners. It is possible that partners who were more involved with their spouses were more likely to participate in this study. This self-selection bias might then have resulted in a sample of couples whose relationship was particularly close, which could have influenced the results. In conclusion, the findings of this prospective study indicate that the psychological distress associated with stressful waiting for the breast cancer surveillance appointment, and -after the appointment- for the results, is an interpersonal experience, which is shared within the couple. These findings support the relevance of considering women in relationships as being part of a larger system, who are influenced by - and vice versa influence – their partners.

Our findings underscore the importance of involving partners in the clinical interventions for high-risk women. As couple-based interventions were found to be effective in reducing distress in couples dealing with breast cancer [27, 28], we expect that a couple-based approach might also be beneficial in this cohort. During clinical interventions, close attention should be paid to worries about the children. Furthermore, clinicians need to be aware of the importance of the affective component of risk perception, i.e. the way the couple experiences the woman's increased risk for breast cancer. Further investigation is warranted to evaluate whether cognitive intervention strategies may be beneficial. Finally, future research should focus on unraveling the different origins of distress in partners and women, as their concerns regarding cancer might be different.

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Chapter 8

General discussion

DISCUSSION

Breast cancer is a disease as old as womankind. The old Egyptians blamed cancer on the Gods. Much later, Hippocrates led to determine the scientific underpinnings of the disease, eventually attributing its cause to an imbalance in one of the theoretical fluids of the body. Although scientists realised that cancer was clustered in families, it was particularly during the past decades that our understanding of the underlying genetic causes of breast and/or ovarian cancer increased rapidly. Since the beginning of the nineteen nineties it became possible for women from families with clustering of breast (and/or ovarian) cancer cases to opt for genetic counselling and testing, and subsequently to receive a personal life time risk estimation. The knowledge that one is at risk for hereditary breast/ovarian cancer ensues complex decisions regarding risk management options, including regular surveillance or prophylactic surgeries consisting of mastectomy and/or salpingo-ovariectomy. As from the start of genetic testing and counselling, it was clear that more data on the (dis)advantages of the different possible strategies was needed, especially since the risk groups mainly concern young women for whom the different strategies may have major impacts for a long period of time. This not only concerns the medical issues, but also more knowledge about the psychosocial consequences of either strategy is essential in order to adequately inform and support women considering one of these options. At our institution, several psychological studies have therefore been conducted, mainly focusing on the “short-term” psychosocial consequences of being at risk for hereditary breast cancer (1), and either adhering to regular breast cancer surveillance (2) or opting for prophylactic surgeries (3). Other available literature have also mainly addressed the short-term impact of genetic testing, surveillance and/or preventive surgical options, while long-term issues are also relevant, as the main goal of either effort is to improve survival for women from these families.

The objectives of this thesis were to further explore the psychological adjustment to either regular breast cancer surveillance or prophylactic mastectomy in women at risk for hereditary breast/ovarian cancer, and to identify risk factors for long-term maladjustment. Also, based on our findings we aimed to construct a set of recommendations for the early identification of women prone to adjustment problems and for supportive interventions.

8.2 PSYCHOLOGICAL ADJUSTMENT IN WOMEN AT RISK FOR HEREDITARY BREAST CANCER

Understanding of factors that improve or undermine adjustment to being at risk for hereditary breast cancer is an important aspect of research aiming at enhancing well-being for women at risk for hereditary breast cancer. Research on stress and coping in general has emphasized the crucial role of personal and social resources in the adjustment to stressful life-events, as resources may buffer the negative impact of such an event (4-6). The roles of these resources in psychological adjustment to being at risk for hereditary breast cancer have been addressed in chapters 2-4. Moreover, while partners are an important source of support for women facing the threat of hereditary breast cancer, we examined distress in partners in chapter 7.

8.2.1 The importance of personal resources

Knowing that one is at risk for hereditary breast cancer may alter a woman's self-concept, including self-perceptions on domains of future health ("feeling vulnerable"), identity ("feeling abnormal"), body image ("mistrust of the body"), sense of mastery ("feeling not in control of one's health") and self-esteem ("feeling impaired"), which can be considered as important personal resources (7-9). Despite its clinical relevance, the role of these personal resources in the context of adjustment to being at risk for hereditary breast cancer has been studied rarely. Consequently, our data on the influence of several aspects of self-concept on psychological distress in the group of women at risk for hereditary breast cancer, irrespective of either regular surveillance or prophylactic mastectomy, **(Chapters 2 and 4**) are particularly relevant.

Self-esteem and mastery

We found that self-esteem was adaptive, in that high self-esteem was associated with less general distress **(Chapters 2, 4)**. Moreover, mastery was associated with less general distress in women with low self-esteem, and can therefore be considered as another protective personal resource (i.e. a sense of resilience) **(Chapter 2)**. Although both self-esteem and mastery have typically not been addressed in previous studies on high-risk women, our findings hereon have recently been confirmed by Vodermaier et al. studying a large group of female mutation carriers (n=237) (10). In general, women with high levels of self-esteem and mastery may be more likely to use adaptive coping strategies (11-12), to use strategies of positive reinterpretation (13), to be optimistic (14) and to have confidence in their ability to deal with the elevated risk. Our findings on the importance of self-esteem and mastery is consistent with Taylor's cognitive adaption theory, which postulates that restoring self-esteem and regaining mastery and a sense of meaning are central components of adjustment to stressful life-events (15).

Feeling stigmatized

We showed in our group of high-risk women that feelings of stigmatization (e.g. feeling labelled, different and isolated from others (7)), significantly contributed to increased psychological distress **(Chapters 2, 4)**. The concept of stigma is relatively new in the field of hereditary breast cancer. In fact, the impact of stigma has only been addressed in one other study concerning BRCA mutation carriers, performed by Vodermaier et al. (10). Vodermaier et al. confirmed our finding of the negative impact of stigma on psychological distress. Feelings of stigmatization may lead to a reduced self-concept, and may be a consequence of altered perceptions of health, altered relationships and in case of prophylactic surgery (mastectomy or salpingo-ovariectomy) of physical deviance, fear of loss of sexual attraction and femininity, and decreased libido. Moreover, women carrying a BRCA1/2 mutation may be confronted with reproductive choices regarding whether to have offspring or not, or whether to opt for assisted reproduction strategies, such as prenatal diagnosis or pre-implantation genetic diagnosis.

The individual differences in a woman's personal experiences with breast and/or ovarian cancer as well as other aspects of the self (cognitive processing, life stage) will affect which aspects of self-concept are most influenced. The observation of Vodermaier et al. reporting that perceiving stigma was associated with younger age probably reflects that young women suffer more from general life disruption through knowledge of an increased breast cancer risk, especially if important life goals have not yet been completed by the time of genetic testing (10). Furthermore, the specific impact on self-concept may depend on what women value most about themselves; for one woman it may be appearance, while for another it may be cognitive abilities or her role as a mother (7).

8.2.2 The importance of social resources

Hereditary breast cancer has a profound impact on individual family members and on their mutual communication and interactions. Our results in the group of women at risk for hereditary breast cancer either being under breast cancer surveillance or having opted for preventive mastectomy indicate that open family communication about thoughts and feelings regarding hereditary cancer may promote individual psychological adjustment (**Chapter 3**), being in accordance with previous findings (16-17). Consequently, avoiding to talk about hereditary cancer in order not to upset and burden each other, also called 'protective buffering' (16), might be unbeneficial in this group of women. Furthermore, we observed that support from intimates was important, which is also in line with previous observations (17-21). Moreover, we found that women who felt supported reported increased self-esteem, and that women who were able to talk in an open way about hereditary breast cancer were less likely to report feelings of stigma. To our knowledge, our study is the first to demonstrate that personal resources mediated the relationships between social resources and psychological distress, thereby providing new insights regarding the possible mechanisms by which social resources affect psychological distress **(Chapter 4)**. Interestingly, when considering these findings the theory of attachment may provide a useful perspective. We hypothesize that securely attached women had greater ego resiliency, and felt more competent in recruiting social support and in using that support. In contrast, women with an insecure attachment -which is associated with worries about not being loved, as well as difficulties becoming close to others- may be less likely to receive and/or to benefit from social support. Furthermore, due to lower ego resilience these women may have a more vulnerable self-concept and may be more prone to increased distress. In a previous study of our group focusing on attachment in families with Huntington's disease, the relevance of attachment for psychological well-being in families with genetic disorders has been demonstrated (22). The exact role of attachment style in the adjustment of women at risk for hereditary breast cancer remains currently insufficiently clear and needs further investigation.

