Quality-of-Life Effects of Prophylactic Salpingo-Oophorectomy Versus Gynecologic Screening Among Women at Increased Risk of Hereditary Ovarian Cancer

ABSTRACT
Purpose
Recommendations for women at high risk of ovarian cancer include periodic gynecologic screening (GS) and prophylactic bilateral salpingo-oophorectomy (PBSO). The aim of the current study was to determine the quality-of-life (QOL) effects of PBSO versus GS.

Patients and Methods
Questionnaire data were obtained from 846 high-risk women who had participated in this nationwide, cross-sectional, observational study. Forty-four percent of the women had undergone PBSO, and 56% had opted for GS. Topics addressed by the questionnaire included generic QOL, cancer-specific distress, endocrine symptoms, and sexual functioning.

Results
No statistically significant between-group differences were observed in generic QOL (Short Form-36), with women in both the PBSO and GS groups scoring similarly to the general population. Compared with GS, PBSO was associated with fewer breast and ovarian cancer worries (P < .001) and more favorable cancer risk perception (P < .05). However, the PBSO group reported significantly more endocrine symptoms (P < .001) and worse sexual functioning (P < .05) than the GS group. Eighty-six percent of women would choose PBSO again, and 63% would recommend it to a friend with familial risk of ovarian cancer.

Conclusion
PBSO had no measurable adverse impact on generic QOL of high-risk women. The favorable effects of PBSO in terms of reduced cancer worries and low perceived cancer risk need to be weighed against the increase in endocrine and sexual symptoms. Balanced information will help clinicians and high-risk women to make informed decisions about the optimal preventive health strategy.

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INTRODUCTION
Ovarian cancer is one of the most common and lethal of gynecologic malignancies. In the Netherlands, the average age-adjusted incidence and mortality rates are 13.1 and 9.6 per 100,000 women, respectively, which are comparable to the rates observed in the United States.1,2 A family history of ovarian cancer is considered to be one of the strongest predictors of developing the disease, and it is estimated that 5% to 10% of all ovarian cancer patients have a hereditary basis.3,4 Female carriers of a BRCA1 gene mutation have a lifetime ovarian cancer risk in the range of 39% to 54%.5,6 Women with a BRCA2 mutation have a lower ovarian cancer risk (11% to 23%), but this is still approximately 10-fold greater than the risk of women in the general population.5,6
Principal preventive health strategies for women at increased risk of ovarian cancer include periodic gynecologic screening (GS) and prophylactic bilateral salpingo-oophorectomy (PBSO), which are aimed at early cancer detection and cancer risk reduction, respectively. Although annual GS is offered as a basic surveillance strategy to high-risk women, its efficacy has yet to be established. Current techniques, such as transvaginal sonography and CA-125 serology yield a significant number of false-positive or false-negative results, leading either to unnecessary medical investigations or to undetected early-stage malignancies. Because early ovarian cancer is asymptomatic and the available techniques have not been demonstrated to be effective for early diagnosis in the general population, the majority of diagnosed ovarian cancers are characterized by advanced stages and, therefore, by a poor prognosis.

In view of the uncertainty surrounding screening procedures, high-risk women may opt for surgical removal of their ovaries and fallopian tubes. PBSO reduces ovarian cancer risk in BRCA1/2 mutation carriers by 96% and breast cancer risk by 53%. However, PBSO does not eliminate the risk of ovarian cancer entirely because 1% to 2% of women may develop peritoneal carcinoma. Adverse effects associated with prophylactic surgery in premenopausal women are loss of fertility and immediate onset of menopause as a result of estrogen deprivation, including vasomotor symptoms and possible sexual dysfunction. Estrogen deprivation may also lead to higher risk of developing osteoporosis. To relieve climacteric symptoms, hormone replacement therapy (HRT) is often prescribed. However, the effectiveness of HRT in combating symptoms associated with surgically induced menopause has not yet been established.

