Randomized Trial of a Shared Decision-Making Intervention Consisting of Trade-Offs and Individualized Treatment Information for BRCA1/2 Mutation Carriers


ABSTRACT

Purpose
To evaluate a shared decision-making intervention (SDMI) for BRCA1/2 mutation carriers who have to make a choice between screening and prophylactic surgery for breasts and/or ovaries.

Patients and Methods
The SDMI consisted of two value assessment sessions, using the time trade-off method, followed by individualized treatment information based on (quality-adjusted) life expectancy. After the baseline assessment (2 weeks after a positive DNA test result), women were randomly assigned to the SDMI group (n = 44), receiving the SDMI 2 months after the test result, or to the control group (n = 44). The short- and long-term effects, 3 and 9 months after the test result, were assessed using questionnaires. Data were collected on well-being, treatment choice, and decision-related outcomes.

Results
In the short term, the SDMI had no effect. In the long term, with respect to well-being, patients in the SDMI group had less intrusive thoughts (P = .05) and better general health (P = .01) and tended to be less depressed (P = .07). With respect to decision-related outcomes for the breasts, the SDMI group held stronger preferences (P = .02) and agreed more strongly to having weighed the pros and cons (P = .01). No effect was found on treatment choice. In the long term, interaction effects between the SDMI and cancer history were found. The SDMI showed an overall beneficial effect for unaffected women, whereas affected women tended to experience detrimental effects.

Conclusion
We conclude that the SDMI improved decision making in unaffected BRCA1/2 mutation carriers. Supporting decision making in a systematic way using trade-offs is beneficial for these women.

INTRODUCTION

The identification of the BRCA1 and BRCA2 genes has created the possibility to test for inherited susceptibility of breast and ovarian cancer.1-2 BRCA1/2 mutation carriers, unaffected with cancer, have a high lifetime risk of developing breast (56% to 85%) and ovarian cancer (16% to 63%).3-5 BRCA1/2 mutation carriers already affected with breast cancer have a high risk of developing a second breast cancer (up to 63%).6 In the Netherlands, options available to BRCA1/2 mutation carriers are intensive screening or prophylactic surgery, including prophylactic mastectomy and prophylactic oophorectomy. Screening of breasts and ovaries is associated with the risk of cancer that may be detected too late for effective treatment. Although prophylactic surgery gives a significant reduction in cancer risk and can also be successful in reducing cancer worries,7 it may cause adverse psychologic and social outcomes in some women.8 Thus BRCA1/2
mutation carriers are confronted with a difficult dilemma in which a trade-off between duration and quality of life plays a crucial role.

There is a movement toward greater patient involvement in treatment decisions, which is often referred to as shared decision making. Shared decision making recognizes that there are complex trade-offs in the treatment choice. Shared decision making also addresses the ethical need to fully inform patients about the risks and benefits of the treatment options, as well as the need to ensure that patients’ values play a prominent role. For medical decisions with more than one reasonable option, patient participation in decision making is necessary to make treatment decisions, taking patient values into account. The actual tools to help with shared decision making are called decision aids (DAs).

DAs can be used as an adjunct to standard counseling to prepare patients for decision making. According to the Cochrane definition, DAs are interventions designed to help people make a specific and deliberative choice among options by providing information about the options and outcomes, relevant to a person’s health status. A variety of formats can be used. The most common formats are brochures, audio- and videotapes, decision boards, and interactive computer programs. Some DAs include tasks to clarify individual values to promote better congruence between the individual values and the treatment choice; however, this is an understudied area. A systematic review of randomized trials has shown that DAs improve patient knowledge, comfort, and participation in decision making. It is not clear which type of DA is most powerful, although more comprehensive programs seem to have larger effects.

The goal of our study was to evaluate the use of DAs in women testing for a BRCA1/2 mutation. DAs may facilitate decision making for these women by helping them to arrive at an informed, preference-based treatment choice. We conducted a shared decision-making study that included two different interventions. In the first part of the study, we evaluated the effects of an informative DA and its timing before or after testing positive for a BRCA1/2 mutation. This DA consisted of a brochure and video providing information on screening and prophylactic surgery. In the second part of the study, reported here, we evaluated the effects of a shared decision-making intervention (SDMI) in BRCA1/2 mutation carriers on well-being, treatment choice, and decision-related outcomes. The SDMI consisted of two value assessment sessions, by use of the time trade-off (TTO) method followed by individualized treatment information based on life expectancy (LE) and quality-adjusted life expectancy (QALE) derived from decision analysis. Decision analysis offers a method to combine individual values regarding treatment outcomes with individual risk profiles. For the treatment choice for BRCA1/2 mutation carriers, individual values were shown to be important. Although such interventions have been described previously, they have mainly concentrated on the impact of patient preferences on treatment choice, whereas in our study we focus on a much broader range of outcomes.

