Opening the psychological black box in genetic counseling

Vos, J.

Chapter 4

Perceiving cancer-risks and heredity-likelihood in genetic-counseling:

the analysis of the counselees' recollections and interpretations of BRCA1/2-test results

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Abstract

Background

Previous studies on the counselees' perception of DNA-test results did not clarify whether counselees were asked about their recollections or interpretations, and only focused on patients' own risks and not on the likelihood that cancer is heritable in the family. We tested differences and correlations of four perception aspects: recollections and interpretations of both cancer-risks and heredity-likelihood.

Method

In a retrospective study, women tested for BRCA1/2 on average 5 years ago completed questionnaires about their perception. Participants had received an unclassified-variant (n=76), uninformative (n=76) or pathogenic-mutation (n=51) result in BRCA1/2. Analyses included t-tests, correlations and Structural-Equation-Modelling.

Results

The counselees' perception showed to consist of four distinctive phenomena: recollections and interpretations of cancer-risks and of heredity-likelihood. This distinctiveness was suggested by significant differences between these perception-variables. Moderate to strong correlations were found between these variables, suggesting that these differences between variables were consistent. The relationships between these variables were not influenced by actually communicated DNA-test result, sociodemographics, medical and pedigree information, or framing of cancer-risk questions. The largest differences between recollections and interpretations were found in the unclassified-variant group and the smallest in uninformatives. Cancer-risks and heredity-likelihood correlated least in the pathogenic-mutation-group. Communication of ambiguous genetic-information enlarged the differences.

Discussion

To understand the counselees' perception of genetic-counseling, researchers should study recollections and interpretations of cancer-risks and heredity-likelihood. Genetic-counselors should explicitly address the counselees' recollections and interpretations, and be aware of possible inaccuracies.

1. Introduction

1.1. Background

Since the identification of the BRCA1 and BRCA2-genes in hereditary breast and ovarian cancer, many mutation analyses have been performed in women at increased risk. Usually, a BRCA1/2-test is performed in case of clinically presumed hereditary breast and/or ovarian cancer, primarily in an affected woman with a mutation detection rate of about 10%, or if she has developed cancer at a relatively young age (15).

A genetic-counselor may communicate six pieces of information about the BRCA1/2-result to an index-patient/proband. 1. The DNA-test result category, i.e. a pathogenic mutation in the breast and ovarian cancer–predisposition genes BRCA1 and BRCA2 (PM), Uninformative-Result, i.e. no mutation in the BRCA1/2 genes (UR), or Unclassified-Variant/variant-of-uncertain-clinical-significance, i.e. the contribution of BRCA1/2 sequence variants to cancer risk remains largely undefined (UV). 2. The likelihood that cancer is heritable in the family (i.e. heredity-likelihood; see below). 3. Contralateral breast- and ovarian-cancer-risks for the affected proband 4. Breast- and ovarian-cancer-risks for healthy relatives. The communicated heredity-likelihood and cancer-risks are based on the DNA-test result and cancer-history of the proband and relatives. In UV/UR-families, the counselor communicates cancer-risks mainly based on the pedigree. 5. Options for surveillance and/or preventive surgery (prophylactic bilateral mastectomy, PBM, and bilateral salpingo-oophorectomy, PBSO) of counselees and relatives. 6. Counselees are advised to communicate this DNA-test result to their relatives.

