Opening the psychological black box in genetic counseling

Vos, J.

Chapter 10

Genetic counseling as fulfillment of the cancer-patient's need for certainty:

Description of perceived certainty, need for certainty, and reactions to unfulfilled need for certainty in a prospective study in BRCA1/2-counselees

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Submitted

Abstract

Objective

Many cancer-patients undergo DNA-testing in the BRCA1/2-genes to receive information about the likelihood that cancer is heritable. Previous studies suggested that DNA-testing often does not fulfill the counselees' needs for certainty. We systematically examined the balance between the counselees' Need-for-Certainty and Perceived-Certainty (NfC-PC, i.e. level of fulfillment of NfC) regarding the specific domains of DNA-test result, heredity and cancer. We also examined relationships of NfC-PC with coping styles and distress.

Method

Before disclosure of BRCA1/2-test results for hereditary breast/ovarian cancer (T1), questionnaires were filled-in by 467 cancer-patients. Another questionnaire (T2) was filled-in after disclosure of pathogenic-mutation results (n=30), uninformative results (n=202) or unclassified-variants (n=16).

Results

Before and after DNA-test result disclosure, overall 58% to 94% of all counselees experienced unfulfilled NfC regarding the DNA-test result, heredity and cancer. Compared to T1, the communication of pathogenic-mutations (T2) caused more fulfillment of their need for certainty about the DNA-result, but less about cancer and heredity. Compared to T1, unclassified-variants (T2) did not change the extent of fulfillment of all counselees' needs for certainty (NfC>PC). Compared to T1, uninformative-results (T2) caused more fulfillment of all needs than before disclosure. Counselees differentiated NfC and PC between the domains of DNA-result, heredity and cancer. The unfulfilled needs for certainty (NfC-PC) were uncorrelated with cognitive understanding of the DNA-test result, but correlated strongly with distress, misinterpretation of information and passive coping, correlated moderately with active-coping and barely with acceptance.

Conclusions

The counselees' NfC needs more attention in research and practice, e.g. when the potential uncertainties of testing are discussed. The counselees' NfC should be assessed and used in tailored, mutual communication of DNA-test results.

1. Introduction

1.1. Certain uncertainty

Since the identification of the BRCA1- and BRCA2-genes for hereditary cancer, many cancer-patients have undergone DNA-testing (15). Reduction of uncertainty is an important goal of genetic counseling for women from families with a strong history of breast and/or ovarian cancer. Counselees report that they want to undergo DNA-testing, to receive certainty about their cancer-risks, their relatives' risks, the role of a possible genetic predisposition of cancer in the family to obtain access to periodic screening, and to regain personal control over their own cancer (1-6).

Genetic-counseling and mutation testing in index patients (i.e. the first tested in the family) do not always provide certainty. Even the most conclusive outcome of testing, i.e. the detection of a pathogenic-mutation (PM), does not imply certainty that a counselee will develop cancer (again). In these cases, contralateral breast-cancer risks are communicated for affected women as 30-60%, and primary breast and ovarian-cancer risks for unaffected carriers as respectively 60-80% and 30-60% (BRCA1) / 5-20% (BRCA2). These are population risks and not individual risks, i.e. a PM is generally associated with these risks but does not tell whether this specific counselee will develop cancer. Moreover, a PM-result may evoke new uncertainties in other domains of the counselees' lives, for instance regarding medical-decisions, telling the family, family planning, and DNA-testing and medical-decisions of relatives.

About 85% of all DNA-test results in index cases do not show a PM, but show either an 'uninformative result' (UR), i.e. no mutation in the BRCA1/2 genes, or an 'Unclassified-Variant'/'variant-of-uncertain-clinical-significance' (UV), i.e. a mutation for which the clinical meaning is not known yet (UV). These non-informative -results include even more uncertainty than PM's, because no precise risk-figures are available in these cases but only general risk estimations on the basis of the counselee's pedigree. Counselees are also confronted with other uncertainties regarding cancer-risk estimates, such as limitations in the sensitivity and specificity of the DNA-tests, source credibility and ambiguous information (34). Genetic-counselors and other physicians may also evoke uncertainty by non-verbal communication not consistent with the communicated information (31-33,345,385,386).

Many studies show that counselees experience much uncertainty and lack of personal control regarding the DNA-test result (3,31,164,244,245,362-366,387,388). Reported levels of uncertainty vary considerably, and depend on instruments and samples.

Thus, many counselees ask for genetic-counseling because of a strong need to obtain certainty, but this need often remains partially or completely unfulfilled. It has been suggested, that this unfilled need for certainty is the essence of the experience of being-at-

high-risk-for-cancer and may explain how counselees cope in general with the DNA-test result and distress. (6,62,389,390)

This chapter describes an empirical study about the extent to which the counselees' need for certainty is fulfilled by DNA-test result disclosure, and how this is related to copingstyles and distress. This study has four points which differ from previous studies on uncertainty in genetic-counseling. First, we focus on specific experiences of uncertainty. Second, we focus on the balance between the counselees' need for certainty and their perception of certainty. Third, we describe the relation between uncertainty, copingstyles and distress. Fourth, we focus both on cognitive and affective elements of uncertainty, and not only on cognitive processes as in many previous studies.