Thus far, only four studies have explicitly focused on quality-of-life (QOL) effects associated with PBSO or PBSO versus GS. Several studies have reported beneficial effects of PBSO on cancer-specific distress (eg, cancer worries and anxiety) and perceived cancer risk but adverse effects on sexual functioning and vasomotor symptoms. In these studies, generic QOL was not affected by prophylactic surgery, with oophorectomized women reporting similar levels of QOL as women in the general population. The only study that has compared the QOL effects of PBSO and GS yielded somewhat conflicting results. Oophorectomized women reported significantly worse generic QOL than women in the GS group; however, no comparisons with the general population were provided. Additionally, PBSO was not found to relieve cancer-specific distress or to worsen sexual functioning. Although this latter study was the first to provide a comparison of psychosocial effects of PBSO and GS, its results may not be generalizable to the entire population of high-risk women. It was a single-center study with a small sample size (PBSO, n = 29; GS, n = 28), and not all statistical analyses controlled for possible confounding medical variables (eg, DNA status and history of breast cancer). In this report, we present the results of a nationwide, multicenter, cross-sectional, observational study that was conducted to determine possible differences in the generic and condition-specific QOL effects of PBSO versus GS.

**PATIENTS AND METHODS**

**Sample and Procedures**

Study participants were recruited from the gynecology departments of eight hospitals in the Netherlands. Women were eligible for enrollment if they were between 30 and 75 years of age, came from a hereditary breast or ovarian cancer family, and had sought advice from a gynecologist on preventive measures at one of the eight participating gynecology clinics between 1996 and 2001. Patients were excluded from participation if they had undergone oophorectomy because of any suspicious changes in the ovaries as detected by medical examination, including both benign and malignant conditions; if oophorectomy was performed as adjuvant treatment for breast cancer; or if they had terminal cancer or any other severe medical comorbidity.

Eligible women received an invitation letter by mail, an informed consent form, a questionnaire, and a postage-paid return envelope. In case of nonresponse within 2 weeks, systematic reminders by mail and telephone were used. Patients were classified as nonrespondents if they actively declined to participate by mail or telephone or if they could not be reached after multiple attempts. Age and the type of ovarian cancer prevention strategy used (PBSO vs GS) were the only available data that could be registered for nonrespondents. The study was approved by the institutional review boards of all participating hospitals.

**Measure: Generic QOL**

To assess generic QOL, four of the eight subscales of the Short Form-36 (SF-36) Health Survey general health perceptions, vitality, role limitations caused by emotional problems, and general mental health) and the global QOL item of the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30 were used. All raw scale scores were linearly converted to a 0 to 100 scale, with higher scores indicating higher levels of QOL. Cronbach’s α coefficients in the present sample for the four SF-36 scales ranged from .80 to .86.

**Measure: Condition-Specific QOL**

Condition-specific QOL included measures of cancer-specific distress (intrusive thoughts, cancer worries, and anxiety), cancer risk perception, endocrine symptoms, and sexual functioning.

Cancer-specific distress: Intrusive thoughts, cancer worries, and postoperative anxiety. The seven-item intrusion subscale of the Impact of Events Scale (IES) measures the frequency of intrusive thoughts experienced because of a specific stressor, which was defined in the present study as an increased risk of developing breast or ovarian cancer. A higher sum score (range, 0 to 35) corresponds to more distress (Cronbach’s α = .90). The recommended cutoff sum score for identifying persons likely to meet criteria for post-traumatic stress syndrome (PTSD) is 20.

Five Likert-type items, adapted from Lerman, were used to assess worries about breast and ovarian cancer. These included the frequency of ovarian and breast cancer worries (two items), the impact of cancer worries on mood and daily functioning (two items), and the frequency of worries about the possible cancer risk
in family members (1 = rarely or never, 2 = sometimes, 3 = often, 4 = all the time). These five items were summed to create a cancer worry scale (possible range, 5 to 20), with higher scores representing more frequent worries in the last 4 weeks (Cronbach’s α = .70). Additionally, women in the PBSO group were asked to rate the extent to which PBSO reduced their anxiety about developing ovarian and breast cancer, with response choices varying on a 4-point scale from not at all to very much.

Self-perceived cancer risk. Two items adapted from previous studies30,31 assessed patients’ current perceptions of their breast cancer risk. Women were asked to rate their self-perceived risk on a scale 0% to 100%, where 0 corresponded to no risk at all and 100 corresponded to being certain about developing cancer in the future. Women in the PBSO group were also requested to estimate (retrospectively) their presurgery risk of developing breast cancer.