1.2. Assumptions in the literature

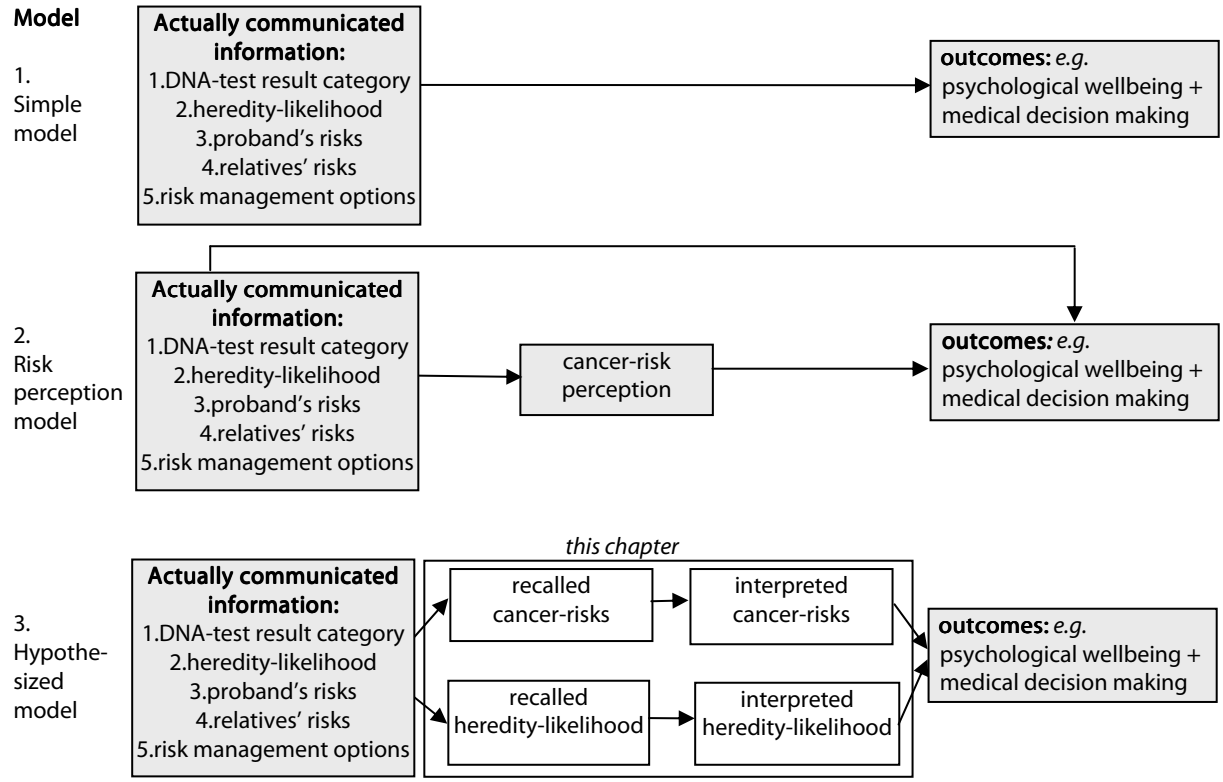
Many studies assume that the communication of a BRCA1/2-result has a direct impact on the counselees' psychological well-being and medical decisions. However, reviews suggested that such studies yielded inconsistent results and showed that DNA-test results rarely predict psychological impact (66,68,70, 71,76). For instance, several studies described disclosure as a stressful experience, mainly after PM communication, but studies differed in distress levels and decrease over time (169,182,199,321,249-255).(figure 1-1)

Not finding a clear direct relationship between the actually communicated DNA-test result and impact-measures caused researchers to turn their focus towards the counselees' perception of the BRCA1/2-results. Recent studies suggested that the receipt of a DNA-test result only has an indirect impact on the counselees' lives, via the mediation of the counselees' perception of cancer-risks (64). Results of these studies seem to be more consistent, and perception-variables explain more variance of the impact-variables. It is suggested that the higher the perceived cancer-risks reported by a counselee are, the more distressed she is (164,169,177-179,199,256-258), the more often she decides to

undergo surgery, and the better she adheres to surveillance of breasts and ovaries (177,257,259-262). Thus, perceived risks are suggested to be better predictors of the impact of genetic-counseling than objective information (cf.77-79). (see figure 1-2) Despite their improved explanation of the impact of genetic-counseling, these risk-perception studies still vary widely in their outcomes, and perception-variables only partially explain the impact (77-79). For example, reported accuracy of perception varies (239): after genetic-counseling, 4% to 37% of all counselees have an improved more accurate risk-perception, but 3-70% of all counselees overestimate their cancer-risks, and 0% to 85% of the counselees perceive their cancer-risks accurately (171-182,249,250,263). Therefore, several authors suggest that risk-perception has been operationalized too simply in previous studies. New measures should be developed to measure the perception of DNA-test results as a multidimensional construct (84,239,264), including personal interpretations of the DNA-test result, risk figures and inheritance (94,239,265).

In this chapter we test four new perception-measures: recollections and interpretations of both cancer-risks and heredity-likelihood (see figure 1-3). We only focus on the counselees' perception of their own cancer-risks and of heredity-likelihood. Other perception-variables are assumed to be implicitly included in these variables: e.g. understanding of the DNA-test result category may be reflected in the counselees' perception of cancer-risks and heredity-likelihood; perception of relatives' risks may overlap with perceived heredity-likelihood.

Figure 1. *Models (1,2) in previous studies and Complex Model of Genetic Counseling (3), as hypothesized in this chapter; in this chapter, only the relationships between recollections and interpretations, and between cancer-risks and heredity-likelihood are studied*



1.3. Recollections and interpretations

In previous qualitative studies, we asked patients to describe their risk to develop cancer (203,239). Several counselees indicated that they did not know whether our question referred to the actually communicated risks, or their own interpretation of that information. They spontaneously mentioned a discrepancy between their recollection of the objective risk, and their personal interpretation of that risk, e.g.: 'I know that the genetic-counselor communicated 'A', but I'm convinced 'B' is true. Therefore, I trust B when considering surgery and surveillance.'