1.2. Specific domains of uncertainty

Previous studies on the counselees' experience of uncertainty have used unspecific instruments (391,227) or have only measured traits (244,366,392,393). Instruments that measure the counselees' need for certainty (NfC) as a trait, or measure the global experience of perceived certainty or uncertainty (PC), may not grasp the counselees' subtle, ever changing experience of different certainties in different situations. For instance, a cancer-patient may feel certain about her cancer –because the tumor is under control- but may feel uncertain about the role of the genetic-predisposition of cancer in the family. A counselee may feel certain about the heredity during the intake-session of genetic-counseling, but after disclosure of the DNA-test result, she may suddenly experience uncertainty. Thus, we suggest that the counselees' experience of certainty should be operationalized specifically in different domains of uncertainty (376,394). Although traits may influence the experience of certainty in specific domains, global trait-instruments may be less useful than specific state-instruments to really understand how counselees experience a specific situation.

We categorized the kinds of uncertainty as described in literature into three groups, and use this categorization in the operationalization of NfC and PC in our study. We have omitted literature on NfC/PC about one's self, personality or life (e.g.137,138,395), to focus on NfC/PC regarding genetic-counseling.

1.DNA-test result: Many studies suggest that uncertainty may be an important part of the counselees' lived experience of being-at-risk to develop cancer (again) (3,6,31,62, 164,244,245,362-366,270,388-390). Counselees feel uncertain about waiting for a long time for the result, and about the possible unclear meaning of the DNA-test result, especially of UR/UV-results. UV-counselees report much uncertainty (203,217,224-226).

2.Heredity: Counselees do not only undergo DNA-testing to receive information for themselves, but also for their relatives, in particular their offspring (1,5). Counselees seem to experience distress because of the (uncertain) meaning of the DNA-result for the

likelihood that cancer is heritable in their family and for their relatives' cancer-risks (e.g.217,277,340).

3.Cancer: Many patients experience uncertainty regarding the diagnosis, the prognosis (376,396), and making medical decisions (35,376,397,398). For example, they decide to undergo surgery to reduce uncertainty (397), and request DNA-testing to receive certainty about their cancer, recurrence risk, and what decisions to make (1,5,35). Genetic-testing may answer the existential question regarding cancer 'why did I have to become ill?', and may be regarded as a way to regain personal control (399,245).

1.3. Need-for-Certainty and Perceived-Certainty

Previous studies have either described NfC or PC in counselees. Both may be required to understand the variety of reactions that different counselees have to a specific situation. For instance, two counselees may perceive the same high level of uncertainty regarding the DNA-test result. The counselee who has a high need to receive certainty about the DNA-test result will experience the situation as more distressful than the counselee who does not strongly need to receive certainty. Thus, the assumption that genetic-information, cognitions, or PC directly lead to distress is too simplistic (227). It is the imbalance between NfC and PC that seems to matter, not NfC or PC *per se*.

NfC implies an awareness of the ideal situation (optimal certainty) and PC implies the perception of the situation in reality. The ideal and realistic perceptions of situations may clash in genetic-counseling.

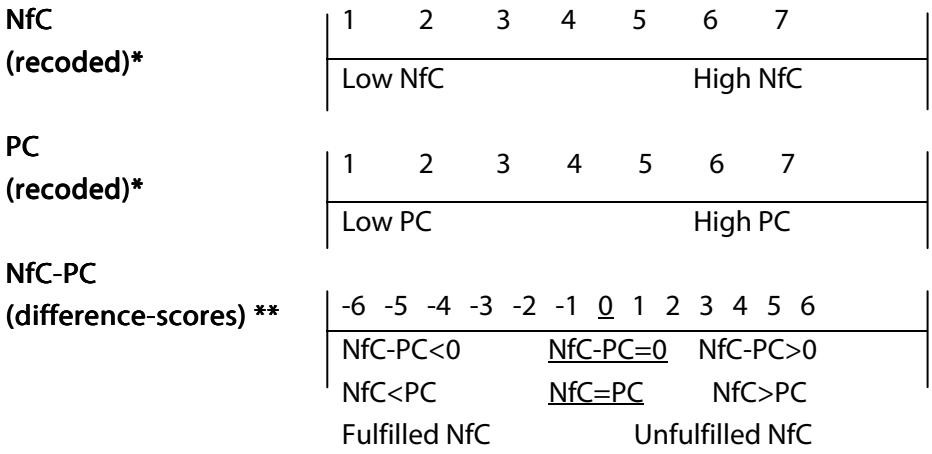
Ideal: Counselees undergo DNA-testing to receive certainty (1,5,6), hope and mastery over their cancer and over their relatives' cancer-risks (148,216,359-361).

Reality: However, DNA-testing does not provide immediate certainty on demand. Counselees have to wait for the results, the result may be ambiguous, may not provide them with the desired options for control, and the communicated cancer-risks may be imprecise and not in line with their own prior interpretations (400). Counselees report that many expectations about genetic-counseling are not met (216,359-361). Confrontation with this uncertain reality of DNA-testing may lead to disappointment and uncertainty (3,31,164,362-366). Thus, the counselees' NfC often collides with the actual PC after genetic-counseling (which is possibly similar to the communication of medical information in other situations).

PC and NfC can be expected to influence each other. Counselees may use their needs and expectations (NfC) as a heuristic background against which they perceive the current situation (PC); thus, NfC may influence PC. Counselees may also adjust their needs and expectations (NfC) in reaction to the actual level of certainty (PC) in this situation. Despite the mutual influence of NfC and PC, we assume that counselees are able to differentiate the actual level of certainty (PC) from their preferred level of certainty (NfC) in a situation, because NfC and PC can be described as fundamentally different processes.

