Opening the psychological black box in genetic counseling

Vos, J.

Chapter 7

A whisper-game perspective on the family communication of DNA-test results:

A retrospective study on the communication process of BRCA1/2-test results between proband and relatives

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Abstract

Objective

The objective was to study how DNA-test result information was communicated and perceived within families.

Method

A retrospective descriptive study in 13 probands with a BRCA1/2 unclassified variant, 7 with a pathogenic mutation, 5 with an uninformative result, and in 44, 14, and 12 of their 1st and 2nd degree relatives respectively. We examined differences and correlations between: (a) information actually communicated (b) probands' perception, (c) relatives' perception. The perception consisted of recollections and interpretations of both their own and their relatives' cancer-risks, and heredity-likelihood (i.e. likelihood that cancer is heritable in the family).

Results

Differences and low correlations suggested few similarities between the actually communicated information, the probands' and the relatives' perception. More specifically, probands recalled the communicated information differently compared with the actually communicated information (R=.40), and reinterpreted this information differently (R=.30). The relatives' perception was best correlated with the proband's interpretation (R=.08), but this perception differed significantly from their proband's perception. Finally, relatives reinterpreted the information they received from their proband differently (R=.25), and this interpretation was only slightly related with the original message communicated by the genetic-counselor (R=.15). Unclassified-variants were most frequently misinterpreted by probands and relatives, and had the largest differences between probands' and relatives' perceptions.

Discussion

Like in a children's whisper-game, many errors occur in the transmission of DNA-test result information in families. More attention is required for how probands disseminate information to relatives. Genetic-*counselor*s may help by supporting the probands in communicating to relatives, e.g. by providing clear summary letters for relatives.

1.Introduction

1.1. Background

Having multiple family members with breast and ovarian cancer may lead an individual to request for DNA-testing. Usually, a DNA-test is first performed in an individual with cancer, a proband. The detection of a pathogenic BRCA1/2 mutation provides probands with precise information about their own cancer-risks. Contralateral breast-cancer recurrence risks for affected women are 30-60%, primary breast and ovarian-cancer risks for unaffected women are respectively 60-80% and 30-60% (BRCA1) / 5-20% (BRCA2). The majority of probands receives an uninformative-result (UR), and about 10% an unclassified-variant/variant-of-uncertain-clinical-significance (UV). In these cases, cancer-risks are primarily calculated on the basis of the pedigree.Vinket al, 2004 Subsequently, risk management options, such as surveillance and prophylactic surgery of ovaries and breasts depend on the pathogenic-result or the pedigree.

Many studies showed that probands may experience a significant influence of DNA-testing on their psychological wellbeing and medical decisions (66,76). Fewer studies have examined how probands communicate DNA-test results to untested relatives, and how a test result influences their relatives' lives. The perception and impact of relatives has not been studied from the relatives' own perspective (109), despite the fact that relatives are often closely involved in genetic-counseling.

First, many relatives provide medical information on the proband's request to complete pedigree information, which is the basis for DNA-testing and risk-estimation.

Second, many probands undergo DNA-testing for the reason of receiving genetic-information for their relatives (1,154,200). Detection of a pathogenic-result enables relatives to request for DNA-testing, and other DNA-results allow calculation of a priori cancer-risks for relatives on the basis of the pedigree.

Third, most relatives are informed by the proband about the DNA-test result, mostly within four months after testing (103). Especially pathogenic-mutations are communicated, in particular to first-degree female relatives from cohesive families for whom DNA-test results may have medical consequences (103-108). The communicated DNA-test result may subsequently cause distress in relatives (105,109-111), awaken familial conflicts and myths (112-114), and influence the relatives' well-being, medical-decisions and intention to request DNA-testing (109,115-120).

1.2. Family communication timeline

We examined the relatives' perception as a part of the family communication timeline of genetic counseling. Family communication of genetic-counseling involves two senders of genetic-information, viz. the genetic-counselor and the proband, and two receivers, viz. the proband and the relative. The communication of genetic-information may involve

'noise', either caused by genetic-*counselor*s and probands who disclose information inaccurately, and/or the probands and relatives who receive information inaccurately.

First, noise may occur in the receipt of information. We showed in previous studies that probands may recall the DNA-test result differently compared to what had actually been communicated (285). Subsequently, these probands did not interpret the risk-information result identical to how they recalled it. Hence, the receival of information – either by probands or relatives- consists of three different processes: actual communicated information, recollections and interpretations.

Second, noise may occur due to ineffective disclosure of genetic-information. In this family study, we focus on the proband, who is not only receiver, but also sender of information. It is unclear how the proband makes this role transformation, and whether she communicates what she recalls or whether she mainly communicates her own interpretation and makes a selection of the information when disclosing to relatives. We expect that the probands' main message is their subjective interpretation because the interpretation has been reported as the most important aspect of their perception, and strongly influences well-being and decision-making (285).