We hypothesize that the counselees' perception combines the processes of recalling and interpreting the communicated DNA-test results. Recollection concerns memorizing and reconstructing what the genetic-counselor has said, Interpreting concerns giving meaning to the recalled information, for instance, by subjectively selecting, weighing and evaluating the information, e.g. as a form of meaning-based coping (131) or by integrating genetic-information in one's identity (61). Both recollections and interpretations may be biased due to selective listening and heuristic information-processing (cf.83), but interpreted information is more deeply processed and more connected with personal meanings than recalled information.

Previous perception studies may have yielded inconsistent results, because they measured either the counselees' recollections (174,172,182,263) or interpretations (169,257,266), or were unclear about this. Most studies operationalized the counselees' perception with aspecific formulations such as: 'what DNA-test result did you receive?' and 'what are your cancer-risks?' Other researchers asked counselees about their cognitions and feelings of risks (87,239,267), in line with the dual-process theory (81-84): 'how do you estimate your chance of developing breast cancer?'; 'what do you feel your chance is?' These questions are also ambiguous, because it is unclear whether the requested estimations are recollections of what the counselor had told, mere subjective interpretations of the communicated risks, or a combination of both. It is also unclear whether feelings about chance include only subjective interpretations or also factual recollections. Due to these ambiguous formulations, different counselees may have given different answers, which may have subsequently caused failure of predicting the impact of DNA-testing.

1.4. Cancer-risks and heredity-likelihood

In our qualitative study, many counselees differentiated between their own cancer-risks and the likelihood that cancer is heritable in the family: 'My own risks do not worry me; I have already had cancer. I worry about the heredity of cancer in my family, and its meaning for my children and sister.' (unpublished part of 203/study in chapter 3).

The sole use of the counselees' perception of their own cancer-risks may explain the poor prediction of outcomes in previous perception studies for two reasons. *Firstly*, only about 10% of all BRCA1/2-test results in affected cases prove pathogenic, and provide exact risk information for the counselee and her relatives. In all other cases, cancer-risks are mainly based on the pedigree and on cancer history, age at onset, and segregation analyses. In these cases, cancer-risks are in general not communicated.

Secondly, one of the main motivations of counselees to request genetic-testing is receiving information about their relatives' cancer-risks (1,5) and heredity-likelihood, i.e. the likelihood that cancer in the family is heritable. Heredity-likelihood is either communicated on the basis of the PM's, or of the pedigree in case of UV's/UR's.

1.5. Research questions

The purpose of this study was to examine relationships between recollections and interpretations, and between perceived cancer-risks and heredity-likelihood. 1.Is the counselees' recollection of genetic-information different from their interpretation? 2.Do recollections predict interpretations? Finding a difference does not imply that variables are unrelated; we expect that recollections and interpretations are correlated, because interpretations are reflections on the counselees' previous recollections of what was communicated. 3.Do counselees perceive heredity-likelihood and cancer-risks differently?

4.Are perceived cancer-risks and heredity-likelihood correlated? We expect these to correlate, because both cancer-risks and heredity-likelihood are high when PM is found, and both are lower in case of UV/UR. 5.Do the answers to the previous questions differ between PM, UV and UR?

2. Method

2.1. Population

This retrospective study was part of a larger Dutch multicenter study on UV's in BRCA1/2 approved by the Medical Ethical Committees of the participating centers. We sent an invitation letter with consent-form and questionnaire to all affected and unaffected adult first tested individuals with cancer (index-cases) from families with intermediate or high risk breast/ovarian-cancer who had received a BRCA1/2-test result in the period 1998-2008 at the Departments of Clinical Genetics of the Leiden University Medical Center, Maastricht University Medical Center, University Medical Central Groningen, and VU Medical Center Amsterdam. We included all index-patients (PM, UR, UV). All results had been communicated face-to-face and summarized in a letter for the counselee. We explicitly asked counselees to not re-read the letter before filling-in the questionnaire.

2.2. Instruments

We asked questions about the counselees' recollections and interpretations of cancer-risks, and of pedigree-based and test-based heredity-likelihood. Questions had been developed in a previous study (203). The presented perception-questions only focused at breast-cancer-risks, because 96% of all counselees reported that they did not experience their ovarian-cancer-risks as strongly influencing their lives, and experienced breast-cancer-risks as relatively more influential.

Recollection-questions were introduced as follows: 'we ask you to recall what your counselor has actually communicated to you, regardless of your own ideas and feelings'. Recollections of cancer-risks were measured by the question 'what cancer-risks did your counselor tell'. Recollections of heredity-likelihood based on the DNA-test result were asked as 'according to your counselor, what does the DNA-test result mean for the likelihood that the cancer in your family is heritable?' Recollections of heredity-likelihood based on the pedigree were asked as: 'regarding your pedigree, what did your counselor communicate about the likelihood that cancer in your family is heritable?' We asked participants to describe their 'own current thoughts and feelings about cancer-risks, test-based and pedigree-based heredity-likelihood regardless of what the counselor has communicated'.