Endocrine symptoms and sexual functioning. The Functional Assessment of Cancer Therapy–Endocrine Symptom, an 18-item endocrine symptom scale, was used to assess menopausal symptoms.32 Occurrence of each symptom in the last 4 weeks was scored on a 5-point Likert-type scale, ranging from not at all to very much. Item scores were summed to obtain a scale score (range, 0 to 72), with lower values indicating more menopausal symptoms. The Cronbach’s α in the present study was .81.

The Sexual Activity Questionnaire (SAQ)33 was used to measure sexual functioning. The SAQ consists of the following three scales: pleasure (six items on desire, enjoyment, satisfaction, and current frequency of activities), discomfort (two items on vaginal dryness and pain and discomfort during penetration), and habit (frequency of sexual activity compared with the usual level). Lower scores represent poorer sexual functioning. In the present sample, Cronbach’s α coefficients for pleasure and discomfort scales were .82 and .77, respectively. The SAQ was introduced during the course of the study and, thus, was administered to only a subset of women (n = 513) from five study centers.

Measure: Satisfaction With Preventive Health Strategies

A series of single items was used to assess the level of satisfaction with or regrets about the decision to undergo PBSO or GS. On a 5-point scale, varying from completely disagree to completely agree, women were asked to indicate their level of agreement or disagreement with the following statements: (1) I am satisfied with the decision I have made, and (2) I have regrets about the decision I have made. Women who chose agree or completely agree as their response to the first or second statement were considered as being satisfied with their decision on the preventive health option or as having regrets about it, respectively. Additionally, women were asked two questions about whether or not they would choose to undergo the same preventive health strategy again and about which preventive option they would recommend to a friend in a similar situation.

Medical and Sociodemographic Data

Medical data were obtained from two sources (a questionnaire and hospital medical records). In case of discrepancies between self-reported and medical record data, the latter were considered as the primary information source. The questionnaire contained a series of questions on reproductive history, personal history of cancer and recent treatment for cancer, prevalence of ovarian and breast cancer among relatives, prophylactic ovarian and breast surgery, and use of HRT. Menopausal status was determined through a series of questions on menstrual history and symptoms during the 6 months preceding PBSO or at the present moment for women who had opted for GS. Premenopause was defined as regular menstrual periods, perimenopause was defined as irregular periods, and postmenopause was defined as complete cessation of menstrual periods for at least 1 year. Women who had had PBSO were classified as postmenopausal. Additionally, clinical variables, such as DNA status, type of prophylactic ovarian or breast surgery, possible use of HRT, history of (breast) cancer, its stage at diagnosis, and cancer treatment, were retrieved from the medical records. Sociodemographic variables (age, marital status, education, and employment) were obtained from the questionnaire.

Statistical Analysis

Descriptive statistics (frequencies, means, and standard deviations [SD]) were generated to characterize the sample in terms of sociodemographics and medical variables. Student’s t-tests and χ² tests were used to explore potential differences in the background characteristics of women who had undergone PBSO and women who had opted for GS.

To test for the statistical significance of group differences in generic and condition-specific QOL, we used one-way analysis of covariance (ANCOVA) controlling for possible confounders (age, BRCA1/2 status, parity, history of breast cancer, and prophylactic mastectomy [PM]). To examine the magnitude of differences between the PBSO and GS groups, effect sizes based on differences between mean scores divided by the pooled SD were calculated. In accordance with Cohen,34 effect sizes of 0.20, 0.50, and 0.80 were considered small, medium, and large, respectively. Using ANCOVA, we also investigated possible differences in the SF-36 mean scale scores between the participating high-risk women and women of similar age from the general Dutch population. The SF-36 general population normative data were based on the sample reported earlier by Aaronson et al.22

A multivariate logistic regression analysis was conducted to investigate the effects of the type of ovarian cancer prevention (GS vs PBSO) on the odds of the presence of cancer worries, when controlling for the potential confounders. Separate items of the cancer worry scale were dichotomized (eg, worried v not worried), with the original categories (sometimes, often, and all the time) describing the frequency of worries and their impact on mood and functioning collapsed into one category (worried). The purpose of this analysis was to determine which specific aspects of distress contributed the most to a PBSO-GS difference.

Within the PBSO group, we also examined whether menopausal status (premenopausal v postmenopausal) at the time of ovarian surgery had a significant impact on the current levels of QOL. Additionally, in an ANCOVA model, we controlled for the time since surgery and current HRT use.