In our study, we measured both NfC and PC, which were assumed to be continuous variables with uncertainty and certainty as end points of one axis. We focused on the balance/relationship between NfC and PC, which was operationalized by the difference between both (NfC-PC); we refer to this difference as 'fulfillment of the counselees' need for certainty'. That is: the counselees' perceived level of certainty fulfills their need for certainty to a lower or higher extent (see figure 1). It is this level of fulfillment, and not NfC or PC per se, that we expect to explain fundamental copingstyles.

Figure 1. *Explanation of the scales of the Unfulfilled Need for Certainty Scale: Need for Certainty (NfC), Perceived Certainty (PC), and level of fulfillment of the need for certainty (NfC-PC)*



**Reverse scaling of the semantic differential in the questionnaire (see table 1); recoding: 1=7, 2=6, 3=5, 4=4, 5=4, 6=2, 7=1; **NfC=PC regards score '0' only; NfC is assumed to be mainly fulfilled when NfC-PC<0 and NfC<PC; NfC is assumed to be mainly unfulfilled when NfC-PC>0 and NfC>PC*

1.4. Coping and distress related to unfulfilled Need for Certainty

We examined the extent to which the counselees' specific needs for certainty are fulfilled in genetic-counseling in this study, because we assumed that counselees experience NfC and PC as important in coping with DNA-test results and with cancer, and unfulfilled NfC may lead to distress (6). In line with the literature, we can identify several ways of coping with the uncertainty of the DNA-test result, of heredity and/or of cancer.

Cancer-patients are assumed to cope optimally with the cancer-experience, when they are able to acknowledge and/or integrate the co-existence of two processes or 'dual realities' (401). This may be understood from the theoretical assumption that two simultaneous positions on certainty are possible (391). First, humans can recognize that the possibility of certainty or complete predictability is an illusion, because the world is fundamentally unpredictable. Second, there is a human drive to reduce uncertainty, to explain the world, and to render it predictable. Both positions may not be mutually exclusive. It has been assumed that patients cope optimally with cancer when they are able to have both positions at the same time, i.e. positively accepting the objective reality of uncertainty, risks and limitations, and at the same time acknowledging and living-out the subjective reality of desires, dreams and needs to reduce uncertainty (138,395,401). Thus, they have to reconcile their perceived lack of certainty/control with their wish for mastery and responsibility (152), and to let uncertainty and hope go hand-in-hand (393,394).

However, unfulfilled NfC may not always go hand-in-hand with acceptance. Counselees may also deny one of the dual realities, i.e. decrease of PC and/or increase of NfC, as suggested by previous studies in cancer-patients (402-404). For instance, cancer-patients may cope by doubting, engaging, denying or by experiencing distress (60); we may apply these copingstyles to the situation of cancer-patients in genetic-counseling, as indicated by previous studies. Counselees may doubt the PC by reinterpreting the actually communicated DNA-test result (221,400). They may actively engage in behaviors to change the situation by undergoing frequent surveillance and/or surgery of breasts and/or ovaries (35,77). They may cope with the DNA-test result by using passive copingstyles such as denial, renaming and/or avoidance (87,405). When uncertainty is not reduced but other copingstyles are unavailable, counselees may experience distress (228). This distress can be described as meta-uncertainty (391), i.e. uncertainty resulting from the question whether PC or NfC is most applicable.

Thus, we assume that counselees may cope with their unfulfilled need for certainty in the ways described above: acceptance, reinterpretation, active coping, passive coping, and/or distress. More specifically, we expect that the more unfulfilled the need for certainty is, the more counselees will report these copingstyles/distress.

1.5. Unfulfilled need for certainty as an affective evaluative process

Previous studies have often operationalized NfC and PC as information-oriented, mainly cognitive processes, such as fulfillment of the counselees' cognitive needs and expectations for information and structure (54,55,406). However, NfC and PC seem to depend on many psychological, appraisal and coping processes and not only on information-oriented processes (see 1.4.); NfC-PC seems to be a general evaluation of a situation in its totality, which includes both cognitive and affective elements (cf.391).

1.6. Research questions

These three points lead to the following research questions in this study. 1.How many counselees experience an unfulfilled need for certainty? 2.Is there a change in the level of fulfillment of NfC after disclosure of test results, and do different DNA-test results cause different changes? 3.Do the domains of unfulfilled need for certainty (i.e. cancer, heredity, DNA-test result) differ from each other? 4.Is the extent to which the counselees' NfC remains unfulfilled after DNA-test result disclosure related to acceptance, reinterpretation, active coping, passive coping, and distress? Each of these questions will be answered separately for PM, UV and UR, because we assume that differences exist between these groups regarding NfC and PC, as described before. 5.Is the extent to which the counselees' NfC is fulfilled independent from the counselees' cognitive understanding of the DNA-test result, cognitive need for structure and the actually communicated DNA-test result?

2. Method

2.1.Study procedure

We decided to include only BRCA1/2-testing in counselees who have (had) cancer, because they are the majority of counselees receiving DNA-test results in the Netherlands. Eligible participants were women with previous or current breast and/or ovarian cancer who had requested a BRCA1/2-test in the period 2006-2009 at the departments of Clinical Genetics of the Leiden University Medical Center, the Maastricht University Medical Center, the University Medical Center Groningen, Erasmus Medical Center Rotterdam, or the VU Medical Center Amsterdam. Eligible counselees received two questionnaires: one after the first genetic-counseling session (T1), one 3 months after the second genetic-counseling session in which the DNA-test result was disclosed (T2).

Actually communicated information was derived from a checklist filled-in after each session completed by the genetic-counselor, from medical files and from summary letters that counselees received within 3 months after the result.