In line with other studies (66,70,164), we asked counselees to rate cancer-risks and heredity-likelihood on a 7-point scale (not likely-very likely). People often use such broad

categories to translate detailed risk information (268-270). We also asked counselees to recall/interpret cancer-risks in percentages, as frequently used (171-182). These answers were excluded from analyses, because most counselees (153/204) did not recall the communicated percentage. Many (69/204) recalled or interpreted cancer-risk of precisely 50% (cf.216,217), indicating stochastic uncertainty; this caused a lack of variation in the counselees' perceptions of percentage-risks.

2.3. Statistical analyses

Analyses with non-parametric tests (not shown here) did not show large differences with parametric tests, and did not lead to different conclusions. Therefore parametric tests are presented. Effect sizes were described with Cohen's d, correlations and standardized B.

Question 1: Differences between recollections and interpretations of cancer-risks and of heredity-likelihood. were tested using the percentage of exact agreement as well as t-tests. Question 2: To test whether recollections predict interpretations, both regarding cancer-risks and heredity-likelihood, we used path-analyses/Structural Equation-Modeling, SEM, in LISREL 8.80 (271) (see final model in figure 2) (e.g.272,273). For evaluation of model fit, the matrix of discrepancies (i.e., the matrix of residual variances and covariances) was investigated (cf.274). We report the overall X^2 statistic with the associated p-value, and the root mean squared error of approximation (RMSEA) (275). Indicative of good model fit are a non-significant X^2 statistic ($\alpha>.05$), and RMSEA $\leq .06$ (276).

Question 3: Differences between cancer-risks and heredity-likelihood, regarding recollections or interpretations, were tested with t-tests. Question 4: The correlations between perceived cancer-risks and heredity-likelihood were estimated using SEM. Question 5: To assess differential effects for different DNA-test results, a separate multi-group analysis was performed using SEM.

Previous studies have been criticized for not taking into account the general context of genetic-counseling (68,74). Therefore, we corrected analyses for several covariates suggested by literature: actually communicated genetic-information (163,164); elapsed time since DNA-test result disclosure (70,165); experiences with cancer and death in the family (164,166-168); cancer history and treatment (35,68,69,71,73); age, education, having-children, religion (164,170); risks measured in percentages (171-182). Most covariates did not significantly influence the relationships between recollections and interpretations, and between cancer-risks and heredity-likelihood. An exception to this was additional explanation provided by the genetic-counselor in summary letters to counselees, such as 'future research may detect a pathogenic-mutation' and using the non-neutral terms 'mutation' or 'deviation'; each explanation predicted a larger difference between recollections and interpretations, but correlations were small (std.ß's<.20,p's<.01). Therefore, covariates are not presented. (see table 1)

Table 1. *Description of moderators/covariates (all showed to be not significant)*

Moderator/covariate name		Operationalisation [1]
actually communicated DNA-test result (derived from medical files, and confirmed by letters summarizing the counseling sessions sent to counselee)	result category[2]	Pathogenic-mutation (PM), unclassified-variant (UV), uninformative-result (UR)
	heredity-likelihood[3]	Low, medium, high
	counselee's cancer-risks[3]	Breast cancer(%); ovarian cancer(%)
	relatives' cancer-risks[3]	Breast cancer(%); ovarian cancer(%)
	counselee's options[3]	Mastectomy (PBM), oophorectomy (PBSO), frequency breast and ovarian surveillance, breast self-examination
	additional explanation in letter to counselee[3]	Explanation of genetics; possible involvement of non-BRCA1/2-genes; indications of heredity (pedigree, etc); future research may show pathogenic-mutation in non-BRCA1/2-genes; DNA-testing is not 100% sensitive to detect changes; use of the term 'deviation' or 'mutation' instead of the neutral term 'change' or 'variation'; autosomal dominant gene; about 10% of all breast-cancer cases are possibly caused to a heritable cause; about 10% of all heritable breast-cancers are detectable by BRCA1/2-testing; in non-pathogenic cases, mentioning of cancer-risk and/or heredity-likelihood if the DNA-test result had shown to be pathogenic
elapsed time	[3]	Years since disclosure of: DNA-test result; 1st, 2nd cancer diagnosis, metastases
pedigree (derived from medical file)	[3]	N and % for: affected, unaffected, deceased 1st degree, 2nd degree, 3rd degree, all relatives
	Cancer[3]	Breast-cancer, ovarian-cancer, unaffected, metastases
medical history	before testing[3]	Mastectomy (PBM), oophorectomy (PBSO),
	after testing[3]	Mastectomy (PBM), oophorectomy (PBSO), chemo, radio, hormone, other
	current [3]	Chemo, radio, hormone, other
sociodemographics	[3]	Age, marital status, having children, educational level, religious, employed
counselees' perception (other than already measured)	result category[3]	Recollection of category (multiple choice question); accuracy of perception (PM: 97%; UI: 97%; UV:75%)
	proband's ovarian cancer-risks[3]	Recollection and interpretation of ovarian-cancer-risks (1-7 Likert scale)
	relatives' cancer-risks[3]	Recollection and interpretation of breast-cancer and ovarian-cancer-risks (1-7 Likert scale)
perceived own cancer-risks in %	[4]	Recollection and interpretation of breast-cancer-risks (%)