All statistical analyses were carried out using SPSS version 11.5.0 (SPSS Inc, Chicago, IL). Because of multiple testing, the significance level was set at P ≤ .01. P values between .01 and .05 were considered to be marginally significant. All statistical tests were two sided.

RESULTS

Study Sample

On the basis of the hospital census data (Fig 1), we identified 1,205 high-risk patients who were potentially...
eligible for participation in the study. After an additional medical record audit, 121 women were excluded because of oophorectomy carried out as treatment for benign or malignant conditions (n = 94), death (n = 23), terminal cancer (n = 3), or severe psychiatric problems (n = 1). In total, 858 (79%) of 1,084 eligible women returned the questionnaires. The main reasons for nonparticipation were lack of motivation (n = 137), poor health (n = 8), and emotional problems (n = 8). The data of 12 women had to be excluded; five of these women reported that the questionnaire was not applicable to their present situation because their cancer risk was found not to be increased according to DNA testing, five women had a high percentage (>50%) of missing values, and two women reported having undergone an oophorectomy before 1996. There were no statistically significant differences between the respondents and nonrespondents regarding the type of ovarian cancer prevention and mean age (data not shown).

The final study sample (n = 846) consisted of 369 women (44%) who had undergone PBSO and 477 women (56%) who had opted for periodic GS (pelvic examination, transvaginal sonography, and CA-125 serology). Among BRCA1/2 mutation carriers (n = 368), 265 women (72%) opted for PBSO, and 103 women (28%) opted for GS.

The demographic and clinical characteristics of the sample are listed in Table 1. Compared with the women in the GS group, the women in the PBSO group were significantly older and were significantly more likely to have been diagnosed with breast cancer, to be BRCA1/2 mutation carriers, and to have undergone (unilateral or bilateral) PM (all P < .001). Women with less education and women having at least one child were also more likely to undergo PBSO, although these associations only reached marginal levels of statistical significance (all P < .05). After PBSO, slightly more than one third of women had used HRT.

Generic and Condition-Specific QOL
Table 2 lists mean scores and SDs of the QOL measures for the PBSO and GS groups. Overall, the study respondents exhibited high levels of generic QOL as assessed by the SF-36, and no significant differences were found between the PBSO and GS groups. The SF-36 scores of both the PBSO and GS groups were, on average, not significantly different from those of similarly aged women from the general population.

There were no significant group differences in mean levels of intrusive thoughts about cancer, and similar percentages of the PBSO and GS groups (9% to 10%) reported intrusive thoughts (sum score ≥20) severe enough to indicate the possible presence of PTSD (Table 2). However, women who had undergone PBSO reported significantly fewer cancer worries (scale mean, 7.0; range, 5 to 14) than...
women in the GS group (scale mean, 7.9; range, 5 to 20; 
$P < .001$; effect size $= 0.44$). The effect of PM and the interaction effect of prophylactic oophorectomy (yes v no) and PM (yes v no) were (marginally) significant ($P < .05$ and .01, respectively). Women who had undergone both PBSO and PM (PBSO v PM) reported significantly lower levels of cancer worries (mean, 6.6; range, 5 to 13) compared with mastectomized women undergoing GS (mean, 8.1; range, 5 to 20). Regarding specific aspects of cancer worries (Table 3), significantly fewer women in the PBSO group indicated being worried about their ovarian cancer risk ($P < .001$), being worried about cancer risk among their family members ($P < .05$), and that cancer worries had affected their mood ($P < .001$) and functioning ($P < .01$). Eighty-two percent and 45% of oophorectomized women reported that their anxiety about developing ovarian and breast cancer, respectively, had decreased substantially since their surgery (Table 2); for the PBSO v PM group,
these percentages were 90% and 57%, respectively. Comparable data were not available for the GS group.

Adjusting for possible confounders, the perceived risk of developing breast cancer was marginally significantly lower among women who had undergone PBSO than among women in the GS group. The effect of PM was statistically significant ($P < .001$; effect size = 0.58), with the lowest estimated risk being in the PBSO + PM + group (mean ± SD, 12.9 ± 11.2) and the highest risk being in women undergoing GS only (mean ± SD, 46.9 ± 26.0). For the entire PBSO group, the perceived risk of breast cancer had decreased, on average, by 29.1 points on a scale 0 to 100 compared with before ovarian surgery (retrospective estimate). For women who had also undergone PM, the decrease was 51.3 points (data not shown).