8.2.3 Distress in partners of high-risk women

In our prospective study examining distress in partners of high-risk women around two bi-annual appointments at the clinic (covering a period of 15 months), we observed low levels of cancer specific distress in partners **(Chapter 7)**. This is in line with the results from another study, reporting low cancer specific distress in partners one to three weeks after test result disclosure (23). Increased levels of distress were reported by both the women and partners on the day of the surveillance appointment, most probably due to the threat that an abnormality or breast cancer might be detected. In the group of partners, having children and an affective risk perception were significantly associated with increased distress.

Importantly, distress in the partner proved to be associated with distress experienced by the at-risk woman, particularly on the day of the surveillance appointment. On the one hand, this positive association may indicate that the worries associated with facing the threat of hereditary cancer are shared by women and partners. On the other hand, this positive association may reflect the strain that breast cancer surveillance puts on the partner relationship. Partners who are distressed may be less able to provide support and to communicate effectively, which we **(Chapter 3)** and others (21, 24-25) found to be associated with distress in the woman. Consistently, relationship problems with the partner were found to be an important reason for referring high-risk women for additional support (26). This finding stresses the importance of considering the context of the partner relationship when seeking to understand psychological adjustment in high-risk women.

8.3 PROPHYLACTIC MASTECTOMY (PM)

8.3.1 Long-term distress and body image

Prospective studies examining the effects of PM on psychological well-being and body image have been scarce, and results regarding body image have been inconsistent. Distress significantly decreased after PM with breast reconstruction (BR) (1, 3, 27-28), which also was observed in our long-term follow-up study **(Chapter 5)**. The decrease in psychological distress most probably indicates relief from fear of developing breast cancer, which is, reassuringly, lasting on the long term.

Regarding body image, we observed a significant increase in problems with breast-related and general body image at 6 months after PM/BR. Subsequently, problems with breast-related body image decreased between 6 months and 7 years after PM/BR, while problems with general body image were sustained. Data from previous studies on body image after PM were not completely consistent, with some reporting an adverse impact of PM on body image at one year follow-up (1, 27), and others not finding evidence for body image problems at 18 months after PM (28). Diverging study results may be a consequence of different assessment moments, small study samples, different types of breast reconstruction, and potentially other factors. The explanation for our findings over time may be that women and partners may experience difficulties in adjusting to the loss of breasts and the new proportions of the body, and in adjusting their sex life to these changes. Reassuringly, the large majority of women did not regret PM/BR and would opt for PM/BR again (29).

Also, despite the persistent body image problems in the long-term, women who opted for PM/BR did not differ from women who opted for regular surveillance regarding self-esteem and feelings of stigma **(Chapter 2)**. We assume that the relief of fear and uncertainty after PM/BR had a positive impact on self-concept, persisting after 7 years, thereby counterbalancing the potential negative effects (altered body image) on self-concept. Consequently, body image may remain unnoticed. More data hereon are warranted, both on the short and the long term.

8.3.2 Risk factors for poor body image

Most studies on risk factors for maladjustment in women opting for PM/BR have focused on predicting psychological distress. Extending on our findings of persistent body image problems after PM/BR, we investigated for risk factors predicting for poor body image after PM/BR **(Chapter 5)**. We observed that general body image prior to PM was predictive for general body image on the long-term, implying that women with a poor general body image before PM/BR were more vulnerable for low body image at long term follow-up. These findings suggest that PM/BR may alter general body image temporarily, but that other factors determine satisfaction with body image over time.

Interestingly, woman's breast-related body image before PM did not predict for breast-related body image after PM/BR. We hypothesize that adverse cosmetic outcomes of the reconstructed breasts, such as visible scars, unnatural look, altered consistency and sensitivity of the reconstructed breasts may play a role in the decreased satisfaction of the women about their breasts after PM/BR. Conversely, it may be that women who were dissatisfied with the look of their breasts before PM/BR accepted their reconstructed breasts more favourably, focussing on the benefits of the new proportions of their body (30). Another finding was that seeking social support and active coping style were predictive for increased satisfaction with both breast-related and general body image after PM/BR on the long-term. To our knowledge, data hereon are not yet available in the literature.

Given the complexity and variety of potential problems after PM/BR, we recommend intensive exploration into an individual woman's reasons for PM/BR, and counselling on the long-term outcomes after PM/BR, before making a final decision and planning this procedure. Also, our findings stress the importance of thoroughly exploring the way the woman (and her partner) experience her body, the potential consequences of PM/BR hereon as well as the way the couple expect to cope with these consequences. In our opinion, this should be done in specialised centres with multidisciplinary expertise on this issue.

8.4 REGULAR SURVEILLANCE

8.4.1 Long-term distress

In our study group of women adhering to breast cancer surveillance, mean distress levels on the long term (after 5-8 years) remained within normal limits and were either lower or similar compared to baseline (**Chapter 6)**. Moreover, women adhering to regular surveillance did not differ in distress levels as compared to women who had opted for prophylactic mastectomy **(Chapter 3)**. It is important to note that women who developed breast and/or ovarian cancer while adhering to regular surveillance were excluded from our study. Consequently, women in our study repeatedly had received favourable results at breast cancer screening, potentially providing reassurance for future control visits. Our finding of low distress add to the growing body of evidence that living with the increased breast cancer risk is not causing distress per se. Our results indicate that women having higher levels of distress on the short-term remained more vulnerable for distress on the long-term, which may reflect that specific personal characteristics are responsible for increased levels of distress. This finding underlines the importance of identifying vulnerable women at an early stage.

Furthermore, living in a family with a susceptibility for breast/ovarian cancer is a burden, even if one is not overtly distressed about the personal increased breast cancer risk. Consistent with previous studies (31-33), we found that distress was increased among women who had lost a first degree relative to breast cancer. Increased distress in this group may reflect blocked or unresolved grief, which indeed has been reported to be one of the main reasons to refer high-risk women for psychological support (26). Additionally, women having family members who died from breast cancer may experience difficulties in communicating about breast cancer, which we also found to be a contributing factor for increased distress (Chapter 3). These findings underline that health care workers should also focus on the impact of hereditary cancer on the whole family system instead of merely focusing on the individual.

8.4.2 Risk factors for long term distress

So far, there is no available tool to identify at an early stage women being vulnerable for psychological distress on the long-term. In our study on high-risk women adhering to regular surveillance, we identified several risk factors predictive for long-term maladjustment **(Chapter 6)**.

One of the most powerful predictors of long-term distress was the types of coping strategies employed by high-risk women. Passive and palliative coping strategies were particularly important, and have been found to predict distress in our short-term analyses as well as in similar studies of others (32, 34-36). Very interesting was our observation that the use of passive coping decreased over time. This finding argues against considering coping styles as stable and trait-like behaviour, and may suggest that the use of a certain coping strategy by an individual is associated with the presence of specific stressful conditions but may be altered, which opens up possibilities to be addressed during psychological interventions.

Other identified risk factors for long-term distress included risk overestimation and excessive breast examination, although the predictive qualities of these factors were only of a small magnitude. Nevertheless, results from other studies confirm that risk overestimation (37-40) and excessive breast examination (2, 41-42) were associated with increased distress. For the accurate interpretation of these results, we should however question whether these factors do not merely reflect an underlying personal vulnerability factor, such as neuroticism, or express underlying unresolved grief.

