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Psychosocial problems in cancer genetic counseling: Detecting and facilitating communication

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Chapter 1

General Introduction

INTRODUCTION

To date, more than 200 hereditary cancer syndromes have been identified,[1] most of them being rare.[2] The most frequently occurring hereditary cancer syndromes with an estimated population incidence of 1/400-500 are the Hereditary Breast and Ovarian Cancer (HBOC) syndrome and Lynch syndrome.[3, 4] HBOC is mainly caused by a mutation in either the *BRCA1* or *BRCA2* gene. These genes are estimated to account for 2-4% of all breast cancer diagnoses.[5] Lynch syndrome, a hereditary cancer syndrome of the colon, is estimated to account for 2-5% of all colon cancer diagnoses.[5] Although each cancer syndrome has its own specific criteria, in general, an individual is classified as being at higher risk of developing cancer if (s)he fulfills one or more of the following criteria: (1) a known DNA-mutation is found in blood-related relatives, (2) a high prevalence of cancer in the family, (3) a cancer diagnosis at a young age, and/or (4) a first-degree relative with a cancer diagnosis at a young age. Individuals who are at high risk of developing cancer can opt for genetic counseling and, where appropriate, DNA-testing.[2, 6] Not only (former) cancer patients, but also non-affected family members are eligible to undergo such counseling and DNA-testing.

Family Cancer Clinics

In the Netherlands, genetic counseling for cancer is provided at 9 family cancer clinics, 8 of which are associated with University Medical Centers and 1 with a specialized cancer hospital (i.e., Antoni van Leeuwenhoek). Genetic counseling and testing is provided by a multidisciplinary team including clinical geneticists, genetic counselors, molecular geneticists, social workers, and psychologists.[6, 7]

Genetic counseling

Resta and colleagues have defined genetic counseling as "the process of helping people understand and adapt to the medical, psychological and familial implications of genetic contributions to disease". They identify the following 3 primary elements of such counseling: (1) Interpretation of family and medical histories to assess the chance of disease occurrence or recurrence, (2) Education about inheritance, testing, management, prevention, resources and research, and (3) Counseling to promote informed choices and adaptation to the risk or condition.[8]

The current model of cancer genetic counseling is based on the counseling protocol of Huntington's disease, a neurodegenerative disease with a very high penetrance (i.e., a very high likelihood that an individual with a Huntington associated gene mutation will develop the disease during his or her lifetime).[9, 10] Changes to this protocol have been introduced for the cancer genetic counseling setting.[11, 12] Within this counseling model, an individual undergoing cancer genetic counseling (hereafter called "counselee") has a minimum of two sessions at the family cancer clinic with a clinical geneticist or genetic counselor (hereafter called "counselor"). Before the first session with the counselor, the counselee is asked to provide details about his/her personal and familial cancer history

by completing a family history questionnaire. Based on this information, the counselor draws a pedigree of the family including its cancer history. This is used during the first face-to-face counseling session at which time the personal and familial history of cancer is discussed.[13, 14]

During the first counseling session, in addition to assessing the personal and familial cancer history, it is recommended that the counselor also performs a psychosocial assessment. This assessment may include the timing and readiness of the counselee to proceed with genetic testing, the anticipated psychosocial reactions to the possible test result, issues regarding the family, and preparing the counselee for how the results will be provided. If indicated, a counselee may be referred to a mental health professional or support groups.[13, 14] If there is an indication for a possible gene mutation and the counselee agrees, a blood sample is taken and a DNA-test is performed. Most counselees eligible for DNA-testing agree to do so. In some cases, the decision is postponed or it is determined that a family member needs to be tested first.[11, 12]

In the second and final counseling session, if applicable, the DNA-test results are disclosed and medical advice is given based upon those results and the personal and familial cancer history of the counselee. Four outcomes of the DNA-test are possible. First, a pathogenic mutation can be found, which means that a counselee has a substantially higher risk of developing cancer due to the mutation. Second, a pathogenic mutation that is already known in the family is not found, which means that the counselee has the same risk of developing cancer as someone from the general population. Third, an unclassified variant (UV) might be identified. These variants are ordered in five categories with a range from 1 (very likely not to be pathogenic) to 5 (very likely to be pathogenic).[15, 16] Fourth, the counselee might receive an inconclusive result, which means that no pathogenic mutation has been found in this family. However, because of the family cancer history, the counselee is still at increased risk of developing cancer.[13]

In case of a mutation positive result, or an UV category 4 or 5, the counselee will be recommended to follow a surveillance program, and if applicable (based on the cancer syndrome for which the testing was performed), the option of prophylactic surgery might be discussed. In case of an uninformative test result, or an UV category 1-3, screening advice will be given based solely on the family cancer history and epidemiological tables that provide risk estimates for that counselee. Non-mutation carriers will be given the advice to follow the same screening procedures as the general population, if available.[6,16,17]

After the final counseling session, all counselees receive a letter summarizing the genetic counseling process, the medical advice and, where applicable, the DNA-test results.[12]

Psychological consequences

In general, cancer genetic counseling has not been found to have an adverse psychological effect on counselees. An updated Cochrane review of the psychological impact of cancer genetic counseling for breast cancer, including eight trials, concluded that cancer genetic

risk-assessment helps to reduce psychological distress.[18] Other reviews, including many prospective and retrospective studies, indicate that approximately one-quarter of counselees experience relatively high levels of anxiety, depression, or distress during the process of genetic counseling, or (years) after DNA-test disclosure.[19-30] Based on the questionnaire used, and the chosen time-point of measurement, a minority of counselees thus experiences high levels of distress during or after genetic counseling and testing.

However, measures used to assess distress do not cover the specific psychosocial problems of individuals undergoing cancer genetic counseling.[30-32] A much higher percentage of counselees report experiencing a range of psychosocial problems. Specifically, the literature indicates that up to three-quarters of counselees experience moderate to severe psychosocial problems during genetic counseling.[33, 34] In families with the hereditary syndromes of Von Hippel-Lindau disease, and Familial Adenomatous Polyposis, one-third reported an unmet need of psychosocial services.[35, 36] In a sample of HBOC women, 27% requested psychological help during genetic counseling, and 16% requested this 3 months after the final counseling session.[31]

Communication in cancer genetic counseling sessions

During the cancer genetic counseling sessions, counselors primarily make use of a 'teaching' style.[37, 38] That is, the counseling is often 'provider-driven' and communication tends to be unidirectional (from the counselor to the counselee). The focus is typically on the pedigree of the counselee, and on providing information about genetics and genetic testing. It has been proposed that a 'psychosocial' style of counseling, in which more effort is made to understand the psychosocial meaning and consequences of risk assessment and counseling, can better serve the counselees' needs.[37, 38] Such a psychosocial counseling style has been demonstrated to reduce levels of depression.[39-41] In contrast, one study reported a significant association between receiving more psychosocial information, having more eye contact between counselor and counselee, and higher anxiety scores.[42]

Patient-reported Outcomes (PROs)

Patient-reported outcomes, such as questionnaires on quality of life or on general distress, are traditionally used in research settings.[43] Recently, there has been increasing interest in using PROs in clinical practice to aid in the management of individuals.[44] The systematic use of PROs can facilitate detecting and discussing health-related issues in clinical oncology practice.[45, 46] Enhancing the discussion of such health-related issues can lead to a multitude of positive effects, including improved patient – provider communication, a higher level of trust, increased clinicians' awareness of their patients' problems, and improved problem management.[47] A few studies have also found that the routine use of PRO's in clinical practice can improve quality of life or lead to lower levels of distress.[48-50]

AIM OF THIS THESIS

The overall aim of the two studies, described in this thesis, was to investigate the prevalence of psychosocial problems in the cancer genetic counseling setting, to develop and test methods for identifying such problems in a valid, reliable and practical manner, and to develop and test interventions to incorporate such assessments as a routine part of the counseling process. More specifically, the primary research objectives addressed in these studies were:

1. To identify and estimate the prevalence of specific psychosocial problems experienced by individuals who undergo cancer genetic counseling and their perceived need for additional psychosocial services.
2. To develop and test the screening properties of a questionnaire designed specifically to assess the psychosocial problems of counselees.
3. To investigate the efficacy of routinely administering the psychosocial screening questionnaire in daily clinical cancer genetic practice in terms of communication, awareness, problem management, and alleviation of psychosocial problems and worries.
4. To investigate the efficacy of a follow-up telephone session one month after the final counseling in combination with administering the psychosocial screening questionnaire on communication, awareness, problem management, alleviation of psychosocial problems and worries, and acceptability of the telephone session.

Design

Two studies are reported in this thesis. The first study comprised the development and testing of a questionnaire to assess and screen for psychosocial problems experienced by individuals undergoing cancer genetic counseling. The second study comprised a randomized controlled trial, in which we studied the efficacy of the routine use of the questionnaire in clinical practice.

Development and testing

The specific questionnaire was developed according to the Guidelines on Questionnaire Module Development of the Quality of Life Group of the European Organisation for Research and Treatment of Cancer (EORTC). After developing the questionnaire, the Psychosocial Aspects of Hereditary Cancer (PAHC) questionnaire, it was tested for its screening properties. To do so, we invited counselees to both complete the questionnaire and an interview with a trained social worker. Additionally we asked participants to complete both the Distress Thermometer (DT), and the Hospital Anxiety and Depression Scale (HADS) to validate the DT for use within this population. This procedure was performed at two time-points within the genetic counseling process: at the time of the first genetic counseling session, and four weeks after the final counseling session.

Randomized controlled trial

The efficacy of the routine use of the PAHC questionnaire in clinical practice was studied in a randomized controlled trial. This trial consisted of two phases: (1) at the time of the first genetic counseling session, and (2) four weeks after the final counseling session, at which time we also introduced an additional, telephone follow-up by the genetic counselor. Within the first phase of the trial, all participants were asked to complete the PAHC questionnaire prior to their planned counseling session. The questionnaire results were summarized (i.e., indicating the areas in which the counselee was experiencing psychosocial problems) and provided to the counselors of those counselees who were randomized to the intervention group only. Four weeks after the initial counseling session, but prior to their final session, the participants were asked to complete a follow-up questionnaire.

In the second phase of the study, participants, who underwent a DNA-test and had a final counseling session within the time frame of the study were asked to complete the PAHC questionnaire prior to the follow-up telephone session. This telephone session was added to the procedure of genetic counseling, four weeks after the final counseling session. Again, the PAHC questionnaire results were only provided to the counselors for those counselees in the intervention group. Four months after the telephone session, a final evaluation questionnaire was administered by mail.

RELEVANCE

The studies reported in this thesis provide an evidence-base for the use of a problem-focused screening instrument in facilitating and optimizing the quality of cancer genetic counseling. These studies also provide insights into the nature and prevalence of a broad spectrum of psychosocial problems experienced by individuals undergoing cancer genetic counseling. These prevalence estimates, combined with information on the perceived need for specialized psychosocial services both during and after the cancer genetic counseling process, can be used to plan clinical and psychosocial care services for this population. In a broader context, these studies can contribute to the larger evidence base on the value of patient-reported outcomes in daily clinical practice in terms of processes of care and health outcomes.

OUTLINE OF THIS THESIS

In **Chapter 2** a review is presented of qualitative studies on specific psychosocial problems as experienced by individuals undergoing counseling for hereditary cancer. In **Chapter 3** the development and testing of the screening properties of the PAHC questionnaire is described, as well as the validity of the DT when used in the cancer genetic counseling setting. In **Chapter 4** the prevalence of specific problems during counseling is investigated, and the association between these problems, and sociodemographic and clinical variables, and generalized psychological distress is reported.

In **Chapter 5** the design of the randomized controlled trial is described. The results of the first phase and the second phase of this trial are reported in **Chapter 6 and 7,** respectively.

In **Chapter 8** the findings of the study are summarized. These findings are discussed, recommendations for clinical practice are provided , and overall conclusions are drawn.

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Chapter 2

Specific psychosocial issues of individuals undergoing genetic counseling for cancer – A literature review

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ABSTRACT

Approximately 25% of individuals undergoing genetic counseling for cancer experiences clinically relevant levels of distress, anxiety and/or depression. However, these general psychological outcomes that are used in many studies do not provide detailed information on the specific psychosocial problems experienced by counselees. The aim of this review was to investigate the specific psychosocial issues encountered by individuals undergoing genetic counseling for cancer, and to identify overarching themes across these issues. A literature search was performed, using four electronic databases (PubMed, PsychInfo, CINAHL and Embase). Papers published between January 2000 and January 2013 were selected using combinations, and related indexing terms of the keywords: 'genetic counseling', 'psychology' and 'cancer'. In total, 25 articles met our inclusion criteria. We identified the specific issues addressed by these papers, and used meta-ethnography to identify the following six overarching themes: coping with cancer risk, practical issues, family issues, children-related issues, living with cancer, and emotions. A large overlap in the specific issues and themes was found between these studies, suggesting that research on specific psychosocial problems within genetic counseling has reached a point of saturation. As a next step, efforts should be made to detect and monitor these problems of counselees at an early stage within the genetic counseling process.

INTRODUCTION

Individuals from families with a known hereditary cancer syndrome and individuals with familial occurrence of cancer may carry a germline mutation. Over 50 hereditary cancer syndromes, such as Hereditary Breast and Ovarian Cancer (HBOC), Lynch syndrome, and Familial Adenomatous Polyposis (FAP) have been identified.[1] Individuals who carry a germline mutation or one of these cancer syndromes have a significantly higher risk of developing cancer compared to the general population. Proven carriers or individuals at high risk of carrying a mutation may benefit from screening options and possible other treatment options if the individual has a cancer diagnosis. For example, *BRCA1/2* carriers are recommended to undergo screening more frequently and at an earlier age, and can opt for prophylactic mastectomy and/or salpingo-oophorectomy to decrease their risk of developing these cancers.[1, 2]

High-risk individuals may choose to undergo cancer genetic counseling, with or without DNA testing. Genetic counseling is defined as: "the process of helping people understand and adapt to the medical, psychological and familial implications of genetic contributions to disease".[3] The National Society of Genetic Counselors (NSGC) guidelines state that within cancer genetic counseling, the personal medical history is evaluated, a pedigree of the family history is created, the cancer risk of the counselee is assessed, and the psychosocial aspects of the counselee are assessed.[4, 5] In order to be aware of the psychosocial aspects and correctly identify these in clinical practice it is essential to know the nature and content of the specific problems as experienced by the counselees.

Previous reviews reported on the psychosocial impact of genetic counseling and testing for HBOC,[6-8] Lynch syndrome,[9] FAP,[10] and "hereditary cancer syndromes" in general.[11,12] More recent reviews have focussed on specific subgroups within known cancer syndromes, such as women recently diagnosed with breast cancer,[13, 14] recently diagnosed colorectal patients,[15] and men from HBOC families.[16] A meta-analysis of studies of cancer-specific distress among individuals counseled for HBOC has also been conducted.[17] These reviews and the meta-analysis indicate that the majority of counselees do not exhibit heightened or clinically relevant levels of depression, anxiety and/or distress as assessed by standardized questionnaires with established score thresholds for clinical relevance. However, dependent on the type and timing of the assessment, approximately 25% of counselees do experience clinically relevant levels of distress.

Known risk factors for increased psychosocial distress among individuals undergoing cancer genetic counseling include low social support,[18-21] young age,[20, 22] previous cancer diagnosis,[23-25] experience of cancer in close relatives,[26] (avoidant) coping style,[20, 21, 27] and low self-efficacy.[27]

Distress, anxiety and/or depression and their known risk factors are often measured with generic questionnaires, such as the Hospital Anxiety and Depression scale (HADS),

the State Trait Anxiety Inventory (STAI), the Impact of Event Scale (IES), and the Center for Epidemiological Studies Depression Scale (CES-D).[28-30] These generic measures, used in quantitative studies, may be too general to identify the specific psychosocial problems experienced by high-risk individuals.[31] The available reviews do not provide detailed information on the nature of such problems. Additionally, these more general psychological problems may be more difficult to address within the genetic counseling sessions, as compared to more specific, genetic-relevant psychosocial problems. This suggests the need for a review of the qualitative studies that have investigated the specific psychosocial issues experienced by counselees within the cancer genetic counseling setting. Identification of the most prevalent of these issues can facilitate their being addressed during genetic counseling. To our knowledge, such a comprehensive review has not yet been performed.

Numerous approaches to conduct such a review have been developed to synthesize data from qualitative articles, such as textual narrative synthesis, meta-study, thematic analysis, grounded theory, meta-ethnography, meta-study, realist synthesis, and content analysis.[32-36] To perform our review we choose the approach of meta-ethnograpy. This approach was proposed by Noblit and Hare in 1988, to be an alternative for meta-analysis.[37] The aim of conducting such a review is to combine and translate concepts of qualitative studies to be able to give a meaningful interpretation. To do so, key metaphors, identified themes, or concepts of the identified articles are collected and translated into each other by means of seven predescribed steps; (1) getting started: identify a research question; (2) decide what is relevant to the initial area of interest: conduct an extensive literature search; (3) read the studies; (4) determine how the studies are related: collect key metaphors and concepts; (5) translate the studies into one another: compare the metaphors and concepts between studies which results in one set of unique translated metaphors and concepts; (6) synthesize translations: relate the translated metaphors and concepts to each other. At this step it is possible to create a higher order synthesis, resulting in a new interpretation; and (7) express the synthesis.[37, 38] This method is widely used, and has proven to be effective in synthesizing qualitative research.[34, 35, 39]

The aim of the current study was to provide an overview of studies that have investigated specific psychosocial issues experienced by individuals undergoing genetic counseling for cancer, to extract the specific psychosocial issues, and to synthesize overarching themes that contain the most important problems encountered by individuals undergoing cancer genetic counseling.

METHODS

This research comprised two phases. First, we performed a systematic literature search to provide a comprehensive overview of the studies. Subsequently, we performed a meta-analysis of the selected articles following the 7-step model of meta-ethnography.

The first three steps of this model (i.e., getting started, deciding what is relevant to the initial interest, and reading the studies) were accomplished by carrying out the systematic literature search. We then carried out steps four to six (i.e., determining how the studies are related, translating the studies into one another, and synthesising translations) by extracting the specific problems out of the identified papers, translating the specific problems into each other, and subsequently defining overarching themes. We observed several patterns of associations across studies. This paper represents the final, 7th step (i.e., expressing the synthesis).

Systematic literature search (step 1 -3)

Four electronic databases (PubMed, PsychInfo, CINAHL and Embase) were used to carry out a systematic literature search using the following MeSH terms, major headings, keywords and combinations of these, grouped as follows: "genetic counseling" AND "psychology" AND "cancer". If available in the databases, subject-related terms of the keywords were used in the search term. Included in the review were English and Dutch-language articles published between January, 2000 and May, 2011 (update January, 2013), in peer-reviewed journals that reported on the specific psychosocial problems of counselees that have, or have had genetic counseling and/or testing within the cancer genetic setting. We included qualitative articles that focused on the specific psychosocial issues as experienced by counselees in the cancer genetic setting. We excluded articles that focused on generic measures of depression, anxiety and/or distress only, on risk factors for distress, on cancer risk perception, and on a single specific topic (e.g., only on family communication) within genetic counseling.

The selection process was performed in four phases (see Figure 1) by the first author (WE). First, all papers were reviewed on the basis of the title and the abstract. When in doubt, the article was selected for the next phase. Duplicates were deleted. Second, the first author reviewed the remaining full text articles. Third, the reference lists of selected articles were checked for additional, relevant studies. Finally, as a confirmatory exercise, the first author carried out a second search in PubMed using the MeSH terms of the articles selected in the first three phases. This last search, performed in January 2013, also served as an update of the literature overview. The final search strategy included the following MeSH terms, which were categorised in 5 groups: (1) genetic counseling OR genetic testing OR genetic predisposition to disease AND (2) breast neoplasms OR ovarian neoplasms OR neoplastic syndromes, hereditary AND (3) psychology OR psychology (Subheading) OR adaptation psychological OR emotions AND (4) English (Language) OR Dutch (Language) AND (5) Between January 2000 and January 2013 (Date of publication).

Data extraction and meta-ethnographic analysis (step 4-6)

The specific issues of all included papers were summarized in a table by the first author. Subsequently we (WE and EB) extracted the themes and concepts as used by the authors of the papers to translate them into each other to provide overarching themes, in line with the fourth to sixth step of the meta-ethnographic approach. We selected the oldest article of the review, that of Appleton et al.[40] and we then reviewed the papers in

chronological order.[38,41] Each subsequent paper was discussed separately, systematically translating the identified problems into each other following the principles of 'reciprocal translation'.[37] We compared the problems of the first paper with those of the second, and the synthesis of these papers with the third paper, and so on. Together with this process, we synthesized the translated problems until we (WE and EB) reached a saturation point where all identified problems could be placed within a given second-order theme. This point was reached after discussion of eight papers, and all themes were identified. After we reached the saturation point, the first author continued the process of translating the identified problems into each other, placed these translations of specific issues under the identified second-order themes, and constructed a final grid overview. Possible new specific issues found in other articles which were not yet identified in the first eight papers were discussed (WE and EB) and placed within a second-order theme after reaching agreement. Additionally, we observed patterns of association between the identified specific problems, the study characteristics and the medical characteristics.

RESULTS

Systematic literature search (step 1-3)

Identification of relevant studies

As shown in Figure 1, we identified a total of 1.144 papers in the first phase. After deleting duplicates, we excluded the large majority of papers because they did not focus on the *content* of the specific issues experienced by counselees. For example, these were studies on the impact of cancer screening, the recall of cancer risks, communication preferences, or that used general measures of depression, anxiety and/or depression. In total, we selected 68 papers based on a review of titles and abstracts. If in doubt, we included papers to be included for the second phase. Of these 68 papers, we excluded 52, primarily because general measures of depression, anxiety or distress were used as an outcome, the studies were focused on a single aspect of genetic counseling (e.g., barriers to participate in counseling, family communication, or fertility issues), and/or the study population included high-risk individuals who had not (yet) received genetic counseling. Checking the reference lists of the remaining (n=16) selected articles resulted in two additional papers. In January 2013, we conducted an additional PubMed search that differed slightly from the first search, also including MeSH terms abstracted from the previously included articles. This was done to double-check the first search strategy employed in May 2011, and to perform an update of the literature search (May 2011-January 2013). This yielded another seven relevant articles. In total, the search resulted in 25 papers that met our inclusion criteria (see Figure 1). One study was described in two papers.[42, 43]

Characteristics of the studies

All included articles were published in English-language peer-reviewed journals, and focused on psychosocial problems within the context of HBOC (n=19) (see Table 1), or Lynch/FAP/mixed tumor syndrome groups (n=6) (see Table 2). Because most studies

focused on HBOC, the majority included women only (n=13), while two papers focused exclusively on men. Eight studies included both males and females, and two studies did not specify the gender of the population. As shown in Table 1 and Table 2, the countries contributing to the majority of the articles were the USA (n=6), the United Kingdom (n=5), Canada (n=3), and Australia (n=3). The other studies were carried out in New Zealand (n=1) and different European countries (n=7).

Most studies (n=20) used interviews [in depth-, or (semi-) structured], while four studies employed focus groups. Two studies were part of a larger, questionnaire-based investigation. All studies included relatively small samples (varying from 6 to 47 participants).

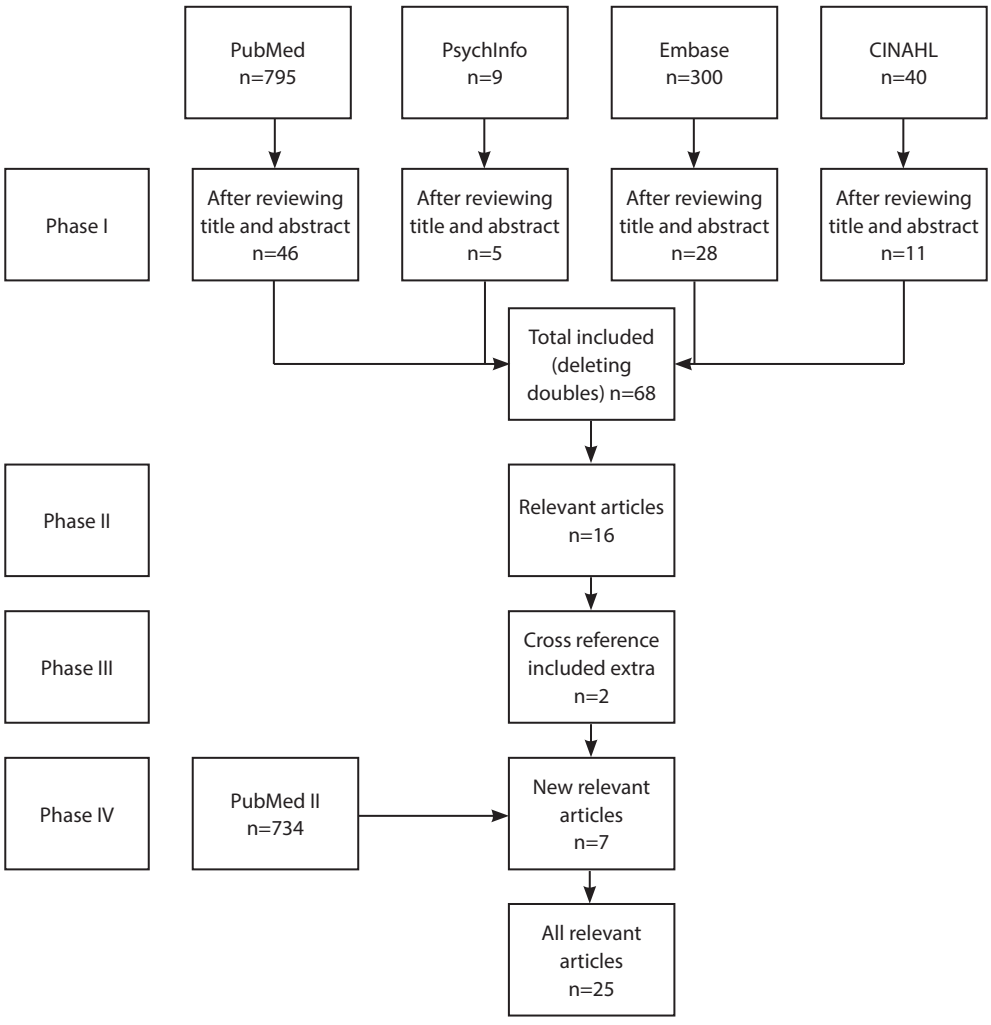

Figure 1. Selection process

Table 1. Review of studies investigating psychosocial issues experienced in HBOC families

First author, year, country	n (male)	Age mean [range]	Period before/ after testing (in years)*	DNA-test result [a]	Having had cancer	Research aim	Measurement	Extracted themes [b]
d'Agincourt-Canning (2006) Canada	39 (5)	? [early 20's – over 60]	After testing (?)	28 + 11 - 0 ±	14 yes 25 no	Does genetic testing change the way people think about themselves or relate to others?	Interviews	Carriers: a) Coping with cancer risk d) Children related problems e) Living with cancer Non-carriers: c) Family and social problems f) Emotions
Appleton (2000) United Kingdom	25 (0)	41.3 [27-51]	After testing (2,5 – 6,5)	0 + 0 - 25 ±	0 yes 25 no	To explore the long-term consequences of being informed about an increased risk of breast cancer in terms of: the effect on daily life, the coping strategies and the unmet needs in terms of current service.	Telephone focus groups	a) Coping with cancer risk c) Family and social problems d) Children related problems e) Living with cancer f) Emotions
Bakos (2008) USA	13 (0)	49 [43-57]	After testing (?)	0 + 13 - 0 ±	0 yes 13 no	Explore the experience of risk among *BRCA1/2* mutation-negative women from HBOC families.	(telephone) Interviews	a) Coping with cancer risk c) Family and social problems e) Living with cancer f) Emotions
Bennett (2010) United Kingdom	30 (0)	48.1 [?]	After testing (6)	0 + 0 - 30 ±	? yes ? no	Exploring factors associated with high levels of cancer worry and the utilization of services	Interviews	a) Coping with cancer risk e) Living with cancer f) Emotions
Crump (2010) New Zealand	6 (0)	43.7 [28-52]	? 2 not tested	3 + ? - 1 ±	1 yes 5 no	Explore how women lived with the knowledge of being from HBOC family	(2x) Interviews	a) Coping with cancer risk c) Family and social problems f) Emotions