**PATIENTS AND METHODS**

**Study Population**

The study was implemented in the Family Cancer Clinics of the University Hospitals of Nijmegen (beginning March 1999), Groningen (beginning June 1999), and Maastricht (beginning January 2000). Study entry closed in November 2001. Both women affected and unaffected with breast/ovarian cancer who had chosen to undergo DNA testing were eligible. Women were excluded if they were unable to give informed consent, had insufficient knowledge of the Dutch language, were diagnosed with distant metastases, had undergone both bilateral mastectomy and oophorectomy, or had been treated with chemotheraphy, radiotherapy, or surgery for breast/ovarian cancer less than 1 month before blood sampling. Women were ongoing in the study only when a deleterious BRCA1/2 mutation was found.

**SDMI**

The SDMI was provided by a trained research assistant and consisted of three sessions with an interval of 1 to 2 weeks. In the first session, individual values for the treatment options (screening and prophylactic surgery) were assessed in a face-to-face interview by use of the TTO method. In the second session, the TTO interview was repeated by telephone. The questions asked in the face-to-face and telephone interview were identical. In a previous study, in a comparable study sample, we judged the TTO method to be feasible, reliable, and valid and strongly predictive of treatment intentions. Many women commented that the trade-off task led to a thoughtful evaluation of the health outcomes and considered the trade-off to be relevant. The TTO interview is described in detail in the next paragraph. Decision analysis was used to arrive at individualized treatment information based on LE and QALE. QALE is calculated by multiplying the TTO value by the LE: TTO values were used as a weighing factor to adjust the remaining life years for the quality of life that will be experienced. In the third session, individualized treatment information was shared with the women using two bar charts, one for LE and one for QALE. The bar charts presented the treatment options relative to each other (see Appendix). Absolute LE and QALE information was not given because we also included women with cancer, who were not always fully aware of their prognosis. However, we did present the absolute gains and losses in LE and QALE of prophylactic surgery compared with screening. To avoid the derivation of prognosis, the bar charts were not to be taken home.

**TTO Interview**

The TTO interview started with an introduction, an example, and a flow-chart in which the women had to answer a series of questions. The value assessment started as follows: the health states following the treatment options were described in bullet-point format on laminated cards, and the women were asked to rank them in order of preference. Values for each health state were then elicited with a flow-chart using the TTO method. Women were asked to choose between two certain options. Option 1 is to continue living with prophylactic surgery for a fixed time t (such as the rest of life until age 80 years). Option 2 is to continue living with screening for a time x less than t. Using forced choices, we...
found how many years (x) in the health state screening was equivalent to a defined time (t) in the poorer health state prophylactic surgery. Time was used as the unit of comparison. By comparing the two times x and t, the value for each health state could be calculated. The TTO value for prophylactic surgery was calculated as \((x/t)\). For example, a respondent who was indifferent between living with prophylactic surgery for 40 more years and living with screening for 20 more years was assigned a TTO value of 0.5 \((20/40)\) for prophylactic surgery. We used the ping-pong technique to identify the indifference point. This involved alternating between long- and short-term time periods x for screening. To mitigate any ordering effects, the presentation of health states was randomly allocated before the interview.

**Study Procedure**

Data described here were collected during a longitudinal randomized study (T1 to T3) evaluating an informative DA and its timing (T1 to T3)\(^\text{11}\) and the SDMI (T3 to T5; Fig 1). The study was approved by the hospital ethics boards. Clinical geneticists or genetic counselors briefly introduced the study after a blood sample for \(BRCA1/2\) testing was obtained. A research assistant subsequently contacted these women by phone to confirm eligibility and to discuss the study. Women who gave verbal consent were enrolled and were mailed an informative letter describing the study and a consent form.