8.5 STRENGTHS, LIMITATIONS AND DIRECTIONS FOR FUTURE RESEARCH

The studies described in this thesis have several strengths, but also drawbacks. Particular strengths of the studies were the prospective designs, the large sample of high-risk women in the surveillance group and the long-term follow up period, the latter being unique for this type of studies. During data analyses, however, it became clear that there were a number of limitations. Hereunder, we will address these limitations, which we can learn from for future research. First, as with many studies on long-term psychological outcomes, the studies described in this thesis suffered from loss to follow-up. Loss to follow-up was caused by: diagnosis of breast and/or ovarian cancer in between, not being under surveillance at the family cancer clinic anymore, finding the questionnaire too burdensome, and having had complications after surgery leading to removal of the prostheses (in case of prophylactic mastectomy). Loss to follow-up might have introduced a selection bias, as women experiencing high levels of distress might have been less inclined to fill in the questionnaires.

Second, the study sample of women at risk for hereditary breast cancer adhering to regular surveillance mainly consisted of women who were not proven BRCA1/2 mutation carriers. To date it is known that both categories of women have different risks of developing cancer.

Furthermore, in the analyses described in the first chapters of this thesis (Chapters 2-4) we identified significant interrelationships between personal resources, social resources and psychological distress in the group of women at risk for hereditary breast cancer. We speculate that the positive relationships between personal and social resources may be explained by an underlying construct, such as attachment style or family climate, which was not measured in the current study. More research is needed on this issue.

In our study psychological distress, measured by means of both global distress measures as well as a breast cancer-specific questionnaire, was considered as an indicator for psychological adjustment. Although the used instruments have been frequently used and their psychometric values have been well established (43-47), these measures might not have been sensitive enough to capture the specific concerns and personal issues of our study population. Hence, for the group of high-risk women who opted for PM we have added body image as an indicator for psychological adjustment, which provided very relevant data regarding outcomes on the long-term (Chapter 5). Future studies aiming to evaluate the psychological outcomes of being at risk for hereditary breast cancer should therefore not only incorporate distress measures, but also incorporate outcome measures specific to the field of hereditary breast cancer. Also, in view of our results on the impact of hereditary breast cancer on self-concept (Chapters 2,4), we support the idea of Esplen et al. (7) that it would be particularly interesting to use the BRCA self-concept scale as an outcome measure for this study group.

Another point of attention is the observation that women may experience significant challenges as a consequence of being at risk for hereditary breast cancer, including decision making about various risk management options, dealing with the consequences of risk reducing strategies, feelings of isolation and family communication challenges, and therefore may need additional psychosocial support. This has not been addressed in our studies, but future research is needed to evaluate the contribution of specific psychosocial interventions to psychological adjustment in the group of women at risk for hereditary breast cancer. A single study evaluating a supportive-expressive group intervention among BRCA1/2 carriers showed promising results (48).

Finally, the analyses in the group of women who had opted for PM/BR (Chapter 5) suffered from the small sample size and consequent small statistical power. Moreover, the majority of these women underwent breast reconstruction by means of implants performed in our institution, making any generalisations to women who underwent other types of breast reconstruction difficult. In addition, this group was heterogeneous as both women without and with a history of breast cancer were included. Notwithstanding these limitations, our findings on long-term body image after PM/BR and potential risk factors for poor body image are of extremely clinical relevance, and further research is warranted to confirm and extend these findings.

8.6 CLINICAL IMPLICATIONS

For the majority of high-risk women, their choice for either regular surveillance or for prophylactic mastectomy did not result in major adverse psychological consequences. In other words, on average, women did not experience clinical levels of distress warranting extensive psychological treatment. On the other hand, a subgroup of high-risk women might benefit from additional support (24, 39, 49-51), and it is known that not all women needing additional support actually receive it (24). Despite the absence of severe psychopathology, women may feel stigmatized and vulnerable (Chapters 2,4), experience difficulties in the partner relationship (Chapter 7) and/or family relationships (Chapters 3,4), have problems adjusting to an altered body image (Chapter 5), have unresolved grief (Chapter 6) and experience existential concerns, potentially requiring additional support (52). Throughout our analyses, we have identified several risk factors for long-term maladjustment which should be addressed in clinical practice for this respective patient group. In Table 1, the specific factors to pay attention to are enumerated, as well as some suggestions for the health care worker on how to address these factors.

An increased awareness in healthcare workers involved in the care of these women might contribute to a better empathic understanding and communication between healthcare workers and the women. It is unlikely that all women will respond similarly to being at increased risk, as women have unique expectations, strengths, values and resources. For instance, some women have a high need for certainty (53-54), and consequently may experience greater difficulties managing the anxiety associated

Table 1. Factors to address in consultation, to further explore and/or to refer for additional psychosocial support

Risk factors	Suggestions for items of attention and support
Self-concept	- Explore alterations in self-concept - Elaborate unacknowledged strengths (e.g. earlier experiences of successful coping) - Focus on self-concept aspects which are relatively unaffected or improved - Focus on aspects of life where the woman has control - Emphasize the advantages of direct behavioral efforts to control the cancer risk, such as regular surveillance and/or prophylactic surgery - Filling in information gaps / educational groups - Supportive counseling interventions / support groups - Positive reappraisal (e.g. rethinking of attitudes and life goals, reappraising the situation as an opportunity for growth) / meaning-making interventions
Social resources	- Explore the dynamics in family interaction and communication - Provide information about the consequences of inhibited communication - Explore barriers for receiving appropriate support
Partner relationship	- Involve the partner in counseling, particularly in case of prophylactic mastectomy - Explore couple dynamics - Provide couple-focused interventions
Passive and palliative coping	- Explore the origins of passive / palliative coping strategies - Stimulate active coping strategies, such as mobilizing support and appraisal focused coping
Loss of close relatives due to cancer	- Explore unresolved grief and disrupted family relationships due to loss experiences - Offer grief counseling / grief therapy

with the increased breast cancer risk, potentially adversely affecting their self-esteem, while other women may feel empowered and feel a sense of control about managing the breast cancer risk. In addition, addressing how a woman has coped with previous difficult experiences may provide insight into her psychological resilience.

Furthermore, social resources need to be monitored. Exploration of the dynamics in family interaction and communication within families may provide valuable information for the determination of strengths and weaknesses and of the need to refer the woman for psychological counseling. Open communication with intimates about hereditary breast cancer should be stimulated and barriers to open communication need to be identified. Similarly, support from intimates needs to be monitored and barriers for receiving support should be identified. A couple-focused approach may be beneficial in case a woman perceives little support from her partner.

Special attention ought to be paid to women with a passive coping style (i.e. feeling overwhelmed by the problem, isolating oneself from others, and escaping into fantasies while facing problems) and/or palliative coping style (i.e. distracting one's attention from the problems, decrease pressure by smoking and drinking) (Chapter 5, 6). Referral to a psychologist or social worker may be needed. Exploring whether a woman's use of passive and palliative coping strategies is associated with the presence of specific stressful conditions, lack of social support, dynamics within the couple or personal dispositions might provide a starting point for interventions aimed at enhancing adequate coping strategies.

Furthermore, special attention is needed for women who have lost close family members to cancer, while this continues to affect women many years later (Chapter 5). Women who suffered significant losses may require additional interventions, aimed at the expression of grief and the emotions associated with earlier (and sometimes ongoing) sense of loss (55). Some indicators of unresolved grief include: the woman is unable to talk about the lost relative without experiencing intense/fresh grief, avoidance of thoughts/reminders about the lost relative and an intrusive/distressing preoccupation with or phobia of breast cancer and death.

Finally, healthcare workers involved in the care of high-risk women adhering to regular surveillance should be aware of signals of risk overestimation and excessive breast self-examination as they might cover underlying factors, such as unresolved grief or neuroticism.