[1]Variables with two levels were included as dichotomous variables (e.g. female 0, male 1); other variables were included on ratio/linear-level. [2]Covariate was included in analyses of research questions 1 and 3 by doing separate t-tests for each category; covariate was included in analyses of research questions 2 and 4 by doing multi-group analyses in SEM; [3]All analyses are corrected for the influence of the DNA-test result category. Inclusion of these covariates in SEM-analyses was impossible due to multicollinearity and small n; therefore, regression and correlation analyses were performed (cf.figure 2), in which one covariate at a time was used in predictions: recalled risks →interpreted risks; recalled heredity-likelihood →interpreted heredity-likelihood; partial-R between recalled cancer-risks and recalled heredity-likelihood, between interpreted cancer-risks and interpreted heredity-likelihood. Covariate was included in analyses of research questions 1 and 3 by doing a separate t-test, for each level of each covariate (e.g. 2 levels: mastectomy; no mastectomy). Covariate was included in analyses of research questions 2 and 4 by doing Separate ANCOVA (analyses of covariance) and partial correlation analyses, including each covariate; [4] Covariate was included in analyses of research questions 1 and 3 by doing separate t-tests, categorical-risks replaced by %-risks. Covariate was included in analyses of research questions 2 and 4 by doing separate ANCOVA; categorical-risks replaced by %-risks.

3. Results

3.1. Study sample

Four-hundred-and-twelve out of 484 eligible probands who had received a DNA-result in the past were invited to participate in our study. Reasons for exclusion were: being deceased, comorbid diagnoses or psychopathology (resp. 7%; 4%; 4%). Half of the probands consented (206/412=50%), and completed the questionnaire. Sixty-three women declined; 145 did not respond. Cited reasons for decline were: being too ill to participate, unresolved feelings, and lack of motivation (resp. 12%; 8%; 7%).

All participants were women, because DNA-testing had not been performed in male probands in our sample; this is in line with the Dutch policy of first testing individuals with breast and/or ovarian cancer from high-risk families, and the large majority of them are women. Mean time elapsed since DNA-test disclosure was 5 years (sd=2.0 yrs). UV was communicated to 76 women (36.8%), UR to 77 women (37.4%), and PM to 53 women (25.8%). As part of standard counseling, letters summarizing the disclosed genetic information were sent by the genetic counselor to all participants; exact cancer-risk information was written in 126 out of the 204 letters (62%), the remaining 78 letters did not include risk information. Most participants (n=57; 28%) belonged to a family with high cancer-risks (30 to 40%), 11(5%) belonged to a family with intermediate cancer-risks between (20-30%) and 10(5%) belonged to a family with low cancer-risks (10-20%). Mean communicated cancer-risk on the basis of the pedigree differed significantly between UV(m=32%,sd=14.0), UR(m=25%,sd=14.7) and cancer-risks on basis of PM(m=64%,sd=10.6).

The majority had a diagnosis of cancer before genetic-counseling (88.3%). Hundred-seventy-three had breast cancer (83.9%), 16 ovarian cancer (7.7%), 5 both (2.0%), and 34 metastatic cancer (16.7%). Table 2 presents sociodemographics. Medical variables and sociodemographics were equally distributed among specific groups of DNA-test results, participants, decliners and non-responders.

3.2.1. Question 1: recollections and interpretations differ

Tables 3-4 and figure 2 show the results for the counselees' recollections and interpretations of (1) cancer-risks and (2) heredity-likelihood.

Counselees recalled intermediate cancer-risks of 4.5 on a 7-point Likert scale (sd=1.4) and interpreted intermediate risks of 4.0(sd=1.6). Recollections and interpretations differed significantly t=-3.4,p<.01,d=.33), except for UR(p>.05,d=.13). 38% of all counselees recalled and interpreted cancer-risks identically, 31% interpreted cancer-risks as higher and 30% interpreted cancer-risks as lower compared to their recollections of the cancer-risks. (see table 3).