No significant differences in the level of sexual activity were observed between the PBSO and GS groups (Table 2). However, women in the PBSO group reported marginally significantly more discomfort (vaginal dryness and dyspareunia; $P < .05$), less pleasure and satisfaction during sexual activities ($P < .05$), and significantly more endocrine symptoms ($P < .001$) than the GS group. No significant differences were observed between HRT users and nonusers after ovarian surgery in the levels of endocrine symptoms and sexual functioning (data not shown). Menopausal status at the time of PBSO (premenopausal vs postmenopausal) and the time since PBSO were not significantly related to the current levels of generic and condition-specific QOL reported by oophorectomized women (data not shown).

Table 2. QOL Assessments by Preventive Health Strategies for Ovarian Cancer: PBSO Versus GS

<table>
<thead>
<tr>
<th>QOL</th>
<th>PBSO (n = 369)</th>
<th>GS (n = 477)</th>
<th>$P$ (PBSO vs GS)</th>
<th>Effect Size</th>
<th>Population Norm (n = 487)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD†</td>
<td>Mean</td>
<td>SD†</td>
<td></td>
</tr>
<tr>
<td><strong>Generic QOL† score</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global health status</td>
<td>74.9</td>
<td>19.0</td>
<td>76.1</td>
<td>19.4</td>
<td>.51</td>
</tr>
<tr>
<td>General health perceptions</td>
<td>70.3</td>
<td>22.4</td>
<td>70.9</td>
<td>19.7</td>
<td>.73</td>
</tr>
<tr>
<td>Vitality</td>
<td>62.7</td>
<td>18.7</td>
<td>64.0</td>
<td>17.2</td>
<td>.55</td>
</tr>
<tr>
<td>Mental health</td>
<td>73.7</td>
<td>15.9</td>
<td>72.9</td>
<td>15.7</td>
<td>.29</td>
</tr>
<tr>
<td>Role–emotional</td>
<td>75.4</td>
<td>37.2</td>
<td>79.2</td>
<td>33.8</td>
<td>.95</td>
</tr>
<tr>
<td><strong>Condition-specific QOL</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intrusive thoughts§</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sum score</td>
<td>6.8</td>
<td>7.8</td>
<td>7.0</td>
<td>7.7</td>
<td>.37</td>
</tr>
<tr>
<td>Patients scoring ≥ 20, %</td>
<td>8.9</td>
<td>9.6</td>
<td></td>
<td></td>
<td>.73</td>
</tr>
<tr>
<td>Cancer worries, ‡ score</td>
<td>7.0</td>
<td>1.9</td>
<td>7.9</td>
<td>2.2</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Women reporting a large decrease in anxiety about ovarian cancer after PBSO, %</td>
<td>82.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women reporting a large decrease in anxiety about breast cancer after PBSO, %</td>
<td>44.9</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perceived breast cancer risk before PBSO (0-100), score</td>
<td>58.6</td>
<td>29.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Currently perceived breast cancer risk (0-100), score</td>
<td>29.5</td>
<td>28.0</td>
<td>39.0</td>
<td>28.2</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Endocrine symptoms, § score</td>
<td>56.0</td>
<td>9.5</td>
<td>59.7</td>
<td>9.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sexually active women, † %</td>
<td>75</td>
<td>81</td>
<td></td>
<td></td>
<td>.11</td>
</tr>
<tr>
<td>Sexual functioning, † score</td>
<td>9.6</td>
<td>3.5</td>
<td>10.7</td>
<td>3.2</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Pleasure</td>
<td>4.4</td>
<td>1.7</td>
<td>5.1</td>
<td>1.4</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Discomfort</td>
<td>0.9</td>
<td>0.5</td>
<td>0.9</td>
<td>0.5</td>
<td>.73</td>
</tr>
<tr>
<td>Habit</td>
<td>0.9</td>
<td>0.5</td>
<td>0.9</td>
<td>0.5</td>
<td>.73</td>
</tr>
</tbody>
</table>

Abbreviations: QOL, quality of life; PBSO, prophylactic bilateral salpingo-oophorectomy; GS, gynecologic screening; SD, standard deviation; ANCOVA, analysis of covariance.