Usually, genetic-counselors disclosed the following information: DNA-test result category, the likelihood that cancer is due to a genetic predisposition in this family (i.e. heredity-likelihood), cancer-risks for female relatives and for the counselee, risk management options (surgery, surveillance) for relatives/counselee and the possibility for relatives to undergo DNA-testing (340).

2.2. Instruments

We developed the Unfilled-Need-for-Certainty-Scale (UNCS) on the basis of our model of four domains (DNA-test result, heredity, cancer, self), and differences between NfC and PC. The initial 80-item UNCS was based on literature and tested in a pilot study, and the number of items was reduced by factor-analyses which *Finally* showed good reliability and validity (e.g.203).

This resulted in a 19-item UNCS administered at T1 and at T2. Both at T1 and T2, we measured 6 subscales: NfC and PC about the DNA-test result, heredity-likelihood and cancer (see table 1). Counselees were asked to rate items 'for the preceding month' on semantic differentials, ranging from 1, high, to 7, low, NfC. For instance: 'I did not feel much uncertainty' to 'I felt much uncertainty', and 'I need certainty' to 'I do not necessarily need certainty'. To facilitate interpretation of the scores, we recoded these items so that '1' indicates low NfC/PC and '7' high NfC/PC. PC was measured with multiple items on each domain, and all PC-scales showed good reliability (see table 1). NfC was measured with only one item on each domain; we selected this item from the initial 80-item UNCS because of its general formulation and strong correlations with other initial items.

Unfulfilled need for certainty (NfC-PC) for a domain was measured by substracting the mean of all PC-questions on that domain from the NfC on that domain (see table 1); using Z-scores yielded similar results and is not shown. We assumed that NfC and PC can be substracted because the items had been formulated similarly, and both PC and NfC seemed to measure comparable concepts as shown by large overall Cronbach's α (see table 1) and strong correlations between PC and NfC (R's=.60-.80). Study results did not differ when we measured NfC-PC with only one item for NfC and one item for PC.

Other instruments are shown in table 2. For validation purpose, we used multiple instruments to operationalize each phenomenon under study.

Table 1. *Description of items (semantic differentials) and their reliability of the 19-items Unfulfilled Need for Certainty Scale (UNCS) administered at T1 and T2*

After intake-session ***(overall α=.78)***		**After DNA-test result disclosure session** ***(overall α=.78)***	
Need for certainty (NfC)* *(overall α=.74)*	Perceived certainty (PC) * *(overall α=.79)*	Need for certainty (NfC)* *(overall α=.75)*	Perceived certainty (PC)* *(overall α=.78)*
T1 NfC Cancer I need/do not necessarily need certainty about cancer	**T1 PC cancer (c): α=.85** *I did not feel(1)-I felt (7)…* 1.uncertainty about c. in general 2.certainty about c. in general** *I felt uncertain (1)/certain(7) about…* 3. treatment/surveillance of c. 4. daily life coping with c. 5. the development of c. in future	**T2 NfC Cancer** I need/do not necessarily need certainty about cancer	**T2 PC cancer (c): α=.87** *I did not feel(1)-I felt (7)…* 1.uncertainty about c. in general 2.certainty about c. in general** *I felt uncertain (1)/certain(7) about…* 3.treatment/surveillance 4. daily life coping with cancer 5.development of cancer in future
T1 NfC DNA-test result I need/do not necessarily need certainty about the DNA-test result	**T1 PC DNA-test result (tr) : α=.88** *I did not feel(1)-I felt (7)…* 1.uncertainty about tr in general 2.certainty about tr in general** *I felt uncertain (1)/certain(7) about…* 3.consequences of tr for myself 4.consequences of tr for relatives 5.meaning of tr for my future 6.unchangeability of tr	**T2 NfC DNA-test result** I need/do not necessarily need certainty about the DNA-test result	**T1 PC DNA-test result (tr) : α=.85** *I did not feel(1)-I felt (7)…* 1.uncertainty about tr in general 2.certainty about tr in general** *I felt uncertain (1)/certain(7) about…* 3.consequences of tr for myself 4.consequences of tr for relatives 5.meaning of tr for my future 6.unchangeability of tr
T1 NfC heredity I need/do not necessarily need certainty about the heredity of cancer in the family	**T1 PC heredity (her) : α=.86** *I did not feel(1)-I felt (7)…* 1.uncertainty about her in general 2.certainty about her in general** *I felt uncertain (1)/certain(7) about…* 3.consequences of her for my cancer 4.consequences of her for my future 5.consequences of her for relatives	**T2 NfC heredity** I need/do not necessarily need certainty about the heredity of cancer in the family	**T1 PC heredity (her) : α=.89** *I did not feel(1)-I felt (7)…* 1.uncertainty about her in general 2.certainty about her in general** *I felt uncertain (1)/certain(7) about…* 3.consequences of her for my cancer 4.consequences of her for my future 5.consequences of her for relatives

All items were measured with semantic differentials ranging from 1, high PC/high NfC, to 7, low PC/low NfC; for presentation purpose, all items are reverse-coded in this chapter so that '1' means low PC/NfC and '7' high PC/NfC (see figure 1); **reverse coded to match the scale of the other items (1=low PC/NfC-7=high PC/NfC); * All items had been formulated like states, i.e. counselees were asked to rate the items regarding 'the last month', except for questions regarding the self which had been formulated like traits, i.e. 'in general I'm a person who…'; the self-items are not presented in this chapter because we want to focus on state-items; α=Cronbach's α; c=cancer, tr=DNA-test result, her=heredity*