Table 1. *(continued)*

First author, year, country	n (male)	Age mean [range]	Period before/ after testing (in years)*	DNA-test result [a]	Having had cancer	Research aim	Measurement	Extracted themes [b]
Di Prospero (2001) Canada	8 (1)	51.3 [23-71]	After testing (?)	9 + 0 - 0 ±	6 yes 2 no	Obtain feed-back about how genetic testing had affected people with mutation positive result	Interviews # whole study includes questionnaires	d) Children related problems e) Living with cancer Not telling family: c) Family and social problems d) Children related problems
Frost (2004) USA	15 (0)	? [?]	After testing (?)	4 + 5 - 6 ±	8 yes 7 no	How do women at high risk for developing breast cancer deal with uncertain clinical information?	Focus groups + interviews	a) Coping with cancer risk c) Family and social problems
Hallowell (2004) United Kingdom	30 (0)	? [39-71]	After testing (2 months – 4 years)	10 + 12 ± 8 awaiting result	30 yes 0 no	Explore women's perceptions and experiences of genetic testing and to establish their information and support needs both before and after they received a result	Interviews	a) Coping with cancer risk c) Family and social problems e) Living with cancer f) Emotions
Hallowell (2006) United Kingdom	17 (17)	Median 55 [39-75]	After testing (3/4 – 6)	5 + 12 - 0 ±	? yes ? no	Explore the impact of predictive *BRCA1/2* testing on men	Interviews	c) Family and social problems d) Children related problems Non-carriers: c) Family and social problems f) Emotions Carriers: a) Coping with cancer risk d) Children related problems
Hamilton (2009) USA	7 (0)	? [25-51]	After testing (>4)	7 + 0 - 0 ±	0 yes 7 no	Explore the range of understandings and a ssociated actions, related to conditions and past experiences	Interviews (2x)	a) Coping with cancer risk c) Family and social problems d) Children related problems

Table 1. *(continued)*

First author, year, country	n (male)	Age mean [range]	Period before/ after testing (in years)*	DNA-test result [a]	Having had cancer	Research aim	Measurement	Extracted themes [b]
Hamilton (2010) USA	11 (0)	? [18-35]	After testing (1 month – 3 years)	11 + 0 - 0 ±	4 yes 7 no	To explore the experiences of young/ single women who are increased risk for HBOC because of a BRCA mutation	Interviews	a) Coping with cancer risk c) Family and social problems e) Living with cancer
Kenen (2003) United Kingdom	21 (0)	? [24-61]	Before test	n/a	n/a	How can healthy women from HBOC families live with their heightened awareness of their risk?	Interviews	a) Coping with cancer risk c) Family and social problems d) Children related problems e) Living with cancer
Lim (2004) Australia	47 (0)	? [24 -76]	After test (1 month – 5 year)	23 + 24 - 0 ±	0 yes 47 no	Discover the emotional and social impact of receiving results of genetic testing for HBOC	Interviews	a) Coping with cancer risk c) Family and social problems f) Emotions
Lodder (2001) The Netherlands	14 (14)	47 [29-67]# # whole study sample	After test (2 weeks)	4 + 10 - 0 ±	? yes ? no	In-depth perspective of the male's experience and feelings	Interviews # whole study includes questionnaires	Mutation carriers a) Coping with cancer risk d) Children related problems Non-mutation carriers e) Living with cancer f) Emotions
MacDonald (2010) USA	22 (0)	56.3 [43-71]	11 only counseling/ 11 after (7-45 months)	3 + 8 - 0 ±	18 yes 4 no	To explore the personal and family impact of genetic cancer risk assessment	Focus groups	a) Coping with cancer risk b) Practical problems c) Family and social problems d) Children related problems e) Living with cancer
Maheu (2009) Canada	20 (0)	? [41-70]	After testing (?)	0 + 0 - 20 ±	20 yes 0 no	Explore women's experiences of living with both a breast cancer diagnosis and a strong family history of breast cancer	Semi structured interview	a) Coping with cancer risk c) Family and social problems e) Living with cancer

Table 1. *(continued)*

First author, year, country	n (male)	Age mean [range]	Period before/ after testing (in years)[a]	DNA-test result *	Having had cancer	Research aim	Measurement	Extracted themes [b]
Strømsvik (2010) Norway	15 (15) 7 partners	? [26 – 73]	After testing (2 – 8)	15 + 0 - 0 ±	1 yes 14 no	To explore male experience of genetic counseling/testing, being identified as carriers, current partners experiences and family communication/ dynamics	(2x) Interviews	a) Coping with cancer risk c) Family and social problems d) Children related problems f) Emotions
Strømsvik (2011) Norway	15 (15) 7 partners	? [26 – 73]	After testing (2 – 8)	15 + 0 - 0 ±	1 yes 14 no	To gain a deeper understanding of male *BRCA1/2* muation carriers' experiences	(2x) Interviews	c) Family and social problems d) Children related problems e) Living with cancer
Vadaparampil (2008) USA	9 (0)	43 [n/a]	?	? + ? - ? ±	9 yes 0 no	Better understand the experiences of recently diagnosed breast cancer patients attending genetic counseling	Interviews	a) Coping with cancer risk b) Practical problems c) Family and social problems

[a] + mutation positive result, - mutation negative result, ± inconclusive result

[b] a) Coping with cancer risk, b) Practical problems, c) Family and social problems, d) Children related problems, e) Living with cancer, f) Emotions

?=not reported value, n/a=not applicable

Table 2. Review of studies investigating psychosocial issues experienced in Lynch/FAP/mixed syndrome group

First author, year, country	n (male)	Age mean [range]	Type	Period before/after testing (in years)	DNA-test result [a]	Having had cancer	Research aim	Measurement	Extracted themes [b]
Bonadona (2002) France	23 (6)	Median 47 [27-72]	Lynch + HBOC	After testing (?)	23 + 0 - 0 ±	23 yes 0 no	Evaluate the consequences of the disclosure of a positive genetic test result to patients affected with cancer	Semistructured interview (open and close questions)	a) Coping with cancer risk b) Practical problems c) Family and social problems d) Children related problems e) Living with cancer f) Emotions
Carlsson (2007) Sweden	19 (9)	Carriers 51 [33-75] Non-carriers 47 [36-64]	Lynch	After testing (1-2)	11 + 8 - 0 ±	? yes ? no	Explore experiences from and perceived impact on life after genetic testing for Lynch syndrome	Interveiws	a) Coping with cancer risk c) Family and social problems
Duncan (2008) Australia	18 (8)	21.8 [14-26]	FAP (10) + HD (8)	After testing (4.8, mean)	7 + 11 - 0 ±	n/a yes n/a no	Broaden the view of potential effects associated with predictive genetic tests in young people	Interviews	a) Coping with cancer risk b) Practical problems c) Family and social problems f) Emotions
Landsbergen (2009) The Netherlands	n/a	n/a	Lynch	?	? + ? - ? ±	8 yes 0 no	Explore the reactions of colorectal cancer patients with a MSI positive tumor, being offered genetic testing	Interviews	Impact of colorectal cancer: a) Coping with cancer risk b) Practical problems c) Family and social problems e) Living with cancer Impact of genetic testing: a) Coping with cancer risk c) Family and social problems

Table 2. *(continued)*

First author, year, country	n (male)	Age mean [range]	Type	Period before/after testing (in years)	DNA-test result [a]	Having had cancer	Research aim	Measurement	Extracted themes [b]
Mendes (2011) Portugal	10 (?)	? [>18]	Hereditary cancers	After testing (?) 3 awaiting result/ 2 not yet tested	3 + 2 - 5 ±	1 yes 9 no	Examines how individuals experience genetic counseling for hereditary cancers	Interviews	a) Coping with cancer risk b) Practical problems c) Family and social problems d) Children related problems f) Emotions
Mireskandari (2009) Australia	11 (5)	26 [19-34]	FAP	?	8 + ? - ? ± 3 not tested	7 yes 4 no	What is the impact of FAP?	In depth interviews	a) Coping with cancer risk b) Practical problems c) Family and social problems d) Children related problems e) Living with cancer

[a] + mutation positive result, - mutation negative result, ± inconclusive result
[b] a) Coping with cancer risk, b) Practical problems, c) Family and social problems, d) Children related problems, e) Living with cancer, f) Emotions
?=not reported value, n/a=not applicable

Five studies solely used a cohort of patients who were diagnosed for cancer in the past. In four studies, only individuals without a previous cancer diagnosis were included. Ten studies reported on a mixed group of individuals with/without a previous cancer diagnosis, and six studies did not provide information about diagnosis.

A few studies included counselees who underwent genetic counseling, but had not (yet) received their DNA-test results. The study of Kenen et al. is the only one that investigated female counselees after the initial counseling, but prior to their test disclosure.[44] Some studies included a mixed group of counselees regarding their knowledge of the test result, while all others included only individuals with a known test result. Six studies included mutation carriers only, 1 study non-carriers only, 3 studies focused exclusively on individuals with non-informative test results, and 11 studies included a mixed sample with regard to DNA-status. Information on DNA-status was not reported in 4 studies.

Meta-analysis

Identified themes across studies (step 4-6)

Despite differences between sample characteristics (male–female ratio, history of cancer, type of cancer syndrome), methodology (interviews, focusgroups), and timing of the assessment (before or after testing, time since testing), a large overlap in reported issues was found between the different studies. We identified six themes; a) coping with cancer risk, b) practical problems, c) family-related problems, d) children-related problems, e) living with cancer, and f) emotions (see Table 3). These themes are explained in more detail below.

a) Coping with cancer risk

Various stategies have been reported in order to cope with the cancer risk. These vary from a reassessment of their life and priorities after genetic counseling,[40, 45-47] a fatalistic way of coping to positive thinking,[48-50] changing lifestyle behavior,[40, 44, 45, 48] and a focus on the present.[51] Some counselees reported that they were (highly) vigilant in performing breast self-examination,[49] are sensitive towards breast cancer cues,[40] and others indicated that they avoided talking about cancer or watching/reading media reports on the subject. Individuals gain a sense of control when they are reassured by obtaining access to medical care, such as extra screening, and the continuing support from the clinic.[45,52-57] Another study reported that the screening will never be sufficient to reassure them.[58] In order to cope with their cancer risk, counselees are confronted with several decisions. The question whether or not to undergo DNA-testing,[44,59] whether or not to undergo (prophylactic) surgery and/or surveillance,[44, 46, 59] and in some cases whether or not to have (more) children are reported as burdensome.[43, 55, 57, 60, 61]

Table 3. Specific issues within six themes

a) Coping with cancer risk	b) Practical problems	c) Family and social problems	d) Children-related problems	e) Living with cancer	f) Emotions
Reassessment of life and priorities Fatalistic view of life Changing lifestyle behaviour Focusing on the present Positive thinking Vigilant performing breast self-examination Avoiding cancer as a topic Obtaining access to medical care Obtaining support from the clinic *Decision making/ decisional conflict about* Genetic testing (prophylactic) Surgery Having children or not	Obtaining life insurance/loans Employment Procedural aspects of genetic testing	Communication problems with family members Partners lack insight in feelings Change in family atmosphere Feeling responsible for family members (survivor) Guilt towards their family	*In general* Concerns for children's increased risk Informing children about their risk Guilt towards children Fear of leaving your children *Specifically related to their daughters* Concerns for daughters' increased risk How to inform the daughters	Concern/fear/thinking about (risk of) developing cancer (hereditary) Cancer is a continuing issue Pain about the loss of family members Intrusion with daily living Side effects of treatment	*Negative emotional reactions* Stress, fear, (cancer) worries Shock or distress Anger, frustration or disappointment Anxiety or loneliness Feelings of loss Questions with spirituality Uncertain about the future *Positive emotional reactions* Reassurance Relief Reduced anxiety

b) Practical problems

Practical problems that have been reported, include concerns about access to health or life insurances,[52, 54] and concerns about negative implications of the DNA-test results for employment.[47, 56, 61] In addition, procedural aspects of the genetic counseling and testing, including a waiting time of several months before learning the DNA-test results, have been reported as burdensome.[57, 59]

c) Family-related problems

Problems related to the family are frequently reported and span a wide range of possible issues. The communication within the family continues to be a problem reported by the counselees. Specifically, the disclosure of the test result to the family members can be burdensome for some counselees.[43, 51, 55, 57, 61, 62] In addition, concerns about changes in the family atmosphere have been described, related to different reactions of members within families.[44,46,47,52,55,56,59] Some counselees did not feel understood or supported by their partner or family members.[40,46,57,60,61,63] Others reported feeling a heavy, for some burdensome, responsibility for their family.[42,45,48,49,53,55,59] Specific emotional reactions included feelings of guilt towards family members (e.g., being a non-carrier but having a relative who is a carrier).[46, 50, 55, 56, 64] In studies of individuals with known DNA-test results, the experience of stronger family ties was described.

d) Children-related problems

Worries that one's child might be at increased risk of developing cancer was a frequently reported motive for undergoing genetic counseling.[42, 43, 50, 52, 59, 62] Many counselees expressed concerns and uncertainty about how best to inform their children about their possible increased risk.[43, 57, 61, 62] These concerns were specifically directed towards their daughters.[40, 45, 65] D'Agincourt-Canning et al., Lodder et al., and Strømsvik et al. reported feelings of guilt towards children.[43, 64, 65] Kenen specifically reported on the importance of the age of the counselee and their children. When mothers were young and had young children, they were more upset for their own survival because they did not want their children to grow up without a mother. Whereas older women were more concerned about the risk of their (grand) children.[44]

e) Living with cancer

Many articles reported fear of developing cancer (again), and thoughts about the risk of developing cancer as an important problem area.[47, 49, 52, 64] This way, cancer continues to be a part of their future.[62, 65] Some counselees reported on the intrusion of having had cancer and the treatment for cancer on their daily life (e.g., the need for frequent visits to the toilet among patients with FAP).[61] Side-effects of preventive risk reducing strategies were another reported source of concern.[40, 53, 59] Several articles described the impact of cancer of family members and the impact of the loss of family members because of cancer to the counselees.[44, 51]

f) Emotions

Emotional reactions to the genetic test-outcome were frequently reported, ranging from positive to negative reactions. Two articles reported on a wide range of negative emotions encountered by individuals, without specifying these emotions.[40, 56] Other articles used terms like stress, fear, (cancer) worries,[46, 52, 57, 58] shock and distress,[44, 50] anger, frustration or disappointment,[43] anxiety and loneliness,[43, 51] and feelings of loss.[60] Questions or feelings about spirituality,[43, 51] and uncertainty about the future [49, 50] were also reported as being linked to these emotional reactions. Positive emotions were also frequently reported, and mostly within studies including individuals with known DNA-test results, including feeling reassured, relief, and reduced anxiety and/or worries as a result of the genetic test outcome.[40, 46, 50-52, 59, 64]

Observed patterns of association between sample characteristics and reported problems

We observed several patterns of association between a number of sample characteristics (e.g., age, gender, and DNA-test result) and the type of reported problems. The most notable of these are discussed below.

Sociodemographic characteristics

A few studies had a young population, with individuals younger than 35 years.[56, 60, 61] Insurance and work-related problems were mostly reported within this age group (only reported once within an older age group [52]). Additionally, the problems reported within the young group tended to focus on 'genetic-related problems' and 'family problems', whereas older respondents tended to more often report problems in other areas such as children-related problems and living with cancer. The studies including men only, feelings of responsibility towards family members and children were frequently reported.[42, 43, 50, 65]

Medical characteristics

Individuals with a cancer diagnosis reported that: (1) the genetic test outcomes were less stressful than their cancer diagnosis,[53] (2) they were already familiar with possible treatment options,[54] (3) the DNA-testing provided them with an explanation for their cancer,[59] and (4) knowing their DNA-test result did not change their lifestyle, whereas their cancer diagnosis did.[63] No clear pattern of association was observed between other medical characteristics (e.g., the type of cancer syndromes) and reported problems.

DISCUSSION

Since most papers on the impact of genetic counseling and/ or testing for cancer do not provide information on the specific content of the problems experienced by counselees, a systematic review of the qualitative literature was performed to obtain an overview of the specific issues that may explain the 'distress' encountered by counselees. We identified 25 relevant articles reporting on specific psychosocial issues experienced by individuals who

had undergone genetic counseling, with or without DNA-testing, for hereditary cancer syndromes. After synthesis of the published concepts of these 25 papers, we identified six important problem themes that are relevant to counselees: a) coping with cancer risk, b) practical problems, c) family-related problems, d) children-related problems, e) living with cancer, and f) emotions.

This review indicates that 'distress' or 'emotions' is just one of the six important problem-themes encountered by counselees. The themes and associated issues identified with this literature review suggest that many of the widely used measures (e.g., the HADS, STAI, IES, CES-D) within the cancer genetic counseling setting may be too general. When using these measures, approximately 25% of counselees are reported to have clinically relevant levels of distress. Moreover, in a study by Coyne et al. in which a diagnostic interview for psychiatric disorders was used, only 1% of the participants was found to have a major depressive disorder as formulated in the DSM-IV.[66] Clearly, most counselees do not suffer from psychiatric levels of depression, or clinically relevant levels of anxiety, and distress. However, this does not mean that counselees do not encounter psychosocial problems. It is therefore of great importance to focus on more cancer-specific and/or genetic-specific issues. A questionnaire focused specifically on cancer genetic-specific psychosocial problems could be particularly useful in facilitating their recognition, discussion and management. This is in line with the strategy of developing condition-specific questionnaire modules to complement more generic quality of life measures (e.g., the FACT-B for breast cancer [67] or the QLQ-CR38 for colorectal cancer [68]).

Risk factors for distress as described in other studies have largely been confirmed in the current review. For instance, 'little social support' is frequently reported and described within the theme 'family-related problems'. Also 'a previous personal cancer diagnosis' and 'cancer diagnoses in close relatives' as risk factors for distress are reported within the theme 'living with cancer'. Although it is important to be aware of these risk factors, we believe that the timely identification of specific problems provides the type of information that can best facilitate appropriate client-counselor dialogue and clinical management.

Some of the identified themes have been the subject of previous research. For instance, a large body of literature is available on the subject of family communication.[69-81] The current review adds to the literature by (1) providing a comprehensive overview of studies on the various specific problems and (2) identifying a limited number of overarching themes within which the specific issues can be placed.

Study limitations

In the current review, a number of studies with a small sample size, or otherwise limited methods were included. There is a debate within the literature on meta-ethnography about whether or not to include a 'critical appraisal' of the included studies, as is common when performing a systematic review. We decided against performing such an appraisal. We decided not to exclude any study on the basis of quality, since the information of in-depth interviews or focus groups was of added value. Although the characteristics of

the study populations varied widely, and the subjective nature of qualitative research complicated the interpretation of data, we were able to identify a common set of psychosocial problems relevant to the cancer genetic setting. Our overview and extracted themes are subjective as well, but we are fairly confident of the robustness of the themes extracted in this overview. Our search started in January, 2000 and therefore excluding possible important papers published before that date. However, we do not believe that adding more qualitative articles from an earlier time period would change the conclusions drawn from this review.

Research recommendations

We are of the opinion that future studies on the psychosocial impact of counseling and testing for cancer should go beyond the level of distress. With the current review we have identified six specific problem-themes encountered by counselees. Since many papers have not referred to each other, the studies identified for this review were conducted independently. Interestingly, all results pointed in the same direction and suggest that research on specific problems of genetic counseling and/or testing within the cancer genetic setting is saturated. Moreover, the literature review written by Walter et al. on the lay understanding of familial risk including studies with individuals with a family history of coronary heart disease, cancer and diabetes mellitus also shows results that point in the same direction.[82] They also discuss the importance of communication about specific psychosocial issues that are of importance to counselees. This suggests, that most problem themes identified in this review could probably be generalised to other areas with counselees who are at high risk of developing a disease due to a hereditary mutation.

This review can not give information on the prevalence of the identified problems within cancer genetic counseling. Therefore, future studies should pay attention to these issues. Furthermore, future studies should investigate the possible differences between specific cultural and ethnic groups facing hereditary tumor syndromes and the ways in which they deal with counseling and testing issues. Also studies from non-western countries, such as Asian countries, could yield new specific issues.

Practice implications

We recommend that clinical geneticists and counselors standardly screen for, and if needed, address the range of psychosocial problems as identified in this review. In concordance with the NSGC guidelines, we would recommend that genetic counseling include a psychosocial assessment. The issues and themes as identified in this review provide concrete information on the nature of the possible problems encountered within this setting. Stimulating the discussion of psychosocial problems may lead to a number of positive effects including increased counselors' awareness of their clients' problems, increased trust in the counselor, better management of problems (including referrals to other health care providers, where appropriate), and ultimately reduction or resolution of the counselees' problems.[83] Our group is currently developing and testing a brief psychosocial cancer genetic questionnaire to aid in identifying relevant psychosocial problems experienced by counselees. The goal is to ensure that relevant psychosocial

issues are more easily identified so that they can be addressed in a timely and effective manner. The questionnaire can be used as a means to start the discussion of psychosocial problems during the genetic counseling itself, or can prompt the genetic counselor to refer the counselee to appropriate ancilllary health care services. For example, a counselor may provide extra information on the procedures involved in genetic counseling and DNA-testing, may advise the counselee to visit a website containing relevant information, or may refer the counselee to additional psychosocial services. This may lead to improved quality of care and may, ultimately, lead to reduction of or even amelioration of the counselee's psychosocial problems.

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Chapter 3

Psychosocial Aspects of Hereditary Cancer (PAHC) questionnaire: Development and testing of a screening questionnaire for use in clinical cancer genetics

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ABSTRACT

Background

Up to three-quarters of individuals who undergo cancer genetic counseling and testing report psychosocial problems specifically related to that setting. The objective of this study was to develop, and evaluate the screening properties of a questionnaire designed to assess specific psychosocial problems related to cancer genetic counseling.

Methods

We adopted the EORTC Quality of Life Group guidelines to develop the Psychosocial Aspects of Hereditary Cancer (PAHC) questionnaire, a 26-item questionnaire organized into six problem domains: genetics, practical issues, family, living with cancer, emotions, and children. The Distress Thermometer and a question per domain on the perceived need for extra psychosocial services were included as well. We administered the questionnaire and the Hospital Anxiety and Depression Scale to 127 counselees at the time of genetic counseling and 3 weeks after DNA-test disclosure. As a gold standard to evaluate the screening properties of the questionnaire, participants underwent a semi-structured interview with an experienced social worker who assessed the presence and severity of problems per domain.

Results

A cutoff score representing responses of "quite a bit" or "very much" to one or more items within a given problem domain yielded moderate to high sensitivity across domains. A cutoff of 4 on the Distress Thermometer yielded high sensitivity. The questions regarding the perceived need for extra psychosocial services yielded high specificity and negative predictive values.

Conclusion

The PAHC questionnaire in combination with the Distress Thermometer can be used as a first-line screener for psychosocial problems within the cancer genetic counseling setting.

INTRODUCTION

Systematic use of patient-reported outcomes (PROs) can facilitate the detection and discussion of both physical and psychosocial health problems in daily clinical oncology practice.[1-6] Enhanced communication can, in turn, result in better understanding and trust between clinicians and their patients, and better patient management.[7] Studies of the effect of routine PRO assessment in clinical practice on patients' functioning and wellbeing have yielded mixed results.[3-6] It has been suggested that PRO assessments are more likely to impact favorably on psychosocial health when the information provided is concrete and specific to the setting in which it will be used.[1, 8]

Approximately one-quarter of those who undergo genetic counseling and testing for cancer report clinically relevant levels of distress, anxiety or depression.[9] These emotional reactions are measured typically with generic questionnaires, such as the Hospital Anxiety and Depression scale (HADS), the State Trait Anxiety Inventory (STAI), the Impact of Event Scale (IES), and the Center for Epidemiological Studies Depression Scale (CES-D).[10-12] These generic questionnaires do not, however, assess the specific psychosocial problems of individuals undergoing genetic counseling.[13, 14]

It has been reported that up to approximately three-quarters of individuals experience specific problems during cancer genetic counseling.[15] Ideally, these problems should be addressed during genetic counseling to help individuals understand and adapt to the psychosocial implications of their situation.[16] However, genetic counselors tend to communicate unidirectionally and focus primarily on biomedical issues.[17] Within the cancer genetic counseling setting, where individuals typically have only two contacts with their genetic counselor, the use of a specific psychosocial screening questionnaire may be of particular value in facilitating communication, enhancing care, and ultimately in resolving the counselees' problems.[18]

There are several questionnaires available for assessing psychosocial issues in the genetic counseling setting, including the Psychological Adaptation to Genetic Information Scale (PAGIS),[19] the Multidimensional Impact of Cancer Risk Assessment (MICRA) [20] and the Genetic Risk Assessment Coping Evaluation (GRACE).[15, 21] The PAGIS and MICRA were both developed to measure the psychological impact and adaptation to genetic test results (thus after the genetic counseling process is completed), and therefore do not address other potentially relevant issues concerning cancer genetic counseling such as worries about undergoing cancer risk assessment. Although the GRACE measures specific concerns and coping during genetic counseling and is a promising tool for use in daily clinical practice, it does not assess some important areas such as the burden of having (had) cancer or experiencing cancer in the family.

The primary objective of the current study was to develop and evaluate a questionnaire designed specifically to identify a broad range of psychosocial problems experienced by ndividuals undergoing genetic counseling and testing in the oncology setting.

METHODS

Development of the Psychosocial Aspects of Hereditary Cancer (PAHC) questionnaire
We adopted the four phases of the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Group guidelines for questionnaire development.[22] First, we conducted an extensive literature search (February, 2009) in PubMed with the MeSH terms "genetic counseling", "neoplasms", "psychology", and combinations thereof. This search resulted in a total of 167 relevant articles. Simultaneously, we undertook semi-structured interviews with 8 health care providers experienced in cancer genetics (4 to 20 years of experience). This included clinical geneticists, genetic counselors, psychologists, and social workers. Combined, the information derived from the literature search and the expert interviews resulted in a provisional list of 52 issues specific to the cancer genetic setting. A questionnaire with this provisional list of issues was then sent to another group of experts (n=18, range of experience 1 to 17 years), all of whom were members of the Dutch Society for Psychosocial Oncology's Working Group on Familial Cancer. Based on their feedback, 22 issues were deleted as being either insufficiently relevant or redundant. Subsequently, four former counselees who had completed the genetic counseling process were interviewed about the relevance of the 30 issues included in the revised, provisional list, and were asked if there were any additional issues that they believed should be added. Based on these latter interviews, four issues were deleted; none were added.