Counselees recalled an intermediate heredity-likelihood of 4.4(sd=1.4), and interpreted this as 4.8(sd=1.3). Recollections and interpretations differed significantly (t=-2.4,p<.05,d=.30), except for PM(p>.05,d=.00). 48% of all counselees recalled and interpreted heredity-likelihood identically, 35% interpreted this as higher, and 17% interpreted this as lower compared to their recollections.

Table 2. *Overview of sample*

Variable	N (%)	Mean(sd)
DNA-test result		
time since disclosure (years)		5.0 (2.0)
unclassified-variant(UV)	76(36.8)	
uninformative-result(UR)	77(37.4)	
pathogenic-mutation(PM)	53(25.8)	
Development of first cancer		
after counseling	22(10.8)	
before counseling	182(89.2)	
Cancer, time since diagnosis (years)		
breast cancer	173(83.9)	9.0 (7.6)
ovarian cancer	16(7.7)	11.0 (8.9)
metastatic cancer	34(16.7)	6.0 (4.9)
Percentage of female relatives with breast and/or ovarian cancer		
1st degree relatives	37(37.0)	
2nd degree relatives	5(16.0)	
3rd degree relatives	2(10.0)	
Demographic variables		
age (years)	54.0(10.5)	
being married	164(79.6)	
having children	189(91.7)	
having daughters		1.2(0.8)
having sons		1.0(0.8)
high school or higher		73(35.4)

3.2.2. Question 2: recollections predict interpretations

Figure 2 provides the path model testing all relationships simultaneously: The statistical model provided a good fit to the data (χ^2 (2) =.77, p=.67; RMSEA=.00). The recollection of cancer-risks and heredity-likelihood predicted their interpretation (resp. $\beta_{\text{cancer-risks}}$= .47, $\beta_{\text{heredity-likelihood}}$= .76), resulting in respectively medium and strong explained variances (22%; 58%).

Figure 2. *Statistical model for the recollections and interpretations of cancer-risks and heredity-likelihood: coefficients for the final Structural Equation Model, and for simple regression analyses (shown between brackets)*

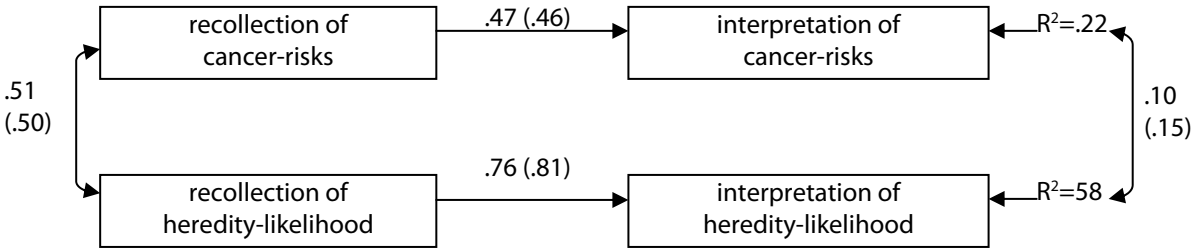


Table 3. *Results of recalled versus interpreted cancer-risks*

DNA-test result	recalled cancer-risks		interpreted cancer-risks		Relationship between recalled and interpreted cancer-risks			
	M (sd)	Median	M (sd)	Median	t (p)	% recalled > interpreted	% recalled < interpreted	% recalled = interpreted
mean	4.5 (1.4)	4	4.0 (1.6)	4	-.34 (.007)	30.4	31.3	38.3
unclassified variant	4.5[a] (1.5)	4	4.6[a] (1.8)	4	-3.25 (.002)	11.4 [a]	47.7 [a]	40.9 [a]
uninformative	3.8[a] (1.1)	4	3.4[a] (1.2)	4	ns	29.6 [a]	29.6 [a]	40.7 [a]
pathogenic mutation	4.9[a] (1.2)	5	4.2[a] (1.7)	5	2.94 (.005)	43.2 [a]	15.9 [a]	40.9 [a]

M=mean, sd=standard deviation, R=correlation, t=t-test, p=p-value, n.s.=not significant. Recollections and interpretations of cancer-risks measured on 7-points scale, ranging from 1 to 7 (not–complete at risk). A= significant column differences between scores of a measure between DNA-test results (Kruskal-Wallis, p<.01).

3.2.3. Question 3: cancer-risks and heredity-likelihood differ

Overall, counselees recalled intermediate cancer-risks of 4.5 (sd=1.4), and heredity-likelihood of 4.4 (sd=1.4; d=.07). Counselees interpreted intermediate cancer-risks of 4.0 (sd=1.6), and significantly higher heredity-likelihood of 4.8 (sd=1.3) with a strong effect size (t=-3.6, p<.0001, d=.55) (see tables 3-4). No differences were found between the DNA-test results (p (K-W)>.05).