Table 2. *Overview of instruments other than the UNCS*

Research question	Theme	Scales	Range of total scores(low/high)	Cronbach's Alpha
1, 2	**Actual DNA-test result**	Actually communicated DNA-test result categories: PM, UR, UV*	0-1 (not/ communicated)	
4	**Level of cognitive understanding and actually communicated cancer-risks**	1.Level of understanding according to the counselee; 2. counselees' level of understanding according to the genetic-counselor*; 3.actually communicated DNA-test result: counselees' own cancer-risks, relatives' cancer-risks*; 4.Need-for-structure: 12-items, subscales 'desire for structure' and 'reaction to lack of structure' (407,370,406)	1&2:1-7 (bad-good understanding); 3:%; 4: scales: 4-24, 7-42	4: .82; .83
5	**Acceptance**	1.COPE:acceptance-copingstyle, 2 items (318); 2.uncertainty is bearable, i.e. sum of the answers to the question 'uncertainty is unbearable' on the domains of cancer, DNA-test result, heredity and self <12	1:2-8; 2:4-28	1:.79
	Reinterpre-tation	difference score between actually communicated own cancer-risks* and counselees' interpretation of their own cancer-risks (correlated and square-root); scales are measured in 1-7 verbal categories (285)	0-6	
	Active coping	1.COPE:active-copingstyle, 2 items (318); 2.changes in life: 2 scales, i.e. psycholo-gical, medical-physical (203,277); 3.intention to undergo: a.surveillance/surgery of ovaries (PBSO), b.mastectomy (PBM), c. breast surveillance	1:2-8; 2: scales: 7-35, 3-15 3:1-7	1: .85, .84 2: .87, .86
	Passive coping	1.COPE:denial and renaming copingstyle, 2 items (318); 2.Impact of Events Scale: avoidance (408)	1:2-8; 2:8-32	1: .79 2: .81
	Distress	1. uncertainty is unbearable' on the domains of cancer, DNA-test result, heredity and self; 2. two distress-factors 'negativity' and 'worries' (m=0), resulting from principal-component-analyses (prosp-2) on the following general-distress and cancer-specific distress scales: Hospital Anxiety and Depression Scale, Positive Affect Negative Affect Scale, Lerman's Cancer-Worry Scale and Impact of Events Scale(1)(288,290)(2)(291)(3)(286,289); 3. Esplen's BRCA-specific distress, subscales: feeling stigmatized, vulnerable to develop cancer, mastery over cancer (75,277).	1:1-7; 3: 7-49, 5-35, 4-28	2: .90, .87 3: .75, .73, .59

Table 2. *Continued*

Covariates and moderators	**Cancer history**	1. breast or ovarian cancer, 2. metastases, 3. kind of cancer treatment (binary items: PBM, PBSO, chemotherapy, radiotherapy, other therapy), 4. months since disclosure of cancer diagnoses, metastases, treatment and of genetic-counseling	1-3: 0-1 (not/applicable); 4: months	
	Inner resources	Personality: 1.Ryff's conceptual well-being scales (319): mastery, purpose in life, self-acceptance, autonomy, vitality, inner strength 2. Optimism (320); 3.experience with few/much uncertainty in life until now	1: 7-42, except autonomy=8-56; 2:10-50; 3: 1-7	1:.81, .82,.80 .84, .86, .83 2: .79
	Social resources	1. openness to discuss hereditary cancer in the family (409) in nuclear family, and in current family; 2. Dutch Relational Ethics Scale (344) in nuclear family, and in current family: trust/justice, loyalty, negative entitlement	1:7-28 2:6-30; 3-15; 3-15	1: .82, .83 2: .84, .82,.81 .79, .80, .81
	Family characteristics	pedigree information**, i.e.: number and percentage of with-cancer-affected and deceased 1st, 2nd and/or 3rd degree relatives.	n,%	
	Socio-demographics	1.living together with a partner, 2. having children, 3.being religious, 4. having a job, 5.educational level (0, no-7, university)	1-4: 0-1 (not/applicable)	

***derived from the checklist filled-in by the genetic-counselor; **derived from medical-file; all other items derived from the questionnaire filled-in by the counselee*

Table 3. *Results of questions 1 and 2*

Domain	Need for certainty = NfC (1, low - 7, high)				Perceived certainty = PC (1, low – 7, high)				Unfulfilled need for certainty = NfC-PC (<0, fulfilled - >0, unfulfilled)			
	Intake (n=467)	PM (n=30)	UR (n=202)	UV (n=16)	Intake (n=467)	PM (n=30)	UR (n=202)	UV (n=16)	Intake (n=467)	PM (n=30)	UR (n=202)	UV (n=16)
Cancer	5.9 (1.5) [2]	6.3 (1.3) [12]	5.6 (1.7) [12]	6.1(1.2) [2]	4.5 (1.3) [2]	4.3 (1.2) [23]	5.0 (1.3) [123]	5.1 (1.2) [123]	1.4 (2.2) 76% [4]	2.0 (1.7) 73% [134]	.6 (2.4) 77% [134]	1.0 (1.6) 87% [34]
DNA-result	5.9 (1.3) [2]	5.5 (2.1) [1]	5.5 (1.8) [1]	6.3 (1.4) [2]	3.9 (1.4) [2]	4.6 (1.8) [13]	5.4 (1.3) [13]	4.6 (1.5) [123]	2.0 (2.1) 86% [4]	.9 (2.9) 67% [134]	.1 (2.4) 64% [134]	1.7 (2.0) 88% [34]
Heredity	6.2 (1.2) [2]	6.7 (.5) [13]	6.2 (1.4) [3]	6.2 (.8) [3]	4.2 (1.3) [2]	3.7 (1.7) [123]	4.7 (1.3) [123]	4.3 (1.3) [23]	2.0 (1.8) 91% [4]	2.5 (1.9) 89% [134]	1.5 (2.1) 82% [134]	1.9 (1.6) 94% [34]