In the first part of the study (T1 to T3; Fig 1),\(^\text{11}\) not reported here, women were randomly assigned to the DA group (the DA

Fig 1. Study design: T1 to T3, first part of the study (not reported here); T3 to T5, second part of the study (reported here). X, usual care; DA, (informative) decision aid; SDMI, shared decision-making intervention.
was provided 2 weeks after blood sampling) or to the control group (receiving usual care). The DA was added to usual care and was to be viewed at home. It consisted of a brochure and video providing information on screening and prophylactic surgery, and the physical, emotional, and social consequences. At T2 (4 weeks after blood sampling), the DA group was compared with the control group. After testing positive, the control group too received the DA. At T3, 2 weeks after disclosure of a positive test result, we compared the impact of timing (before or after a positive test result) of the DA. The DA had positive effects on information-related outcomes only (subjective knowledge, satisfaction with information, and risk perception); timing of the DA had no effect.14 Women were ongoing in the study only if a deleterious BRCA1/2 mutation was found.

In the second part of the study (T3 to T5; Fig 1), described here, T3 formed the baseline assessment for the evaluation of the SDMI. After T3, women were randomly assigned to the SDMI group or to the control group (receiving usual care). The SDMI was added to usual care and was scheduled 2 months after the test result. This time point was chosen so that information from the consultations with the specialists from the Family Cancer Clinic could be weighed into the trade-offs. These consultations usually take place within 1 to 2 months after disclosure of a positive test result. At T4 and T5, 3 and 9 months after the test result, a follow-up questionnaire was sent to evaluate the short- and long-term effects of the SDMI.

Outcome Measures
All measures were obtained at baseline (T3) and at short (T4) and long-term follow-up (T5), unless indicated otherwise.

Well-Being
We collected data on anxiety (state anxiety subscale of the Spielberger State-Trait Anxiety Inventory),17 depression (Center for Epidemiologic Studies Depression Scale),18 and intrusive and avoidance thoughts about cancer in the family (intrusion and avoidance subscale from the Impact of Event Scale).19 Furthermore, women were asked to rate their general health during the last week on an 11-point scale (0, very bad; 10, excellent).

Treatment Choice
Women were asked to indicate their intended treatment choice for the breasts and/or ovaries. When women had no breasts or ovaries because of previous curative or prophylactic surgery, this question was not applicable. Intended treatment choice included prophylactic surgery, screening, and undecided. To test differences in intended treatment choice, it was dichotomized in prophylactic surgery versus the rest (screening and undecided). We have combined the treatment choice screening with undecided, because these women will receive the same clinical treatment, namely, screening. Also, the undecided group was too small: undecided choices decreased from 2% to 1% for the breasts, and from 5% to 0% for the ovaries for T3 and T5, respectively. Furthermore, women were asked to rate prophylactic surgery and screening on a 10-point rating scale (1, very bad; 10, excellent) in answering the question, “How suitable do you find prophylactic mastectomy for yourself?” Data on the actually performed treatment were also collected by questionnaire.

Decision-Related Outcomes
The decision-related outcomes were asked separately for the breasts and ovaries. When women had no breasts or ovaries because of previous curative or prophylactic surgery, these questions were not applicable.

Strength of treatment preference. Strength of treatment preference was asked for the treatment options prophylactic surgery and screening on a four-point Likert scale (1, weak preference; 4, very strong preference). Those who had chosen undecided as treatment choice were assigned a value of zero (no preference).

Decision uncertainty. Decision uncertainty was measured with three items related to the uncertainty subscale of the Decisional Conflict Scale by O’Connor.20 Our items were “I doubt what to choose,” “This decision is hard for me to make,” and “I am not sure what to choose,” measured on a five-point scale (1, strongly disagree; 5, strongly agree). A sum score was created by averaging the items.

Perceived participation in decision making. Perceived participation in decision making was measured with two decision-making items from the Problem-Solving Decision-Making Scale from Deber et al.14 The items were as follows: “Given the risks and benefits of the possible treatment options, who has decided how acceptable those risks and benefits are for you?” and “Who has decided which treatment option should be selected?” These were measured on a five-point scale (1, doctor alone; 3, doctor and I equally; 5, I alone). A sum score was created by averaging the items. This item had no baseline assessment.

Weighing treatment choice. Because trade-offs were prominent in the SDMI, we included a single item, “I weighed the pros and cons,” from a decision evaluation scale (Stalmeier et al, manuscript submitted for publication). It was measured on a five-point scale (1, strongly disagree; 5, strongly agree). This item had no baseline assessment.