Hopefully, the items and suggestions, as described in table 1, offer practical directions being helpful for 1) the psychologist/social worker and 2) any health care worker dealing with high-risk women. We would propose that if one or more of the mentioned risk factors are present, referral to a specialized psychologist or social worker, being available at the family cancer clinics and/or departments of clinical genetics of an academic center, ought to be considered. Although the identified risk factors may help health care workers to identify vulnerable women at an early stage, we do realise that thoroughly checking for all the mentioned issues is time-consuming for which there is not sufficient time in what is already a tight clinic schedule. Therefore, the use of a standardized screening questionnaire may be efficient. Hereby, the distress thermometer and problem list have shown to be useful and easy to administer for clinicians involved in the care of women at risk for hereditary breast cancer (56). We suggest an adjustment of the problem list by adding items that correspond with the risk factors identified in this study.

Some specific notes concern the decision making regarding preventive mastectomy with breast reconstruction. The findings of our long-term follow-up study in women who underwent this procedure suggest that the potentially negative consequences of prophylactic mastectomy on a woman's body image on the short- and long-term should be incorporated in the information given to a woman considering this radical procedure (Chapter 5). Counseling should preferably be done with both partners present. The ways the woman and her partner perceive the woman's body, the potential consequences of prophylactic surgery hereon as well as the way the couple expect to cope with these consequences need to be thoroughly explored prior to surgery. In addition, unrealistic expectations, for example regarding aesthetic outcomes of breast reconstruction, need to be clarified (57). In our opinion, this should be done in specialised centres with multidisciplinary expertise on this issue.

Also, we recommend that the issues of body image and sexual functioning are discussed with the couple after prophylactic surgery. It is our clinical impression that after prophylactic surgery, it is difficult for women to address these issues themselves and to seek referral to a psychologist or sexuologist. We suggest developing a group intervention for women who had prophylactic mastectomy and their partners, focusing on issues such as body image, changes in sexuality and communication with the partner.

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SUMMARY

INTRODUCTION

It is estimated that 5-10% of all breast- and/or ovarian cancer cases are due to a genetic predisposition, which is recognised by a clustering within families of breast and/or ovarian cancer, mainly occurring at young ages (< 50 years of age). With the identification of the two breast cancer susceptibility genes BRCA1 and BRCA2 in 1994 and 1995, respectively, it became possible for women from families with clustering of breast (and/or ovarian) cancer to opt for genetic counselling and testing, and subsequently to receive a personal life time risk estimation. To date, the life time risk for developing breast cancer for a female BRCA1 or BRCA2 mutation carrier is being estimated to range between 43-87%, while the ovarian risk is 40-62% for BRCA1, and 15-20% for BRCA2 mutation carriers. Also, over the years it became clear that by means of the currently available genetic testing facilities a BRCA1/2 mutation is only identified in approximately 15-20% of the families with clustering of breast/ovarian/fallopian tube cancer, leaving the great majority of such families unidentified. In these so-called non-BRCA1/2 families, either the mutation in BRCA1/2 has been missed (due to the available testing facilities), or the responsible genetic factor is not yet known or identifiable. Women from these non-BRCA1/2 families, however, remain at increased risk for breast cancer compared to the female population risk (to date being 12-13% in the Netherlands). The personal life time risk for these women is being estimated using pedigree data and genetic epidemiological tables.

One of the risk management options for women at increased risk of hereditary/familial breast and/or ovarian/fallopian tube cancer is regular surveillance (outside of population screening) aiming to detect cancer at an as early stage as possible. As regular surveillance, however, does not prevent cancer to develop, it does neither prevent cancer to occur nor guarantee that cancer is detected before lymphatic spreading has occurred. Women at very high risk for breast (and/or ovarian/fallopian tube) cancer, mainly applying to BRCA1/2 mutation carriers, may therefore opt for prophylactic surgery, being either prophylactic mastectomy (PM; removal of all fibroglandular breast tissue) mainly in combination with breast reconstruction (BR), and/or prophylactic salpingo-oophorectomy (PSO; removal of both ovaries and fallopian tubes). These surgical strategies are highly effective in reducing the risk of developing breast and/or ovarian/fallopian tube cancer, but may also have irreversible consequences potentially negatively affecting physical and psychological functioning.

While both breast cancer surveillance as well as prophylactic surgeries are important and recognized management options for high-risk women, more data on the (dis)advantages of the different strategies was needed, both regarding medical and psychosocial consequences, in order to adequately inform and support women considering these options.

THE STUDY

In 1999, two prospective studies were initiated at the Family Cancer Clinic of the Erasmus University Medical Centre-Daniel den Hoed Cancer Centre, in Rotterdam, evaluating the psychological consequences of either adhering to regular breast cancer surveillance or opting for PM and/or PSO in high-risk women (MRISC-B study and PREVOM-B study, respectively) encompassing a study period of approximately 12 months. In both short term studies, several subgroups of women being more vulnerable for psychological distress were identified. From these studies as well as from clinical practice it became clear that data on the long-term also were needed. As prospective data on long-term outcomes were lacking in the literature, a follow-up study was initiated in women still under follow-up at the Family Cancer Clinic in Rotterdam in the context of a breast cancer surveillance program or still under follow-up after a PM.

The aims of the follow-up study were: 1) to explore psychological adjustment of the women in the MRISC-B and PREVOM-B cohorts on the long term, and 2) to identify risk factors of maladjustment through time.

The follow-up study included a total of 248 women, consisting of 206 women from the MRISC-B study and 42 women from the PREVOM-B study. Assessments in the context of this long-term study included completion of questionnaires 4-9 years after participation in the short-term study. The study procedure is described in more detail in *Chapter 1*. This thesis reports on the results of the follow-up studies.

In *Chapters 2-4*, the results regarding the impact of personal and social resources on psychological distress in the total group of women being at risk for hereditary breast cancer, irrespective of the choice for either regular surveillance or prophylactic mastectomy, are reported. In *Chapters 5-6* we describe the results of the analyses on long-term psychological adjustment to either having undergone prophylactic mastectomy (follow-up PREVOM-B cohort) or adhering to regular breast cancer surveillance (follow-up MRISC-B cohort). Furthermore, psychological adjustment in partners of high-risk women adhering to regular surveillance is addressed in *Chapter 7*.

THE IMPORTANCE OF PERSONAL RESOURCES

In *Chapter 2* the level of psychological distress, studied in 246 women, is described in relation to several aspects of self-concept, distinguishing between general self-esteem and several self-concept aspects specifically related to the risk of developing hereditary breast cancer. We found that women having a high level of self-esteem reported less general distress. Moreover, in the group of women with low self-esteem, a greater sense of mastery was associated with less general distress. These findings suggest that both self-esteem and mastery reflect a sense of resilience, and may buffer the stressful effects of being at risk for hereditary breast cancer. Another important finding was that feelings of stigmatization, implying feeling labelled, different and isolated from others, were significantly associated with increased psychological distress levels. Feelings of stigmatization may contribute to a negative self-concept, and may be a consequence of altered perceptions of health, altered relationships and in case of prophylactic surgery (mastectomy/breast reconstruction, and/or salpingo-ovariectomy) of physical deviance and fear of lowered or loss of sexual attraction and femininity. These findings suggest that exploration of the self-perception of women at risk for hereditary breast cancer is worthwhile. Specifically, addressing the issues of feelings of stigmatization, self-esteem and mastery may provide clues for tailoring counselling and support.