In the second phase, we operationalized these issues into questionnaire items. We organized the questions into 6 problem domains: genetics, practical issues, family, living with cancer, emotions, and children. The number of questions generated per topic area ranged from 2 (for practical issues) to 6 (for family related problems). Each item had a four-point Likert-type response scale ranging from 1, 'not at all' to 4, 'very much'. Additionally, for each problem domain, a question was included about interest in talking with a psychosocial health care professional (response choices *yes* or a *no*). The Distress Thermometer (DT), a visual analog scale ranging from 0-10 ("no distress" to "extreme distress") was also added to the questionnaire as a measure of general psychological distress.[23]

In the third phase, the provisional questionnaire was sent to 56 former counselees to further evaluate the relevance of the questions, their phrasing, and whether any additional issues needed to be included. Completed questionnaires were received from 25 individuals, of whom 17 were subsequently interviewed by telephone to obtain more qualitative information about their questionnaire responses. This resulted in a few minor changes in the phrasing of the questions; no changes were made in the questionnaire content. An online version of the provisional questionnaire, the HADS [24] and the sociodemographic questions was pilot tested among 15 counselees of the family cancer clinic of the Netherlands Cancer Institute in Amsterdam. The questionnaire was translated from Dutch to English using forward-backward translation procedures.

The fourth and final phase of the questionnaire development process consisted of testing the resulting questionnaire, the Psychosocial Aspects of Hereditary Cancer (PAHC) questionnaire in a larger group of counselees. The methods and results of this fourth phase are reported below.

Participants

Between January and December, 2010, all individuals, index patients as well as relatives, who were scheduled for genetic counseling with a clinical geneticist or genetic counselor at the family cancer clinic of the Netherlands Cancer Institute were eligible to participate in the study. Participants had to be older than 18 years of age and have sufficient command of the Dutch language to be able to complete the questionnaires. For logistic reasons, counselees were initially invited only if it was possible to also schedule an interview with a psychosocial worker prior to the counseling session.

Study procedures

Eligible individuals were asked to return the consent form by mail. A reminder letter was sent one week before the genetic counseling session. Participants completed sociodemographic questions, the provisional PAHC questionnaire, the HADS, and the DT. Additionally, participants underwent a semi-structured interview with one of three experienced social workers about their psychosocial problems. All participants completed questionnaires and interviews at two points in time: (1) at the time of the initial genetic counseling session; and (2) approximately 3 weeks after the counseling session during which DNA-test results were disclosed. Participants who did not undergo DNA-testing were not invited for the second assessment.

We originally planned to have all participants complete the first questionnaire and undergo the semi-structured interview *prior* to seeing their genetic counselor. Toward this end, participants were asked to come to the clinic 40 minutes prior to their counseling session. However, due to practical reasons, one-third of participants completed the questionnaires immediately after their counseling session, and underwent the semi-structured interview by telephone within 3 days.

At the second assessment after DNA-testing, the provisional PAHC questionnaire was modified slightly. For example, because at this time the DNA-test result had already been disclosed, items related to concerns about whether or not to go for testing were deleted. The modified PAHC questionnaire, the HADS, and the DT were mailed to the participants three weeks after the counseling session during which the DNA-test results were disclosed. A telephone interview with the psychosocial worker was scheduled within a week after the questionnaires had been returned. Reminders were sent via mail after two weeks. The institutional review board approved the study.

Gold standard: Ratings by the psychosocial workers

Because no comparable, validated questionnaire was available, interviews conducted by experienced social workers were used as "gold standard". This is in line with development

procedures of other screening tools.[25] The interviews were carried out by three clinical social workers experienced in counseling individuals with psychosocial problems related to cancer genetics. They were instructed to pose questions about all six domains covered by the PAHC questionnaire, but without being aware of the specific content (i.e., items) of the questionnaire. For each domain, they rated the presence and severity of possible problems on a 3-points scale: (1) no problem; (2) a minor problem that could probably be dealt with by the genetic counselor; or (3) a major problem requiring referral to specialized psychosocial services. All interviews were audiotaped for purposes of assessing inter-rater reliability. In total, the three social workers independently rated 5 audiotaped interviews of each of the other social workers.

Statistical analysis

To evaluate the screening properties of the PAHC questionnaire, we first dichotomized the scores of both the questionnaire and the interview to establish two cutoffs or thresholds per psychosocial domain; one more liberal and one more stringent. For the questionnaire, which employs a 4-point response scale, the more liberal cutoff was based on the following criteria: the respondent had a score of 2 or more (i.e., indicating "a little," "quite a bit" or "very much") on at least one item within a given problem domain. The alternative, more stringent cutoff was based on a score of 3 or more on at least one item within a given domain (i.e., "quite a bit" or "very much").

Similarly, the social workers' ratings based on the clinical interview (1=no problem, 2=minor problem, and 3=major problem) were dichotomized in two ways, one more liberal and the other more conservative, namely: (1) the counselee had any degree of problem within a given domain (i.e., either minor or major problems) or not (2) the counselee had a major problem within a given domain that required referral to specialized psychosocial services (versus having no or only a minor problem).

The combinations of these thresholds yielded four different sets of 2x2 tables. A first 2x2 table was based on both liberal thresholds. The second 2x2 table was based on the more stringent threshold for the questionnaire (i.e., a score of 3 or greater) and the more liberal rating of the social worker (minor or major problem versus no problem). The third 2x2 table was based on both stringent thresholds. And finally, the fourth 2x2 table was based on the more liberal threshold on the PAHC questionnaire with the more stringent rating of the social worker. This latter 2x2 table was considered less relevant, and thus results based on that categorization are not presented.

We calculated the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the PAHC questionnaire based on these sets of 2x2 tables. Sensitivity is the proportion of true cases (as classified by the social worker) that was detected as such by the screening questionnaire. Conversely, specificity is the proportion of true negative cases (again as classified by the social worker) that was detected as such by the questionnaire. The PPV is the proportion of true positive cases detected by the questionnaire and so classified by the social workers versus the total number of cases

identified by the questionnaire. Finally, the NPV is the proportion of true negative cases detected by the questionnaire and so classified by the social workers versus the total number of cases which were identified as negative based on the questionnaire alone. In all of these analyses, the social workers' ratings were used as the 'gold standard' against which the questionnaire scores were evaluated. Prior to evaluating the screening properties of the questionnaire, we first examined the inter-rater reliability of the social workers' ratings (percentage of agreement).

We also evaluated the screening properties of the items that asked the participant if (s)he felt that (s)he needed professional help for any given problem domain. Here, again, the ratings based on the interviews held by the social workers (i.e., should the participant be referred) were considered the "gold standard". Finally, we calculated the area under the curve (AUC) of the receiver operating characteristics (ROC) curve and evaluated the screening properties of the DT, using the HADS as the criterion measure (a cutoff of 15 for the total score of the HADS).

In selecting the preferred cutoff scores for the questionnaire domains and for the DT, we were primarily concerned with achieving a relatively high sensitivity (i.e., capturing those individuals with a problem) and preferably a high PPV (i.e., a high percentage of those who screen positive actually having a problem).[26] This optimizes the likelihood of correctly identifying counselees experiencing problems that merit further attention. Sensitivity, specificity, PPV and NPV were rated as follows: poor (< 0.2), fair (0.2 ≤ 0.4), moderate (0.4 ≤ 0.6), good (0.6 ≤ 0.8), and very good (0.8 ≤ 1).[27] Finally, the percentage of participants who screened positive on the questionnaire was taken into account in establishing the optimal threshold.

RESULTS

Participants

In total, 263 eligible counselees were invited to participate in the study, of whom 139 (53%) agreed to do so. Reasons for non-participation included, logistical/scheduling problems (n=23), perceived emotional burden (n=20), lack of interest (n=13), and not wanting to be audiotaped (n=3). Thirty-nine counselees provided other reasons, and 26 did not provide a reason.

Complete data (both questionnaire and interview) were available for 127 of the 139 participants (91%) at the first assessment. Of the 139 participants, some did not undergo DNA-testing (n=35), did not return the second questionnaire (n=13), or did not have complete interview data at the second assessment (n=17). Complete data of 74 participants were available at the second assessment. To evaluate the screening properties of the DT at the second assessment, we also included the 17 participants who completed these questionnaires (without having undergone an interview), resulting in 91 cases. Table 1 presents the sociodemographic characteristics of the participants.

Inter-rater agreement

Inter-rater agreement between the social workers was moderate, ranging from 53% to 62% across the problem domains. Given this, all statistical analyses were first conducted for each psychosocial worker separately. The results were very similar across the individual social workers, and thus we based the final analyses on the combined ratings of the social workers.

Questionnaire screening properties

Table 2 shows the results of three 2x2 tables comparing the counselees' questionnaire scores with the ratings of the social workers. First, we compared the most liberal criteria for both sources (i.e., any degree of problem). The sensitivity of the questionnaire domains ranged from 0.79 for 'practical issues' to 1.0 for 'living with cancer'. The PPV ranged from 0.41 for 'practical issues' to 0.73 for 'genetics'. Specificity ranged from 0 for 'living with cancer' to 0.43 for 'practical issues', with a NPV ranging from 0 for 'living with cancer' to 1 for 'children-related issues'. Using this liberal cutoff score for the questionnaire, the percentage of patients who screened positive varied between 65% for practical issues to 100% for living with cancer.

Table 1. Sociodemographic characteristics of the study sample (n=127)

Age (years) [range]	Mean 47	[18-78]
	n	(%)
Gender		
Male	23	18
Female	104	82
Marital status		
Married/steady relationship	100	78
Single	15	12
Divorced	7	6
Widow/widower	5	4
Education level [a]		
Low	29	23
Middle	39	31
High	58	46
(former) Cancer diagnosis		
Yes	64	50
No	63	50

[a] n=126, 1 participant has unknown education level

Second, we compared the same results when using a cutoff of 3 or higher (i.e., "quite a bit" or "very much") on at least one item within a given questionnaire problem domain and a minor or major problem as rated by the social worker. In this case, sensitivity ranged

from 0.35 for 'practical issues' to 0.91 for 'living with cancer,' and the PPV ranged from 0.57 for 'problems with family' to 0.87 for 'genetics'. Specificity ranged from 0.30 for 'living with cancer' to 0.88 for 'practical issues,' with a NPV ranging from 0.38 for 'children-related issues' to 0.73 for 'practical issues.' Using this cutoff, between 20% (for genetic-related issues) and 83% (for living with cancer) of the counselees screened positive on the PAHC questionnaire.

Table 2. Screening properties of the questionnaire with different cutoffs

	%	Sensitivity	Specificity	PPV	NPV
2 or greater (counselee rating) versus minor or major problem (social worker rating)					
Genetics	94	0.97	0.14	0.73	0.63
Practical issues	65	0.79	0.43	0.41	0.80
Problems with family	89	0.95	0.18	0.55	0.79
Living with cancer	100	1	0	0.64	0
Emotions	89	0.95	0.23	0.70	0.71
Children	98	1	0.04	0.58	1
3 or greater (counselee rating) versus minor or major problem (social worker rating)					
Genetics	47	0.58	0.78	0.87	0.43
Practical issues	20	0.35	0.88	0.60	0.73
Problems with family	48	0.54	0.58	0.57	0.55
Living with cancer	83	0.91	0.30	0.70	0.67
Emotions	29	0.35	0.82	0.78	0.40
Children	58	0.57	0.41	0.59	0.38
3 or greater (counselee rating) versus major problem (social worker rating)					
Genetics	47	0.84	0.59	0.27	0.96
Practical issues	20	0.67	0.81	0.08	0.99
Problems with family	48	0.83	0.54	0.08	0.98
Living with cancer	83	1	0.19	0.13	1
Emotions	29	0.63	0.76	0.27	0.93
Children	58	1	0.45	0.13	1

%; percentage of individuals who were screened positive with this cutoff on the PAHC questionnaire
Abbreviations; PPV: positive predictive value; NPV: negative predictive value

Third, we compared the results based on a cutoff of 3 or higher on at least one item within a given questionnaire domain and a rating of a major problem by the social worker. With these cutoffs, the sensitivity of the questionnaire ranged from 0.63 for 'emotions' to 1.0 for 'living with cancer,' and the PPV from 0.08 for 'practical issues' and 'problems with family'

to 0.27 for genetics and emotions. The specificity ranged from 0.93 for 'emotions' to 1.0 for 'living with cancer' and 'children,' with a NPV ranging from 0.93 for 'emotions' to 1.0 for 'children-related issues' and 'living with cancer.' Using this cutoff, between 20% (for genetic-related issues) and 83% (for living with cancer) of counselees screened positive on the PAHC questionnaire.

The analysis of the data from the second assessment, three weeks after the DNA-test disclosure, yielded a very similar pattern of results to that based on the first assessment (data not shown).

Based on these results, we choose a cutoff of 3 (i.e., 'quite a bit' or 'very much') on any item within a domain of the questionnaire as indicative of a problem meriting further attention (i.e., screen positive). Using this cutoff we were able to avoid a situation in which almost all counselees would screen positive on at least one domain, but still have sufficient sensitivity and PPV. Also, with a cutoff of 3, the specificity and NPVs were within acceptable ranges.

Perceived need for professional psychosocial services

The screening properties of the questionnaire item regarding the perceived need for psychosocial care per domain are shown in Table 3. The sensitivity of this item ranged from 0.21 for 'living with cancer' to 0.71 for 'children,' with a PPV ranging from 0.06 for 'practical issues' to 0.39 for 'emotions.' Specificity ranged from 0.73 for 'children-related issues' to 0.88 for 'living with cancer,' with a NPV ranging from 0.88 for 'genetics' to 0.99 for 'practical issues.' Based on this single item, between 13% (for 'living with cancer') and 30% (for 'children') of participants was found to be interested in receiving additional psychosocial services at the first assessment. The perceived need for psychosocial care was consistently much lower at the second assessment (data not presented).

Table 3. Screening properties of the perceived need for psychosocial care at the first assessment

	%	Sensitivity	Specificity	PPV	NPV
Genetics	25	0.42	0.78	0.25	0.88
Practical issues	27	0.67	0.74	0.06	0.99
Problems with family	20	0.67	0.83	0.16	0.98
Living with cancer	13	0.21	0.88	0.18	0.90
Emotions	22	0.69	0.85	0.39	0.95
Children	30	0.71	0.73	0.18	0.97

%; percentage of participants that requested extra services
Abbreviations; PPV: positive predictive value; NPV: negative predictive value

The Distress Thermometer (DT)

ROC curve analysis of the DT against the HADS (cutoff =15) at the first assessment yielded an area under the curve (AUC) of 0.81. A cutoff for the DT score of 4 resulted in the most optimal balance between sensitivity and specificity. The sensitivity of the DT was 0.84, the PPV was 0.33, the specificity was 0.63, and the NPV was 0.94 (Table 4). Results of this analysis for the second assessment were comparable (data not shown).

Table 4. Screening properties of the Distress Thermometer at the first assessment

Score on DT	%	Sensitivity	Specificity	PPV	NPV
1	86	1	0.17	0.21	1
2	74	0.96	0.31	0.23	0.97
3	60	0.87	0.46	0.26	0.94
4	46	0.83	0.63	0.33	0.94
5	39	0.78	0.69	0.36	0.94
6	33	0.74	0.75	0.40	0.93
7	26	0.56	0.81	0.39	0.89
8	14	0.39	0.91	0.50	0.87
9	2	0.04	0.98	0.33	0.82
10	0	0	1	0	1

%; percentage of participants who screened positive when using this cutoff
Abbreviations; PPV: positive predictive value; NPV: negative predictive value

DISCUSSION

In this paper we have reported the results of a study that investigated the screening properties of the Psychosocial Aspects of Hereditary Cancer (PAHC) questionnaire, together with the Distress Thermometer (DT) in detecting counselees' specific psychosocial problems. We were unable to identify a single cutoff value for the PAHC questionnaire that yielded optimal screening properties across all of the problem domains, and that did not result in all participants screening positive on at least one domain. This suggests that, from a pure measurement perspective, it might make most sense to select a different cutoff value for each of the domains of the questionnaire. However, from a practical perspective, we believe that such a strategy would be cumbersome and confusing to genetic counselors in the daily clinical practice setting. As a compromise, we have chosen a cutoff of 3 (i.e., "quite a bit" or "very much") for all domains of the PAHC questionnaire, and a cutoff of 4 for the DT.

In establishing the threshold score for the PAHC questionnaire, we gave more weight to sensitivity and PPV as screening properties, as opposed to specificity and NPV. We did so in order to correctly identify counselees experiencing problems that merit further

attention, which is of particular importance in the clinical practice setting. With the chosen cutoff of 3, the PPVs were quite reasonable, but not all domains yielded high sensitivity for detecting individuals with *any degree* of problem (minor or major). However, the questionnaire's sensitivity was good to very good in identifying counselees with a major problem (see Table 2).

The question regarding the perceived need for psychosocial care was found to have very good screening properties for identifying counselees who *do not* wish to talk with a specialized psychosocial worker and do not require such specialized services (i.e., high specificity and NPV). This question is less useful in identifying those who express a desire for extra counseling and actually require it (i.e., low to moderate sensitivity and PPV). This emphasizes the importance of having the genetic counselor probe further when a counselee expresses interest in speaking with a specialized psychosocial worker. This also suggests that the counselor should pay extra attention to those who do not express interest in being referred to specialized psychosocial services, but do report serious problems on the PAHC questionnaire as it has frequently been observed that highly distressed patients often do not make use of specialized psychosocial services.[28, 29]

Our goal was to develop a questionnaire for use in clinical practice. Therefore we emphasize again that the thresholds that we recommend here are based, in part, on practical considerations arising from the need to easily interpret the results of the questionnaire in the context of a busy clinical practice. This questionnaire, with its simple thresholds, can guide genetic counselors toward problems areas that merit discussion during genetic counseling.

To our knowledge, this is the first report on the validity of the DT when used in the cancer genetics setting. We found that a threshold score of 4 yielded the best trade-off between sensitivity (high) and specificity (moderate). Within the oncology setting in the Netherlands, the recommended threshold for the DT is 5.[30] As has been the case in previous studies, we found that a threshold of 4 yields high NPVs, but low PPVs. This emphasizes the need to use the DT only as a first-line screener for generalized distress, requiring further probing by the counselor before referrals are made to specialized psychosocial services.[31]

Several limitations of the study should be noted. First, only 53% of those invited to participate in the study did so. However, there were no significant difference between participants and non-participants on available socidemographic and clinical variables. Also, response rates are less important for this type of study in that the focus is on comparing self-reported problems with social workers' ratings *within* subjects. Second, the inter-rater reliability of the social workers' ratings of the participants' problems was only moderate. However, no other "gold standard" was available, and similar procedures have been used in other questionnaire validation studies. We would also note that the screening properties of the PAHC questionnaire based on the combined ratings of the social workers were very similar to those based on each social worker's ratings separately.

The study also has several noteworthy strengths. First we used a standardized and structured procedure for developing the questionnaire, which involved both health care professional and patient input. Second, we evaluated a range of possible thresholds for defining an individual as having clinical relevant problems, and we were able to identify a single threshold value for all of the questionnaire domains; one that exhibits quite reasonable screening properties. The availability of a single cutoff across the questionnaire domains will facilitate its use in daily clinical practice.

In conclusion, the PAHC questionnaire, together with the DT, can be used as a first line screener for detecting psychosocial problems of individuals undergoing cancer genetic counseling and testing. Future work is needed to determine the best ways of implementing the questionnaire in daily clinical practice, and to investigate how its use affects counselor-counselee communication, timely detection of psychosocial problems, and the management of those problems. Toward this end, we are currently conducting a randomized, controlled trial in which use of the PAHC questionnaire is being compared with usual care.

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Chapter 4

Prevalence and detection of psychosocial problems in cancer genetic counseling

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ABSTRACT

Objective

Although a minority of individuals who undergo cancer genetic counseling experience heightened levels of distress, many more experience a range of psychosocial problems. The aim of this study was to estimate the prevalence of such problems, and to identify sociodemographic and clinical variables associated significantly with them.

Methods

Participants were invited to complete the Psychosocial Aspects of Hereditary Cancer (PAHC) questionnaire, the Hospital Anxiety and Depression Scale (HADS) and the Distress Thermometer (DT) prior to or immediately following their counseling session.

Results

More than half of the 137 participants reported problems on three or more domains of the PAHC. Most frequently reported problems were in the domains 'living with cancer' (84%), 'family issues' (46%), 'hereditary predisposition' (45%), and 'child-related issues' (42%). Correlations between questionnaires were low. Sociodemographic and clinical background variables explained only a small percentage of the variance in distress or in the PAHC domains (2-14%).

Conclusion

The majority of counselees experience specific problems in the context of cancer genetic counseling. No background variables were identified as important predictors of distress or psychosocial problems.

Practice Implications

To identify counselees with psychosocial problems we recommend using the PAHC questionnaire or a similar problem-oriented questionnaire routinely in cancer genetic counseling.

INTRODUCTION

The main message of studies on the psychosocial impact of genetic counseling for cancer is that, after the process of genetic counseling and risk assessment, mean distress levels of counselees return to or are even lower than baseline levels.[1-3] However, approximately one-quarter of counselees experience heightened levels of distress during and/or after the genetic counseling process.[4]

The psychosocial impact of genetic counseling is most frequently measured with the Hospital Anxiety and Depression scale (HADS), the State Trait Anxiety Inventory (STAI), the Impact of Event Scale (IES), or the Center for Epidemiological Studies Depression Scale (CES-D).[5-7] However, these questionnaires may be too generic to capture the entire spectrum of psychosocial issues relevant to the cancer genetic setting.[8] They do not capture other important issues and concerns, such as existential problems, family related problems, issues surrounding genetic risk, the burden of living with cancer, and possible practical problems related to genetic counseling (e.g., insurance issues).[8-10]

Several methods are available to assist genetic counselors in detecting counselees with serious psychosocial problems. Esplen and colleagues have developed a screening questionnaire based partly on factors associated with distress after the counseling process.[11] Vadaparampil and colleagues recommend inquiring routinely about previous contacts with psychosocial caregivers as a means of identifying counselees potentially in need of such services.[7]

Increasingly, the Distress Thermometer (DT) with an accompanying problem checklist is being recommended as a first-line screening method for distress in daily clinical oncology practice.[12] The DT, together with a revised checklist designed specifically for women at high risk of developing breast cancer has proven to be useful in screening for distress at the time women undergo mammography.[13]

Recently, we developed the Psychosocial Aspects of Hereditary Cancer (PAHC) questionnaire as a tool for identifying psychosocial issues and concerns experienced during cancer genetic counseling.[14] The PAHC questionnaire consists of 26 items, organized into six domains. We have established a threshold per domain of the PAHC questionnaire for identifying counselees who may need further psychosocial care.[14]

Knowledge of the specific psychosocial problems and distress levels experienced by counselees, as well as factors that may be associated with such problems can provide genetic counselors with useful information that they can use during the genetic counseling session. In this paper, we report on a study of the prevalence of cancer genetic-specific psychosocial problems and their association with more generalized levels of distress as assessed by the HADS and the DT. We also investigated whether sociodemographic and clinical variables are associated significantly with psychological distress and psychosocial problems experienced during genetic counseling.

METHODS

The data reported here were collected as a part of a larger study that evaluated the screening properties of the PAHC questionnaire and the DT in the cancer genetic counseling setting.[14]

Participants

Individuals were eligible to participate when they were scheduled for a visit at the family cancer clinic of the Netherlands Cancer Institute to undergo genetic counseling for cancer in the period January through December, 2010, were over 18 years of age, and had a sufficient command of the Dutch language.

Procedure

Eligible counselees received a letter of invitation from the head of the family cancer clinic and, if interested, were requested to return a signed consent form by mail. A reminder letter was sent one week before the genetic counseling session. Participants completed a questionnaire on a touchscreen computer at the clinic with demographic questions, the PAHC questionnaire, the DT and the HADS. The preference was to have the questionnaire completed prior to the counseling, but this was not always feasible due to planning issues. Thus counselees completed the questionnaire immediately prior to their scheduled genetic counseling session or immediately thereafter.

Sociodemographic and clinical data

The counselees' age, sex, marital status, education level, number of children, the number of affected first degree relatives, and use of psychosocial services in the past was obtained via self-report. Data on whether (s)he was diagnosed with cancer in the past and, if so, at what age, and whether there was a known gene mutation in the family were extracted from the medical records.

The PAHC questionnaire

The PAHC questionnaire consists of 26 questions addressing psychosocial problems and concerns that are specifically relevant to counselees within the cancer genetic counseling and testing setting. The content of the PAHC questionnaire is organized into the following six domains: (1) hereditary predisposition; (2) practical issues; (3) family and social issues; (4) general emotions; (5) living with cancer; and, for those who have children (6) children-related issues. The number of items per domain varies between 2 and 6. All 26 items are scored on a 4-point Likert-type scale ranging from 1 ("not at all") to 4 ("very much"). Based on a detailed analysis of the screening properties of the PAHC questionnaire, a threshold was established for clinical relevance.[14] Specifically, if one or more items within a domain was scored with a 3 or a 4 (i.e., indicating a moderate to severe problem), that domain is considered as a positive case. Additionally, per problem domain, the respondent is asked to indicate whether (s)he would like to receive professional psychosocial support. The PAHC questionnaire is supplemented by the DT, a visual analogue scale ranging from 0-10 ("no distress" to "severe distress").[12] The timeframe of the PAHC questionnaire and the DT is the previous week.

The HADS

The HADS was used to assess general psychological distress. It includes 14 questions and yields a total score and subscale scores for anxiety and depression. In the current analysis, we used only the total score, with a possible range of 0-42. Higher scores represent higher levels of distress. The HADS has been validated for use in the Netherlands.[15]

Statistical analysis

Chi-square analysis and Student's t-tests were used to examine potential differences in responses to the PAHC questionnaire, the HADS and the DT as a function of timing of questionnaire completion (i.e., prior to or immediately following the counseling session). The association between the PAHC questionnaire domains, the HADS and the DT was assessed by calculating Pearson's correlation coefficients and partial correlations that controlled for inter-correlations between the domains of the PAHC questionnaire.

Chi-square and Student's t-tests were employed to investigate which sociodemographic and clinical variables, if any, were associated significantly with the PAHC questionnaire domains, the HADS, and the DT. Any variable with a p-value below 0.10 was entered subsequently into a logistic (for the PAHC domain scores) or a linear regression model (for the HADS, and the DT). The domain 'children-related issues' was only completed by those participants who had children. Thus the analyses relating to this domain were performed on the subgroup of participants with children (n=100).

RESULTS

Participants

In total, 263 eligible counselees were invited to participate in the study, of whom 139 (53%) agreed to do so. Reasons for non-participation included logistical or scheduling problems (n=23), perceived emotional burden (n=20), lack of interest (n=13), and not wanting the counseling session to be audiotaped (n=3) (audiotaping was employed for another part of the study). Thirty-nine counselees provided other reasons, and 26 did not provide a reason. Two additional cases were excluded from the analysis because their clinical data were not available. This resulted in a total of 137 cases for the analysis.

The sociodemographic characteristics of the sample are reported in Table 1. The mean age of the sample was 47.1 years (range 18 to 78), and the large majority was female (82%). Most respondents were married or in a steady relationship, had children, and reported that they were not aware of any DNA-mutation in the family. Approximately half of the sample was relatively highly educated, had had contact with a psychologist or social worker at some time in the past, and had previously been diagnosed with cancer. There were no statistical significant differences on any of these background variables between those who completed the questionnaires before (n=91) or after (n=46) the genetic counseling session.