Perceived preference of the specialists. Women were asked whether they felt that the specialists held a treatment preference (yes/no) and, if so, its strength (strong/weak). We combined the two answers in strong preference versus weak or no preference. These items were only asked at T4.

Support and advice from specialists. Women were asked whether they had wanted more support and advice from their specialists regarding their treatment choice on a seven-point scale (1, strongly disagree; 7, strongly agree). These items were only asked at T4.

Sample Size and Power
We assumed that the SDMI would have a larger effect on decision uncertainty than our informative DA.14 The SDMI is face-to-face and more intensive, and the sample consisted of BRCA1/2 mutation carriers who are actually facing the choice between screening and prophylactic surgery. To detect a difference of at least 25% in the decision uncertainty score between the two groups with a 5% two-sided significance level and a power of 80%, we needed a sample size of 45 women in each group.

Randomization and Blinding
Randomization of the SDMI took place by family (first-degree up to and including third-degree relatives) to avoid contamination. The randomization schedule, stratified by medical history of breast/ovarian cancer and by timing of the informative DA, was generated by computer in blocks of 10. Neither study participants nor members of the study staff were blinded to intervention assignment.

Statistics
Data were analyzed using the Statistical Package for the Social Sciences (SPSS 10.0.5; SPSS Inc, Chicago, IL). We analyzed data on an intention-to-treat basis. For missing items from multi-item scales, we imputed the mean of the remaining items when at least
half of the items were completed. To identify potential confounding variables, we compared the SDMI and control group on baseline characteristics using χ² tests for categoric variables and Student’s t tests for continuous variables.

To evaluate the effects of the SDMI, we compared the SDMI and control group on the outcome measures. For continuous measures, comparisons were done using analyses of covariance, including, when present, the baseline assessment as a covariate. Effect sizes were calculated as the adjusted mean of the SDMI group minus the adjusted mean of the control group divided by the SD of the difference score. When no baseline assessment was present, effect sizes were calculated from the unadjusted mean scores. For the two categoric variables of treatment choice and perceived preference of the specialists, comparisons were made using χ² tests. We used a P level of .05 to indicate statistical significance. The number of patients providing data for the various analyses varied because of missing data and because of nonapplicability of some questions.

Because randomization took place by family, and because family members were not independent on the outcome measures, statistical significance will be inflated when all women are treated as independent units. The sample contained nine families with multiple members (range, two to three members), with a total of 21 women. To counter inflation, we further examined significant effects by incorporating only the first included family member in the analyses.

Because previous findings showed that women affected with breast or ovarian cancer experienced worse well-being than unaffected women, we included cancer history in the primary analyses to examine the interaction effect between the SDMI and cancer history. Furthermore, we conducted separate analyses for women affected and unaffected with cancer to report the various effect sizes.

RESULTS

Participants

Figure 1 presents the study design for the whole study (T1 to T5). At study entrance, 453 women were eligible and 390 patients (86%) gave informed consent. Of the women followed up to the test result, 89 had a deleterious BRCA1/2 mutation (positive test result). Thus after the first part of the study (T1 to T3), 89 women were eligible for the second part of the study reported here (T3 to T5). One woman withdrew after T3 because of high emotional distress. Of the remaining 88 women, 44 women were randomly assigned to the SDMI group and 44 women to the control group. In the SDMI group, two women did not receive the SDMI, one unaffected woman because her mother just had died of breast cancer, and one affected woman because she had already undergone both bilateral mastectomy and oophorectomy. The follow-up at T4 was 100%. At T5, one woman from the control group was lost to follow-up.

Baseline Characteristics

No significant differences were found between the SDMI and control group (Table 1). The stratification for medical history and for the allocation of timing of the informative DA was successful.

Well-Being

In the short term (Table 2, T4), the SDMI had no effect on any of the well-being outcomes. In the long-term (Table 2, T5), the SDMI group had less intrusive thoughts about cancer in the family (F1,83 = 3.91; P = .05; effect size [d] = −0.30), a better general health (F1,79 = 6.53; P = .01; d = 0.40), and tended to be less depressed (F1,84 = 3.40; P = .07; d = −0.28). No effect was found on anxiety.