Cells show the results for the questionnaire filled-in by counselees after the intake (T1) and after one of the three possible DNA-test results (T2: PM, UR or UV). Figures are means (standard deviations), and % of counselees with NfC-PC<0; see figure 1 for explanation of the scores.[1]Difference between intake and DNA-test result as shown by t-tests with p<.01 and Cohen's d>.14 (i.e. medium effects or larger); [2]Difference between NfC and PC (either at intake or at PM/UR/UV) as shown by t-tests with p<.01 and Cohen's d>.14 (i.e. medium effects or larger); [3]Difference between PM, UR, UV measured with Kruskal-Wallis test, either for NfC or PC (p<.01);[4]Difference from 0 as shown by one-sample t-tests with p<.01 and Cohen's d>.14 (i.e. medium effects or larger).

2.3. Statistics

1. We described the percentage of counselees who experienced an unfulfilled need for certainty (i.e. NfC>PC; see figure 1); t-tests were used to show whether NfC was mainly unfulfilled, i.e. larger than PC. 2. Differences between intake(T1) and PM/UR/UV(T2) were calculated with t-tests (effect sizes are shown with Cohen's d), and differences between the disclosure of PM, UR and UV with Kruskal-Wallis-tests and t-tests(t/d). 3. We calculated differences in NfC-PC-scores between the domains of cancer, DNA-test result and heredity with t-tests (t/Cohen's d). 4. Relationships between NfC, PC, NfC-PC and cognitive-understanding-variables were calculated with correlations, corrected for PM/UR. 5. For each domain, we calculated correlations between NfC-PC and the coping- and distress-variables.

Inclusion of other variables as either covariates or moderators in analyses did not substantially change answers to the research questions and are therefore not presented (see table 2; see selection of variables in 340). Significance level was defined as $p<.01$. This level reflected a balance between the explorative nature of this study (suggesting to set a high p-value to avoid type-II error), and the large number of tests (suggesting a low p-value to avoid type-I error).

3. Results

3.1. Population

We approached 654 cancer patients who had undergone BRCA1/2-testing. Of them, 467(71%) filled-in the T1-questionnaire and 248(54%) the T2-questionnaire. Mean time since cancer-diagnosis was 5 years (sd=2); 94% had had breast cancer and 6% ovarian cancer. Metastases were detected in 26% of all participants. Before DNA-testing, 56% had undergone therapeutic mastectomy, 6% therapeutic and 5% preventive bilateral salpingo-oophorectomy (PBSO). Mean age was 56 years, 42% had visited high school or higher, 84% were married, 87% had children (see chapter 6).

3.2.1. Question 1: description of unfulfilled need for certainty

On all domains, after intake and after DNA-test result disclosure, NfC was always significantly larger than PC (all $p(t)<.01$, $d>.14$; see [2] in table 3). On each domain, between 58% and 94% of all counselees experienced NfC as mainly unfulfilled (NfC>PC; see percentages in table 3).

3.2.2. Question 2: change in unfulfilled need for certainty after DNA-test result

Compared to T1, PM-counselees experienced more fulfillment of their NfC about the DNA-test result, but less fulfillment of their NfC about cancer and heredity (p(t)'s<.01, d's>.14). (see table 3) Compared to T1, UV-counselees experienced no changes in fulfillment of NfC in all domains (p(t)'s >.05). Compared to T1, UR-counselees experienced more fulfillment of their NfC in all domains.

PM-counselees experienced less fulfillment of their NfC regarding cancer and heredity than counselees with an UV/UR (p(t)'s<.01, d>.14). Compared to PM/UR-counselees, a larger percentage of UV-counselees experienced unfulfilled NfC on all domains, and their mean unfulfilled NfC was larger than UR-counselees on all domains (p(t)'s<.01, d>.14). Compared to PM/UV-counselees, UR-counselees experienced more fulfillment on all domains (p(t)'s<.01, d>.14).

3.2.3. Question 3: differences between domains

The counselees' scores on the unfulfilled NfC (NfC-PC) differed significantly between all domains. More specifically: scores differed between cancer and DNA-test result (d's: intake:.41; PM:.29, UR:.25, UV:.16; p(t)'s<.01), between cancer and heredity (d's: intake:.14; PM:.72, UR:.35, UV:.56; p(t)'s<.01), DNA-test result and heredity (d's: intake:.15; PM:.81, UR:.62 , UV:.33; p(t)'s<.01).

3.2.4.Question 5: correlations with coping and distress

Table 4 shows how the level to which the counselees' NfC remained unfulfilled (NfC-PC) correlated with coping styles and distress. NfC-PC correlated barely with the extent to which counselees had an accepting-coping style, but correlated moderately with another operationalization of acceptance, i.e. experiencing the uncertainty as bearable. NfC-PC correlated strongly with reinterpretations of cancer-risks, i.e. with the level to which the risks were perceived inaccurately. NfC-PC correlated moderately with active-coping, i.e. with an active-coping style, psychological and medical changes, intention to undergo surveillance/surgery of ovaries (PBSO), mastectomy (PBM), and breast surveillance. NfC-PC correlated moderately with passive coping styles, i.e. with the level of avoidance, denial and renaming. NfC-PC correlated strongly with distress, i.e. with the level of uncertainty about cancer, DNA-test result and heredity perceived as unbearable, and with negative emotions, worries, feeling stigmatized, low mastery over cancer and large vulnerability to develop cancer.