3.2.4. Question 4: cancer-risks and heredity-likelihood correlate

The path model of question 2 also showed that recollection of cancer-risks and heredity-likelihood correlated quite strongly (R=.51, p<.001).

Table 4. *Results of recalled and interpreted test-based versus pedigree-based heredity-likelihood*

DNA-test result	recalled heredity-likelihood		interpreted heredity-likelihood		Relationship between recalled and interpreted heredity-likelihood			
	M (sd)	Median	M (sd)	Median	t (p)	% recalled > interpreted	% recalled < interpreted	% recalled = interpreted
mean	4.4 (1.4)	4	4.8 (1.3)	5	-2.41 (.017)	17.2	35.1	47.8
unclassified-variant	4.6[a] (1.6)	4	4.6[a] (1.6)	4	-4.85 (.000)	23.5	32.4	44.1
uninformative	3.0[a] (1.5)	3	3.4[a] (1.9)	4	-1.68 (.009)	20.8	41.5	37.7
pathogenic mutation	6.9[a] (0.4)	7	6.9[a] (0.4)	7	ns	5.9[a]	5.9[a]	88.2[a]

M=mean, sd=standard deviation, R=correlation, t=t-test, p=p-value, ns=not significant. Recollections and interpretations of heredity-likelihood measured on 7-points scale, ranging from 1 to 7 (not-certainly heritable). A= significant column differences between scores of a measure between DNA-test results (Kruskal-Wallis, p<.01)

3.2.5. Question 5: DNA-test result category

To investigate differences between UV, PM, and UN, a multigroup structural equation model was formulated and tested simultaneously in each group. This model provided a reasonably good fit to the data (χ^2 (6) =11.11, p=.09; RMSEA =.11). Although RMSEA was slightly higher than the threshold, X^2 was still non-significant. Results showed that in all three DNA-test result groups, recollections predicted interpretations of cancer-risks as well as heredity-likelihood. Recalled cancer-risks explained a smaller percentage of variance in interpreted cancer-risk for UV-counselees than PM/UR-counselees (resp. 13%, 31% and 40%). Recalled heredity-likelihood explained a small percentage of variance in interpreted heredity-likelihood in UV, a larger percentage for PM/UR (resp.9%, 45%, 42%). Correlations between cancer-risks and heredity-likelihood were small for PM and large for UV/UR (resp. .09, .54, .50) (see table 5).

Table 5. *Results of structural equation modeling*

	overall	unclassified-variant	pathogenic-mutation	uninformative-result
Prediction of interpreted cancer-risks by recalled cancer-risks (R^2)	.22	.13	.31	.40
Prediction of interpreted heredity-likelihood by recalled heredity-likelihood (R^2)	.58	.09	.45	.50
Correlation between cancer-risks and heredity-likelihood	.51	.54	.09	.50

4. Discussion

4.1. Conclusions

In previous studies on the impact of genetic-counseling on counselees' lives, risk-perception has been operationalized in unspecific ways. It remained unclear whether counselees reported their recollections or interpretations of the DNA-test result. Moreover, counselees were asked about their own cancer-risks, and not about heredity-likelihood, which is indicated by many counselees as a major reason to undergo DNA-testing (1,5). The use of these presumably non-valid perception-measures may explain the relatively small effect sizes and inconsistencies between those studies. We have showed that at least four new perception-measures are required to explain the impact of DNA-testing on the counselees' lives (277).

Our research shows a significant differentiation between perceived recollection and interpretion of the DNA-test result, and between cancer-risks and heredity-likelihood. This differentiation was not influenced by covariates: the actually communicated DNA-test result, elapsed time, experience with their own and relatives' cancer and treatment, sociodemographics and measuring cancer-risks in percentages.

4.2. Explanations

We suggest two explanations why most counselees differentiated between recollections and interpretations, and why almost half of them did not.

Firstly, counselees may interpret the DNA-test result differently compared to their recollection, due to ambiguity or uncertainty of the genetic-information (cf. 81-84). For instance, differences were larger when UV's were communicated Differences increased slightly when genetic-counselors provided additional explanations, e.g. 'future research may detect a pathogenic-mutation in yet unknown genes'. Counselees may react to such uncertain/ambiguous information by processing information in dual ways (cf.81-84).

Secondly, personality traits may explain individual differences. For instance, more autonomous individuals may be more likely to create their own interpretation, independently from their recollections of the counselors' message. Autonomous counselees may rely more on their own opinion and use other sources of information (suggested by unpresented a-posteriori analyses).