Treatment Choice

Intended treatment choice was only asked when applicable. At baseline (T3), short (T4), and long term (T5), no differences were found between the SDMI and control group, neither on the intended treatment choice nor on the actually performed treatment for breasts and ovaries (data not shown). No differences were found for the ratings of the treatment options (data not shown).

Overall, 33% (28 of 85 patients) intended to undergo prophylactic mastectomy at T3, of whom 50% (n = 14) had undergone this treatment at T5; none of the other women...
had undergone prophylactic mastectomy at T5. Overall, 68% (56 of 82 patients) intended to undergo prophylactic oophorectomy at T3, of whom 54% (n = 30) had undergone this treatment at T5; four of the other women had undergone prophylactic oophorectomy at T5.

**Decision-Related Outcomes**

With respect to the decision-related outcomes for the breasts, in the short term (Table 3, T4), no effects were found. In the long term (Table 3, T5), the SDMI group held a stronger treatment preference \((F_{1,68} = 6.11; P = .02; \text{d} = 0.41)\) and more strongly agreed to having weighed the pros and cons \((F_{1,69} = 6.45; P = .01; \text{d} = 0.42)\); no effects were found for the other decision-related outcomes. With respect to the decision-related outcomes for the ovaries, no effects were found, neither in the short nor in the long term (data not shown).

With respect to the behavior of the specialists, more women in the SDMI group (29%) felt that the specialists held a strong preference for one or the other breast treatments compared with the control group (3% \(\chi^2 = 10.47; P = .001\)). This difference was not found for the ovaries; 33% in the SDMI group, and 35% in the control group experienced a strong preference \((\chi^2 = 0.03; P = .87)\). Although not significant, women in the SDMI group wanted more support and advice from the specialists regarding their treatment choice for the breasts \((F_{1,78} = 2.94; P = .09; \text{d} = 0.27)\); this finding was less strong for the ovaries \((F_{1,74} = 2.22; P = .14; \text{d} = 0.24)\).

**Additional Analyses: Controlling for Family**

Significant differences found above were further tested by including only the first family member. Therefore, 12 persons were excluded from the analyses, seven from the SDMI group and five from the control group. Only the long-term effect on intrusion became insignificant \((F_{1,71} = 2.14; P = .15; \text{d} = 0.24)\).

**Interaction Effects Between SDMI and Cancer History**

In the short term, no interaction effects between the SDMI and cancer history were found for any of the well-
Decision Making for BRCA1/2 Mutation Carriers

We evaluated an SDMI for BRCA1/2 mutation carriers who were facing the choice between screening and prophylactic surgery for the breasts and/or ovaries. The SDMI consisted of trade-offs and individualized treatment information. To our knowledge, this is the first randomized study to evaluate such an intervention on a broad range of outcomes as a decision support tool. Previous studies, combining value assessment and decision analysis, have mainly concentrated on the impact of patient preferences on treatment choice.18–23 In the short term, 3 months after the test result, the SDMI had no effect. In the long term, 9 months after the test result, the SDMI group reported less intrusive thoughts about cancer in the family, better general health, and a trend toward less depressive thoughts. Moreover, they reported a stronger treatment preference and more strongly agreed to having weighed the pros and cons for the breast treatment. It is noteworthy that two previous studies on DAs also found stronger effects in the long term.34,35

Several types of DAs exist. The issue of what type of DA is most effective is still unresolved.9 Our randomized study shed some light on this issue. The informative DA had shown beneficial effects on information-related outcomes only,11 whereas the SDMI showed beneficial effects on a broader range of outcomes. In a previous uncontrolled before-after study of our group, we evaluated the informative DA and the SDMI as one package.36 Then we found beneficial effects on information-related outcomes as well as on more general outcomes, suggesting that the beneficial effects of the two interventions add up. Our current study design, with all participants receiving the initial informative DA before the randomization of the SDMI, precluded an evaluation of the interacting effects between the informative DA and the SDMI. This might be a subject for future research.