Table 4. *Results for question 5*

Coping and distress related to the level of unfulfilled need for certainty (NfC-PC)			Level of unfulfilled need for certainty after DNA-test result disclosure (NfC-PC)					
	Measurement	Subscales	NfC-PC-cancer		NfC-PC-DNA		NfC-PC-heredity	
			High scores (%)*	(R)	High scores (%)*	(R)	High scores (%)*	(R)
Acceptance	*-Copingstyle*	Acceptance	28	ns	29	ns	29	ns
	-'Uncertainty is bearable'		4	.30	4	.21	6	.31
Misinter-pretation	*-Perception*	Level of inaccuracy of counselees' interpretation of their own cancer-risks	76	.40	78	.36	69	.55
Active coping	*-Copingstyle*	Active	15	.27	17	.15	24	.26
	-Changes in life	Psychological	15	.31	14	.20	13	.26
		Medical-physical	8	.26	8	.12	7	.18
	-Intention to undergo surveillance and/or surgery	Surveillance or surgery of ovaries (PBSO)	42	.15	46	.10	46	.19
		Mastectomy (PBM)	41	.20	54	.16	46	.20
		Breast surveillance	65	.13	66	.10	67	.10
Passive coping	*-Copingstyle*	Avoidance	19	.37	18	.27	16	.28
		Denial	35	.22	3	.20	3	.18
		Renaming	14	.20	14	.18	15	.22
Distress	*-'Uncertainty is unbearable'*	Cancer	19	.60	20	.42	25	.47
		DNA-test result	37	.34	32	.42	41	.34
		Heredity	10	.31	12	.35	17	.52
		Self	26	.45	26	.39	33	.40
	-Distress	Negativity	60	.66	60	.51	56	.60
		Worries	60	.67	60	.46	62	.52
		BRCA-stigma	5	.56	5	.50	4	.51
		BRCA-mastery	24	.46	20	.46	23	.47
		BRCA-vulnerability	18	.61	18	.47	16	.49

*Ns=not significant; *Cells show percentages of counselees with NfC-PC<0 who has 'high' mean scores, i.e. acceptance copingstyle>5, sum of 'uncertainty is unbearable'<16, inaccuracy>0, psychological change>15, medical-physical change>9, denial/renaming>6, avoidance>20, uncertainty is unbearable>4, negativity>0, worries>0, stigma>34, mastery<13, vulnerability>24*

3.2.5. Question 4: correlations with cognitive understanding

The counselees' unfulfilled NfC (NfC-PC) was not correlated with the counselees' level of understanding according to themselves and the genetic-counselor, and not with the actually communicated DNA-test result and cognitive-need for structure (R's<.20, p(R)'s>.05).

4. Discussion

4.1. Conclusions

Before and after receiving DNA-test results, the majority of counselees experienced an unfulfilled need for certainty about the DNA-test result, heredity and cancer. The communication of PM decreased uncertainty about the DNA-test result, but increased uncertainty about cancer and heredity (i.e. meaning for relatives); this is understandable because one's genetic status may have consequences for medical treatment as well as for one's relatives. The communication of UV's did not fulfill any of the counselees' needs for certainty, and on all domains of uncertainty, UV-counselees experienced a more unfulfilled need for certainty than PM/UR-counselees. UR-counselees experienced more fulfillment of their NfC compared with PM/UV-counselees and with the intake-measurement.

Counselees differentiated the unfulfilled NfC between the domains of cancer, DNA-test result and heredity. The unfulfilled NfC did not correlate with the counselees' cognitive-understanding of the DNA-test result.

This study is limited by its relatively large and specific number of decliners (which is comparable to other studies in the Netherlands) and by lack of baseline-measurement. We only described the short-term impact of DNA-testing and included cancer-patients only; however, similar results were found when we performed (unpublished) analyses in retrospective studies in unaffected counselees and their untested, unaffected relatives (277,321). NfC-scores and PC-scores may have influenced each other and/or may both reflect other variables such as personality; however, such influence would lead to a small difference between NfC and PC, but we did find large differences between both (d's>.6).

The extent to which the counselees' need for certainty remained unfulfilled after genetic-counseling, correlated strongly with distress, misinterpretation of genetic-information, and passive coping. It correlated moderately with active-coping and only weakly with acceptance. Thus, only few counselees accept unfulfilled NfC, and the majority transformed their perception, reacted passively and/or experienced distress.

If we regard acceptance of the dual reality of genetic-uncertainty and the counselee's wish for certainty as psychologically beneficial (138,395,401), psychological care may help them living meaningfully while accepting uncertainties. It may help them in the acceptance of dual realities, by finding/creating some extent of subjective certainty,

without denying the reality of being a cancer-patient (e.g.378). In other terms, they may learn to neither try to deny PC nor give-up their NfC, and accepting the situation and experiencing the uncertainty as bearable.

On the basis of the results, we suggest six shifts in the implicit/explicit hypotheses that psychological researchers may have about DNA-testing.

4.2. Unspecific-trait-hypothesis

Previous studies on genetic-counseling focused on general, trait-like variables, but did not clarify how these general concepts were related to specific experiences of uncertainty. We examined state-items about DNA-testing, heredity and cancer, which showed differences, changed after DNA-test result disclosure, and were strongly related with copingstyles. Additionally, we also measured trait-items about the self, but non-presented analyses showed that these trait-items did not appear to be sensitive enough to track the impact of DNA-testing. Because these trait-items did not change after DNA-test result disclosure and were not correlated with copingstyles and distress. This suggests that the counselees' experience of uncertainty is understood in most detail when measured with sensitive items about the current experience of NfC/PC in specific domains. Future studies should examine how specific-NfC/PC relates to the cancer-patients' general experience/needs of certainty, vulnerability and assumptions about life (131,137,410,411).