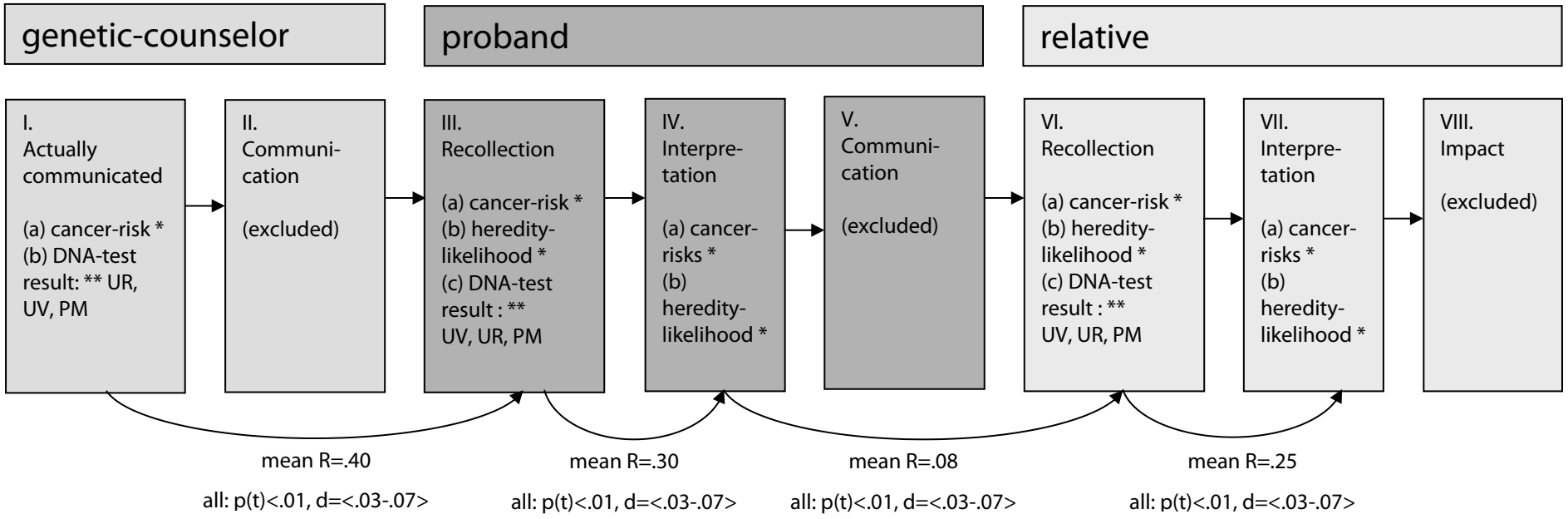
Figure 1 depicts our hypothesized family communication timeline of genetic counseling. I.A DNA-test result and cancer-risks are obtained; II.the genetic-*counselor* communicates this to a proband. III.The proband recalls and IV.interprets this information. V.The proband communicates her interpretation of the DNA-test result to the relative, which is VI.recalled and VII.interpreted by the relative, and VIII.may have consequences for the relatives' lives. Because of logistic reasons, II, V and VIII were excluded from this study.

1.3.Hypotheses and research questions

The difficulty of communicating information accurately can be illustrated by children's whisper games, in which one child whispers a word to another child who subsequently whispers the word to another child. In most cases, the last child in the line of whisperers understands another word than the initial word.

We hypothesized that the family communication of a DNA-test result functions like a whisper game, in which the originally communicated information fades out more at every step in the communication timeline. More specifically, we asked: 1.Is there a significant difference between each step in the family communication timeline of genetic-counseling? The steps in the family communication timeline of genetic-counseling consist of the genetic-information actually communicated by the genetic-*counselor* (i.e. DNA-test result category and cancer-risks), and the recollections and interpretations that probands and relatives have regarding this genetic-information (cf.figure 1). We expected to find significant differences between all variables of respectively steps I-III, III-IV, IV-VI, and VI-VII.

Figure 1. *Family communication timeline of genetic counseling, showing variables included in this article, and the found correlations and differences.*



'Excluded' boxes were not studied in this article;
R= mean Pearson's correlations between all variables of two steps; all= results (t/d) regard all tested variables of two steps;
p(t)=significance of t-tests between variables of two steps; d=value-range of Cohen's d of differences between variables of two steps;
**=measured on Likert scale ranging from 1 (not at risk/heritable) to 7 (complete at risk/heritable);*
***=each DNA-test result is included as dichotomous variable: communicated/recalled/interpreted (1) or not (0).*

2.Does the initially communicated genetic-information fade out more and more at every next step in the communication model? More specifically: does the information transmitted at the first step correlate less and less with each step further away from the first step? We expected that the correlations would decrease between the following steps, i.e.: I-III>I-IV>I-VI >I-VII; III-IV>III-VI>III-VII; IV-VI>IV-VII; small correlations between VI-VII.