Nevertheless, from the present study, it is unclear which specific element of the SDMI is effective. One possible explanation is the additional attention paid by the research assistant. However, the time spent with the research assistant was relatively short when compared with the time spent with the specialists from the Family Cancer Clinic. Perhaps the provision of individualized treatment...
information is effective. However, as our informative DA had only beneficial effects on information-related outcomes and none whatsoever on well-being and decision-related outcomes,\textsuperscript{11} this seems unlikely. Another explanation, which needs to be followed up in future work, is that during decision support, negative emotions are expressed more strongly.\textsuperscript{37} This is known to enhance well-being over the long term.\textsuperscript{38}

On the basis of our own data, we hypothesize that the trade-offs are the effective component of the SDMI. These trade-offs explicitly required women to consider their values in the light of quality and length of life. The effect of the trade-offs is evident as women in the SDMI group more strongly agreed to having weighed the pros and cons, suggesting a more deliberated treatment choice. This might lead to stronger treatment preferences in women from the SDMI group, as indeed we found. Furthermore, as these women explored their own preferences, they might more easily discern their own preferences from the preferences of the specialists, as indeed we found. Our hypothesis is further supported by psychologic work showing that contrasting the future with reflections on present reality (the trade-offs have that effect) strengthens goal commitments, which may lead to improved well-being.\textsuperscript{39} If indeed the beneficial effects could be attributed to the trade-offs, decision making might be improved by actively exploring individual values for the treatment options in a systematic way using trade-offs.

Next to establishing the essential elements of a DA, there is also a need to identify the people who are most likely to benefit.\textsuperscript{33} In the long term, we found various interaction effects between the SDMI and cancer history. Subgroup analyses revealed that the SDMI had an overall beneficial effect for unaffected women and detrimental effects for affected women, although the SDMI was evaluated equally by affected and unaffected women (data not shown). Several explanations may apply. First, affected women may have received individualized treatment information that was discordant with their treatment intention more often. However, the opposite was found: treatment intentions and the best option based on QALE agreed in 70% of the affected women and in 44% of the unaffected women. Second, affected women (45 years) were older then unaffected women (37 years), and it may be that the SDMI is less effective in older women. However, in the unaffected sample, the beneficial effects of the SDMI were independent of age. Furthermore, affected and unaffected women did not differ at baseline (T3) on other potential explanatory variables such as risk perception and preference for decision making (data not shown). So it remains unclear why the SDMI is not effective in affected women. Previously, we found that affected women tended to react more strongly toward a positive DNA test result.\textsuperscript{33} Perhaps the additional confrontation with trade-offs is simply too taxing for affected women, in view of the burden of being at risk for a second cancer. Further studies are needed with larger sample sizes to confirm these effects.

In general, DAs are meant to supplement, not replace, the traditional process of patient counseling by clinicians. Can the present SDMI be implemented into a Family Cancer Clinic? The present study shows it is feasible to implement such an intervention in the clinic within a research context. Our study reveals that the SDMI is acceptable to women; further study is needed about the acceptability to counselors. However, the TTO interview is labor-intensive, requiring on average of 1 hour per patient when performed face-to-face and 30 minutes when repeated by telephone. The time needed to perform the decision analysis, including sensitivity analyses, depends on the cancer history. For affected women, the prognosis needs to be determined and included in the decision analysis, which may take some hours. For unaffected women, the decision analysis takes half an hour. Furthermore, performing TTO interviews, conducting individual decision analyses, and sharing treatment information requires well-trained personnel. Of course, the SDMI is not complete without using the informative DA.\textsuperscript{11} This information material and the decision model need to be kept up-to-date. Time pressure and costs of implementing decision aids are frequently cited as barriers for using decision aids.\textsuperscript{40} Despite these barriers, we believe that a simplified version of the SDMI, perhaps involving only the trade-offs, can be integrated into a consultation with a social worker or genetic counselor. This may not require much extra time per patient, as the trade-offs could be used as a basis for further deliberations.

It is acknowledged that some of the significant differences observed in this study could be due to chance, given the number of statistical tests. However, for unaffected women, all measures consistently pointed in a beneficial direction. Furthermore, the sample size is relatively small. Other limitations are that we know nothing about its cost effectiveness and how the counselors view the SDMI.

We conclude that the SDMI improved decision making in unaffected BRCA1/2 mutation carriers. Our advice is to support decision making in these women in a systematic way using trade-offs. The SDMI is not recommended for affected women. Future research should concentrate on how and for whom this intervention could be implemented profitably in the clinical practice of Family Cancer Clinics.

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Appendix

The appendix is included in the full-text version of this article, available online at www.jco.org. It is not included in the PDF (via Adobe® Acrobat Reader®) version.

Authors' Disclosures of Potential Conflicts of Interest

The authors indicated no potential conflicts of interest.

REFERENCES