4.3. Uncertainty-causes-distress-hypothesis

It has been suggested that the communication of uncertain genetic-information directly evokes distress (86,203). However, this study suggests that neither the actually communicated DNA-test result nor the counselees' PC or NfC strongly predicted distress as sole predictor. It is the balance between NfC and PC, i.e. the level to which the NfC remains unfulfilled after genetic-counseling, that strongly predicted distress.

4.4. Accuracy-matters-hypothesis

From the perspective of genetic-counselors, DNA-testing is offered as a means to inform counselees about their cancer-risks and medical options, and to help them to make well-informed medical decisions (cf.412,413). From this perspective, several studies have focused on the accuracy of the counselees' perception, and on how counselors may improve this (66,70,78). In contrast, counselees describe health care professionals 'to rely on numbers to fulfill certain obligations to inform patients, to steer decision making, and to prevent unrealistic expectations', and thought professionals 'are insensitive toward the more general impact that numerical information could have within their illness experience' (149, p.327-8). This description is understandable because counselees do not ask for DNA-testing in order to become 'accurate' and 'well-informed' (1,5,6), and frequently value their own opinion as more important than that of the genetic-counselor (203,285). They want to

receive certainty about their own and their relatives' cancer-risks and to know which medical decisions to make (1,5,6). That is, they want to find meaningful ways to live with the uncertainties about cancer, and to find a basis for hope (149).

Before DNA-testing, genetic-counselors assess counselees' needs and motivations to have a test, and inform them about the potential uncertainty that may result from DNA-testing. We suggest developing genetic-counseling as a personal, two-directional and reciprocal process (283) with explicit focus on these needs and interpretations.

One may argue that for some counselees, accuracy of perception is less important than knowing what to think, what to do, and what to hope for (i.e. NfC-PC). As long as the necessary medical care is provided, some counselees may benefit more from psychosocial help to learn to live meaningfully with the uncertainty of cancer and heredity than from undergoing expensive genetic-counseling, which has a large likelihood of detecting uncertain UR/UV-results, followed by uncertainty, distress and poorly-informed medical-decisions (277,340). The counselees' needs may also be taken into account when considering communicating UV's, low-penetrance-genes and unexpected findings in whole-genome-sequencing. Such information may not fulfill the counselees' motivation to undergo DNA-testing, cause misinterpretation and distress.

4.5. Cognitions-cause-uncertainty-and-distress-hypothesis

Many studies focused on the counselees' perception of the communicated cancer-risks, and tried to predict uncertainty and distress by their cognitive-understanding of the DNA-test result (70,66,277). These authors seemed to assume that cognitions cause uncertainty and distress. However, the counselees' cognitions were often poor predictors of the counselees' reactions (66,68,76). The best predictors of distress were not the counselees' (mainly cognitive) recollections but their interpretations (277,340). The current study underlines these criticisms. PC, NfC and NfC-PC were not related with cognitive understanding, but to social and inner resources, such as purpose-in-life, self-acceptance and open family communication (see method). Thus, information-focused variables, i.e. the actually communicated DNA-test result and cognitive risk-perception, did not strongly predict distress but counselee-centered variables did (i.e. NfC-PC) (cf.400).

4.6. Paternalism-hypothesis

The intention of genetic-counseling is to counsel in a non-directive way, give counselees a free choice, and respond to the counselees' needs (40-42). In practice, genetic-counseling sometimes represents more a teaching-model than a counseling-model (99,311,414,415), meaning that counselors may verbally dominate the dialogue and advise directively (416). From such a paternalistic perspective, authors assumed a direct relationship between the genetic-counselor's role and false cognitions (78) which seemed to lead them to the conclusion that counselors should improve risk communication skills (54,56,311,264).

However, these paternalistic assumptions seem oversimplified. Genetic-counselors may actually have little influence on the counselees' lives. For instance, the counselees' perception is not only connected with the communicated genetic-information, but also with their experiences with their own and their relatives' cancer (35,68,71,73,164,166-169). Therefore, the accuracy of the counselees' perception does not strongly depend on the communicated message (400), but on individual processes, such as coping and (mis)interpretation of the DNA-test result. This is confirmed by studies suggesting that patient-centered aspects of interventions change the counselees' perception more than information-centered aspects (327,400).

4.7. Non-tautology-hypothesis

Many studies have searched for possible predictors of distress, such as social-support, stigma and vulnerability (417), uncertainty (418), and risk-perceptions (70,66,277). However, these predictors may not be other phenomena than distress, only differently measured by different instruments. Distress may underlie all these predictors. Therefore, examining how variables such as uncertainty relate to distress, may be similar to stating a tautology: e.g. NfC-PC strongly correlated with negativity and worries. That is, one aspect of distress was related to another aspect, but we do not know their causal directions. Such tautologies should be studied with correlations to show consistencies, as we did, and not with regression analyses to show predictions.

When we assume that variables such as stigma, vulnerability and uncertainty are different expressions of the same distress, the criterion that defines a variable as 'bad' or 'good' transforms. Previous studies have searched for predictors with the largest effect sizes, but it may be more important to search for variables that express the counselees' lived experience of distress most fully and fundamentally. Qualitative studies suggest that feelings of uncertainty are the essence of the counselees' lived experience of being at risk for cancer (6,62,389,390). More studies are needed to understand the counselees' experience of uncertainty in genetic-counseling and other diseases.