THE IMPORTANCE OF SOCIAL RESOURCES

In *Chapters 3 and 4* the results regarding the specific impact of social factors on the long-term psychological distress in 222 high-risk women are reported. First, we found that open family communication about thoughts and feelings regarding hereditary cancer was associated with less distress, and in fact may promote individual psychological adjustment (*Chapter 3*). In addition, social support from intimates (family and friends) had positive effects on psychological distress. Our findings suggest that providing support by communicating in an open way about feelings regarding hereditary cancer is most beneficial. Moreover, our results of further analyses on the interrelationships between personal and social resources suggest that social resources may strengthen personal resources *(Chapter 4)*. More specifically, women who felt supported by intimates reported increased levels of self-esteem. Additionally, women who were able to talk in an open way about hereditary cancer with their partner reported less feelings of stigmatization and vulnerability. These findings underline the importance of social resources, and indicate that monitoring of family communication and social support is relevant regarding the assessment of a woman's vulnerability. Also, health care workers should focus on the impact of hereditary cancer on the whole family system instead of merely focusing on the individual.

LONG-TERM PSYCHOLOGICAL CONSEQUENCES OF PROPHYLACTIC MASTECTOMY: FOLLOW-UP OF THE PREVOM-B STUDY COHORT

Data on the course of psychological distress and body image problems in 36 high-risk women who opted for prophylactic mastectomy with breast reconstruction (PM/BR) are discussed in *Chapter 5*. Women completed questionnaires before PM/BR (T0), at 6 months (T1) and 6-9 years (T2) after PM/BR. Levels of breast cancer specific as well as general distress were significantly decreased 6 months after PM/BR, and, subsequently, even further decreased 6-9 years after PM/BR, which most probably indicates relief from fear of developing breast cancer. Concerning body image, we observed a significant increase in problems regarding both breast-related and general body image at 6 months after PM/BR. At long -term follow-up (after 6-9 years), problems with breast-related body image had decreased in comparison with the 6 months follow-up, although the pre-surgery level was not reached, while problems with general body image were sustained.

Additional analyses aiming to identify risk factors predicting for poor body image on the long term revealed that general body image prior to PM was predictive for general body image on the long-term. Women having a poor general body image before PM/BR were more vulnerable for poor body image at long-term follow-up. Additionally, it was observed that seeking social support and having an active coping style were predictive for fewer problems with both breast related and general body image after PM/BR. In our opinion, these findings, although limited by the small sample size, are very important for clinical practice. The potentially negative consequences of PM/BR on a woman's body image both on the short and the long term should be discussed with a woman considering this surgical procedure and her partner. We suggest that a consultation with a psychologist or social worker is warranted as standard of care in the counseling of women considering PM/BR. Careful attention should be paid to the body image prior to PM/BR and the coping styles of the woman, in order to identify vulnerable women before surgery, and refer these women for additional support.

LONG-TERM PSYCHOLOGICAL CONSEQUENCES OF ADHERING TO REGULAR SURVEILLANCE: FOLLOW-UP OF THE MRISC-B STUDY COHORT

In *Chapter 6* findings on the long-term versus the short-term psychological distress in 197 high-risk women adhering to regular breast cancer surveillance are described. Furthermore, we examined which women may be more vulnerable for experiencing increased psychological distress. We found that mean psychological distress levels on the long-term (after 5-8 years) remained within normal limits and were either lower or similar compared to baseline levels. Furthermore, it was observed that women who had lost a first degree relative to breast cancer reported increased breast cancer specific distress levels both on the short-term and on the long-term, possible reflecting unresolved grief.

Several risk factors for long-term maladjustment were identified. We observed a positive association between short-term and long-term levels of distress. This means that women with higher levels of distress in the short-term study remained more vulnerable for distress over time. In our opinion, this finding underlines that it is important to identify vulnerable women at an early stage. Of great interest was the observation that one of the most powerful predictors of long-term distress was the type(s) of coping strategies employed by the respective women. Both passive and palliative coping strategies were predictive for increased long-term psychological distress, whereas, in contrast, coping through fostering reassuring thoughts had a positive impact on psychological distress. Another important observation was that the use of passive coping decreased over time, while coping through fostering reassuring thoughts increased over time. The latter findings interestingly argue against considering coping styles as stable and trait-like behaviour. Furthermore, women overestimating their cancer risk and women examining their breasts excessively, as has previously been recognized, were confirmed as vulnerable subgroups for long-term distress.

On the one hand, the findings of similar or even lower mean distress levels on the long term in high-risk women adhering to a regular breast cancer surveillance programme are reassuring as breast cancer surveillance can last for many years. On the other hand, the results indicate that several factors are predictive for increased psychological distress on the long term. It is important to identify vulnerable women at an early stage and offer them additional support, focusing on the particular stressors of a specific woman.

PARTNERS

The data on levels and courses of breast cancer-specific distress in 77 partners and high-risk women, assessed around two bi-annual appointments at the family cancer clinic (covering a period of 12-15 months), are described in *Chapter 7*. In general, the partners reported low levels of breast cancer specific distress. Increased distress levels in the partner were associated with having children (fatherhood) and a high affective risk perception of the breast cancer risk of the woman. Both the women and their partners reported increased levels of distress on the day of the surveillance appointment at the clinic, most probably due to the threat that an abnormality or breast cancer might be detected. Importantly, the level of distress reported by the partner proved to be associated with the degree of distress experienced by the at-risk woman, particularly on the day of the surveillance appointment. On the one hand, this positive association may indicate that the worries associated with facing the threat of hereditary cancer are shared by the woman and her partner, but, on the other hand, also reflects the strain that breast cancer surveillance puts on the partner relationship. Partners who are distressed may be less able to provide support and to communicate effectively, which, in turn, may lead to increased distress in the woman. This finding stresses the importance of considering the context of the family and the partner relationship when seeking to understand psychological adjustment in high-risk women.

CONCLUSIONS

In *Chapter 8*, the main findings of the analyses performed in the context of the long-term follow-up study, as presented in the current thesis, are discussed. Furthermore, recommendations regarding clinical practice and regarding possible future studies are proposed. For the majority of high-risk women, their choice for either regular surveillance or for prophylactic mastectomy (with breast reconstruction) did not result in major adverse psychological consequences on the long term, in terms of psychological distress. As it is important to identify the subset of women being in need for additional psychological support correctly and at an early stage, our data provide further knowledge about the risk factors to be addressed and can help health care workers involved in the care of high-risk women to identify vulnerable women for whom referral to a specialized psychologist or social worker may be considered. Furthermore, the findings of our long-term follow-up study after prophylactic mastectomy/breast reconstruction indicate that women may experience significant problems regarding body image after surgery, both on the short and on the long term. The potential (negative) consequences on body image should be incorporated in the information discussed with a woman (and her partner) prior to PM/BR. We also strongly advise that a consultation with a psychologist or social worker is warranted as standard of care for women considering PM/BR in order to thoroughly explore the way the woman and her partner expect to cope with the potential consequences of PM/BR on body image and sexual functioning. In our opinion, it is essential to re-discuss these issues after the surgery, and to refer women to a psychologist or sexologist if necessary.

SAMENVATTING

INTRODUCTIE

Naar schatting wordt ongeveer 5 tot 10% van de gevallen van borst- en eierstokkanker veroorzaakt door een erfelijke aanleg. Wanneer borstkanker en/of eierstokkanker veelvuldig in de familie voorkomt kan dit wijzen op een erfelijke aanleg, vooral als deze soorten kanker op jonge leeftijd optreden. In 1994 en 1995 zijn er twee genen geïdentificeerd die in geval van een mutatie predisponeren voor borst- en eierstokkanker, de zogenaamde BRCA1 en BRCA2 genen. Daarmee werd het voor vrouwen uit families met clustering van borst- en/of eierstokkanker mogelijk om middels genetisch onderzoek te laten nakijken of er sprake is van een mutatie in de familie en/of bij henzelf, en vervolgens een individuele risicoschatting te krijgen. Vrouwen met een geïdentificeerde mutatie in BRCA1 of BRCA2 hebben gedurende het leven 43-87% kans op borstkanker. Bovendien is het risico op het ontwikkelen van eierstokkanker 40-62% voor BRCA1 en 15-20% voor BRCA2 mutatiedraagsters. Echter, slechts bij 15-20% van de families waar een erfelijke aanleg wordt vermoed wordt daadwerkelijk een mutatie in BRCA1/2 geïdentificeerd. In deze non-BRCA1/2 families is er waarschijnlijk sprake van een voor ons nog onbekende erfelijke factor, of de mutatie in BRCA1/2 is mogelijk niet opgepikt (door de huidige beschikbare testmethoden). Voor vrouwen uit dergelijke families geldt dat het risico op borst kanker verhoogd is in vergelijking met het risico voor de algemene vrouwelijke populatie (12-13% in Nederland). Dit individuele risico op het krijgen van borst- en/of eierstokkanker wordt berekend aan de hand van familiegegevens en genetisch epidemiologische tabellen.