Table 1. Sociodemographic and clinical characteristics of the study sample (n=137)

Age (years) [SD]	47.1	[11.3]
	n	(%)
Sex		
Male	25	(18)
Female	112	(82)
Marital status		
Married/steady relationship	123	(90)
Single/Divorced/Widow/widower	14	(10)
Education level [a]		
Low	31	(23)
Middle	43	(32)
High	62	(46)
Children		
Yes	100	(73)
No	37	(27)
Previous contact with psychosocial worker		
Yes	69	(50)
No	68	(50)
First in family being referred to cancer genetic counseling		
Yes	87	(64)
No	50	(36)
Mutation in family before counseling		
Yes	33	(24)
No	104	(76)
Personal history of cancer		
Yes	71	(52)
No	66	(48)

[a] n=136, 1 participant has an unknown education level

Prevalence of psychosocial problems and their relation to distress

Approximately 10% of the participants did not report any problems included in the PAHC questionnaire that were of a sufficient magnitude (i.e., a score of 3 or 4 on an item within any given domain) to be considered relevant for further discussion. More than half of the participants reported at least one problem that met the threshold for clinical relevance on 3 or more domains (see Table 2). The domain with the highest prevalence was 'living with cancer' (84%), followed by the domains 'hereditary predisposition' (46%), 'family and social issues' (45%), and 'child-related issues' (42%). The domains 'general emotions' (29%), and 'practical issues' (19%) had the lowest prevalence in our sample (see Table 3).

All of the PAHC questionnaire domains were correlated significantly with psychological distress as measured by the HADS, when based on a Pearson correlation coefficient. However, when correcting for inter-domain correlations, only the domains 'family and social issues' and 'general emotions' remained statistically significantly associated with the HADS. All of the partial correlations were low, with the exception of the domain 'general emotions,' which has a strong conceptual overlap with distress as assessed by the HADS.

Table 2. Frequency and percentages of PAHC questionnaire domains with scores above the threshold

	Frequency (n=137)	Percentage (%)	Cumulative percentage (%)
None	14	10.2	10.2
1 domain	30	21.9	32.1
2 domains	19	13.9	46.0
3 domains	27	19.7	65.7
4 domains	27	19.7	85.4
5 domains	15	10.9	96.4
6 domains	5	3.6	100

The domains 'hereditary predisposition', 'practical issues', and 'general emotions' had statistical significant Pearson's correlations with distress as measured by the DT. These domains remained statistically significant when correcting for inter-domain correlations (see Table 3). However, the magnitude of the (partial) correlations was relatively low.

Table 3. Percentage of counselees with PAHC questionnaire scores above the threshold for clinical relevance per domain and correlations with the HADS and DT [a]

		HADS [b]		DT [c]	
Domain	Above the threshold (%, n=137)	Pearson's correlation	Partial correlation [d]	Pearson's correlation	Partial correlation [d]
Hereditary predisposition	46	0.33**	0.16	0.31**	0.24**
Practical issues	19	0.23**	0.09	0.26**	0.17*
Family – and social issues	45	0.33**	0.19*	0.16	0.03
General emotions	29	0.54**	0.49***	0.29**	0.25**
Living with cancer	84	0.29**	0.14	0.14	0.02
Child – related issues	42	0.24**	-0.05	0.09	-0.10

* p<0.05; ** p<0.01; *** p<0.001
[a] Pearson's correlation between HADS and DT = 0.58***
[b] distress as measured with the HADS, Adjusted R square of the model=0.37
[c] distress as measured with the DT, Adjusted R square of the model=0.15
[d] association between variables controlling for inter-correlation between the domains
Abbreviations; HADS: Hospital Anxiety and Depression Scale; DT: Distress Thermometer

Sociodemographic and clinical variables associated with general distress

Education level, having had previous contact with a psychosocial worker, and having a personal history of cancer were statistically significantly associated with general distress as measured by the HADS (see Table 4). When entered in a linear regression model, only having had previous contact with a psychosocial worker (p=0.001), and having a personal history of cancer (p=0.03) remained statistically significant. However, only 10% of the variance in distress scores was explained by these three variables.

Marital status, having had previous contact with a psychosocial worker, having a known mutation in the family, and having a personal history of cancer were statistically significantly associated with the DT. However, none of these variables remained statistically significant when entered in a linear regression model. The variance in distress scores explained by these four variables was 8%.

Table 4. Sociodemographic and clinical variables associated with general distress, assessed with the HADS and the DT

			95% CI for B	
	B (SE)	exp b	Lower	Upper
HADS [a]				
Education level	-0.10 (0.68)	-0.01	-1.45	1.26
Previous contact with psychosocial worker	3.61 (1.08) **	0.28	1.48	5.74
Personal history of cancer	2.45 (1.09) *	0.19	0.31	4.60
DT [b]				
Marital status	1.11 (0.77)	0.12	-0.40	2.64
Previous contact with psychosocial worker	0.79 (0.47)	0.14	-0.13	1.71
Known mutation in family	-0.52 (0.58)	-0.08	-1.67	0.63
Personal history of cancer	0.73 (0.50)	0.13	-0.25	1.71

[a] Adjusted R square of the model=0.10
[b] Adjusted R square of the model=0.08
* p<0.05; ** p<0.01
Abbreviations; HADS: Hospital Anxiety and Depression Scale; DT: Distress Thermometer

Sociodemographic and clinical variables associated with PAHC questionnaire domains
Having children was statistically significantly associated with the domain 'hereditary predisposition'. Age and having had previous contact with a psychosocial worker were statistically significantly associated with the domain 'practical issues'. Having children, being the first in the family to undergo genetic counseling, and sex were statistically significantly associated with the domain 'family and social issues'. Having had previous contact with a psychosocial worker and having a personal history of cancer were statistically significantly associated with the domain 'general emotions'. Sex, the total number of children, and a known DNA-mutation in the family were statistically significantly associated with the domain 'living with cancer'.

At the multivariate level, having children was the only variable associated significantly with the domains 'hereditary predisposition (p=0.02) and 'family and social issues' (p=0.007). Having had former contact with a psychosocial worker was associated significantly with the domain 'practical issues' (p=0.04). No sociodemographic or clinical variables exhibited statistically significant associations with the domains 'general emotions', 'living with cancer' or 'child-related issues'. The variance in the PAHC domain scores explained by these regression models ranged from 2% to 14% (see Table 5).

Table 5. Sociodemographic and clinical variables associated with PAHC questionnaire domains

			95% CI for exp b		
	B(SE)	exp b	Lower	Upper	Nagelkerke R square
Hereditary predisposition					0.05
Having children	0.94(0.41) *	2.56	1.14	5.74	
Practical issues					0.10
Age	-0.37(0.02)	0.96	0.93	1.00	
Previous contact with psychosocial worker	-0.97(0.47)*	0.38	0.15	0.96	
Family – and social issues					0.14
Having children	1.27(0.47)**	3.56	1.41	8.94	
First in family to undergo genetic counseling	0.72(0.39)	2.06	0.96	4.39	
Sex	-0.33(0.54)	0.72	0.25	2.06	
General emotions					0.06
Previous contact with psychosocial worker	-0.57(0.39)	0.57	0.27	1.21	
Personal history of cancer	-0.75(0.39)	0.47	0.22	1.02	
Living with cancer					0.02
Sex	-0.35(0.87)	0.71	0.13	3.91	
Total number of children	0.29(0.38)	1.33	0.64	2.79	
Known mutation in family	0.53(0.68)	1.70	0.45	6.42	

Note: the domain of 'Child-related issues' did not yield any statistical significant factors
* $p<0.05$; ** $p<0.01$
Abbreviation; PAHC: Psychosocial Aspects of Hereditary Cancer questionnaire

DISCUSSION AND CONCLUSION

Discussion

In this paper we have reported on the prevalence of specific psychosocial problems experienced by counselees at the time that they attended a family cancer clinic for their first cancer genetic counseling session. Many counselees reported moderate to severe problems in the various domains assessed by the PAHC questionnaire, such as 'living with cancer', 'hereditary predisposition', 'family and social issues', and 'child-related problems'. These results are in line with those reported by Bennett and colleagues who, using a different questionnaire, found that up to two-thirds of counselees experienced concerns related to the impact of genetic counseling and testing on family members.[16] In our study, 54% of counselees reported problems on at least three different domains meriting discussion with the genetic counselor. It is important that such problems are being detected and discussed during genetic counseling,[17, 18] as that can lead to an improved relationship between counselor and counselee, and ultimately may result in lower levels of distress and possibly to alleviation of psychosocial problems.[19]

We also investigated the association between cancer genetic-specific problems as measured by the PAHC questionnaire and more generalized distress as measured by the HADS and the DT. The results showed that, with the exception of the domain 'general emotions', the correlations were low. This indicates that the specific domains of the PAHC are measuring problems that are only modestly related to psychological distress as measured by the HADS and the DT. This suggests that neither the HADS nor the DT should be employed as an initial screening instrument, if one is interested in detecting specific, cancer genetic problems. To do so would result in a significant loss of clinically relevant information about the problems and concerns of counselees undergoing cancer genetic counseling.

Some investigators have proposed using sociodemographic and clinical risk factors or risk profiles to identify individuals who are likely to be(come) distressed.[20, 21] We were able to identify some variables that are associated significantly with both generalized distress and specific cancer genetic-specific problems. However, the percentage of variance explained by these variables was consistently low. This suggests that sociodemographic and clinical variables cannot be used to identify particularly vulnerable subsets of genetic counselees. Rather, such background variables can be used as probes once a counselee reports being distressed and/or having specific psychosocial problems related to the genetic counseling process. For example, if a counselee reports family and social issues at the time of counseling, the counselor can inquire further about the potential role of having children and of being the first in the family being referred to genetic counseling.

We would stress the potential importance of asking counselees about their specific psychosocial problems at the time of cancer genetic counseling, prior to undergoing DNA-testing and receiving the DNA-test results. The PAHC questionnaire has the potential for being a valuable tool for clinical genetic counselors in increasing communication about psychosocial problems, and addressing those problems in a timely manner. Studies of the routine use of patient-reported outcome measures in daily clinical oncology practice have demonstrated their value in enhancing communication between patients and their health care providers.[22-26] We are currently conducting a randomized, controlled trial to determine if a similar procedure, using the PAHC questionnaire, yields similar benefits in the cancer clinical genetics setting.[27]

There are several limitations of the current study that should be noted. First, the large majority was female and was being counseled for hereditary breast and ovarian cancer. It is important to determine if the results obtained in our study hold equally for men, and for those at risk for other hereditary cancer syndromes. Second, questionnaires were administered either prior to or immediately following the genetic counseling session. This could potentially affect the prevalence of psychosocial problems as measured by the PAHC questionnaire, and the associations observed between the PAHC questionnaire and the HADS and DT, and between the PAHC questionnaire and various sociodemographic and clinical variables. However, our analyses indicated that the prevalence of psychosocial problems did not vary significantly as a function of the timing of the questionnaire

administration. Third, the domains of the PAHC questionnaire were correlated. While this could potentially complicate the interpretation of observed correlations between the PAHC, and other measures and variables, the use of partial correlations corrected for this.

The study also has a number of strengths. First, the sample was representative of the population undergoing genetic counseling in our clinic. Second, we included a number of commonly used measures and variables for identifying (potentially) distressed counselees, thus facilitating an analysis of the comparative usefulness of those screening methods.

Conclusion

Our results indicate that the majority of counselees experience specific problems in the context of cancer genetic counseling. More than half of the participants reported problems in at least three different domains of the PAHC questionnaire. None of the sociodemographic or clinical variables investigated proved to be important predictors, explaining only a small percentage (2-14%) of the variance in distress (HADS or DT) or the psychosocial problems (PAHC questionnaire).

Practice implications

Despite the fact that only a minority of individuals who undergo cancer genetic counseling suffer from high levels of psychological distress, the large majority reports a range of psychosocial problems related specifically to cancer genetic counseling. Sociodemographic and clinical background characteristics do not facilitate identifying those counselees with significant psychosocial problems, and more general measures of distress correlate only weakly with such problems. The PAHC questionnaire is a potentially useful tool for identifying relevant psychosocial problems that merit further attention in clinical practice. Use of such a tool may contribute significantly to enhancing the quality of communication between genetic counselors and their clients, to providing client-centered care, and to addressing relevant psychosocial problems in a timely manner.

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Chapter 5

The efficacy of a standardized questionnaire in facilitating personalized communication about problems encountered in cancer genetic counseling: Design of a randomized controlled trial

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ABSTRACT

Background

Individuals with a personal or family history of cancer, can opt for genetic counseling and DNA-testing. Approximately 25% of these individuals experience clinically relevant levels of psychosocial distress, depression and/or anxiety after counseling. These problems are frequently left undetected by genetic counselors. The aim of this study is to evaluate the efficacy of a cancer genetics-specific screening questionnaire for psychosocial problems, the Psychosocial Aspects of Hereditary Cancer (PAHC) questionnaire together with the Distress Thermometer, in: (1) facilitating personalized counselor-counselee communication; (2) increasing counselors' awareness of their counselees' psychosocial problems; and (3) facilitating the management of psychosocial problems during and after genetic counseling.

Methods

This multicenter, randomized controlled trial will include 264 individuals undergoing cancer genetic counseling in two family cancer clinics in the Netherlands. Participants will be randomized to either: (1) an intervention group that completes the PAHC questionnaire, the results of which are made available to the genetic counselor prior to the counseling session; or (2) a control group that completes the PAHC questionnaire, but without feedback being given to the genetic counselor. The genetic counseling sessions will be audiotaped for content analysis. Additionally, study participants will be asked to complete questionnaires at baseline, three weeks after the initial counseling session, and four months after a telephone follow-up counseling session. The genetic counselors will be asked to complete questionnaires at the start of and at completion of the study, as well as a checklist directly after each counseling session. The questionnaires/checklists of the study include items on communication during genetic counseling, counselor awareness of their clients' psychosocial problems, the (perceived) need for professional psychosocial support, cancer worries, general distress, specific psychosocial problems, satisfaction with care received, and experience using the PAHC questionnaire.

Discussion

This study will provide empirical evidence regarding the efficacy of a relatively brief psychosocial screening questionnaire in terms of facilitating personalized communication, increasing counselors' awareness, and optimizing management of psychosocial problems in the cancer genetic counseling setting.

Trial registration

This study is registered at the Netherlands Trial Register (NTR3205) and ClinicalTrials.gov (NCT01562431).

BACKGROUND

Genetic counseling is offered to individuals who are at high risk of carrying a cancer gene mutation and who are at high risk of developing hereditary cancer. Factors related to *hereditary* cancer are: a cancer diagnosis at a young age, multiple relatives with a similar cancer diagnosis or a specific combination of cancers and a proven gene mutation in the family.[1] Reviews of previous studies indicate that, on average, genetic counseling does not have adverse psychological effects (i.e., depression, anxiety, distress). However, approximately 25% of high risk individuals experience clinically relevant adverse psychosocial effects after counseling.[2-13]

It has been estimated that approximately one-third of counseless have some level of unmet need for psychosocial services in relation to genetic counseling.[14, 15] This is not entirely suprising, in that genetic counselors focus primarily on gathering and communicating biomedical information, and often have a 'teaching' communication style.[16] This creates a situation where there is less time available to discuss potentially relevant psychosocial issues.

Patient reported outcome (PRO) measures have been used in a range of health care settings as a tool to improve communication between patients and their health care providers about relevant physical and psychosocial health problems.[17-20] Facilitating such communication has been hypothesized to have a cascade of effects, including improved provider awareness of their patients' problems, improved patient care and management, including appropriate referrals, and ultimately, improved health outcomes.[21-24]

Recently, we developed a psychosocial screening questionnaire specifically for the clinical cancer genetics setting, the Psychosocial Aspects of Hereditary Cancer (PAHC) questionnaire.[25] The PAHC questionnaire comprises: (1) 26 items organized into 6 problem domains (i.e., hereditary predisposition, family- and social issues, practical issues, general emotional issues, cancer-specific issues, and, for those who have children, children-specific issues), with response options ranging from 1 ("not at all") to 4 ("very much"); (2) a question, per problem domain, about the desire to talk to a specialized psychosocial health professional; and (3) the Distress Thermometer (DT), a single item visual analogue scale ranging from 0-10, with 0 representing "no distress", and 10 "severe distress".[26]

The aim of this randomized, controlled trial is to evaluate the efficacy of the PAHC questionnaire when used routinely in daily clinical cancer genetics practice in: (1) facilitating communication during genetic counseling sessions about relevant psychosocial issues; (2) increasing genetic counselors' awareness of the psychosocial problems of their counselees; and (3) facilitating the appropriate management of these cancer genetic-specific psychosocial problems.

Specifically, our primary research hypotheses are that the use of the PAHC questionnaire during genetic counseling will:
(1) increase significantly the number of psychosocial issues discussed during genetic counseling sessions;
(2) increase significantly the genetic counselors' awareness of the psychosocial problems experienced by their counselees; and
(3) improve significantly the management of cancer genetic-specific psychosocial problems as evidenced by the referrals to psychosocial care and/or to sources of information about psychosocial issues.

Additionally, we hypothesize that the routine use of the PAHC questionnaire will:
(4) increase significantly the number of discussed issues initiated by the counselor;
(5) increase significantly counselees' satisfaction with the counseling process;
(6) decrease significantly counselees' levels of cancer worry and distress during and after the genetic counseling process;
(7) decrease significantly the cancer genetic-specific problems experienced by the counselee after the genetic counseling process; and
(8) *not* increase significantly the total duration of the genetic counseling session.

METHODS/DESIGN

This is a prospective, multicenter, randomized controlled trial in which participants will be randomly allocated to: (1) an intervention group that completes the PAHC questionnaire prior to genetic counseling, the results of which are provided to the genetic counselor; or (2) a control group that completes the PAHC questionnaire, without feedback being given to the genetic counselor. The study consists of two phases. In the first part of the study, the focus is on the efficacy of the intervention during the first face-to-face genetic counseling session. The second phase of the study is concerned with the efficacy of the intervention during a telephone follow-up held approximately 4 weeks after DNA-test results are disclosed in a final face-to-face counseling session.

The primary outcome measures are counselor-counselee communication about psychosocial problems, counselors' awareness of their counselees' psychosocial problems, and improved management of those problems. Secondary outcomes include satisfaction with the counseling process, cancer worries, psychological distress, and prevalence of psychosocial problems. The design of the study and the anticipated flow of participants are displayed graphically in Figure 1.

The institutional review boards of the Netherlands Cancer Institute in Amsterdam, and the University Medical Center Utrecht have approved the study. This study follows the CONSORT guidelines 27 and is registered at the Netherlands Trial Register (NTR3205) and ClinicalTrials.gov (NCT01562431).

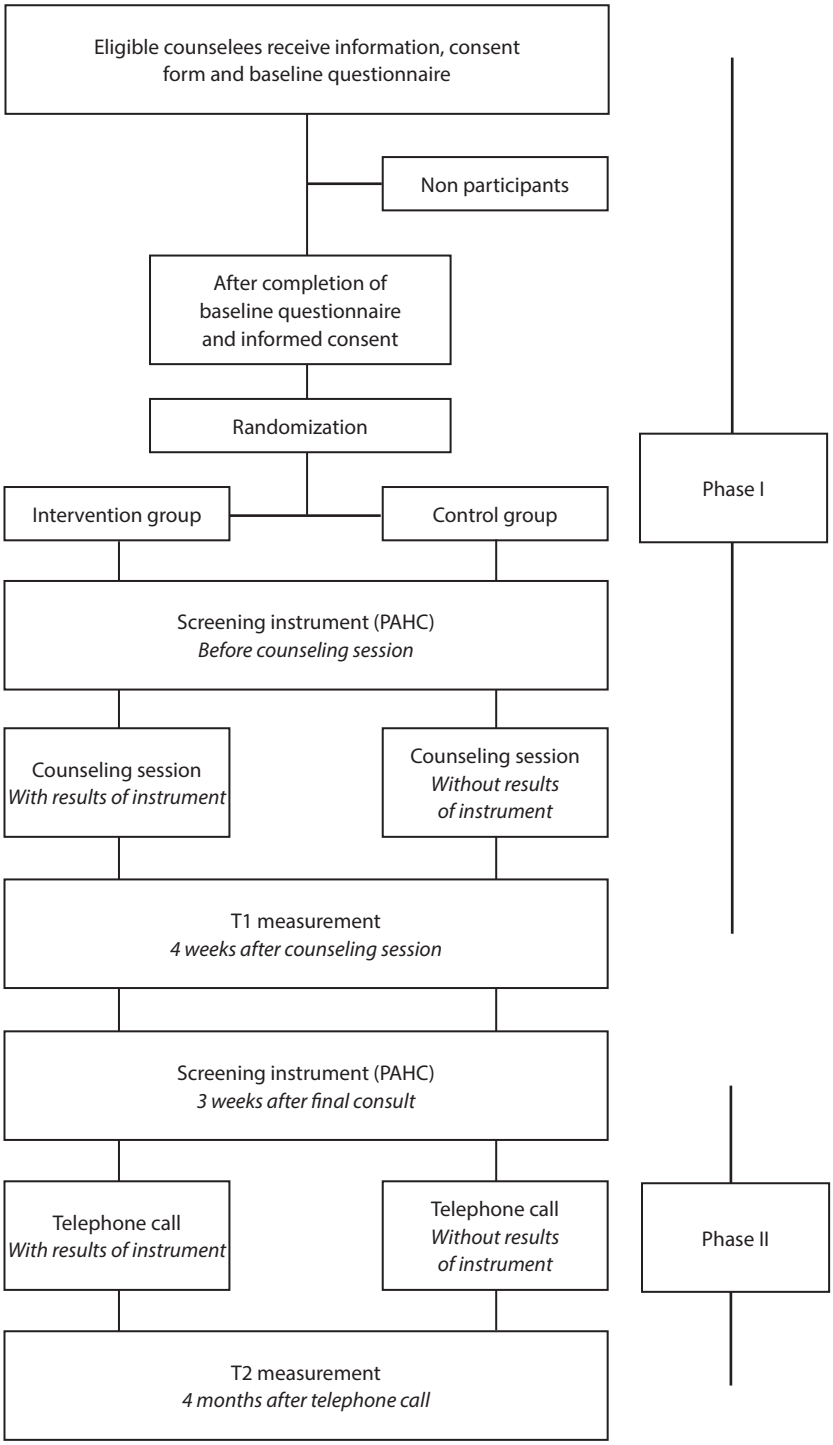

Figure 1. Design of the trial

Study sample

The study sample will be composed of 264 counselees who request genetic counseling at either the Netherlands Cancer Institute in Amsterdam or the University Medical Center Utrecht. Counselees will be excluded from the study if they are younger than 18 years of age, do not have basic fluency in the Dutch language or are participating in another study that would interfere with the current study.

Recruitment and randomization

All eligible counselees will receive an invitation letter from the family cancer clinic, an informed consent form, a baseline questionnaire, and a return envelope three weeks before their first counseling session. Upon returning the completed informed consent form and the baseline questionnaire, we will randomize the participants on a 1:1 basis to either the intervention group or the control group. The minimization method will be used to balance the intervention and control group for each counselor in terms of gender and the cancer syndrome for which genetic counseling is requested.[28] Neither the counselees nor the counselors will be (or can be) blinded to group assigment.

Intervention group procedure

Within the Netherlands, individuals seeking cancer genetic counseling routinely undergo a first consultation with a genetic counselor or a clinical geneticist and, when opting for a DNA-test, a final counseling session during which the DNA-test results are disclosed to the counselee. If indicated, screening recommendations for the patient and relatives are discussed within these sessions. The study intervention will take place within this standardized process, at the time of the first face-to-face genetic counseling session (phase I), and by telephone 4 weeks after the final face-to-face counseling session (phase II). The participants in the intervention group will be asked to complete the PAHC questionnaire either via the internet or, if preferred, by mail shortly before the face-to-face and the telephone follow-up counseling sessions. The counselee's responses to the PAHC questionnaire will be made available to the genetic counselor prior to the counseling sessions.

The PAHC questionnaire consists of 26 questions addressing psychosocial problems and worries that are specifically relevant to counselees within the cancer genetics counseling and testing setting. The content of the PAHC questionnaire is organized into the following six domains: (1) hereditary predisposition; (2) family- and social issues; (3) practical issues; (4) general emotional issues; (5) cancer-specific issues; and, for those who have children (6) children-specific issues. The number of items per domain varies between 2 and 7. All 26 items are scored on a 4-point, Likert-type scale ranging from 1 ("not at all") to 4 ("very much"). The PAHC questionnaire is supplemented by the Distress Thermometer (DT), a visual analogue scale ranging from 0-10 (no distress-severe distress). The timeframe of the PAHC questionnaire and the DT is the previous week. Per problem domain assessed by the PAHC questionnaire, the respondent is asked to indicate whether (s)he would like to receive professional psychosocial support.[25]

The results of the PAHC questionnaire + DT will be printed and attached to the counselee's medical record so that they are available to the genetic counselor prior to the relevant counseling session (face-to-face in phase I and telephone-based in phase II). To facilitate the genetic counselor's rapid review of the questionnaire output, all problem domains for which the counselee responds "quite a bit" or "very much" to at least one item are color coded *red*, indicating a problem area that should preferably be discussed during the counseling session. All other problem domains, are color coded *green*, indicating that there is, in principle, no need to discuss it during the counseling. Additionally, based on the literature and analysis of a validation of the DT in a previous study by our group using a heterogeneous sample of counselees for cancer in the Netherlands, a score of 4 or greater on the DT is used to indicate a clinically relevant level of distress.[25, 29] Finally, the counselor will receive information about whether the counselee is interested in obtaining additional professional psychosocial support for any given problem area. Scores on the DT above the cut-off point, and counselees' requests for additional psychosocial support are also color coded *red.* Additionally, to increase the ease of interpretation of the results, all items above the threshold will be printed in a bold font, and those items that are not above the threshold will be printed in light-grey. All counselors will receive written instructions/ guidelines and training in the use of the PAHC questionnaire and the DT.

Control group procedure

Counselees in the control group will complete the PAHC questionnaire and DT as described above for the intervention group. However, the results of these questionnaires will not be provided to the genetic counselors.

Timing and content of study measures

Counselees will be asked to complete questionnaires at: (1) baseline, prior to randomization; (2) approximately 4 weeks following the first genetic counseling session, before the final counseling session takes place; and (3) approximately 4 months after the telephone-based counseling session.

The counselors will be asked to complete a baseline questionnaire at the start of the study, a checklist at the end of each counseling session, and a final questionnaire at the end of the study. Both the in-person and the telephone-based genetic counseling sessions will be audiotaped by two independent raters (WE, GNS) for purposes of content analysis (see below). Inter-rater reliability will be assessed by double coding 10% of the audiotaped sessions, equally divided between the intervention group and control group sessions.

Sociodemographic and clinical data

The counselees' age, gender, marital status, education level, number and age of children, and use of psychosocial services in the past and during the study, will be obtained via the self-report questionnaires (see Table 1). Data on whether (s)he was diagnosed with cancer in the past and, if so, at what age, whether there is a known gene mutation in the family, the counselees' genetic test results, and the number of genetic counseling sessions will be extracted from the medical records.

The counselors' age, gender, and the number of years working at the family cancer clinic will be determined by questionnaire.