*Population norm scores were available only for the Short Form-36 scales (general health perceptions, vitality, mental health, and role–emotional). None of the comparisons between the general population scores and those of high-risk women (PBSO and GS groups) were statistically significant (all $P > .3$). All analyses were adjusted for age.

†Unadjusted means, $P$ values, and effect sizes for the main effect. PBSO versus GS in ANCOVA. All analyses were controlled for age, DNA status, parity, history of breast cancer, and prophylactic mastectomy. Effect sizes were calculated according to the following formula: Cohen’s $d = M_{PBSO} - M_{GS}/\sigma_{pooled}$, where $M_{PBSO} - M_{GS}$, $\sigma_{PBSO}^2$, and $\sigma_{GS}^2$ indicate, respectively, a difference in mean QOL scores and score variances of the PBSO and GS groups and where $\sigma_{pooled} = \sqrt{(\sigma_{PBSO}^2 + \sigma_{GS}^2)/2}$. Effect sizes are indicated only for $P < .05$.

‡ Higher scores correspond to better functioning or less symptoms.

§ Higher scores indicate more intrusive thoughts or worries.

¶ The Sexual Activity Questionnaire was administered to a smaller sample of women (PBSO, n = 248; GS, n = 265). Scores for sexual functioning apply only to women who reported that they had been sexually active in the last 4 weeks. Higher scores represent higher levels of sexual functioning.
"Satisfaction With Preventive Health Strategies"

Ninety-seven percent of women who had undergone PBSO reported being satisfied with the decision they had made compared with 82% of women in the GS group (P < .01). Regrets about the decision on the preventive health strategy were expressed by 5% of the PBSO group and 6% of the GS group (P > .05). Eighty-six percent of women would choose PBSO again, and 63% would recommend it to a friend with familial risk of ovarian cancer. In the GS group, 14%, 4%, and 15% of women intended to undergo PBSO within 5 years, within 10 years, and at some unspecified time in the future, respectively. Dissatisfaction with GS was not related significantly to the intention to undergo PBSO in the future.

To our knowledge, this is the largest cross-sectional, observational study to date that describes the psychosocial issues of ovarian cancer prevention in high-risk women. The results provide a comprehensive assessment of the generic and condition-specific QOL in 846 women who had opted either for PBSO or periodic GS.

All study participants reported high levels of generic QOL that were not significantly different from the QOL levels of women in the general Dutch population. Despite the fact that PBSO is an irreversible procedure with major consequences for the bodily hormonal balance, which, in turn, may affect the level of the patients’ general well-being, we found no adverse impact of PBSO on generic QOL. These results are consistent with earlier findings\textsuperscript{17,18} but in contrast with one study\textsuperscript{20} that suggested impairments in generic QOL as a result of PBSO. The discrepant results of the latter study may be a result of methodologic issues, such as a small sample size and the lack of statistical control for possible confounding medical factors.

Our results indicate that PBSO is associated with significantly lower levels of cancer worries compared with GS, with the fewest worries being expressed by women who had undergone both PBSO and PM. Additionally, 45% and 82% of women also indicated that PBSO had led to a large decline in anxiety about breast and ovarian cancer, respectively. As expected, the anxiety reduction was even larger for women who had undergone both prophylactic ovarian and breast surgery. Our findings are in line with other reports\textsuperscript{17-19,34} that have found a postsurgery reduction in cancer-specific distress but contrast with the results of Fry et al\textsuperscript{20} who found no beneficial effects of PBSO over GS on cancer worries. This discrepancy may be a result of the fact that Fry et al\textsuperscript{20} used a different measure of cancer worries\textsuperscript{36} than the measure used in our and other studies. Also, their sample was small, and it may not have been representative of the larger population of high-risk women. Their sample was recruited from a single center and, compared with our sample, included fewer women with a history of breast cancer (31%), more women who were premenopausal at PBSO (50%), and no women who had undergone PM.