Vrouwen met een verhoogd risico op borstkanker op grond van een aangetoonde of aangenomen erfelijke aanleg worden geadviseerd om zich regelmatig te laten controleren. Het doel van een controleprogramma is om kanker in een zo vroeg mogelijk stadium te ontdekken, maar de onderzoeken kunnen niet voorkomen dat kanker optreedt, en er kan evenmin garantie gegeven worden dat kanker ontdekt wordt voordat er sprake is van uitzaaiingen in bijvoorbeeld de lymfeklieren. Een deel van de vrouwen met een sterk verhoogd risico op borst- en/of eierstokkanker (meestal vrouwen met een BRCA1/2 mutatie) kiest daarom voor een operatie uit voorzorg: preventieve mastectomie (PM; verwijdering van het borstklierweefsel) al of niet in combinatie met een borstreconstructie (BR) en/of preventieve salpingo-ovariectomie (PSO; verwijdering van eierstokken en eileiders). Deze chirurgische ingrepen blijken zeer effectief in het reduceren van het risico op kanker, maar zijn onomkeerbaar en hebben in meer of mindere mate gevolgen op het fysiek en psychologisch functioneren.

Aangezien zowel het borstkankercontrole programma als de preventieve operaties belangrijke handelingsopties zijn die met hoog-risico vrouwen worden besproken, werd het vanaf het begin van belang geacht om de voor- en nadelen van beide opties in kaart te brengen, niet alleen betreffende de lichamelijke aspecten, maar ook ten aanzien van de psychosociale consequenties. Meer kennis hierover is belangrijk om vrouwen die deze opties overwegen adequaat en optimaal te kunnen informeren en te steunen.

DE STUDIE

In 1999 werden vanuit de Polikliniek Erfelijke Tumoren van het Erasmus MC-Daniel den Hoed Oncologisch Centrum in Rotterdam twee prospectieve onderzoeken gestart om de psychologische gevolgen van enerzijds het participeren aan een borstkankercontrole programma en anderzijds het ondergaan van PM/BR en/of PSO (respectievelijk de MRISC-B, en de PREVOM-B studie) bij vrouwen met een verhoogd risico op borstkanker op basis van een aangetoonde erfelijke aanleg of duidelijke familiebelasting in kaart te brengen. De studieperiode in beide onderzoeken omvatte ongeveer 12 maanden (= korte termijn). In beide studies werden subgroepen geïdentificeerd van vrouwen die meer kwetsbaar zijn voor psychologische distress op de korte termijn. Uit deze studies en de dagelijkse praktijk werd echter ook duidelijk dat het belangrijk was om te weten hoe deze vrouwen op de lange termijn functioneerden, en hierover bestonden vooralsnog geen prospectieve data. Daarom werd in 2007 een vervolgstudie gestart met als doel: 1) het in kaart brengen van het psychologische welbevinden van de vrouwen in zowel de MRISC-B als PREVOM-B cohorten op de lange termijn, en 2) het identificeren van vrouwen die kwetsbaarder zijn in termen van psychologisch welbevinden, bij voorkeur in een zo vroeg mogelijk stadium. In het lange termijn vervolgonderzoek participeerden 248 vrouwen; 206 vrouwen uit de MRISC-B studie en 42 vrouwen uit de PREVOM-B studie. De vragenlijsten in dit vervolgonderzoek werden ingevuld 4-9 jaar na de eerdere participatie in het kader van MRISC-B en PREVOM-B studies. Details over de studieopzet zijn beschreven in *Hoofdstuk 1*. In dit proefschrift wordt verslag gedaan van de resultaten verkregen tijdens het vervolgonderzoek.

In de *Hoofdstukken 2-4* worden de resultaten beschreven betreffende de impact van zowel persoonlijke als sociale factoren op het psychologisch welbevinden op de lange termijn in de gehele groep van vrouwen met een erfelijke/familiaire aanleg voor borstkanker, ongeacht de keuze voor regelmatige controles of preventieve operatie. In de *Hoofdstukken 5-6* beschrijven we de resultaten van de analyses naar het psychologisch welbevinden op de lange termijn van vrouwen die een profylactische mastectomie ondergingen (follow-up PREVOM-B cohort) of die nog gecontroleerd werden op de Polikliniek Erfelijke Tumoren in het kader van borstkankercontrole (follow-up MRISC-B cohort). Ook de mate van psychologische distress bij partners van hoog-risico vrouwen die participeren aan een borstkankercontrole programma werd onderzocht *(Hoofdstuk 7)*.

BELANG VAN PERSOONLIJKE KENMERKEN

In *Hoofdstuk 2* wordt gerapporteerd over de invloed van verschillende aspecten van het zelfconcept op de mate van psychologische distress die hoog-risico vrouwen ervaren (n=246). Hierbij werd onderscheid gemaakt tussen algemene eigenwaarde en verschillende specifieke aspecten van zelfconcept gerelateerd aan erfelijke borstkanker. We vonden dat vrouwen met een hogere mate van eigenwaarde minder algemene distress rapporteerden. Bovendien vonden we dat onder vrouwen met een lage eigenwaarde een sterker gevoel van subjectieve controle ('mastery') geassocieerd was met minder algemene distress. Deze bevindingen duiden erop dat zowel gevoelens van eigenwaarde als van controle ('mastery') adaptieve persoonlijke kenmerken zijn, die mogelijk als een buffer fungeren tegen psychologische distress in vrouwen met een erfelijke/familiaire aanleg voor borst en/of eierstokkanker. Een andere belangrijke bevinding was dat gevoelens van stigmatisering, dat wil zeggen het gevoel hebben getekend, geïsoleerd en anders dan anderen te zijn, geassocieerd waren met een hogere mate van psychologische distress. Gevoelens van stigmatisering kunnen bijdragen aan een negatief zelfconcept, en kunnen onder andere het gevolg zijn van veranderde percepties van gezondheid, veranderde relaties en, in geval van preventieve operaties, van het gevoel fysiek "abnormaal" en seksueel minder aantrekkelijk en vrouwelijk te zijn.

Deze resultaten wijzen erop dat het belangrijk is dat hulpverleners aandacht besteden aan de zelfperceptie van vrouwen met een erfelijke/familiaire aanleg voor borstkanker. Specifieke onderwerpen om te bespreken zijn gevoelens van stigmatisering, eigenwaarde en subjectieve controle ('mastery'), en kunnen aanknopingspunten bieden voor het aanpassen van de counseling en ondersteuning.

BELANG VAN SOCIALE RELATIES

In de *Hoofdstukken 3 en 4* werd de impact van sociale factoren op psychologische distress onderzocht bij 222 vrouwen. Allereerst vonden we dat open communicatie over gedachten en gevoelens betreffende erfelijke borstkanker in de familie geassocieerd was met minder algemene distress, en dus een positief effect had op het individuele psychologische welbevinden van de vrouw (*Hoofdstuk 3)*. Ook sociale steun van intimi (familie en vrienden) had een gunstig effect op distress, waarbij voornamelijk steun in de vorm van open gesprekken over erfelijke borstkanker belangrijk lijkt. Bovendien bleek uit de analyses naar onderlinge samenhang tussen sociale en persoonlijke factoren, dat de sociale omgeving ook positieve effecten had op verschillende aspecten van zelfconcept *(Hoofdstuk 4)*. Vrouwen die zich gesteund voelden door intimi rapporteerden een hogere eigenwaarde. Bovendien rapporteerden vrouwen die open communiceerden over erfelijke borstkanker met hun partner minder gevoelens van stigmatisering en kwetsbaarheid. Deze bevindingen benadrukken het belang van sociale relaties. Het exploreren van communicatiepatronen binnen families en sociale steun kan waardevolle informatie opleveren bij het inschatten van de psychische kwetsbaarheid en weerbaarheid van hoog-risico vrouwen. Bovendien onderstrepen deze bevindingen dat hulpverleners oog dienen te hebben voor de impact van erfelijke borst- en/of eierstokkanker op de familie als systeem in plaats van enkel op het individu.