Table 1. Content and timing of study measures

	Content of the measurement	Timing of measurement
Counselees		
Baseline (first) questionnaire	Cancer worries	Before randomization
	General distress	
	Demographic data	
Second questionnaire (T1)	Evaluation of screening instrument	4 weeks after genetic counseling, before final consult, end of phase I
	Evaluation of counselor	
	General distress	
	Need for extra support	
	Cancer worries	
Third questionnaire (T2)	Specific psychosocial problems	4 months after the telephone call,
	Need for extra support	end of phase II
	Cancer worries	
	Evaluation of screening instrument	
	Satisfaction	
	General distress	
Counselors		
Checklist	Counselors' awareness	After each counseling session and telephone call
Baseline questionnaire	Demographic data	Before the beginning of trial
First questionnaire	Evaluation of screening instrument	After finishing the trial
Counselees and counselors	Audio tapes	Genetic counseling
		Telephone call, 4 weeks after DNA-test disclosure

Primary outcome measures

The primary outcomes of the trial are: (1) discussion of psychosocial problems; (2) counselors' awareness of the counselees' psychosocial problems; and (3) management of psychosocial problems during and after genetic counseling.

Discussion of psychosocial problems

Counselor-counselee communication about psychosocial issues will be assessed via content analysis of the audiotaped counseling sessions. Using a study-specific questionnaire, each counseling session will be coded for the specific psychosocial issues discussed during the counseling session. The coding reflects the 26 psychosocial issues of the PAHC questionnaire. Additionally, the percentage of counseling time devoted to the discussion of psychosocial issues will be calculated.

Counselors' awareness

Counselors' awareness of the psychosocial problems as experienced by their counselees will be assessed with a checklist completed by the counselors directly after the counseling sessions. The counselor will be asked to report whether (s)he believes that the counselee is experiencing problems in each of the 6 problem domains covered by the PAHC questionnaire on a 4-point scale ranging from (1, "no problem" to 4, "a severe problem"). The counselors' ratings will be compared to the responses provided by the counselees on the PAHC questionnaire.

Management of psychosocial problems

The audiotapes of the counseling sessions will also be used to evaluate how the counselees' psychosocial problems are managed. Specifically, the study-specific checklist will be used to code whether counselees were referred to additional sources of information about how to deal with psychosocial problems (e.g., websites or written materials) or to additional psychosocial counseling. The counselees will be asked to report their actual use of psychosocial services.

Secondary outcome measures

Secondary outcomes include: (1) initiation of problem discussion; (2) the time devoted to discussing each psychosocial problem and the total duration of the counseling session; (3) cancer worries and general psychological distress; (4) cancer genetics-specific psychosocial problems; and (5) counselees' and counselors' satisfaction with the genetic counseling and with the intervention (the latter for the intervention group only).

Initiation of psychosocial issue discussion, and time devoted to such discussions

The audiotapes of the counseling sessions will be coded for who initiated the discussion of each specific psychosocial issue (i.e., the counselee or the counselor), the amount of time spent talking about psychosocial issues, and the total length of the counseling session.

Cancer worries and general psychological distress

Cancer worries will be assessed using an adapted version of the Cancer Worry Scale (CWS) as used in previous studies.[14, 15, 30] The CWS is an 8-item questionnaire measuring the frequency of cancer worries, the impact of worries on mood, and the impact of worries on daily functioning.

The Hospital Anxiety and Depression Scale (HADS) will be used to assess general psychological distress.[31] The HADS includes 14 questions and yields a total score, as well as subscale scores for anxiety and depression. It has been validated for use in the Netherlands.[32]

Specific psychosocial problems

The PAHC questionnaire will be used to assess (changes over time in) specific psychosocial problems experienced by counselees in both the intervention and the control group. This will be evaluated at both the individual item as well as the problem domain level.

Satisfaction, evaluation and feasibility

Counselee and counselor satisfaction with both the genetic counseling itself and with the intervention (the latter for the intervention group only) will be assessed using an adapted version as used in a study by Bleiker et al.[33]

Sample size and power calculations

We have based the sample size estimates on expected differences between the intervention group and the control group in communication between the genetic counselors and counselees about psychosocial issues. Overall power calculations for estimating sample size requirements were based on the following criteria for defining a substantively meaningful statistical association: (1) power of 0.80, (2) α of 0.05, and (3) an effect size "*d*" of 0.4. With these criteria, 99 cases per study arm are needed, resulting in a total sample size of 198 cases.

We anticipate that approximately 25% of the counselees will not have more than one counseling session and thus will not have a DNA-test disclosure session. Therefore, in order to have sufficient power in the second phase of the trial, we will include 264 participants at the start of the trial.

Statistical analyses

All analyses will be performed on an intention-to-treat basis. Missing data on the HADS and CWS will be imputed using half-scale mean substitution methods. Data of participants who complete and return their first follow-up questionnaire after their final counseling session will be omitted from the analysis, because knowing the DNA-test result might influence questionnaire responses. Between rater agreement on the audiotaped sessions will be assessed by calculating the percentage of absolute agreement. Effect sizes will be calculated using standard statistical approaches.

Non-participant analysis

Based on experience with other studies, we anticipate that approximately 40% of eligible participants will decline to participate in the study. The non-participants will be compared with participants on available sociodemographic and clinical data using appropriate statistics (e.g., Student's t-test, or non-parametric test).

Comparability of intervention and control group

The comparability of the intervention and control groups at baseline will first be evaluated in terms of sociodemographic and clinical characteristics. Student's t-test or appropriate non-parametric tests will be used. If, despite the stratified randomization procedures, the groups are found to be statistically different on one or more baseline characteristics, these variables will be adjusted for in subsequent analyses.

Main research hypotheses

We will evaluate group differences in the number of psychosocial issues discussed during the genetic counseling sessions using analysis of (co)variance. We will assess counselors' awareness of their counselees' psychosocial problems by calculating the agreement between counselees' and counselors' on their ratings, per domain, of the psychosocial problems experienced by the counselees. We will calculate an Intraclass Correlation Coefficient (ICC2.1.A[34]) per domain for both the intervention and control group. Group differences will be assessed by treating the ICC's as Pearson correlation coefficients and using Fisher's r-to-z transformation to test for statistical differences per domain. Analysis of (co)variance will also be used to evaluate group differences in referral to additional information sources and/or referral to psychosocial care services, and the actual use of such services.

Secondary research hypotheses

We will employ analysis of (co)variance to evaluate group differences in the frequency with which the genetic counselor initiated the discussion of psychosocial issues. Analysis of (co)variance will also be used to evaluate group differences in the amount of counseling time spent discussing psychosocial issues, and the total length of the counseling session. To evaluate group differences in cancer worries and general distress, we will use analysis of covariance, with the previous scores on these questionnaires as covariate. Logistic regression analysis will be used to evaluate differences between groups in the prevalence of cancer genetics-specific problems. Group differences in satisfaction with the genetic counseling process will be examined with Student's t-tests and chi-square tests, where appropriate. Intervention group and counselor satisfaction with the intervention will be reported descriptively.

DISCUSSION

Previous studies have shown that psychosocial problems experienced by individuals undergoing genetic counseling for cancer are often left undetected and thus untreated. One way that has been proposed to address this problem is to make use of patient-reported outcome (PRO) measures in routine clinical practice to first identify, and then to manage relevant psychosocial issues. Previous studies that have evaluated the efficacy of implementing PRO measures in clinical settings have shown an increase in communication about health-related issues and an increase in clinicians' awareness of their patients' problems and, to a lesser extent an improvement in patient management and health over time.[21-23, 35] To our knowledge, no previous studies have investigated the value of using such PRO data in daily clinical cancer genetic counseling.

This clinical trial will evaluate the efficacy of using a relatively brief, psychosocial screening questionnaire, the PAHC questionnaire, in improving communication about, recognition of, and management of psychosocial problems among individuals undergoing cancer genetic counseling and testing.

Methodological issues

A major strength of the study is its use of a randomized design that will ensure high levels of internal validity. The relatively large sample size, the multicenter approach, and the heterogeneity of the study sample will increase the external validity and generalizability of the findings.

Several possible limitations of the study should also be noted. First, due to the nature of the intervention, it is not possible to blind the genetic counselors, nor the counselees, nor the raters of the audiotapes to group allocation. This carries with it the risk of contamination, particularly on the part of the counselors. That is, any given genetic counselor will be seeing both counselees assigned to the intervention group and the control group. Thus, it is conceivable that the counselors' experience with the intervention (i.e., receiving personalized feedback regarding the counselees' self-reported psychosocial problems) will also affect the way they interact with counselees in the control group. We would note, however, that any such carry over effect will have a conservative effect on the study (i.e., that, if anything, it will make it more difficult to observe significant group differences on the primary study outcomes). A second possible limitation of the study will depend on the observed prevalence of psychosocial problems among counselees. If the prevalence is low, then it will be more difficult to detect group differences in the various study outcomes. Finally, due to funding limits, the follow-up period for the second phase of the trial is relatively short (only 4 months).

CONCLUSION

If proven efficacious, the introduction of a standardized procedure for assessing the psychosocial problems and needs of individuals undergoing cancer genetic counseling and testing will be a welcome addition to current clinical practice. It will facilitate timely discussion, detection and treatment of psychosocial issues specific to the cancer genetics setting. This is particularly important given the fact that the number of requests for genetic counseling is expected to continue to increase in the future. This will place additional demands on the time and resources of genetic counselors. Tools that facilitate early detection and treatment, or referral of those with specific psychosocial problems and concerns, are welcome.

Authors' contributions

NKA, IK, DEEH, and EMAB are the principal investigators of this study. WE is the PhD student on this study, and generated the first draft of this manuscript based on the study protocol. MGEMA is the clinical geneticist at University Medical Center Utrecht. GNS is the research assistant on this study. All authors approved the final version of the manuscript.

Competing interests

The authors declare that they have no competing interests.

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Chapter 6

The effect of routine assessment of specific psychosocial problems on personalized communication, counselors' awareness, and distress levels in cancer genetic counseling practice: A randomized controlled trial

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ABSTRACT

Purpose

This study evaluated the efficacy of a cancer genetics-specific questionnaire in facilitating communication about, awareness of, and management of psychosocial problems, as well as in lowering distress levels.

Methods

Individuals referred to genetic counseling for cancer at two family cancer clinics in the Netherlands were randomly assigned to either an intervention or a control group. All participants completed the psychosocial questionnaire prior to counseling. In the intervention group, the counselors received the results of this questionnaire prior to the counseling session. All sessions were audiotaped for content analysis. Primary outcomes were the frequency with which psychosocial problems were discussed, the genetic counselors' awareness of these problems, and their management. Secondary outcomes included cancer worries and psychological distress, duration and dynamics of the counseling, and satisfaction.

Results

The frequency with which psychosocial problems were discussed with 246 participating counselees was significantly higher in the intervention group (n=127) than the control group (n=119; p=0.004), as was the counselors' awareness of psychosocial problems regarding 'hereditary predisposition' (p<0.001), 'living with cancer' (p=0.01), and 'general emotions' (p<0.001). Counselors initiated more discussion of psychosocial problems in the intervention group (p<0.001), without affecting the length of the counseling session. No significant differences were found on management (p=0.19). The intervention group reported significantly lower levels of cancer worries (p=0.005), and distress (p=0.02) after counseling.

Conclusion

The routine assessment of psychosocial problems by questionnaire facilitates genetic counselors' recognition and discussion of their clients' psychosocial problems, and reduces clients' distress levels.

This trial is registered at ClinicalTrials.gov, number NCT01562431.

INTRODUCTION

In general, genetic counseling for cancer does not have serious adverse psychological effects,[1-3] but approximately 25% of counselees experience heightened levels of anxiety, depression and/or distress during or after counseling.[4-9] In addition, less than or equal to three fourths of counselees report some degree of psychosocial problems related specifically to genetic counseling and testing for cancer.[10] This includes, among other issues, coping with cancer risk and living with cancer in the family.[11, 12] Ideally, such problems should be recognized and discussed during genetic counseling.[13] However, genetic counselors tend to focus primarily on biomedical issues, with relatively little attention being paid to counselees' psychosocial problems.[14]

Research within the broader field of clinical oncology has demonstrated that the routine use of patient-reported outcome (PRO) measures in clinical practice facilitates the discussion of health-related issues without lengthening the consultations.[15] Facilitating such discussion can have multiple positive effects, including improved physicians' awareness of their patients problems, improved management of patients' problems, increased patient satisfaction, and improved health outcomes.[16] These effects are all part of raising the quality of patient-centered care.[17]

We have developed a PRO measure for assessing psychosocial problems specific to the cancer genetic setting. The Psychosocial Aspects of Hereditary Cancer (PAHC) questionnaire covers six domains (see Intervention Procedure) and has thresholds indicating whether a specific problem area merits further discussion during the counseling session.[18]

In the current randomized controlled trial we have evaluated the efficacy of using the PAHC questionnaire to provide genetic counselors with important information on the psychosocial problems experienced by their counselees. Our primary research hypotheses were that the routine use of the PAHC questionnaire would increase significantly the frequency with which a range of psychosocial problems are discussed during genetic counseling, increase significantly genetic counselors' awareness of their counselees' psychosocial problems, and improve significantly the management of these psychosocial problems, as evidenced by referrals to psychosocial care and/or to sources of information about psychosocial issues. Second, we hypothesized that the routine use of the PAHC questionnaire would result in genetic counselors taking more initiative in raising and addressing psychosocial issues, decrease significantly counselees' levels of cancer worries and generalized psychological distress, increase significantly counselees' satisfaction with genetic counseling, and not increase significantly the total duration of the genetic counseling session.

METHODS

Study sites and participants

All counselees who underwent genetic counseling for cancer at the Netherlands Cancer Institute in Amsterdam or the University Medical Centre Utrecht were invited to participate if they were older than 18 years, had basic fluency in the Dutch language, and were not participating in competing psychosocial studies. All eligible counselees received a letter providing information on: the purpose of the study, the study procedures, including randomization and audiotaping the counseling session, and an informed consent form, together with the baseline questionnaire via the mail 3 weeks before their counseling session. A reminder letter was sent, and an adjacent phone call was made 1 week before the counseling session. All participants provided written informed consent prior to randomization.

Trial design and randomization

Participants were randomly assigned to an intervention group or a control group. The minimization method was used to balance the intervention and control groups in terms of counselor, gender and the cancer syndrome for which the counselee was referred.[19] Because of the nature of the intervention, it was not possible to blind the counselees, the counselors, or the raters to group assignment.

The institutional review boards of the two participating hospitals approved the study. The trial is registered at the Netherlands Trial Register (NTR3205) and ClinicalTrials.gov (NCT01562431), and is reported in accordance with the CONSORT guidelines.[20-22] A detailed description of the trial design is reported elsewhere.[23]

Intervention procedure

In the Netherlands, the cancer genetic counseling procedure routinely includes an initial face-to-face counseling session during which personal and familial cancer history are discussed, pedigree data are discussed, the personal medical history is taken, and psychosocial problems and concerns are addressed. Most counselees opt for a DNA-test at the end of this session. During a subsequent counseling session, the results of DNA-testing are disclosed, if applicable, and screening advice for the counselee and relatives is provided.[24]

Our trial consisted of two distinct phases: a first phase with an intervention at the time of the initial counseling session and a second phase with an intervention, including a novel telephone contact 4 weeks after the final counseling session. The supplemental telephone session was not a standard procedure within the genetic counseling process, and thus, the second phase of the trial cannot be viewed simply as a follow-up of the first phase. Therefore, the results of this second phase will be reported in a subsequent paper.

Participants in both study groups were asked to complete the PAHC questionnaire by Internet or mail before their counseling session. A summary of the questionnaire results was attached to their medical file prior to the counseling session of the intervention group counselees only.

The 26-item PAHC questionnaire is cancer genetics-specific and is grouped into six domains: hereditary predisposition, practical issues, family and social issues, general emotions, living with cancer, and child-related issues for those who have children. All 26 items are scored on a four-point Likert-type scale ranging from 1 (not at all) to 4 (very much). The PAHC questionnaire is supplemented by the Distress Thermometer (DT), a visual analogue scale ranging from 0 to 10 (no distress to severe distress).[25] The timeframe used is the previous week. Per problem domain counselees are asked to indicate whether they would like to receive professional psychosocial support.

In a previous study, we established a threshold per domain on the PAHC questionnaire. If one or more items within a domain had a score of three or higher (i.e., at least one problem of moderate intensity within a domain), or the score on the DT was four or higher, then this was considered relevant for discussion during the genetic counseling.[18]

The summary of the questionnaire was color coded such that, if a domain and/or the DT score was above the threshold or if the counselee indicated wishing to receive additional psychosocial support, this was highlighted in red. All other scores were colored green. In addition, the text of the items with a score of three or four on the questionnaire was printed in bold type versus light gray for all others. Counselors received guidelines and training in how to interpret scores on the PAHC questionnaire, ask follow-up questions, and provide referrals to other health care services.

Outcomes and study measures

Sociodemographic and clinical characteristics

Before random assignment (baseline), participants completed a brief questionnaire on sociodemographic characteristics, the use of psychosocial services in the past, and whether they were the first in the family requesting cancer genetic counseling. Clinical characteristics were extracted from the medical record. Participating counselors completed a short series of questions on sociodemographics and years of work experience.

Primary outcome measures

Discussion of psychosocial problems. The genetic counseling sessions were audiotaped and content analyzed using a checklist to determine how many items from the PAHC questionnaire, the DT, or other problems were being discussed during the counseling session (range, 0 to 28). Two independent raters (WE and GNS) coded the audiotapes. A 10% random sample was double coded to assess inter-rater reliability. Agreement between the raters was good (76%). Each rater rated approximately an equal number of intervention and control group audio-taped sessions.

Counselors' awareness. After the counseling session, counselors completed a brief checklist that covered each of the six problem domains of the PAHC questionnaire on a four-point scale ranging from 1, (no problem) to 4 (a severe problem). These ratings were compared to the counselees' ratings on the PAHC questionnaire.

Management of psychosocial problems. The content analysis checklist was also used to code whether counselees received extra psychosocial-related patient information (e.g., written materials, Web sites) or referral to psychosocial services. Actual use of psychosocial services was assessed four weeks after the counseling session by counselee self-report.

Secondary outcome measures

Initiation of discussion of problems and total duration of the counseling session. The content analysis checklist was also used to determine whether the counselor, the counselee, or the partner or family member (if present) initiated the discussion of any given psychosocial problem, and to record the total duration of the session.

Cancer worries and general psychological distress. Cancer worries were assessed using an adapted version of the Cancer Worry Scale (CWS).[26] The CWS is an eight-item questionnaire, with a four-point response scale (range, 8 to 32). General distress was measured with the Hospital Anxiety and Depression Scale (HADS).[27] The HADS includes 14 questions, with a four-point response scale (range, 0 to 42). Cronbach's α coefficient for the CWS and the HADS was 0.83 and 0.90, respectively.

Satisfaction and evaluation. Counselees' satisfaction with the initial counseling session was assessed 4 weeks after counseling with an adapted version of a 24-item questionnaire used in previous research in the cancer genetic counseling setting.[28]

Sample size and power calculation

Sample size calculations were based on similar, previous studies,[29, 30] by using expected differences in the discussion of problems. With power set at 0.80, α at 0.05, and effect size (Cohen's *d*) at 0.4, a total of 99 cases per study arm were needed, resulting in a required sample of 198 cases for the first study phase.

Statistical analyses

All statistical analyses were performed on an intention-to-treat basis. We used analysis of variance and chi-square tests to compare study participants and nonparticipants, as well as the two study groups on sociodemographic and clinical characteristics. Missing data on the HADS and CWS were imputed using half-scale mean substitution methods. Follow-up data completed and returned after the DNA-test disclosure, if applicable, were omitted from the analysis, because the DNA-test result itself might have had an impact on distress and cancer worries.

We used multilevel analysis to evaluate differences between groups in the number of psychosocial issues discussed during the counseling session. Counselors' awareness of the

counselees' psychosocial problems was assessed by calculating the intraclass correlation coefficient 2.1.A [31]) per domain for both the intervention and control group. Subsequently, we used Fisher's *r*-to-*z* transformation to obtain *z* scores.[32] The between-group differences were divided by the standard error to yield a standard *z* score, which was used to test for significance. We used chi-square tests to assess group differences in the management of psychosocial problems and the use of psychosocial services.

Multilevel analysis was used to compare groups on the frequency with which the counselor initiated the discussion of psychosocial problems, the total length (in minutes) of the counseling session, cancer worries, and general distress. Baseline scores of cancer worries and general distress were used as covariates. We used chi-square tests to evaluate group differences in satisfaction. Effect sizes (Cohen's *d*) were calculated by dividing the mean group differences by the pooled standard deviation. The 95% CIs of the means, intraclass correlation coefficients, and effect sizes were calculated.

All statistical tests were two-sided, with *α* set at 5%. To control for multiple comparisons, we calculated false discovery rates, which take into account the ranking of the obtained P values and the number of tests.[33] Calculation of the false discovery rate did not alter our conclusions, with all observed p-values falling below the established thresholds.

RESULTS

Sociodemographic and clinical characteristics

Between October 2011 and December 2012, we invited 571 eligible individuals, of whom 246 (46%) agreed to participate and were randomly assigned to the intervention (n=127) or control group (n=119) (Figure 1). No statistically significant differences in sociodemographics or clinical variables were found between participants and nonparticipants, between the intervention and the control group, or between participants who were or were not included in the analysis at 4 week follow-up.

The mean age of participants was 48 years (range, 19 to 77 years) and most were female, had a steady relationship, and had children. Approximately half of the participants were relatively highly educated, approximately 60% had a family history of breast and/or ovarian cancer, and slightly less than half had a personal history of cancer (Table 1).

A total of 11 counselors, 5 at the Netherlands Cancer Institute and 6 at the University Medical Centre Utrecht, participated in the study, of whom one discontinued participation because of change of job. Their mean age was 40 years (range, 26 to 56 years), with an average of six years of working experience in cancer genetics (range, 0 to 16 years).

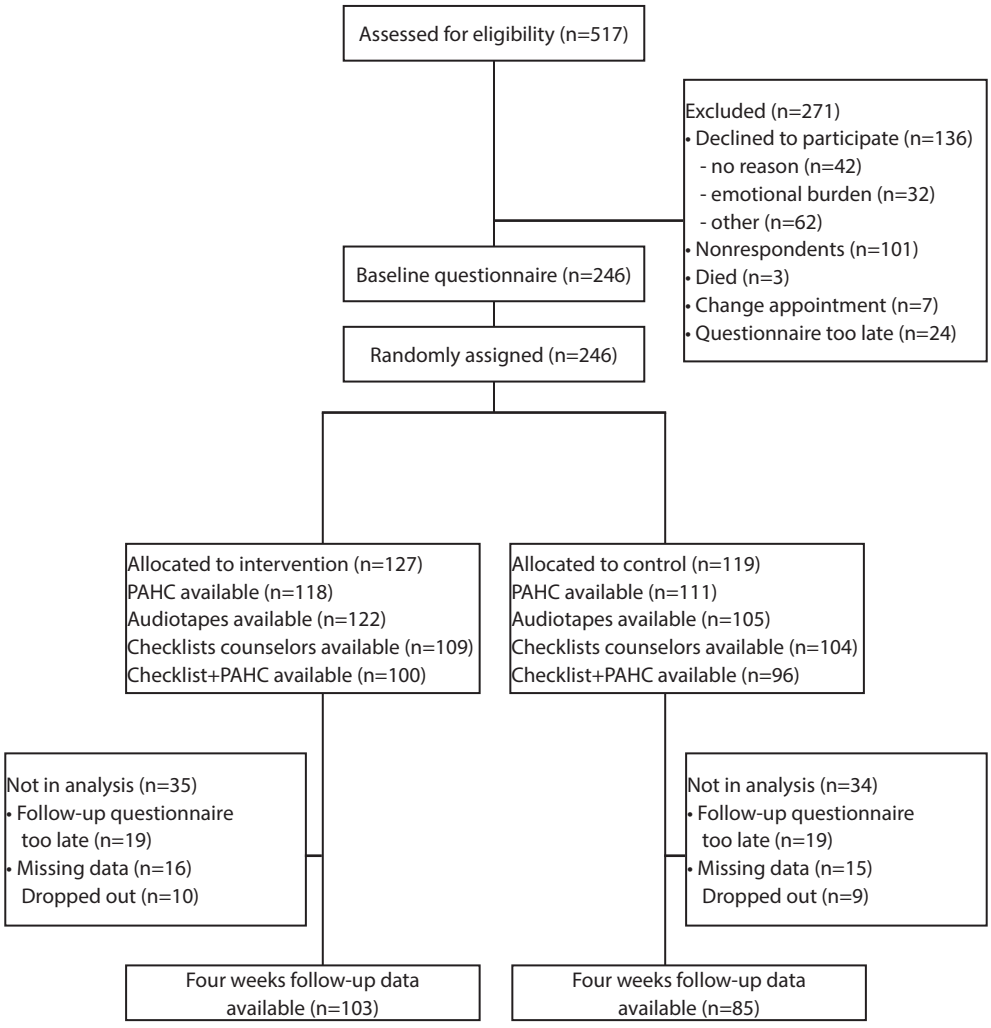

Figure 1. Flow diagram

Primary outcomes

Discussion of psychosocial problems

The mean number of psychosocial problems discussed during the counseling session was significantly higher in the intervention group (8.81; 95% CI, -0.55 to 18.17) than the control group (7.27; 95% CI, -1.33 to 15.87; p=0.004, *d*=0.15; Table 2).

Counselors' awareness

Counselors' awareness on all domains of the PAHC questionnaire was higher in the intervention group compared to the control group. Group differences reached statistical significance for the problem domains of 'hereditary predisposition' ($p<0.001$) 'general emotions' ($p<0.001$), and 'living with cancer' ($p=0.01$).

Management of psychosocial problems

There were no statistically significant between-group differences in the management of psychosocial problems or in the actual use of psychosocial services.

Table 1. Sociodemographic and clinical characteristics of participants at baseline assessed prior to randomization, and prevalence of problems assessed with the PAHC questionnaire prior to the counseling session

	Intervention (n=127)		Control (n=119)	
	n	%	n	%
Age (years)				
Mean	48.51		47.60	
SD	12.06		13.90	
Gender				
Male	26	20	24	20
Female	101	80	95	80
Marital status				
Married/in a relationship	100	79	98	82
Single/not in a relationship	27	21	21	18
Educational level				
Low (< high school)	30	24	25	21
Middle (≥high school)	36	28	34	29
High (≥college)	61	48	60	50
Children				
Yes	94	74	88	74
No	33	26	31	26
Former contact with a psych. worker	n=126		n=118	
Never	58	46	52	44
0-5	26	21	26	22
5-10	11	9	19	16
>10	31	24	21	18
First in family requesting genetic counseling	n=126		n=116	
Yes	81	64	73	63
Yes, together with others	7	6	10	9
No	38	30	33	28

Table 1. *(continued)*

	Intervention		Control	
	n	%	n	%
Cancer syndrome for which counseling is requested	n=127		n=119	
Breast	76	60	74	62
Colon	16	13	13	11
Other	35	28	32	27
Former cancer diagnosis				
Yes (1 or more diagnoses)	58	46	54	45
No	69	54	65	55
Prevalence of problems at counseling session	n=118		n=111	
Hereditary predisposition	40	34	47	42
Practical issues	15	13	17	15
Family issues	24	20	30	27
General emotions	22	19	26	23
Living with cancer	91	77	93	84
Child related problems	40	34	38	34

Note: No statistically significant differences were found between groups on any variable
Abbreviation: SD, standard deviation

Secondary outcomes

Initiation of the discussion of psychosocial problems and the total duration of the counseling session

The counselors initiated discussion of psychosocial problems significantly more often in the intervention than in the control group ($p<0.001$, $d=0.27$; Table 3). The total length of the counseling session did not differ significantly between the groups (approximately 40 minutes).

Cancer worries and general psychological distress

Four weeks after the counseling, participants in the intervention group reported significantly lower levels of cancer worries ($p=0.005$, $d=0.41$), and general psychological distress ($p=0.02$, $d=0.33$) than did the control group.