We did not only find differences, but also large correlations between recollections and interpretations, and between perceived cancer-risks and heredity-likelihood. This could be caused by the high risks and heredity-likelihood in PM. These strong/significant correlations may also suggest that the differences between the perception-variables were consistent, i.e. most counselees interpreted cancer-risks higher than in their recollections, which caused significant differences and strong correlations.

4.3. DNA-test results

Differences were found between the three groups of DNA-test results. First, PM-carriers recalled and interpreted heredity-likelihood identically, probably due to a ceiling effect caused by high cancer-risks communicated by the genetic-counselor. Cancer-risks were reported as much lower than heredity-likelihood, and correlations were small; this was not due to post-testing preventive mastectomy (PBM) or oophorectomy (PBSO), as shown by covariate-analyses.

Second, in line with our previous study (203), the counselees' interpretation of UV's was poorly predicted by their recollections. Thus, they did not base their interpretations on their recollections of what the genetic-counselor had communicated. This could be caused by the ambiguity of UV's.

Third, in UR-counselees, we found relatively strong correlations and lack of differences between both recollections and interpretations, and strong correlations between cancer-risks and heredity-likelihood. Thus, the four perception-variables were more strongly related than in PM/UV. This suggests a more balanced perception compared to the more 'dissociated' perception in PM/UV.

4.4. Limitations

The retrospective design of this study only allowed exploratively measuring the long-term impact of genetic-counseling, and not the short-term impact. Causal relationships were suggested, but could not be conclusively determined. Other limitations are: only genetic-counseling for BRCA1/2 was included, genetic-information was communicated in a non-standardized way, and the retrospective design only allowed studying the short-term impact of DNA-test result disclosure in patients who had been diagnosed with cancer with a mean of 9 years ago. We focused only on the counselees' recollections and interpretations of breast cancer risks, and not of ovarian cancer risks; new studies should also focus on the latter. We used four single items to measure the counselees' perception, which does not exclude the possibility that these variables are indicators of one underlying construct measured by slightly different scales; therefore, multiple-item-measures should be developed. We suggest developing more elaborate models on the basis of longitudinal studies, including several genetic-diseases.

4.5. Implications

We suggest genetic-counselors to avoid communication of ambiguous information, which counselees could misinterpret. Our study suggests that counselors should especially be careful in communicating UV's and additional explanations.

Many counselees had forgotten the communicated numerical risks, which suggests that cancer-risks are better measured in verbal categories than in percentages. This finding could explain the finding of previous studies that the use of percentage-scales causes

larger differences between subjective and objective lifetime risk than categorical scales (77). Moreover, percentage-risks were often interpreted as 50%, i.e. black-or-white: 'either I get cancer or I do not get cancer' (216,217). Categorical scales may be more in line with the counselees' own way of describing risks (239), and seem to lead to less overestimation (278). For these reasons, we suggest that future researchers operationalize cancer-risks as categories. Currently, empirical evidence lacks for the efficacy of the communication of risks in percentages, despite the genetic-counselors' preference for this communication format (279). More intervention studies are required to examine which format (categories, percentages, proportions, or a combination) lead to the most accurate perceptions, least distress and best informed medical decisions of counselees (243,280,281).

Genetic-counselors may contribute to diminishing the discrepancy between the counselees' recollections and interpretations, by tailoring the information to the counselees' own interpretations. Before and after disclosing DNA-test results, genetic-counselors could explicitly ask counselees about their perception of cancer-risks, heredity-likelihood, possible causes and treatments of cancer, reason for requesting DNA-testing, and possible medical consequences, and they could adjust their communication to these perceptions of counselees (cf.264). It has shown that counselees may indeed benefit from tailoring risk-information, as suggested by a pilot study showing that explicitly discussing the counselees' pre-existing interpretations increases the accuracy of their risk-perception (282).

Counselors could ask counselees to rephrase the DNA-test result in their own words, and reflect on their ideas and feelings, such as: 'did you expect this result?'; 'how do you feel about this result?'; 'what does this mean for your relatives?'; 'do you believe this result?'; 'what medical decisions are you reflecting upon after having received this information?' Additional explanation may be formulated in the terminology and metaphors of the counselees.

In summary, counseling should be a personal, two-directional/reciprocal process including tailoring of risk-information (283). This is also in line with Edwards et al (284) who suggested that the positive effects of interventions in genetic-counseling are not explained by the information elements, but by the emotional and psychosocial elements of these interventions. Thus, genetic-counseling should not only focus at merely disclosing genetic-information such as cancer-risks, but also on the context and personal meaning (i.e. interpretation) of this information for counselees (38). Intervention studies may focus on improving interaction and tailoring of information to the needs and personality of the counselees. This may help counselees to make well-informed medical decisions, improve well-being and communication to relatives.