LANGE TERMIJN PSYCHOLOGISCHE CONSEQUENTIES VAN PROFYLACTISCHE MASTECTOMIE: FOLLOW-UP VAN DE PREVOM-B COHORT

In *Hoofdstuk 5* werd het beloop van psychologische distress en problemen met het lichaamsbeeld onderzocht bij 36 vrouwen die een preventieve mastectomie met borstreconstructie (PM/BR) ondergingen. Vrouwen vulden vragenlijsten in voorafgaand aan PM/BR (T0), zes maanden na PM/BR (T1) en 6-9 jaar na PM/BR (T2).

Algemene en borstkankerspecifieke distress waren significant afgenomen 6 maanden na PM/BR, en namen vervolgens zelfs nog verder af 6-9 jaar na PM/BR, wat hoogstwaarschijnlijk duidt op een afname van angst om borstkanker te ontwikkelen. Resultaten met betrekking tot het lichaamsbeeld lieten zien dat vrouwen een significante toename in problemen met het algemene en borstgerelateerde lichaamsbeeld rapporteerden 6 maanden na de operatie. Bij de meting 6-9 jaar na PM/BR waren de problemen met het borstgerelateerde lichaamsbeeld significant afgenomen, hoewel deze niet afnamen tot het niveau van voor de operatie, terwijl de problemen met het algemene lichaamsbeeld bleven bestaan.

In verdere analyses werd onderzocht of bepaalde factoren voor de operatie voorspellend zijn voor problemen met het lichaamsbeeld op de lange termijn. Algemeen lichaamsbeeld voorafgaand aan PM/BR was voorspellend voor algemeen lichaamsbeeld op de lange termijn. Vrouwen met een laag lichaamsbeeld voorafgaand aan een PM/BR bleken meer kwetsbaar voor een verlaagd lichaamsbeeld na de operatie. Verder bleken een actieve copingstijl en het zoeken van sociale steun voorspellend voor minder problemen met zowel het algemene als borstgerelateerde lichaamsbeeld op de lange termijn.

Naar onze mening zijn deze bevindingen, ondanks de kleine onderzoeksgroep, van grote waarde voor de praktijk. De potentieel negatieve consequenties van PM/BR op het lichaamsbeeld zowel op de korte als de lange termijn dienen besproken te worden met een vrouw die de operatie overweegt en haar partner. Voorts geven de resultaten van deze studie aan dat een psychologisch consult voorafgaand aan een preventieve mastectomie geïndiceerd is. In dit consult dient men aandacht te geven aan het lichaamsbeeld en de manier waarop de vrouw met problemen omgaat, met het oog op het vroegtijdig identificeren van kwetsbare vrouwen, en deze vrouwen eventueel te verwijzen voor aanvullende ondersteuning.

LANGE TERMIJN FOLLOW-UP VAN VROUWEN DIE PARTICIPEREN AAN REGELMATIGE BORSTKANKER CONTROLES

In *Hoofdstuk 6* worden de resultaten beschreven van de psychologische distress op de lange termijn in vergelijking met de korte termijn bij 197 vrouwen met een erfelijke/familiaire aanleg voor borstkanker die gecontroleerd werden op de Polikliniek Erfelijke Tumoren van het Erasmus MC-Daniel den Hoed. Voorts werd onderzocht welke vrouwen het meest kwetsbaar zijn voor distress op de lange termijn. We vonden dat het gemiddelde niveau van psychologische distress op de lange termijn (5-8 jaar follow-up) binnen normale spreidingswaarden bleef. Borstkankerspecifieke distress was significant lager op de lange in vergelijking met de korte termijn, terwijl er geen significante verandering in algemene distress was. Verder bleek dat vrouwen die een eerstegraads familielid aan borstkanker hadden verloren meer borstkankerspecifieke distress rapporteerden dan vrouwen die deze ervaring niet hadden, hetgeen werd gevonden op zowel de korte als de lange termijn. Verhoogde borstkankerspecifieke distress in deze groep van vrouwen is mogelijk een symptoom van gecompliceerde rouw.

Verschillende factoren waren voorspellend voor psychologische distress op de lange termijn. We vonden dat de mate van distress op de korte termijn voorspellend voor de mate van distress op de lange termijn. Vrouwen die een hoge mate van distress rapporteerden in de korte termijn studie waren meer kwetsbaar voor verhoogde distress op de lange termijn. Naar onze mening onderstreept deze bevinding het belang van het vroegtijdig identificeren van kwetsbare vrouwen. Van groot belang was de bevinding dat de copingstijl die een vrouw hanteert (de manier van omgaan met problemen) een aanzienlijke impact had op de mate van psychologische distress. Vrouwen die een meer passieve en palliatieve copingstijl hadden bleken meer distress te rapporteren op de lange termijn, terwijl vrouwen die geneigd waren geruststellende gedachten te hanteren minder distress rapporteerden. Een andere belangrijke observatie was dat het gebruik van een passieve copingstijl afnam in de loop van de studieperiode, terwijl het hanteren van geruststellende gedachten toenam. Deze veranderingen pleiten tegen de opvatting van copingstijl als een stabiele persoonlijkheidstrek. Verder vonden we dat vrouwen die hun borstkankerrisico overschatten en vrouwen die hun borsten overmatig controleren, welke meer kwetsbaar werden gevonden voor distress op de korte termijn, eveneens meer kwetsbaar waren voor verhoogde distress op de lange termijn.

Enerzijds zijn deze bevindingen met betrekking tot gelijke of zelfs afgenomen psychologische distress op de lange termijn in hoog-risico vrouwen die participeren in een borstkankercontrole programma geruststellend, aangezien participatie langdurig kan zijn. Anderzijds geven de resultaten aan dat bepaalde factoren voorspellend zijn voor meer psychologische distress op de lange termijn. Het is belangrijk om kwetsbare vrouwen vroegtijdig te herkennen en de hulpverlening erop aan te passen.

PARTNERS

De mate en beloop van kankerspecifieke distress rondom twee opeenvolgende halfjaarlijkse controleafspraken werd onderzocht bij 77 partners en hoog-risico vrouwen (*Hoofdstuk 7)*. De partners rapporteerden gemiddeld een laag niveau van borstkankerspecifieke distress. Factoren die geassocieerd waren met een verhoogd distress niveau bij de partner waren vaderschap en een hoge gevoelsmatige (affectieve) risicoperceptie van het borstkankerrisico bij de vrouw. Zowel de vrouwen als hun partners rapporteerden een verhoogde mate van kankerspecifieke distress op de dag van de controle afspraak bij de arts, waarschijnlijk door de dreiging dat borstkanker gedetecteerd zou kunnen worden. Verder vonden we een positieve samenhang tussen de mate van distress ervaren door de vrouw en de mate van distress ervaren door haar partner, welke het sterkst was op de dag van de controle afspraak. Enerzijds kan deze bevinding erop wijzen dat de zorgen over kanker gedeeld worden door de vrouw en haar partner, anderzijds kan deze wijzen op spanningen binnen de partnerrelatie. Partners die meer distress ervaren zijn mogelijk minder in staat om de vrouw adequaat te steunen, wat vervolgens kan leiden tot meer distress bij de vrouw. Deze bevindingen benadrukken dat het belangrijk is om aandacht te besteden aan de gezinscontext, en aan de partnerrelatie.