Counselees' satisfaction

No significant group differences were observed in counselees' satisfaction with the genetic counseling session (results not shown).

Table 2. Primary outcomes; Number of discussed psychosocial problems, counselors' awareness of experienced problems, and management of the psychosocial problems

	Intervention (n=122)		Control (n=105)				
	Mean	95% CI	Mean	95% CI	p-value [b]	effect size	95% CI
Total number of discussed problems (0-28) [a]	8.81	- 0.55 to 18.17	7.27	-1.33 to 15.87	0.004	0.15	-0.11 to 0.41
Counselors' awareness (ICC 2.1.A)		n=100		n=96			
Hereditary predisposition issues	0.52	0.36 to 0.65	-0.03	-0.22 to 0.17	<0.001		
Practical issues	0.40	0.22 to 0.55	0.19	-0.01 to 0.38	0.11		
Family issues	0.36	0.16 to 0.53	0.22	0.02 to 0.41	0.30		
General emotions	0.51	0.33 to 0.65	0.02	-0.18 to 0.22	<0.001		
Living with cancer	0.41	0.17 to 0.59	0.07	-0.07 to 0.22	0.01		
Child related problems	0.46	0.26 to 0.62	0.30	0.08 to 0.49	0.19		
Management of the psychosocial problems		n=122		n=105	0.19		
No actions	51		53				
1 or more	71		52				
Actual use of psychosocial services at follow-up					0.82		
Yes	10		10				
No	93		75				

[a] Adjusted for clustering at counselor and hospital levels

[b] Controlled for multiple testing with the FDR procedure: rank of the p-value (low to high) divided by the number of tests multiplied by the α for type I error. If the statistically significant p-value is lower than the accompanying FDR value, H_0 can be rejected

Abbreviation: ICC, Intraclass Correlation Coefficient

Table 3. Secondary outcomes; Total duration of the counseling session, initiation of the discussion about psychosocial problems, general distress, and cancer worries

	Intervention group		Control group				
	Mean	95% CI	Mean	95% CI	p-value [h]	effect size	95% CI
Duration of the counseling session (minutes) [a, b]	41.09	37.28 to 44.89	39.67	35.76 to 43.57	0.37	0.07	-0.19 to 0.33
Total number of discussed problems initiated by the counselors [b,c]	4.55	-0.23 to 9.32	3.06	-1.35 to 7.46	<0.001	0.27	0.01 to 0.53
HADS							
Baseline [d]	8.31	7.07 to 9.55	9.03	7.77 to 10.29			
Follow-up [e,f]	6.29	4.98 to 7.59	8.38	6.96 to 9.81	0.02	0.33	0.04 to 0.62
CWS							
Baseline [d]	13.86	13.22 to 14.49	14.32	13.66 to 15.01			
Follow-up [e,g]	12.63	11.93 to 13.34	14.09	13.30 to 14.87	0.005	0.41	0.12 to 0.70

[a] Adjusted for clustering at counselor level
[b] Number of participants in analysis; 122 in intervention group, 105 in control group
[c] Adjusted for clustering at counselor and hospital levels
[d] Number of participants; 127 in intervention group, 119 in control group
[e] Adjusted for baseline and clustering at the counselor level, measured 4 weeks after the counseling session
[f] Number of participants in analysis; 102 in intervention group, 85 in control group
[g] Number of participants in analysis; 103 in intervention group, 84 in control group
[h] Controlled for multiple testing with the FDR procedure: rank of the p-value (low to high) divided by the number of tests multiplied by the α for type I error. If the statistically significant p-value is lower than the accompanying FDR value, H0 can be rejected
Abbreviations: HADS; Hospital Anxiety and Depression Scale, CWS; Cancer Worry Scale

DISCUSSION

As hypothesized, providing genetic counselors with information about specific psychosocial problems via a standardized questionnaire increased significantly the frequency with which such problems were discussed. However, the magnitude of the effect was quite modest and lower than that observed in other studies on the use of PRO measures in clinical practice.[29,30,34] The intervention had a stronger effect on the frequency with which the counselors' initiated discussion of psychosocial issues. Importantly, use of the questionnaire did not increase the duration of the counseling sessions, a finding that has been reported in earlier studies.[29, 34]

The effect of the intervention on counselors' awareness of counselees' psychosocial problems was substantial, particularly with regard to problems in the area of 'hereditary predisposition', 'general emotions', and 'living with cancer'. Effects on awareness were of approximately the same magnitude as those observed in a similar study among cancer nurses and patients undergoing chemotherapy.[30]

Importantly, we observed a statistically and clinically relevant effect of the intervention on general distress and cancer worries. This has rarely been observed in previous studies.[15,35,36] The differences we observed in HADS scores exceeded the 1.5 point difference used to define clinical relevance.[37] The observed effect sizes for distress and cancer worries (0.33 and 0.41, respectively) are substantially larger than those reported previously (0.16).[38]

The intervention did not alter behavior in terms of the counselors' management of problems or actual use of psychosocial services, yet we did observe a significant effect on distress and worry scores. This suggests that counselors' awareness and acknowledgement of problems may, in and of itself, have a salutary effect on counselees' well-being without the need for any additional interventions. Additional research is needed to determine whether certain qualitative elements of communication (e.g., empathic utterances, or non-verbal communication) can elucidate the pathways through which this intervention contributes to reducing distress and cancer worries.

Our study had several limitations that should be noted. First, because the genetic counselors counseled both intervention and control group patients, there was a risk of a contamination effect. However, secondary analyses of data from the control group (i.e., difference in the frequency with which psychosocial issues were discussed between the first five and the last five sessions) did not suggest any such effect. If such an effect had been present, it would have had a conservative effect on the study results.

Second, all study participants completed the PAHC questionnaire before their counseling session. Although this could have potentially affected the communication of problems in the control group, a study by Velikova et al.[34] found no evidence of such an effect.

Third, the raters of the audiotapes were not be blinded to the randomization. This was unavoidable, because the PAHC questionnaire was frequently mentioned explicitly during the intervention group sessions.

Fourth, the percentage of individuals who participated in the study was relatively low (46%). However, this participation rate is similar to that observed in comparable studies.[39,40]

Fifth, our study sample consisted of predominantly highly educated women, and a relatively high percentage of individuals who had had previous contact with a psychosocial worker. This suggests that participants in our study may have had more interest in or concern with psychosocial issues than the larger population of counselees from which they were drawn. However, participants did not differ from the nonparticipants on any available background variables. In addition, follow-up data on the HADS and the CWS were available for only 84% and 71% of the intervention and control group, respectively.

Our study also had several strengths, including its randomized design, its multicenter nature, the use of both observational and self-reported outcomes, and the use of standardized outcome measures, where possible.

In conclusion, our results indicate that providing genetic counselors with summaries of counselees' self-reported, cancer genetic-specific psychosocial problems primarily raises counselors' awareness of those problems and facilitates their discussion. Importantly, this relatively simple intervention appears to also have a salutary effect on distress levels, at least in the short term. Although it is important to replicate these findings in future studies, the results are sufficiently robust to recommend introduction of this intervention in daily cancer clinical genetics practice.

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Chapter 7

Routine assessment of psychosocial problems after cancer genetic counseling: Results from a randomized controlled trial

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ABSTRACT

Introduction

Approximately 70% of counselees undergoing cancer genetic counseling and testing (CGCT) experience some degree of CGCT-related psychosocial problems. We evaluated the efficacy of an intervention designed to increase detection and management of problems four weeks after completion of CGCT.

Methods

In this randomized, controlled trial, 118 participants completed a CGCT-related problem questionnaire prior to an -audiotaped- telephone session with their counselor one month after DNA-test disclosure. For those randomized to the intervention group (n=63), a summary of the questionnaire results was provided to the counselor prior to the telephone session. Primary outcomes were discussion of the problems, counselors' awareness of problems, and problem management. Secondary outcomes included self-reported distress, cancer worries, CGCT-related problems, and satisfaction.

Results

Counselors who received a summary of the questionnaire were more aware of counselees' problems in only one psychosocial domain (practical issues). No significant differences in the number of problems discussed, in problem management, or on any of the secondary outcomes were observed. The prevalence of problems was generally low.

Conclusions

The telephone session, combined with feedback on psychosocial problems, has minimal impact. The low prevalence of psychosocial problems one month post-CGCT recommends against its use as a routine extension of the CGCT procedure.

This trial is registered at Clinicaltrials.gov (NCT01562431).

INTRODUCTION

Approximately one-quarter of counselees experience heightened levels of distress, depression and/or anxiety after cancer genetic counseling and testing (CGCT).[1] A large percentage of counselees (up to 83%) report a broader range of CGCT-related psychosocial problems, including family communication issues, coping with the DNA-test result, and fear of developing cancer while awaiting the test results.[2, 3]

Most CGCT protocols involve direct, face-to-face contact with counselees.[4, 5] Van Oostrom and Tibben have proposed a counseling model that includes a follow-up telephone contact with counselees approximately 2-3 weeks after having received a positive test result for a *BRCA1/2* gene mutation.[6] Intensive post CGCT telephone counseling has been shown to reduce short term distress in female mutation carriers.[7] However, not only mutation positive individuals seek psychosocial support after completion of the CGCT procedure.[8]

Previous research has demonstrated that the routine use of a questionnaire in clinical practice has a multitude of positive effects on both process of care and patient outcomes.[9] In a two-phase randomized controlled trial we investigated the efficacy of providing genetic counselors with a summary of the results of a CGCT-related psychosocial problem questionnaire (the PAHC questionnaire).[10] Key results of the first phase, at the initial counseling session, were that the counselors' awareness of counselees' problems was increased substantially, and levels of general distress and cancer worries decreased.[11]

In this paper, we report the results of the second phase of the trial in which we investigated the efficacy of the routine provision of information about the psychosocial problems of counselees to genetic counselors as part of a telephone session held one month after the CGCT procedure. As was the case in the first phase of the RCT, it was hypothesized that the intervention would increase the frequency with which psychosocial problems were discussed, counselors' awareness of and management of such problems, and would have a positive effect on general distress, cancer worries, satisfaction and acceptability, and prevalence of specific CGCT-related problems. We also hypothesized that the duration of the telephone session would not be affected by the intervention.

METHODS

The design of the RCT and the results of the first phase of the trial have been reported elsewhere.[10, 11] Here we describe briefly the overall trial design, and provide more details on the methods of the second phase of the trial.

Study sites and subjects

All individuals who underwent genetic counseling for cancer at the Netherlands Cancer Institute or the University Medical Center Utrecht in the period October, 2011 to December, 2012 were invited to participate. Participants had to be 18 years of age or older, have basic fluency in the Dutch language, and not be participating in competing psychosocial studies. Those counselees who underwent diagnostic or presymptomatic DNA-testing themselves and had their final counseling session prior to December 15, 2012 were eligible to be included in the second phase of the trial.

Eligible individuals received an information letter from the family cancer clinic, an informed consent form, a baseline questionnaire and a return envelope via the mail approximately three weeks before their first scheduled genetic counseling session. Participants provided written informed consent prior to randomization.

Trial design and randomization

Participants were randomized to an intervention group or control group using the minimization method to balance the groups in terms of counselor, gender and the cancer syndrome.[12] Blinding of the randomization was not possible due to the nature of the intervention.

The institutional review boards of both hospitals approved the study. The trial is registered at the Netherlands Trial Register (NTR3205) and ClinicalTrials.gov (NCT01562431), and is reported in accordance with CONSORT guidelines.[13-15]

Intervention procedures

In the Netherlands, counselees undergoing genetic counseling for cancer routinely have an initial face-to-face counseling session. Possible DNA-test results are disclosed in a final counseling session, at which time screening or other advice for the counselee and relatives is provided.[6]

In phase 2 of this trial, we introduced a telephone session one month following completion of the CGCT procedure. The intent of this telephone session was for the genetic counselor to ask the counselee if (s)he had any unanswered questions about the CGCT process, the DNA-test result, the screening advice that was given, and other issues, including psychosocial problems.

Before the telephone session all participants were asked to complete the PAHC questionnaire via the internet or, if preferred, by mail prior to the session with their counselor. A summary of the results of the questionnaire was provided to the counselor only for those counselees in the intervention group.

The PAHC questionnaire used after completion of the CGCT procedure consists of 24 items, grouped into six domains: (1) hereditary predisposition; (2) practical issues; (3) family – and social issues; (4) general emotions; (5) living with cancer; and (6), where relevant,

child-related issues. All items are scored on a 4-point, Likert-type scale ranging from 1 ("not at all") to 4 ("very much"). It is supplemented by the Distress Thermometer (DT), a visual analogue scale ranging from 0-10 (no distress-severe distress).[16] The timeframe used is the previous week. Per problem domain on the PAHC questionnaire, participants can indicate their need for professional psychosocial support. Thresholds per domain on the PAHC questionnaire and the DT have been established previously.[3] Briefly, if one or more items within a domain was rated as 3 or higher (i.e., "quite a bit" or "very worried"), or the score on the DT was 4 or higher, then this domain was flagged as possibly meriting attention during the initial counseling or telephone session. Prior to the start of the trial, the genetic counselors received guidelines and training in how to interpret the scores on the PAHC questionnaire.

Study measures

Sociodemographic and clinical characteristics

Before randomization (baseline), participants completed a brief questionnaire on sociodemographic characteristics, the history of genetic counseling for cancer in the family, and on past use of psychosocial services. Clinical data were extracted from the medical records.

Primary outcome measures

Discussion of psychosocial problems. The telephone sessions were audiotaped and content analyzed using a checklist to document the frequency with which issues covered by the PAHC questionnaire, the DT as well as other topics were discussed (range 0-28). Two independent raters (WE, GNS) coded the audiotapes. Both raters coded a random sample of 7% of the audiotapes to assess inter-rater reliability. Krippendorff's *α* was 0.76.[17]

Counselors' awareness. After the telephone session, counselors completed a brief checklist, rating each of the six problem domains of the PAHC questionnaire on a 4-point scale ranging from (1, "no problem" to 4, "very much a problem"). These ratings were compared to counselees' ratings on the PAHC questionnaire.

Management of psychosocial problems. The content analysis checklist was also used to code whether counselees received extra psychosocial-related patient information (e.g., written materials, websites, availability of psychosocial services), or if they were referred to psychosocial services. Actual use of psychosocial services was assessed at follow-up by counselee self-report.

Secondary outcome measures

Initiation of discussion of problems and total duration of the counseling session. The content analysis checklist was also used to determine who had initiated the discussion of any given psychosocial problem during the telephone session, and to record the total duration of the session.

Cancer worries and general psychological distress. Cancer worries were assessed using an adapted version of the Cancer Worry Scale (CWS), an 8-item questionnaire with a 4-point response scale (range, 8 to 32).[18] General distress was measured with The Hospital Anxiety and Depression Scale (HADS), composed of 14 questions scored on a 4-point scale (range, 0 to 42).[19] Cronbach's *α* were 0.92 and 0.90 for the CWS and the HADS, respectively. Both questionnaires were addressed at baseline, 1 month after the initial counseling session, and 5 months after the final counseling session.

Specific psychosocial problems. The PAHC questionnaire was used to assess specific psychosocial problems. Counselees were asked to complete the PAHC questionnaire at three time points: (1) prior to the initial counseling session (i.e., first phase of the trial); (2) shortly prior to the telephone session, one month after the final counseling session; and (3) at follow-up, five months after the final counseling session.

Satisfaction and acceptability. At follow-up, study-specific questions were used to assess the counselees' satisfaction and perceived acceptability in terms of usefulness, of the extra telephone session. The genetic counselors were asked a series of questions regarding the acceptability and perceived value of the extra session at the end of the trial.

Statistical analyses

All primary statistical analyses were performed on an intention-to-treat basis. We used analysis of variance and chi-square tests to compare whether those who were eligible for the second phase of the study differed from those who were not, and to compare the baseline sociodemographic and clinical characteristics of the intervention and control groups. Missing data on the HADS and CWS were imputed using half-scale mean substitution methods.

We used multilevel analysis to evaluate differences between groups in the number of psychosocial issues discussed during the telephone session. Counselors' awareness of the counselees' psychosocial problems was assessed by calculating the Intraclass Correlation Coefficient (ICC2.1.A [18]) per domain. Group differences between ICC's were assessed using Fisher's *r*-to-*z* transformation and were subsequently tested for significance. We used chi-square tests to assess group differences in the management of psychosocial problems and the use of psychosocial services.

Multilevel analysis was also used to compare groups on the frequency with which the counselor initiated the discussion of psychosocial problems, the duration (in minutes) of the telephone session, general psychological distress, and cancer worries. Baseline scores for cancer worries and distress were used as covariates. Finally, we used logistic regression analysis to evaluate group differences on specific psychosocial problems and chi-square tests to evaluate satisfaction of both counselees and counselors.

Effect sizes (Cohen's *d*) were calculated by dividing the adjusted mean group differences by the pooled standard deviation. The 95% confidence intervals of the means, ICC's, and effect sizes were calculated. All statistical tests were 2-sided, with *α* set at 5%.

We performed secondary analyses of the total sample using the Friedman test and the post-hoc McNemar test to evaluate changes between different time-points in the CGCT-related problems as assessed by the PAHC questionnaire. For these analyses, we employed predefined thresholds to identify cases.[3] The prevalence of self-reported need for psychosocial services at follow-up is reported descriptively.

RESULTS

Sociodemographic and clinical characteristics

Of the 246 individuals who took part in the first phase of the trial, 118 (63 from the intervention group and 55 from the control group) underwent DNA-testing themselves and received their test results, and thus were eligible to participate in the second phase. Twenty-three counselees discontinued participation in the trial during or directly after completion of the first phase. Of those not eligible to participate in the second phase, 84 had not (yet) undergone a DNA-test, and 21 had not had their final counseling session prior to December 15, 2012 (Figure 1).

Counselees in the second phase of the trial were significantly more likely to have a family history of colon cancer and to have a personal history of cancer as compared to those who were not eligible for the second phase of the study. Among the participants in the second phase of the trial, there were no significant group differences at baseline on any sociodemographic or clinical variables, or with regard to DNA-test results. Mean age was 49.5 years (range, 21 to 73 years). The majority of participants had a personal cancer history, were counseled for hereditary breast and ovarian cancer, were female, and had a relatively high education level (Table 1).

Primary outcomes

Discussion of psychosocial problems, counselors' awareness of and management of psychosocial problems

As shown in Table 2, there were no significant between group differences in the frequency with which psychosocial issues were discussed during the telephone session or in problem management. Counselors' awareness of counselees' problems on most domains was higher in the intervention group. However, the only statistically significant between group difference was for counselors' awareness of 'practical issues' (p=0.006).

Secondary outcomes

Initiation of discussion of problems, total duration of the counseling session, cancer worries, general distress, and specific problems

No significant between group differences were found for the frequency with which the counselors initiated discussion of psychosocial issues, nor for the duration of the telephone session. There were no statistically significant group differences for cancer worries or general distress (Table 3). Neither were there significant group differences observed for the prevalence of CGCT-related problems over time (i.e., between the initial counseling session and follow-up) (Table 4).

Satisfaction and acceptability

High levels of satisfaction with the overall genetic counseling process were reported by both the intervention (93%) and the control group (90%). The telephone session was evaluated positively by 48% of the participants. One-third of the participants would recommend calling all counselees, but 55% would recommend calling only those who indicate wanting to receive such a call. The 10 genetic counselors did not find the telephone session useful for all counselees, but indicated that it might be useful to contact those counselees who experience difficulties coping with their (positive) DNA-test result (not reported in table).

Secondary analyses

Table 4 shows the prevalence of genetic counseling-specific problems at the initial counseling session, the telephone session, and at follow-up. The prevalence of psychosocial problems differed significantly between assessment points, with the exception of the domain 'general emotions' (p=0.10). Family-related problems were increased significantly at follow-up as compared to the initial counseling session. Conversely, the prevalence of problems in the areas of 'practical issues' and 'general emotions' decreased significantly during this time period. Other domains (i.e., 'hereditary predisposition', 'living with cancer', and 'child-related problems') decreased from the initial counseling session to the telephone session, but at follow-up were increased again to approximately the levels observed at the initial counseling session. At follow-up, only 5% of participants expressed a need to talk to a psychosocial worker about problems identified via the PAHC questionnaire.

DISCUSSION

In the second phase of this trial, we evaluated the efficacy of an extra telephone session one month after disclosure of DNA-test results, in combination with providing the genetic counselors with a summary of the results of a standardized problem-oriented questionnaire versus the telephone session alone. No statistically significant results were observed in any of the outcomes of interest, except for an increase in counselors' awareness of their counselees' 'practical issues'. In part, this may reflect the low prevalence of problems reported by counselees, as ICC's are sensitive to prevalence rates. We would note that, although the group differences in HADS scores were not statistically significant,

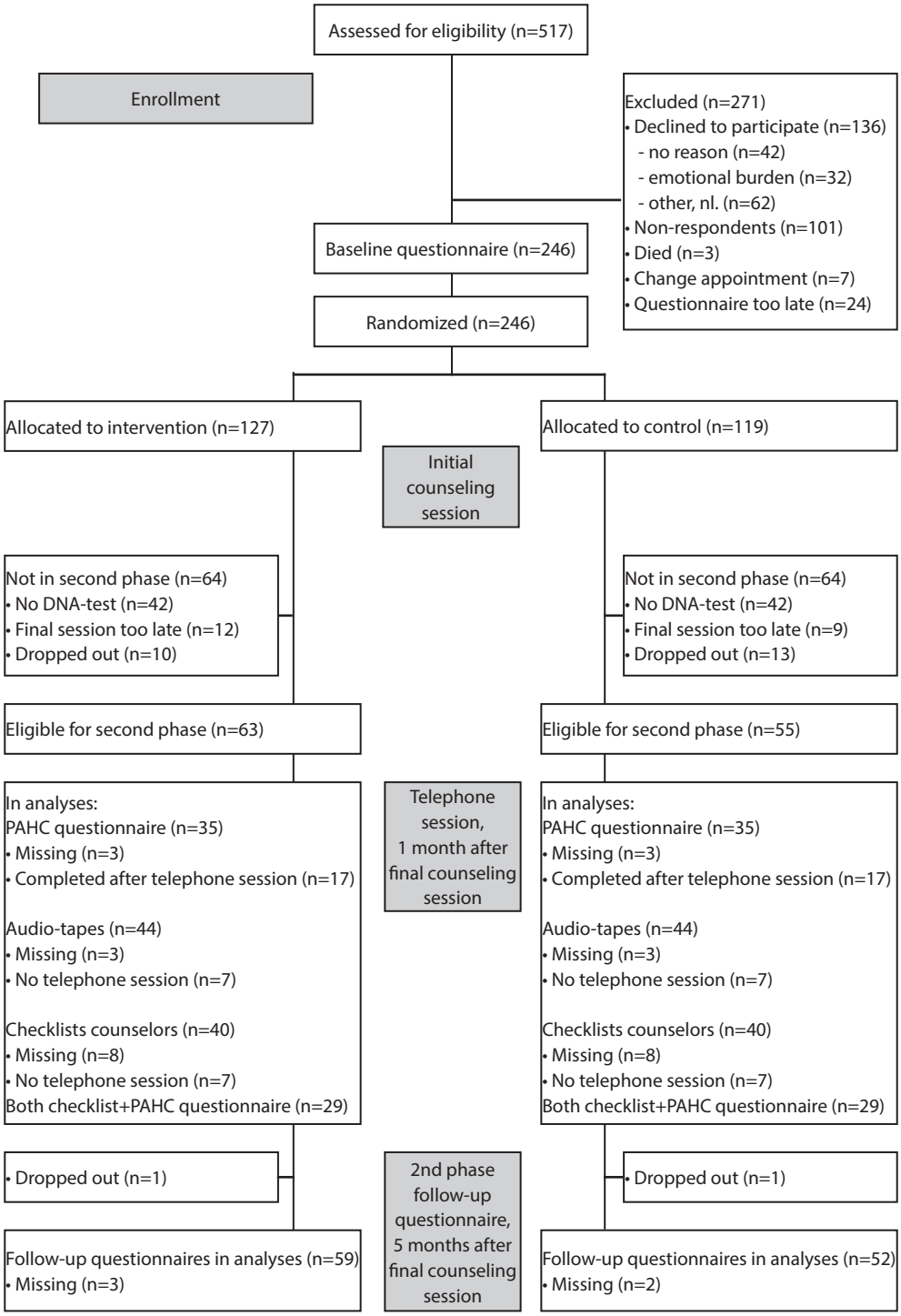

Figure 1. Flow diagram

Table 1. Sociodemographic and clinical characteristics of participants in the second phase as assessed at baseline

	Intervention n=63		Control n=55	
Characteristic	n	%	n	%
Age				
Mean	49.52		49.38	
SD	10.99		12.08	
Gender				
Male	11	21	9	16
Female	52	79	46	84
Marital status				
Married/in a relationship	49	78	45	82
Single/not in a relationship	14	22	10	18
Educational level				
Low (< high school)	17	27	14	26
Middle (≥high school)	13	21	15	27
High (≥college)	33	52	26	47
Children				
Yes	43	68	41	75
No	20	32	14	25
Former contact with a psych. worker	n=62		n=54	
Never	28	45	24	44
0-5	13	21	10	19
5-10	9	15	9	17
>10	12	19	11	20
First in family requesting genetic counseling	n=62		n=53	
Yes	44	71	34	64
Yes, together with others	2	3	6	11
No	16	26	13	25
Cancer syndrome for which counseling is requested	n=63		n=55	
Breast	43	68	37	67
Colon	4	6	2	4
Other	16	26	16	29
Former cancer diagnosis				
Yes (1 or more diagnoses)	40	63	39	71
No	23	37	16	29

Note: No statistical between group differences were found at baseline on any characteristic of participants in the second phase

Table 2. Primary outcomes; Number of discussed psychosocial problems, counselors' awareness of experienced problems, and management of the problems

	Intervention n=47			Control n=44			
	Mean	95% CI lower	upper	Mean	95% CI lower	upper	p-value	effect size
Total number of discussed problems (0-28) [a]	3.29	2.61	3.96	2.82	2.11	3.54	0.23	0.22
Counselors' awareness (ICC 2.1.A)		n=38			n=29			
Hereditary predisposition issues	0.48	0.12	0.71	0.24	-0.10	0.54	0.28	
Practical issues	0.45	0.16	0.67	-0.23	-0.52	0.14	0.006	
Family issues	0.46	0.16	0.68	0.45	0.10	0.70	0.98	
General emotions	0.30	-0.02	0.57	0.31	-0.04	0.60	0.96	
Living with cancer	0.19	-0.08	0.45	0.28	-0.05	0.57	0.70	
Child related problems	0.21	-0.16	0.53	-0.06	-0.42	0.33	0.29	
Management of the psychosocial problems (frequency)		n=47			n=44		0.88	
No actions	39			36				
1 or more [b]	8			8				
Actual use of psychosocial services at follow-up		n=59			n=51		0.75	
Yes	8			8				
No	51			43				

[a] Adjusted for clustering at counselor level
[b] Additional psychosocial information given or referral to psychosocial services
Abbreviation: ICC, Intraclass Correlation Coefficient

they exceeded 1.5 points, which has been used as a criterion for minimal important difference.[21] The effect size for the group difference in HADS scores (d=0.31) was similar to that observed in the first phase of the trial, suggesting either a sustained effect over time of the use of the PAHC questionnaire and/or a salutary effect of the subsequent telephone session plus PAHC questionnaire. This effect size is substantially larger than that reported in similar studies investigating the efficacy of the routine use of patient-reported outcomes in daily clinical practice.[22, 23]

Problems on four out of six PAHC questionnaire domains were more prevalent at follow-up (five months after the final counseling session) as compared to the time of the telephone session (one month after the final counseling session). This suggests that the timing of the telephone session may have been premature; that it might be more useful to conduct the telephone session some months later.