In addition to the cancer worry scale, we also administered the intrusion subscale of the IES to assess cancer-specific distress. No significant differences were observed in the level of intrusive thoughts about breast and ovarian cancer between the PBSO and GS groups. The cancer worry scale can be viewed as a subclinical distress measure, whereas the intrusive thought subscale of the IES is intended to assess a more severe form of distress, capturing symptoms of PTSD. In our study sample, approximately 10% of all women exhibited symptoms suggesting the presence of PTSD, with breast and ovarian cancer risk as an underlying stressor. It is worth noting that, although PBSO reduces objective cancer risk, it does not eliminate high levels of cancer-specific distress in some women.

After controlling for possible confounders, a significant difference was observed in breast cancer risk perception, with the PBSO group scoring significantly lower than the GS group. A comparison between the pre- and postoperative (retrospective) assessments of perceived breast
cancer risk indicated a decrease, on average, of 29% after PBSO and 51% after both PBSO and PM. Our results suggest that high-risk women benefit both medically and psychologically from prophylactic surgery by the reduction of both their objective cancer risk and their perceived risk of developing cancer and that this benefit is the greatest among women who undergo both ovarian and breast surgeries.

As expected, PBSO was associated with more endocrine symptoms and worse sexual functioning than GS. The use of HRT had relatively limited impact on the level of menopausal and sexual symptoms in the PBSO group (detailed data on this issue will be reported in a separate article). Although the PBSO and GS groups included comparable numbers of sexually active women, prophylactic surgery was associated with more discomfort and less pleasure and satisfaction during sex. Post-surgery increase in levels of menopausal symptoms and declines in sexual functioning caused by estrogen deprivation symptoms (eg, vaginal dryness, dyspareunia, and vasomotor symptoms) have also been reported in other studies. However, no significant PBSO-GS differences in sexual functioning were detected in the study by Fry et al using the same measure of sexual functioning. This may be because of their smaller sample size and lower rates of sexually active women (66.1%) compared with our investigation.

Our findings suggest that the beneficial QOL effects of PBSO may outweigh the adverse effects because almost all women who had undergone PBSO reported being highly satisfied with the procedure. These findings are in line with previous studies. The vast majority of women in the PBSO group would undergo surgery again, whereas less than two thirds of women undergoing GS would choose screening again. Almost one third of women in the GS group expressed the intention to undergo PBSO in the future. These results suggest that high-risk women may perceive GS as only a temporary preventive health strategy.

Given its multicenter nature and the relatively high response rate, we believe that the study sample was representative of high-risk women in the Netherlands. However, some possible limitations of our study should be noted. First, we did not include measures of perceived anxiety reduction or a retrospective report of changes in self-perceived cancer risk in the GS group. Given the cross-sectional study design and the longitudinal nature of screening itself, there was no clear reference point in time for the GS group that would be comparable to that for women who had undergone PBSO. Data from our ongoing, longitudinal study will be able to inform this issue. Second, because of the cross-sectional design of the study, possible changes in QOL over time induced by prophylactic treatment or screening could not be assessed prospectively. A prospective, multicenter study is currently being conducted to obtain a more thorough picture of the QOL and symptom experience over time of high-risk women who opt for PBSO versus GS. Third, women who had undergone PBSO or GS may come from slightly different populations regarding their objective risk of developing ovarian cancer because more than half of the GS group did not have DNA testing. Although we controlled for known risk factors in our analyses, statistical adjustments for confounding factors may not have entirely ruled out possible selection bias resulting from nonrandomized comparison groups. However, given the known benefits of PBSO for ovarian cancer risk reduction and the unknown efficacy of the current GS techniques in early ovarian cancer detection, a randomized trial is not feasible and would not be ethical.

In conclusion, this study has documented both beneficial and adverse QOL effects associated with the two major health strategies for ovarian cancer in high-risk women. Physicians should discuss both the pros and cons of PBSO and GS with high-risk women seeking medical advice about their risk management. Among the benefits, reduced cancer worries after PBSO should be emphasized. The likely increase of climacteric and sexual symptoms, which may not be alleviated by the postsurgical use of HRT, should be included in discussions of adverse effects of PBSO. Balanced information will help clinicians and high-risk women to make informed decisions about the optimal preventive health strategy. Finally, our results indicate that a minority of oophorectomized women may experience high levels of distress after prophylactic treatment. Such women should be identified in a timely manner, and they should be offered (additional) psychosocial care after PBSO.

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Authors’ Disclosures of Potential Conflicts of Interest
The authors indicated no potential conflicts of interest.

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