CONCLUSIES

In *Hoofdstuk 8* worden de resultaten van de verschillende analyses verricht in de context van de lange termijn studie, zoals beschreven in dit proefschrift, verder in perspectief geplaatst. Verder worden er aanbevelingen gedaan voor de klinische praktijk en voor mogelijk toekomstig onderzoek. Voor de meerderheid van de hoog-risico vrouwen heeft de keuze voor ofwel regelmatige borstkankercontroles of het ondergaan van een preventieve mastectomie (in combinatie met borstreconstructie) gelukkig geen verregaande emotionele gevolgen in termen van psychologische distress. Echter, in de verschillende analyses werden verschillende factoren geïdentificeerd die voorspellend waren voor het ervaren van verhoogde distress. Kennis over risicofactoren is van belang voor artsen en hulpverleners om vrouwen die het in psychologisch opzicht zwaarder kunnen krijgen vroegtijdig te herkennen, en eventueel te verwijzen naar een gespecialiseerde psycholoog of maatschappelijk werker.

De bevindingen van de prospectieve, lange termijn studie na profylactische mastectomie met borstreconstructie (PM/BR) tonen aan dat vrouwen na de operatie significante problemen met het lichaamsbeeld kunnen ervaren, zowel op de korte als de lange termijn. De potentiële (negatieve) consequenties op het lichaamsbeeld dienen geïncorporeerd te worden in de informatie die voorafgaande aan de PM/BR met de vrouwen (en hun partner) wordt besproken. Voorts is het wenselijk om vrouwen die een PM/BR overwegen in het voorbereidingstraject een gesprek met een psycholoog of maatschappelijk werker aan te bieden, om te exploreren hoe de vrouw (en haar partner) verwachten om te gaan met de potentiële consequenties van PM/BR op het lichaamsbeeld en het seksueel functioneren. Naar onze mening is het ook wenselijk om deze onderwerpen opnieuw na de operatie met de vrouw (en haar partner) te bespreken, en indien nodig vrouwen te verwijzen naar een psycholoog of seksuoloog.

DANKWOORD

Het is zover, het proefschrift is af! Zoals zo velen al voor mij geschreven hebben: een proefschrift schrijven doe je zeker niet alleen. Op deze plaats wil ik dan ook iedereen bedanken die op directe of indirecte wijze aan de totstandkoming van dit proefschrift heeft bijgedragen. Een aantal mensen wil ik in het bijzonder bedanken.

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CURRICULUM VITAE

Mariska den Heijer was born on May 8th, 1984 in Terneuzen, the Netherlands. She graduated from secondary school (VWO, Zeldenrust Steelantcollege, Terneuzen) in 2002. In 2005 she obtained her Bachelor's degree in Psychology cum laude at the University of Tilburg and received an excellence scholarship. In 2007 she received her Master's degree in Psychology and Mental Health with honor ('met genoegen'), after completing her internship in a mental healthcare institution for adults (GGZ). For her Master's thesis, she conducted a study on the contribution of a self-report personality inventory (the Dutch Short Form of the MMPI) in distinguishing patients with ADHD from a control group of patients from the general psychiatric population.

In February 2009, she began her PhD study as described in this thesis at the Department of Medical Psychology and Psychotherapy at the Erasmus Medical Centre in Rotterdam, in collaboration with the Daniel den Hoed family Cancer Clinic. The main focus of her research is on the psychological adjustment to either regular breast cancer surveillance or prophylactic mastectomy in women at risk for hereditary breast/ovarian cancer, and on risk factors for long-term maladjustment. In addition to research, she is involved in teaching medical psychology and communication skills in the medical curriculum at the Erasmus MC.

Since 2010, she is working as a psychologist at the Department of Clinical Genetics, Erasmus Medical Centre, Rotterdam. She is currently involved in several other research projects in the field of Clinical Genetics. Since 2011, she has been secretary of the working group Hereditary Tumors of the Dutch Association of Psychosocial Oncology.

PhD PORTFOLIO

Name PhD student: Mariska den Heijer
Erasmus MC Departments: Clinical Genetics & Medical Psychology and Psychotherapy
PhD period: 2009-2012
Promotors: Prof. dr. A. Tibben & Dr. C. Seynaeve
Supervisor: Prof. dr. Aad Tibben

1. PhD Training	**Year**
Relevant courses	
Minicursus Methodologie van patiëntgebonden onderzoek en voorbereiding van subsidieaanvragen, Erasmus MC, Rotterdam	2009
Basiscursus didactiek, Erasmus Universiteit Rotterdam	2009
Biomedical English writing and communication, Erasmus MC, Rotterdam	2009
Basiscursus regelgeving klinisch onderzoek, Erasmus MC, Rotterdam	2010
Cursus "Gecompliceerde Rouw", Rino-groep	2011
Presentations	
Psychological distress in women at risk for hereditary breast cancer: the role of family communication and perceived social support, European Meeting on Psychosocial Aspects of Genetics (EMPAG), Gothenburg, Sweden	2010
Long-term psychological distress in women at risk for hereditary breast cancer adhering to regular surveillance, 12th International Meeting on Psychosocial Aspects of Hereditary Cancer (IMPAHC), Amsterdam, Netherlands	2011
Body image and psychological distress after prophylactic mastectomy and breast reconstruction in genetically predisposed women: a prospective long-term follow-up study (poster), IPOS 13th World Congress of Psycho-Oncology, Antalya, Turkey	2011
(Inter)national conferences	
Congres Nederlandse Vereniging Medisch Onderwijs (NVMO), Egmond aan Zee, Nederland	2009
17e Congres van de Nederlandse Vereniging Psychosociale Oncologie "Bewegen en bewogen worden", Amersfoort	2010
European Meeting on Psychosocial Aspects of Genetics (EMPAG), Gothenburg, Sweden	2010
18e Congres van de Nederlandse Vereniging Psychosociale Oncologie "Effectiviteit van interventies", Utrecht	2011
12th International Meeting on Psychosocial Aspects of Hereditary Cancer (IMPAHC), Amsterdam, Netherlands	2011
IPOS 13th World Congress of Psycho-Oncology, Antalya, Turkey	2011
Seminars and workshops	
Workshop "Body awareness: de complexiteit van de eenvoud", NVPO Congres	2010
Workshop "Genetisch counseling van kinderen", LUMC, Leiden	2010
Workshop "Kanker en seksualiteit", NVPO Congres	2011
Workshop "Tailored therapeutic strategies for high risk individuals", IMPAHC	2011
Workshop "Genetic counselling for cancer: Do we meet the needs?", IMPAHC	2011
Workshop "Sex & Cancer: Improving Psychosexual Care", IPOS	2011
Workshop "Supportive-Expressive Group Therapy Advanced Cancer", IPOS	2011
Workshop "Supportive Counselling Mindfulness-based Therapies", IPOS	2011

2. Teaching

Lecturing

Communicatie en Attitude-onderwijs in het medische curriculum	2009 – 2012
Vaardigheidsonderwijs Genetisch counselen, Dysmorfologie, Pijn, Cognitieve gedragstherapie	2009 – 2012
Onderwijs mammacare verpleegkundigen	2011

Workshops

Workshop omgaan met erfelijke belasting, Lynch patiëntendag, Erasmus MC, Rotterdam	2010
Workshop "erfelijkheid & kanker", voorlichtingsdag oncologiepatiënten, Albert Schweitzer Ziekenhuis, Dordrecht	2010, 2011 & 2012

As Time Goes By

The Long-Term Psychological Impact of either Regular Surveillance or Prophylactic Mastectomy in Women at Risk for Hereditary Breast Cancer

Mariska den Heijer

As Time Goes By
The Long-Term Psychological Impact of either Regular Surveillance or Prophylactic Mastectomy in Women at Risk for Hereditary Breast Cancer
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