Table 3. Secondary outcomes; Total duration of the counseling session, initiation of the discussion about psychosocial problems, general distress, and cancer worries

	Intervention group			Control group				
	Mean	95% CI		Mean	95% CI		p-value	effect size
		lower	upper		lower	upper		
Duration of the telephone session (minutes) [a]	7.49	5.58	9.40	5.72	3.70	7.75	0.14	0.29
Total number of discussed problems initiated by the counselors [a]	1.55	1.04	2.05	1.44	0.92	1.96	0.60	0.01
HADS								
Baseline [b]	9.02	7.24	10.79	8.78	6.82	10.75		
Follow-up [c]	6.07	4.76	7.38	7.64	6.25	9.03	0.11	0.31
CWS								
Baseline [b]	13.92	12.95	14.89	14.47	13.39	15.55		
Follow-up [d]	12.93	11.29	14.59	13.27	11.47	15.08	0.71	0.06

[a] Adjusted for clustering at counselor level, number of participants in analysis; 47 in intervention group, 44 in control group
[b] Number of participants; 63 in intervention group, 55 in control group
[c] Adjusted for baseline, measured 5 months after the final counseling session, number of participants in analysis; 59 in intervention group, 52 in control group
[d] Adjusted for baseline and clustering at counselor level, measured 5 months after the final counseling session, number of participants in analysis; 59 in intervention group, 51 in control group (1 CWS not complete)
Abbreviations: HADS; Hospital Anxiety and Depression Scale, CWS; Cancer Worry Scale

Table 4. Prevalence of specific problems at the three different time-points

	At initial counseling session [d]		At telephone session (one month after final counseling session)		At follow-up (five months after final counseling session) [e]	
	Intervention	Control	Intervention	Control	Intervention	Control
	n=59	n=52	n=46	n=35	n=59	n=52
Above cutoff on domain	%	%	%	%	%	%
Hereditary predisposition [b,c]	34	40	2	9	22	33
Practical issues [a,b]	14	19	4	0	3	10
Family issues [a,c]	19	35	20	14	41	40
General emotions [a]	15	23	11	14	5	10
Living with cancer [b,c]	76	83	74	51	83	92
Child-related problems [b,c]	29	42	22	23	27	38

[a] Statistically significant difference between initial counseling and follow-up
[b] Statistically significant difference between initial counseling and telephone session
[c] Statistically significant difference between telephone session and follow-up
[d] PAHC questionnaires of 7 participants were completed after the initial counseling session
[e] No statistically significant between group differences

The prevalence of problems on the domains 'practical issues' and 'general emotions', was lower at follow-up than at the time of the telephone session. This suggests that only a minority of participants experience heightened levels of distress in the long term, a finding similar to that reported previously.[24-26] Additionally, only 5% of participants indicated a need for extra psychosocial services at follow-up. This is lower than the estimate of 16-30% reported in previous studies.[27-29] This lower need might be related to the relatively high uptake of services prior to requesting cancer genetic counseling (i.e., 35% reported having had five or more previous contacts with a psychosocial worker).

Our study had some limitations that should be noted. First, the genetic counselors counseled both intervention and control group participants, and all participants completed the PAHC questionnaire. This might have resulted in some degree of contamination of the control group, which would tend to mask or minimize any true between group differences. Second, the raters of the audiotapes were not blinded to group allocation. This could not be done given the nature of the intervention. Third, our study sample consisted of predominantly highly educated women, although this is representative of a clinic-based population of counselees. Fourth, counselees whose family members were tested were excluded in the second phase of the study. The prevalence of psychosocial problems among these counselees might have been different. Fifth, the sample size was relatively small due to the fact that many of the trial participants either did not undergo a DNA-test or received their DNA-test results after the trial had ended. Thus the study may have been underpowered to detect some smaller, but potentially relevant differences. This is illustrated, for example, by the fact that the effect size observed for the HADS was of a magnitude suggestive of a clinically relevant intervention effect, but the group differences were not statistically significant.

The study also had a number of strengths, including its randomized design, multicenter nature, the use of a clinic-based sample, and the use of both observational and self-reported data.

In conclusion, based on the results of our study, we cannot recommend the introduction of a telephone session, including the provision of the results of the PAHC questionnaire, as a routine procedure for all counselees one month after DNA-test disclosure. It may be a procedure that could be used for selective counselees who express a wish for such a contact or who indicate substantial problems with coping with their test results some months after test disclosure.

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Chapter 8

SUMMARY, GENERAL DISCUSSION AND CONCLUSIONS

INTRODUCTION

Individuals who are at high risk of developing cancer can opt for genetic counseling and, if indicated, DNA-testing.[1] The procedure of genetic counseling usually follows a traditional model [2, 3] that includes the completion of a family history questionnaire by the counselee, a counseling session, and a final session in which the possible DNA-test is disclosed [4, 5] and medical advice is given.[6, 7] The counselee might receive recommendations to follow a screening program (e.g., regular mammograms in the case of heightened risk of breast cancer, or colonoscopies in the case of Lynch Syndrome), or to consider undergoing prophylactic surgery (e.g., surgical removal of the breasts and ovaries in case of mutation positive *BRCA1/2*, or removal of the stomach in case a *CDH1*-mutation is found).[6]

Being a member of a family with a cancer history and requesting genetic counseling for cancer is psychologically burdensome for some counselees. Approximately one-quarter of counselees experience high levels of anxiety, depression, and/or distress that may warrant the need for extra psychosocial services.[8] Even more counselees, around 70%, experience a broader range of problems that are related to the cancer genetic counseling setting.[9] Communication during genetic counseling is primarily focused on counselees' family cancer history.[10] The use of a questionnaire might facilitate the discussion of psychosocial problems.[11-13]

In this thesis, we reported on two studies. First, we developed and tested a questionnaire with items on psychosocial problems that are relevant for the cancer genetic counseling setting. Second, after developing and testing this questionnaire, we performed a randomized controlled trial to assess the efficacy of the routine use of the questionnaire in clinical practice as a means of facilitating communication of psychosocial problems in cancer genetic counseling. We hypothesized that providing the genetic counselor with the results of the questionnaire would lead to more frequent discussions of psychosocial problems, increased counselors' awareness and management of these problems and, ultimately, a decrease in counselees' distress and cancer worries.

Here we summarize and discuss the main findings of our studies, the implications of our findings for clinical practice, as well as future research directions.

SUMMARY AND DISCUSSION OF THE MAIN FINDINGS

Specific psychosocial problems of counselees in cancer genetic counseling

We first investigated the specific psychosocial problems as experienced by counselees in the cancer genetic counseling setting. We performed a review of the literature **(Chapter 2)**. The aim of the review was to include studies with a broad focus; it did not include studies that investigated specific problem areas. Numerous studies have been conducted on specific problem areas or issues, as identified in this review. For example, many studies have focused on the familial impact of cancer and the communication with the family.[14-26]

Out of 25 selected papers, we identified six important problem themes including specific issues that are relevant to counselees. The first theme was 'coping with cancer risk', which includes issues related to the reassessment of life and priorities such as changing lifestyle behavior or adopting a fatalistic view of life, and issues related to decisional conflict such as whether or not to undergo the DNA-test or to have children. The second theme was 'practical problems', which includes issues such as employment or difficulties with obtaining insurance. The third theme was 'family and social problems', which includes issues related to communication problems with family members or feeling responsible for family members. The fourth theme was 'children-related problems', which includes concerns for children's increased risk, and guilt towards children. The fifth theme was 'living with cancer', which includes concerns about cancer being a continuing issue, and negative emotions regarding (the risk of) developing cancer. Finally, the sixth theme was 'emotions', which includes both negative emotional reactions such as stress, fear and feelings of loss, and positive emotional reactions such as reassurance, relief and reduced anxiety.

Measures frequently used to estimate the psychological impact of cancer genetic counseling tend to be generic in nature,[27-30] including such measures as the Hospital Anxiety and Depression Scale (HADS), the State Trait Anxiety Inventory (STAI), the Impact of Event Scale (IES), and the Center for Epidemiologic Studies Depression Scale (CES-D).[31-33] However, as described in our review **(Chapter 2)**, 'emotions' is only one of the six themes relevant to the assessment of the psychosocial impact of genetic counseling and testing. Again, the majority of counselees do not suffer from high levels of distress, anxiety, and/or depression.[30, 34-40] However, this does not imply that counselees do not experience a broader range of problems at a subclinical but still relevant level. It is widely recommended that counselors perform a psychological assessment that includes the broader range of problems that can be experienced during genetic counseling.[3-5, 41]

Development and testing of the questionnaire

Based on the literature, interviews with experts from the field, and interviews with former counselees, we developed a new questionnaire (**Chapter 3**). This Psychosocial Aspects of Hereditary Cancer (PAHC) questionnaire contains 26 items, which are organized into six

domains. We subsequently tested the questionnaire, supplementing it with the Distress Thermometer (DT). We established a single cutoff of 3 for all items of the six domains of the PAHC questionnaire. This means that if one (or more) item(s) in a domain is experienced as "quite a bit" or "very much" a problem, the domain is considered a positive case, and the domain warrants extra attention by the counselor. Furthermore, we established a cutoff of 4 for the DT. Thus if an item is rated as a 4 or higher, this indicates that general distress should be discussed during the counseling session.

The PAHC questionnaire, together with the DT, is intended to be used as a first-line screening instrument. The screening properties with the established cutoffs on the questionnaire and DT are not sufficient to recommend using the instruments in a strictly diagnostic manner. If used as a diagnostic tool only, distress screening has proven not to be beneficial for patients in oncology practice,[42] nor for screening for depression in primary care.[43] Ultra-short screening instruments used to identify psychological disorders, such as depression or distress, generally do not yield high sensitivity in combination with high positive predictive value, which is preferable if one is interested in identifying true cases. In fact, most of the questionnaires and screening instruments perform best when identifying those individuals who do *not* exhibit any psychological disorders. Thus the questionnaires yield high specificity combined with a high negative predictive value.[44, 45] In a study that identified thresholds on the QLQ-C30, a similar pattern of relatively high specificity and high negative predictive value was found, including low positive predictive values, which means that many false positives are being identified.[46] Questionnaires, when used as a screening instrument in clinical practice, should therefore be used in combination with a second-line screen, such as a triage from a nurse or physician.[43, 46-48] Simply asking follow-up questions on a positive screen of a screening instrument would require minimal effort, but one should avoid 'alert fatigue', the possible unwillingness of clinicians to communicate about issues because of the many false positives that are detected by the first-line screening instrument.[46] Second-line screening, or triage, has been shown to alleviate distress in oncology practice.[49]

Prevalence of specific problems

In **Chapter 3 and 4**, we described the testing of the screening properties of the PAHC questionnaire. Also, in secondary analyses of these data we were able to estimate the prevalence of specific problems experienced during genetic counseling. Preceding the genetic counseling session, more than half of the participants experienced three or more problems across the domains of the PAHC questionnaire (**Chapter 4**). Prevalence rates of the problems were as high as 84% for problems with living with cancer, and approximately 45% for the domains 'hereditary predisposition', 'family and social issues', and 'child-related issues'. Two papers of Bennett and colleagues have reported on the prevalence of specific problems *during* genetic counseling, estimating the prevalence of specific problems to be up to 73%.[9, 50] They did not, however, include (an) item(s) on 'living with cancer.' Furthermore, we found that correlations between the scores on the PAHC questionnaire and those of measures of general distress were low, except for the domain 'general emotions', which has great conceptual overlap with distress **(Chapter 4)**.

These results indicate that specific problems are of a different order than general distress. This again stresses the need to include more situation specific items when assessing the psychosocial impact of cancer genetic counseling.[27-30]

We designed a randomized, controlled trial to assess the efficacy of the routine use of the PAHC questionnaire in clinical practice **(Chapter 5)**. In **Chapter 7**, we reported the results of the second phase of the trial as well as the prevalence and differences of specific problems as assessed with the PAHC questionnaire between the intervention and control group during the course of the trial. During the trial, one month after the test disclosure session, there was a statistically significant decrease in the prevalence of specific problems on the domains 'hereditary predisposition', 'practical issues', 'living with cancer', and 'child-related issues'. However, five months after the test result disclosure, only the domains 'practical issues' and 'general emotions' were significantly lower than the levels at the time of the initial counseling session. The prevalence of problems in the other domains returned to the higher levels at the moment of the initial counseling, and that of 'family and social issues' had increased significantly five months after DNA-test disclosure (**Chapter 7**). The high prevalence of problems concerning the family is in accordance with the large amount of literature available on the impact of cancer genetic counseling within families.[14-26] Currently, the efficacy of providing extra information and counseling to families after receiving their DNA-test is being investigated.[51, 52]

We found that 21% of counselees experience problems in the domain 'general emotions' (the only domain of the PAHC questionnaire associated significantly with general distress) at the initial counseling session. This percentage suggests that only a minority of counselees experience high levels of distress. This is not too dissimilar from the prevalence rate of 25% high distress levels reported by several reviews on the psychological impact of cancer genetic risk assessment.[8, 36-38, 40, 53]

Need for extra psychosocial services

Another aim of the study was to obtain information about the perceived need for additional, psychosocial services. We found that, at the moment of the initial genetic counseling session, between 13% ('living with cancer') and 30% ('child-related issues') of counselees expressed such need **(Chapter 3)**. In the trial, approximately one-fifth expressed this need at the moment of counseling, and only five percent at follow-up five months after test disclosure. A total of 14% indicated that they had had contact with a psychosocial worker during or after the genetic counseling procedure (five months after follow-up) **(Chapter 7)**.

In two studies in families with the hereditary cancer syndromes Von Hippel-Lindau disease (VHL) and Familial Adenomatous Polyposis (FAP), which included participants who did not know their DNA status (i.e., 13% and 10%, respectively), it was reported that approximately one-third of the moderately to severely distressed participants indicated an unmet need for extra psychosocial services.[54, 55] The uptake of specialized professional services of the complete samples was 28% for VHL, and 17% for FAP.[54, 55] No data were reported on the

need for psychosocial services of those that were not moderately or severely distressed, and estimates of the psychosocial support needs of the total sample might be somewhat lower. Additionally, those who did receive psychosocial support were left out of these analyses. In another study including counselees for Hereditary Breast and Ovarian Cancer (HBOC) the need for psychosocial services was estimated to be 27% during counseling and 16% three months after the final counseling session, and the actual use of additional services was 20% and 4%, respectively.[28] Thus the prevalence of self-reported need for additional psychosocial counseling found in our study (which consisted predominantly of HBOC counselees) was similar to that reported in an earlier study of HBOC counselees, and was lower than that reported in the studies that included families of hereditary cancer syndromes that have a lower population incidence (e.g., VHL, FAP). The actual use of specialized psychosocial services was different across the studies, but in ours it was somewhat lower. This lower use of psychosocial services during or following genetic counseling might reflect the fact that a relatively high percentage of participants reported having used such services prior to requesting cancer genetic counseling. In total, 34% of the participants reported to have had five or more former contacts with a psychosocial worker or psychologist.

Detecting individuals with problems

Many studies have investigated the contribution of sociodemographic and clinical 'risk factors' as predictors of psychosocial problems or distress. However, as reported in **Chapter 4**, none of the basic sociodemographic and clinical variables were identified as important predictors of distress or specific problems at the moment of genetic counseling, explaining only a small percentage (2-14%) of the variance in distress (HADS or DT) or the six problem domains. These findings are in line with those of the study of Douma and colleagues, who also could not identify sociodemographic or clinical variables as major contributors of variance in general distress in a sample of counselees for FAP.[55] Therefore, attempts at detecting counselees who experience distress and psychosocial problems should not focus primarily on these risk factors.

A recent review described a number of risk factors for psychological distress among women at increased risk of developing breast cancer.[56] Most of these risk factors were personality characteristics, such as personal traits, self-concept, appraisal, and coping strategies. Social factors that were identified were experiences with cancer-related events in the family, family communication, and social support from the partner. Many of these risk factors, and particularly those that are social and thus more readily assessable, have been included in the Vulnerability Index for High-Risk Women.[57] Some overlap is present between the risk factors included in this index and items of the PAHC questionnaire (e.g., family communication, cancer-related events, social support). However, risk factors do not imply that a person experiences this factor as problematic and therefore we would argue that a problem-focused approach would be more useful in clinical practice.

Routine use of the PAHC questionnaire during genetic counseling

In the first phase of our trial, we hypothesized that providing counselors with the

results of the PAHC questionnaire, completed by the counselee prior to the counseling session, would increase the number of psychosocial problems discussed, as well as the counselors' awareness and management of these problems. Secondary hypotheses were that providing counselors with the results of the PAHC questionnaire would increase the likelihood that the genetic counselor would initiate discussion of psychosocial problems, and would result in less distress and cancer worries, and increased satisfaction with the genetic counseling. Finally, we hypothesized that the use of the PAHC questionnaire would not significantly lengthen the duration of the genetic counseling session **(Chapter 6)**.

We observed a statistically significant but relatively small effect (effect size of 0.15) of the intervention on the frequency with which problems were discussed during the counseling session. The small effect size could suggest that the counselors already addressed many of the problems included in the PAHC questionnaire during the counseling session, as recommended by guidelines (i.e., a ceiling effect).[3-5] Another possible explanation for the small effect size might be low compliance of the counselors with the intervention. However, we observed that the PAHC questionnaire was mentioned explicitly in 80% of the counseling sessions in the intervention group. The effect size of 0.15 was smaller than that found in similar studies.[58-60] Some of these other studies did not, however, control for differences between clinicians,[59, 60] which might lead to smaller main effects. Counselors in our study also had more time to discuss all medical and psychosocial issues (i.e., mean duration of a counseling session is approximately 40 minutes), in contrast with consultations of the clinicians in other studies where the average duration ranged from 13 to 20 minutes.

The largest and most clinically relevant effect, with ICC's ranging between 0.36 and 0.52, was found on counselors' awareness of their counselees' problems, which was of a similar magnitude to that found in the study of Hilarius and colleagues.[60] No statistically significant difference was found regarding patient management, an outcome measure with mixed results elsewhere in the literature.[13, 61-63] At least one problem management action was initiated in 50% of the sessions in the control group, indicating a high base rate. The actual use of psychosocial services was low in both groups, which, again might reflect the relatively high use of such services prior to cancer genetic counseling.

Another finding that has frequently been reported in the literature is the absence of a statistically significant effect of the intervention on more distal outcomes, such as health-related quality of life or distress.[12, 63, 64] In contrast, we did find such an effect on general distress, which was both statistically significant and clinically relevant, and of a magnitude that was greater than that reported in another study on distress.[47, 65] The mean between-group difference observed on the HADS exceeded the estimated minimal important difference of 1.5 points.[66] A possible explanation for the fact that our study found an effect on distress levels while many other have not, is that our study was targeted primarily at psychosocial issues, whereas some other studies focused on a broader range of problems and somatic symptoms. Targeted and specific interventions might have a higher

chance of being successful at finding a difference with regard to related outcomes.[65, 67] Unfortunately, our data and coding of the audiotapes could not provide insight into the mechanisms that might have led to these findings, and thus further research is needed. For example, it may be that the counselors, having been prompted to attend to their counselees' psychosocial problems by means of the PAHC questionnaire summary, may have had more empathic responses to their counselees' emotional cues. Such empathetic responses have been reported to be associated with lower depression levels in another study in the cancer genetic counseling setting.[68]

As hypothesized, we found no significant between-group differences in the duration of the counseling sessions, a finding that is similar to that reported in previous studies.[58,59,62] Although comparable studies reported that a similar intervention had a significant, positive effect on satisfaction levels,[11, 61] we did not observe such effect in our trial. This was probably due to a ceiling effect, as almost all counselees were very satisfied with the genetic counseling process. In any case, no major adverse effects were identified in this study, which strengthens our view that this simple intervention is not only efficacious, but also can be practically implemented in clinical practice.

Routine use of the PAHC questionnaire after genetic counseling

In the second phase of the trial, we added a telephone session, which included an intervention similar to that used in the first phase, to detect individuals experiencing problems four weeks after the possible test disclosure. We tested the same hypotheses as in the first phase of the trial, as described above, and added the hypothesis that the intervention would significantly reduce specific psychosocial problems over time. However, the results indicated that the intervention only had a significant effect on the counselors' awareness of the problem domain 'practical issues.' None of the other hypotheses (i.e., increase of discussion of problems, the management of problems, satisfaction, decrease of general distress, cancer worries, and specific problems) were supported by the data **(Chapter 7)**.

Based on our results presented in **Chapter 7**, we concluded that it is not efficacious to systematically conduct a telephone session with all counselees one month after the final counseling session. The two main limitations of the second phase of the trial were a small sample size, which made it difficult to find statistically significant between-group differences, and the low prevalence of self-reported problems as described earlier in this chapter. This low prevalence of problems may, in part, explain the null findings on several outcomes of the second phase of the trial, such as the discussion of problems, management of the problems, and acceptability of the intervention. The small sample size prohibits us from drawing definite conclusions about the efficacy of the intervention. However, of specific interest is the possible between-group difference regarding general distress over time. Although not statistically significant, the difference exceeded the 1.5 point difference used as a criterion for minimal important difference for the HADS.[66] Also, the effect size of 0.31 was similar to that found in the first phase of the trial, and was higher than that reported in similar studies.[47, 65] This suggests a sustainable effect of the

intervention over time and/or a salutary effect of the intervention in the second study phase. The effect found on cancer worries in the first study phase was not observed in the second phase, but this may have been due to the fact that that the mean cancer worry level of the control group had decreased over time as well. Combined, these findings suggest that the intervention in the first phase of the study may have resulted in a relatively rapid decline in cancer worries.

In terms of acceptability of the telephone session, participants were more positive than the genetic counselors. A negative (or at least absence of a positive) attitude of clinicians towards screening for distress has been reported as an important barrier to successful implementation of such a screening intervention.[13] The acceptability of screening has not been reported in most studies of the routine use of patient-reported outcomes in daily clinical practice; when reported, attitudes have generally been favorable.[13] In our study, which had mixed results regarding acceptability of the telephone session, participants indicated that the telephone session might be most useful for those who are in need of a telephone session, and thus the counselors should limit the telephone sessions to counselees who have difficulty coping with their (mutation positive) DNA-test results.

To our knowledge, no systematic psychosocial follow-up intervention for all cancer genetic counselees has been reported in the literature. Van Oostrom and Tibben proposed telephoning all mutation positive counselees 2 to 3 weeks after the final counseling session.[2] This might be useful in terms of discussing medical information. With regard to psychosocial issues, results from our study suggest that contacting counselees five months after the counseling session might be more beneficial than short-term follow-up.

METHODOLOGICAL ISSUES

Two studies have been described in this thesis: the development and testing of the PAHC questionnaire, and the evaluation of the efficacy of administering the PAHC questionnaire in clinical practice. Both studies have some limitations and strengths that should be discussed.

In the first study, we developed and tested the PAHC questionnaire. As part of that study, we assessed the inter-rater reliability of the social workers' ratings of participants' problems. Analyses were first performed for each social worker separately, and differences between social workers were found. However, conclusions for all results across the social workers were similar. Furthermore, no other gold standard was available, and our study procedures were similar to those of other questionnaire validation studies. A second limitation concerns the timing of the involvement of former counselees in developing the questionnaire. Although we did include the opinion of 30 individuals during the development stages, it might have been better if more individuals were asked for their opinion at an earlier stage of development.

In the second study, we performed a randomized controlled trial on the efficacy of the routine use of the PAHC questionnaire in clinical practice. Unfortunately, it was not possible to blind the participants, counselors, or the researchers (i.e., raters of the audiotapes) to the randomization due to the nature of the intervention (i.e., feedback of the results of the PAHC questionnaire). At the counselors' level this might have resulted in a contamination effect. However, if this effect was present, it would have a conservative effect on the results, favoring the control group. Second, due to a slower accrual rate and the limited time available for the completion of the trial, we had a substantially smaller sample size in the second phase. This limited statistical power in the second phase of the trial may explain, at least in part, the failure to observe statistically significant group differences in general distress, although the effect sizes were similar to those in the first trial phase. Third, the genetic counselors' were not particularly enthusiastic about the added telephone session. Such lack of enthusiasm might not only reflect the counselors' experience with the intervention, but might also have impacted on other outcomes (i.e., discussion of problems or management of problems). Importantly, the counselees in the intervention group generally found the intervention, both during genetic counseling and at the time of the telephone session, to be useful, at least for those who express the need for such a follow-up.

In both studies, the participation rate was only moderate, although comparable to other similar studies within the same context in the Netherlands.[69, 70] Of those eligible for the trial, only 48% participated, and in the development and testing study 53% agreed to participate. However, in both study groups the participants did not differ from the non-participants on available sociodemographic and clinical background variables (i.e., distribution of age, sex, former cancer diagnosis, known mutation in the family). Furthermore, in the development and testing study, a lower response rate was considered less important since we focused on comparing the ratings of both the participants and social workers of the problems within subjects in order to establish the thresholds on the questionnaire. Low participation rates in both studies might be due to the fact that counselees already had to complete a family history questionnaire prior to genetic counseling, which might have lowered their willingness to participate.

Our studies also had a number of methodological strengths. First, in developing the PAHC questionnaire, we included input from both professionals and former counselees. This was done in the interest of the content validity of the questionnaire, which is critical if it is to be used as a checklist and first-line screener in clinical practice. Second, we established a cutoff for the PAHC questionnaire domains, indicating areas that warrant further discussion during the genetic counseling session. This is an important step in identifying counselees who experience problems, and in the interpretation of the results for counselors who know that this threshold identifies the majority of counselees who experience mild to more severe problems. Third, the multicenter, randomized design of the trial enables us to draw stronger conclusions regarding the efficacy of the intervention in clinical practice. Finally, our use of multiple outcomes in the trial, all of which are relevant for the clinical practice setting, increased the comprehensiveness with which the efficacy of the intervention was investigated.

CLINICAL IMPLICATIONS

The future of cancer genetic counseling and testing faces a multitude of challenges. First, the number of counselees is still increasing each year, reflecting the growing public awareness of the possibility of such testing, and the scientific advances being made in identifying genes that are associated with a higher risk of developing cancer. As a result of the increased volume of individuals seeking genetic counseling and testing, a variety of service delivery models have been developed and investigated; models intended to accommodate the growing number of counselees, while continuing to provide high-quality genetic counseling. The new models are increasingly pointing toward service delivery with less personal contact, such as counseling by phone,[71] disclosing test results by mail,[72] or providing a DNA-test without a counseling session.[73] Although many counselees do not experience serious levels of distress related to genetic counseling and testing, a subgroup still does.[8] Furthermore, based on our results, the large majority of counselees experience significant psychosocial problems during and after the process of genetic counseling and testing. If new methods for service delivery are tested, these specific problems should be taken into account. One way of doing so would be to implement the PAHC questionnaire in clinical practice.

Based on the results of our studies, we would recommend implementing the PAHC questionnaire in the clinical practice of cancer genetic counseling. Within the present, more traditional model of counseling, it might be done easily by including the PAHC questionnaire with the family cancer history questionnaire that is already being sent to the counselee prior to the first genetic counseling session. Alternatively, the PAHC questionnaire could be completed prior to counseling via a patient portal on the internet, or even in the waiting room immediately prior to the counseling session via a tablet computer.

We do not recommend following-up on all counselees one month after the final counseling session. As suggested by many of the counselees who participated in our trial, it might be more appropriate and efficient to inquire about counselees' need/desire for a follow-up telephone session five months after receiving their test results. This would result in only a subset of counselees receiving such a follow-up session. This could be done by means of a simple question, or by administering the PAHC questionnaire by mail, including a question about whether or not the counselee would like to discuss some of these issues with a counselor either over the telephone or in person.

FUTURE RESEARCH DIRECTIONS

Our studies provide important information on the problems experienced by those undergoing cancer genetic counseling, how to detect those problems, and on the effect of the routine use of a problem-focused questionnaire in clinical practice. The results from our studies also generate ideas and hypotheses for further research.

First, it is important to replicate the results from our trial. Improvements in the design and conduct of the trial might include the following. To avoid contamination at the counselors' level, a cluster-randomized design could be used.[12, 74] We would note, however, that results between RCTs with or without a cluster-randomized design often yield very similar results (e.g., in studies on the collaborative care for depression).[75]

Second, video-taping might be used to check on both verbal and non-verbal cues of the counselor and counselee, and a standardized coding scheme could be used to rate the (video)tapes (e.g., RIAS [76], or VR-CoDES [77]).

Third, future studies may want to include a longer follow-up to gain insight into the long-term trajectory of specific problems following completion of genetic counseling and testing.

Fourth, it could be useful to use another genetics-specific questionnaire with a clear factor structure (e.g., the MICRA [29]) to measure the psychosocial impact of genetic testing, taking not only the first counseling session but also subsequent sessions or telephone calls that occur in clinical practice into account, and monitoring all referrals to specialized services, if applicable.

Fifth, if questionnaire assessment were to be completely digitalized, the PAHC questionnaire might benefit from having different cutoffs across the different domains. Data from our study can be used to define these optimal cutoffs. Also, the ability of genetic counselors to detect specific problems can be studied and this can be expressed in terms of screening properties. The ability of genetic counselors, when used as a second-line screener, together with the PAHC questionnaire, should preferably have high sensitivity and positive predictive value to correctly detect the counselees who are likely to experience more severe problems.

Sixth, the finding that the prevalence of specific problems on four domains of the PAHC questionnaire returned to the baseline levels five months after the DNA-test result was disclosed suggests that many counselees remain worried about psychosocial problems after test disclosure. Future research is needed to better understand these more chronic, long-term concerns, and to design interventions that might alleviate these problems.

Finally, although clinically relevant effects of the intervention were found on cancer worries and general distress, the mechanisms through which the intervention might lead to decreased distress levels remain unclear. Future studies should make an effort to identify which elements of communication (e.g., empathic utterances, or non-verbal communication) have significant effects on distress or problem experience, and via which pathways (e.g., increased trust, more appropriate management strategies) counselees' problems and concerns can be minimized, if not entirely resolved.[78, 79] Additionally, future research is needed to tailor communication and interventions to counselees' information needs and coping styles. For example, different approaches may be needed for those counselees who tend to seek as much information as possible (monitors), as opposed to those who have less need for or interest in being fully informed and engaged (blunters).[80]

OVERALL CONCLUSIONS

- Counselees can experience a wide range of psychosocial problems. These can be related to family, or specifically to children, their experiences with cancer, practical issues, decisional conflicts, or general emotions.
- Generic measures of distress are too general to measure the broad range of problems that may be relevant in cancer genetic counseling.
- The Psychosocial Aspects of Hereditary Cancer (PAHC) questionnaire, which covers 6 'problem domains' with 26 items, can assess the specific psychosocial problems of counselees in cancer genetic counseling.
- The established cutoff per domain increases the applicability of the PAHC questionnaire for identifying counselees who experience specific psychosocial problems.
- Due to the high sensitivity but low positive predictive value of the cutoffs on both the PAHC questionnaire and the DT in ruling in counselees with major psychosocial problems, it is important to include follow-up on the positive cases identified with these instruments.
- Easily accessible sociodemographic and clinical variables explain only a small percentage of variance in distress and specific psychosocial problems (2% to 12%) at the time of genetic counseling. Therefore, these variables cannot be relied upon to detect counselees who are distressed or are experiencing significant problems.
- The correlation between domains of the PAHC questionnaire and general distress is low. Again, measures of general distress do not cover the broad range of psychosocial problems in this population.
- The prevalence of problems that warrant extra attention at the initial genetic counseling session is high, ranging from 20% to 83% on the PAHC questionnaire domains, and decreases shortly after receiving the test results. Five months after the final counseling session, the prevalence of most problem domains returns to or even exceeds baseline levels.

- Approximately 20% of counselees express a need for additional psychosocial services at the time of genetic counseling. This decreases to 5% five months after test disclosure.
- Providing genetic counselors with the results of the PAHC questionnaire at the genetic counseling session results in a significant increase in the frequency with which psychosocial problems are discussed, the frequency with which counselors' initiate such discussions, and counselors' awareness of their counselees' problems. Additionally, the intervention leads to a significant decrease in general distress and in cancer worries one month after the initial counseling session. This is achieved without lengthening the duration of the genetic counseling session itself.
- Conducting a telephone follow-up session for all counselees one month after test disclosure is not efficacious.
- Providing genetic counselors with personalized information on experienced problems improves the quality of care in cancer genetic counseling with regard to psychosocial issues.

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APPENDIX

Appendix 1. Psychosocial Aspects of Hereditary Cancer (PAHC) questionnaire

	Not at all	A little	Quite a bit	Very much	
Hereditary predisposition					
1. Are you worried about the chance of being a carrier of a genetic mutation	1	2	3	4	
2. Are you worried about having to choose whether or not to go for genetic counseling and testing	1	2	3	4	
3. Are you worried about the choice of possible preventive options (screening or surgery)	1	2	3	4	
4. Are you worried about coping with the (future) DNA test results	1	2	3	4	
5. Are you worried about (fulfilling) your plans for having children	1	2	3	4	N/A[1]
Would you like to speak with a psychosocial worker in addition to the clinical geneticist/genetic counselor about these issues?			Yes/No		
Practical issues					
6. Are you worried about the impact of genetic testing on your daily life (at home, at work, at school, or with hobbies)	1	2	3	4	
7. Are you worried about the impact of genetic testing on obtaining insurance or mortgage	1	2	3	4	
Would you like to speak with a psychosocial worker in addition to the clinical geneticist/genetic counselor about these issues?			Yes/No		
Family and social environment					
8. Do you feel misunderstood by your partner/family/social circle with respect to genetic testing	1	2	3	4	
9. Are you bothered by lack of support about genetic testing from your partner, family or your social circle	1	2	3	4	
10. Are you worried about your immediate family's functioning because of genetic testing	1	2	3	4	
11. Are you worried about the contact with family members about genetic testing	1	2	3	4	
12. Are you worried about coping with cancer within the family	1	2	3	4	N/A[1]
13. Are you burdened by feelings of responsibility towards family members related to genetic testing?	1	2	3	4	
Would you like to speak with a psychosocial worker in addition to the clinical geneticist/genetic counselor about these issues?			Yes/No		
Emotions with respect to genetic counseling and testing					
14. Do you feel anxious	1	2	3	4	
15. Do you feel tense	1	2	3	4	
16. Do you feel depressed	1	2	3	4	
17. Do you feel insecure about the future	1	2	3	4	
18. Do you have questions about life and death	1	2	3	4	
Would you like to speak with a psychosocial worker in addition to the clinical geneticist/genetic counselor about these issues?			Yes/No		

Appendix 1. *(continued)*

	Not at all	A little	Quite a bit	Very much	
Living with cancer					
19. How emotionally burdensome is it for you that family members have cancer	1	2	3	4	N/A[1]
20. How emotionally burdensome is losing a family member because of cancer?	1	2	3	4	N/A[1]
21. How emotionally burdensome is your diagnosis or treatment for cancer?	1	2	3	4	N/A[1]
22. Are you worried about the chance of getting cancer (again)	1	2	3	4	
23. Are you worried about the chance that family members will get cancer	1	2	3	4	
Would you like to speak with a psychosocial worker in addition to the clinical geneticist/genetic counselor about these issues?			Yes/No		
If you have children (if you do not have children please proceed to question 27)					
24. Do you feel guilty about the chance of passing on to your children your possible genetic alterations	1	2	3	4	
25. Are you worried about telling your children the results	1	2	3	4	
26. Are you worried about the chance of your children developing cancer	1	2	3	4	
Would you like to speak with a psychosocial worker in addition to the clinical geneticist/genetic counselor about these issues?			Yes/No		
27. Are there any other issues related to genetic testing that bother you or that you are worried about? If yes, which issues?					
Would you like to speak with a psychosocial worker in addition to the clinical geneticist/genetic counselor about these issues?			Yes/No		

[1] N/A; Not applicable

SAMENVATTING

INLEIDING

Mensen met een mogelijk verhoogde kans op kanker kunnen zich aanmelden voor erfelijkheidsadvies, ofwel genetische counseling. De procedure van erfelijkheidsadvies is als volgt; de eerste adviesvrager in een familie krijgt na aanmelding een zogenaamde 'familievragenlijst' met vragen over de historie van kanker in de familie. De adviesvrager wordt vervolgens voor een adviesgesprek uitgenodigd, met een genetisch counselor. In Nederland is dat een klinisch geneticus of genetisch consulent. Indien van toepassing wordt in dit gesprek besloten tot DNA-onderzoek, en wordt er bloed afgenomen. In een tweede, en veelal laatste, gesprek wordt de mogelijke uitslag van de DNA-test besproken en wordt medisch advies gegeven. Dit medische advies kan, in het geval van verhoogd risico op borstkanker, bestaan uit deelname aan een screeningsprogramma, zoals jaarlijkse mammografie, halfjaarlijks lichamelijk borstonderzoek door een arts, en maandelijks borstzelfonderzoek, of, bij een verhoogd risico op dikke darmkanker, een colonoscopie eenmaal in de 2-3 jaar. Ook kan een preventieve operatie worden overwogen, zoals het operatief laten verwijderen van de borsten en eierstokken bij een *BRCA1/2* mutatie of het laten verwijderen van de maag als een *CDH1* mutatie is gevonden.

Voor een lid van een familie waarin veel kanker voorkomt, kan het proces van erfelijkheidsadvies een mentale belasting vormen. Ongeveer een kwart van de adviesvragers ervaart veel emotionele last, depressieve en/of angstige gevoelens. Een veel grotere groep van adviesvragers, rond de 70%, ervaart problemen die minder algemeen van aard zijn, maar meer specifiek gerelateerd zijn aan erfelijkheid en het proces van erfelijkheidsadvies. Uit eerder onderzoek kwam naar voren dat de communicatie tijdens het proces van erfelijkheidsadvies voornamelijk is gericht op de geschiedenis van kanker in de familie, erfelijkheid en de procedure van het erfelijkheidsonderzoek. Hierdoor worden mogelijke psychosociale problemen van adviesvragers wellicht minder goed herkend. Het gebruik van een vragenlijst, als hulpmiddel om problemen te herkennen, kan de discussie over psychosociale problemen stimuleren, het inzicht van de counselor in ervaren problemen verhogen, en het geven van passende voorlichting bevorderen.

In dit proefschrift zijn twee studies beschreven. De eerste studie betrof het ontwikkelen en testen van een vragenlijst met vragen over de specifieke psychosociale problemen die relevant zijn voor erfelijkheidsadviesvragers. De tweede studie betrof een gerandomiseerde studie waarbij werd bestudeerd in hoeverre het gebruik van deze ontwikkelde vragenlijst in de klinische praktijk de communicatie over de psychosociale problemen stimuleerde. Hierbij verwachtten we dat het aanbieden van resultaten van de vragenlijst aan de genetisch counselor zou leiden tot een hoger aantal besproken psychosociale problemen, meer inzicht bij de genetisch counselor in welke problemen de adviesvrager ervaart, een verbeterde behandeling van deze problemen, en uiteindelijk in minder algemene psychosociale last en minder zorgen over kanker.

SAMENVATTING VAN DE RESULTATEN

Specifieke psychosociale problemen van erfelijkheidsadviesvragers voor kanker
Eerst hebben we onderzocht welke psychosociale problemen worden ervaren door mensen die erfelijkheidsadvies vragen voor kanker. Dit hebben we gedaan door een overzicht te maken van de literatuur over dit onderwerp (**Hoofdstuk 2**). Het doel van dit overzicht was om studies te beschrijven die de specifieke problemen van deze groep adviesvragers hebben onderzocht. Studies die gericht waren op één probleemgebied, bijvoorbeeld familiecommunicatie, zijn niet meegenomen in het overzicht.

Uit de 25 geselecteerde artikelen hebben we zes overkoepelende thema's gevonden en beschreven. Het eerste thema was het 'omgaan met het kanker risico'. Onderwerpen die hieronder vielen waren problemen met de levensstijl, het ontwikkelen van een fatalistische kijk op het leven, en conflicten met betrekking tot besluitvorming over het kiezen voor de mogelijke DNA-test of problemen rond de keuze voor het krijgen van kinderen. Het tweede thema was 'praktische problemen'. Hieronder vielen problemen over het dagelijks functioneren of het kunnen krijgen van een levensverzekering. Het derde thema was 'familie en sociale problemen'. Onder dit thema vielen problemen met de communicatie met de familieleden of het verantwoordelijk voelen voor de familie. Het vierde thema was 'kind gerelateerde problemen'. Hierbinnen vielen het zorgen maken voor het mogelijk verhoogde risico voor kinderen en een schuldgevoel tegenover kinderen. Het vijfde thema was 'leven met kanker', met onderwerpen die gaan over de ziekte kanker als een voortdurende terugkerend onderwerp en negatieve gevoelens over het (risico op) het ontwikkelen van kanker. Het laatste, zesde thema, was 'emoties' waarbinnen zowel negatieve emoties als stress en angst, maar ook positieve emoties als opluchting een plaats hebben.

De meeste vragenlijsten die in onderzoek tot nu toe gebruikt zijn naar de emotionele impact van erfelijkheidsadvies gebruiken voornamelijk algemene vragenlijsten die angst, depressie of algemene emotionele last (distress) meten. Het thema 'emoties' blijkt echter slechts 1 van de 6 thema's die in ons literatuuroverzicht terugkomt. De meerderheid van erfelijkheidsadviesvragers ervaart over het algemeen niet veel angst of depressieve klachten, maar vaker wordt gesproken over problemen die specifieker van aard zijn en relevant zijn.

Ontwikkeling en testen van de vragenlijst
We hebben een nieuwe vragenlijst ontwikkeld op basis van de literatuur en interviews met zowel experts uit het veld van de klinische genetica als mensen die het erfelijkheidsonderzoek hadden afgerond (**Hoofdstuk 3**). De Psychosociale Aspecten van Erfelijke Kanker [Psychosocial Aspects of Hereditary Cancer (PAHC)] vragenlijst bestaat uit 26 vragen, verdeeld over 6 domeinen. Iedere vraag kan beantwoord worden met 1=helemaal niet, 2=een beetje, 3= nogal, of 4=heel erg. Na het ontwikkelen van de vragenlijst hebben we deze getest samen met de Lastmeter. Deze laatste bestaat uit een

lijn van 0 (geen last) tot 10 (extreem veel last) waarop kan worden aangegeven hoeveel algemene emotionele last de afgelopen week ervaren is. We hebben een afkappunt van 3 vastgesteld op de domeinen van de PAHC vragenlijst. Dit betekent dat als 1 of meerdere vragen binnen een domein als 'nogal' of 'heel erg' worden aangemerkt, dit domein als 'positief' wordt bestempeld en extra aandacht verdient van de genetisch counselor. Hetzelfde geldt voor het vastgestelde afkappunt van 4 voor de Lastmeter.

De PAHC vragenlijst en de Lastmeter dienen gebruikt te worden als 1e stap in het herkennen van mogelijke problemen bij adviesvragers. Net zoals bij andere studies naar soortgelijke signaleringsvragenlijsten, laat de PAHC zien dat de diagnostische eigenschappen van de vragenlijsten in het herkennen van problemen niet optimaal zijn. Er is sprake van een relatief lage sensitiviteit en lage positieve voorspellende waarden waardoor op basis van de vragenlijsten veel problemen worden aangemerkt als probleem, terwijl het geen probleem is (fout-positief). Het is daarom belangrijk om een 2e stap in het proces van het herkennen van mogelijke problemen te hebben. Bij de PAHC vragenlijst en Lastmeter is dat de genetisch counselor die kan doorvragen over de domeinen die als 'positief' zijn aangemerkt.

Prevalentie van specifieke problemen

In **Hoofdstuk 3** hebben we de ontwikkeling en het testen van de PAHC vragenlijst beschreven. Met secundaire analyses van deze data kunnen we ook de prevalentie van de specifieke problemen inschatten. Voorafgaand aan het eerste adviesgesprek ervaart meer dan de helft van de adviesvragers problemen op 3 of meer domeinen van de vragenlijst (**Hoofdstuk 4**). Meer specifiek maakten 84% van de adviesvragers zich zorgen over 'leven met kanker' en ongeveer 45% maakte zich zorgen over 'erfelijke aanleg', 'familie en sociale omgeving' en/of 'kind gerelateerde problemen'. Daarnaast vonden wij dat de samenhang tussen de domeinen van de PAHC vragenlijst en de vragenlijsten over algemene emotionele last laag waren, met uitzondering van het domein 'emoties'. De hoge prevalentie van de problemen en de lage samenhang met de meer algemene vragenlijsten over emotionele last laat zien dat naast algemene psychologische last er ook aandacht moet zijn voor de meer specifieke problemen die worden ervaren door mensen die erfelijkheidsadvies voor kanker vragen.

In **Hoofdstuk 5** wordt het design van de gerandomiseerde studie beschreven. In deze studie is onderzocht of het aanbieden van de resultaten van de PAHC vragenlijst aan de genetisch counselor de discussie over de psychosociale problemen in de klinische praktijk stimuleerde. Bij de helft van de deelnemers (interventiegroep) werden de resultaten van de vooraf ingevulde PAHC vragenlijst aan de genetisch counselor gegeven, en van de andere helft van de deelnemers (controlegroep) niet. In **Hoofdstuk 7** beschrijven we de resultaten van de 2e fase van deze studie, waarbij ook de prevalentie van de problemen over tijd en tussen de interventie en controle groep van de studie zijn bekeken. In de gerandomiseerde studie was er geen verschil tussen de groepen 1 maand na het eerste counseling gesprek; beide groepen lieten een afname van problemen zien op de domeinen 'erfelijke aanleg', 'praktische zaken', 'leven met kanker' en 'kind gerelateerde problemen'. Vijf

maanden na de laatste sessie echter, waren alleen de domeinen 'emoties' en 'praktische zaken' statistisch significant lager dan bij de eerste counseling sessie. Het percentage adviesvragers dat problemen rapporteerde op de andere domeinen was teruggekeerd naar de eerdere hogere niveaus van het moment van het eerste adviesgesprek. Het percentage adviesvragers dat problemen rapporteerde op het domein 'familie en sociale omgeving' was zelfs statistisch significant hoger.

We vonden dat in totaal 21% van adviesvragers problemen ervoeren op het domein 'emoties', het enige domein dat samenhangt met algemene emotionele last (distress), op het moment van het eerste adviesgesprek. Dit laat zien dat slechts een minderheid van de adviesvragers veel emotionele last ervaart. Dit is in overeenstemming met prevalentie cijfers van rond de 25% uit ander onderzoek over algemene last, depressie en/of angst.

Behoefte aan extra psychosociale zorg

Een ander doel van het onderzoek was om inzicht te krijgen in de behoefte van adviesvragers aan extra psychosociale zorg. Wij vonden dat op het moment van het eerste counseling gesprek tussen de 13% voor het domein 'leven met kanker' en de 30% voor het domein 'kind gerelateerde problemen' aangeeft behoefte te hebben aan een gesprek met een psychosociaal medewerker (**Hoofdstuk 3**). In de gerandomiseerde studie gaf ongeveer één-vijfde aan met een psychosociaal medewerker te willen spreken op het moment van het eerste advies gesprek. Slechts 5% geeft aan deze behoefte te hebben vijf maanden na het laatste gesprek. In totaal heeft 14% aangegeven daadwerkelijk contact te hebben gehad met een psychosociaal medewerker gedurende of na afloop van het proces van erfelijkheidsonderzoek (**Hoofdstuk 7**).

Detecteren van adviesvragers met problemen

Veel studies hebben sociaal demografische en klinische variabelen gevonden die mogelijk 'risico factoren' zijn voor het hebben van algemene psychosociale last. Echter, in onze studie kunnen wij deze bevindingen niet ondersteunen. De sociaal demografische en klinische variabelen die samenhangen met algemene psychosociale last of specifieke problemen verklaren slechts 2% tot 14% van de variantie op het moment van het eerste advies gesprek (**Hoofdstuk 4**). Daarom zal bij het detecteren van adviesvragers die problemen ervaren niet primair gelet moeten worden op mogelijke 'risico factoren', maar zal een probleem georiënteerde vragenlijst in de dagelijkse praktijk waarschijnlijk nuttiger zijn.

Gebruik van de PAHC vragenlijst in de klinische praktijk

In de 1^{e} fase van de gerandomiseerde studie verwachtten we dat het terugkoppelen van de resultaten van de PAHC vragenlijst aan de genetisch counselor bij het eerste adviesgesprek zou leiden tot een hoger aantal besproken psychosociale problemen, een verbeterd inzicht van de genetisch counselor in welke problemen de adviesvrager ervaart, en een verbeterde behandeling van deze problemen. Secundaire hypotheses waren dat het terugkoppelen van de resultaten van de PAHC vragenlijst ertoe zou

leiden dat de counselor meer psychosociale problemen in het adviesgesprek aansnijdt, adviesvragers minder algemene psychosociale last ervaren, adviesvragers minder zorgen over kanker ervaren, en adviesvragers meer tevreden zouden zijn met het adviesgesprek. We verwachtten dat deze interventie het adviesgesprek niet langer zou doen laten duren (**Hoofdstuk 6**).

We vonden een statistisch significant maar klein effect (Cohen's $d = 0.15$) van het aantal besproken psychosociale onderwerpen tijdens het adviesgesprek tussen de interventie groep (waarbij de resultaten waren teruggekoppeld) en de controle groep (waarbij de resultaten niet zijn teruggekoppeld). Overeenkomstig met ander onderzoek was het inzicht van de genetisch counselors in de ervaren problemen van de mensen die erfelijkheidsadvies hebben gevraagd het grootst. De samenhang tussen de ingevulde PAHC vragenlijst en in hoeverre de genetisch counselor op de hoogte was van de problemen (ICC) lag tussen de 0.36 en 0.52. Wij vonden geen verschillen tussen de groepen met betrekking tot de behandeling van de problemen, zoals het aantal doorverwijzingen naar psychosociale hulpverleners.

In onze studie vonden we een sterkere afname in algemene psychosociale last en zorgen over kanker in de interventie groep dan de controle groep, op één maand na het adviesgesprek. Dit verschil was zowel statistisch significant alsook klinisch relevant. Daarnaast nam de genetisch counselor bij de interventiegroep vaker het initiatief om een psychosociaal onderwerp te bespreken. Ook bevestigden de resultaten onze verwachting dat het terugkoppelen van de resultaten van de PAHC vragenlijst de tijdsduur van het adviesgesprek niet veranderde. We vonden geen verschil op tevredenheid over het adviesgesprek tussen de twee groepen.

In de 2^{e} fase van de gerandomiseerde studie hebben we een telefoongesprek toegevoegd aan de normale procedure van genetisch counseling, ongeveer één maand na het laatste adviesgesprek (**Hoofdstuk 7**). Hier hebben we eenzelfde interventie gedaan als in de 1^{e} fase van deze studie, waarbij resultaten van de PAHC vragenlijst van de adviesvragers in de interventiegroep werden teruggekoppeld aan de counselors. In deze 2^{e} fase vonden we alleen een statistisch significant verschil bij het inzicht van de genetisch counselor in de ervaren 'praktische problemen' van de erfelijkheidsadviesvragers. Daarnaast was het verschil op algemene emotionele last, net als in de 1^{e} fase, klinisch relevant. Vanwege de lage prevalentie van psychosociale problemen op één maand na het laatste adviesgesprek, strekt het niet tot de aanbeveling om alle adviesvragers in de toekomst te bellen op dat moment. Mogelijk is het nuttig om adviesvragers enkele maanden na afloop van het erfelijkheidsadvies de PAHC vragenlijst op te sturen, en daarbij te vragen naar de behoefte aan een extra telefoongesprek met een genetisch counselor.

CONCLUSIES

- Mensen die erfelijkheidsadvies vragen voor kanker kunnen een wijd scala aan psychosociale problemen ervaren. Deze kunnen gerelateerd zijn aan problemen met de familie, kinderen, het leven met kanker, praktische zaken, besluitvorming, en/of algemene emoties.
- Vragenlijsten over algemene emotionele last, angst en/of depressie zijn te algemeen om het brede scala aan psychosociale problemen te meten in deze populatie.
- De PAHC vragenlijst die bestaat uit 26 vragen onderverdeeld in 6 domeinen kan de specifieke problemen meten van de erfelijkheidsadviesvragers.
- Het vastgestelde afkappunt op de PAHC vragenlijst vergroot de bruikbaarheid van deze lijst bij het detecteren van de adviesvragers die psychosociale problemen ervaren.
- Vanwege de relatief lage positief voorspellende waarde van zowel de PAHC vragenlijst als de Lastmeter is het van belang om de domeinen en items die als problematisch worden ervaren door de counselor uit te vragen.
- Op het moment van het eerste adviesgesprek verklaren sociaal demografische gegevens en klinische variabelen slechts een klein gedeelte van de algemene emotionele last (2%-14%). Bij het detecteren van adviesvragers met algemeen emotionele last of specifieke problemen dient daarom niet uitgegaan te worden van deze gegevens.
- Er is slechts een kleine samenhang tussen de PAHC vragenlijst en algemene emotionele last. De vragenlijsten naar algemene emotionele last meten niet de specifieke problemen die relevant zijn voor deze populatie.
- De prevalentie van problemen die extra aandacht verdienen in de klinische praktijk varieert tussen 20% en 83% op domeinen van de PAHC vragenlijst en daalt kort na het ontvangen van de DNA-test resultaten. Vijf maanden later echter, keren de meeste problemen weer terug naar het niveau als bij het eerste adviesgesprek, of zijn ze zelfs hoger.
- Ongeveer 20% van de adviesvragers geeft aan behoefte te hebben aan gespecialiseerde psychosociale hulp op het moment van het eerste adviesgesprek. Dit daalt tot 5% op vijf maanden na het laatste adviesgesprek.
- Het terugkoppelen van de resultaten van de PAHC vragenlijst aan de genetisch counselor leidt tot een verhoogd aantal besproken psychosociale problemen tijdens het eerste adviesgesprek, meer initiatief van de genetisch counselor om het gesprek over de problemen te beginnen, en een verbeterd inzicht van de genetisch counselor in de ervaren problemen van de adviesvrager. Dit wordt bereikt zonder het adviesgesprek langer te laten duren. Daarnaast zorgt de interventie voor lagere waarden van algemene emotionele last en minder zorgen over kanker een maand na het adviesgesprek.
- Het is niet aan te bevelen om alle adviesvragers een maand na het laatste adviesgesprek op te bellen om psychosociale problemen te inventariseren.
- Het terugkoppelen van resultaten van persoonlijke informatie over ervaren problemen verbetert de kwaliteit van het erfelijkheidsadvies op psychosociaal gebied.

DANKWOORD

DANKWOORD

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