3.Are there differences in the information transfer (i.e. correlations and decrease in correlations) between unclassified-variants (UV), pathogenic-mutations (PM) and unformative-results (UR)? 4.Do the following covariates influence the information transfer: sociodemographics, pedigree, familial relationship, cancer-history of proband and relative? We expected that the whispergame-effect would be stronger than the communicated DNA-test result and covariates.

2. Method

2.1. Procedure

Eligible participants in current study were probands from families with intermediate or high cancer-risks who had received a BRCA1/2 DNA-test result in the period 1998-2008 at the Leiden University Medical Center or the VU Medical Center Amsterdam (203). Because the primary focus of our study concerns unclassified-variants, we first approached probands with an unclassified-variant, communicated as 'a mutation/genetic-change for which the clinical meaning is not known (yet)'. In addition, we approached women with a PM or UR, with matching year of result-disclosure.

We asked all 89 probands in this study for their approval to contact their 1st and 2nd degree relatives in the affected branch of the family. Subsequently, in line with the proband's preference, we either sent our invitation letter to relatives directly, or to the proband who distributed the letters. We administered the relatives' questionnaire both in a paper-and-pencil-version as in an Internet version. The study was approved by the medical ethical committees of the participating medical centers.

2.2 .Instruments

Development and description of the questions about the probands' and relatives' recollections and interpretations of both cancer-risks and heredity-likelihood have been described elsewhere (203,277,285).(see figure 1;table 1)

Table 1. *Overview of instruments and items*

	Instruments	scaling	Items
Actually communicated information	cancer-risks	cancer-risks in %, rescaled to a 1-7 scale to match counselees' recollections and interpretations (derived from medical file and summary letter sent to proband)	
	DNA-test result	scored as 3 dummy-items: communicated (1) or not (0)	pathogenic-mutation, unclassified-variant, uninformative
Proband's perception	recollection of DNA-test result	1 item with 3 options (see chapters 4 & 5)	options: (a) 'no genetic change detected', (b) 'a genetic change was detected meaning that cancer is heritable in my family', (c) 'a genetic change was detected for which the meaning for breast/ovarian cancer is unknown at this moment, and therefore tells nothing about the heredity of cancer in my family'
	recollections of own cancer-risks and heredity-likelihood	2 items (1-7 scale: not-complete at risk/heritable) (see chapters 4 & 5)	(1) what is your risk to develop cancer (again), according to your genetic-*counselor*; (2) according to your genetic-*counselor*, what does your pedigree/DNA-result mean for the likelihood that cancer is heritable in your family (pathogenic-mutation: result-based; other DNA-results: pedigree-based)
	interpretations of own cancer-risks and heredity-likelihood	2 items (1-7 scale: not-complete at risk/heritable)(see chapters 4 & 5)	What are your own thoughts and feelings about: (1) your risk to develop cancer (again), (2) the likelihood that cancer is heritable in your family
	interpretations of healthy relatives' cancer-risks	1items (1-7 scale: not-complete at risk) (see chapters 4 & 5)	What are your own thoughts and feelings about the risk for a healthy female relative in your family to develop cancer?
Relatives' perception		relative's questionnaire: identical to proband's perception, except 'healthy relatives' risks'	'genetic-*counselor*' was replaced for 'your relative' (i.e. proband)
Covariates		(1) 3 items derived from medical files (%);(2) 6 binary items in questionnaire (yes/no); (3) 8 items (several scales)	(1) percentage of affected 1st, 2nd and 3rd degree relatives; (2) gender: woman, children, married, religiously active, employed, high school and higher, or lower educated; (3) age, breast or ovarian or other cancer, metastases, year of diagnoses, mastectomy, adnexextirpation, radio/chemotherapy in past or now

2.3. Statistical analysis

Research question 1 was answered by performing t-tests to calculate differences: a.between all variables of steps I and III, b.between all variables of steps III and IV, c.between all variables of steps IV and VI, d.and between all variables of steps VI and VII. Figure 1 shows which variables are included in each step. To facilitate presentation of the large number of t-tests, we only present an overview of the results; details can be requested from the authors.

Research question 2 was analyzed in two phases. In phase 1, all applicable correlations between all variables of all steps were calculated (figure 1 shows all variables). In phase 2, mean correlations were calculated between all variables of the steps required for answering research question 2: I-III, I-IV, I-VI, I-VII; III-IV, III-VI, III-VII; IV-VI, IV-VII; VI-VII. To facilitate data presentation, we only present phase 2; data from phase 1 can be requested from the authors.

Research question 3 was answered by calculating mean correlations regarding research question 2 separately for each of the three DNA-test results. Research question 4 was explored by calculating partial correlations for research question 2, corrected for covariates.

Missing values (<2%) were imputed by multiple imputing within each step. To correct for three DNA-test-result categories, p-values smaller than .01 were regarded as significant. Effect sizes were calculated with Cohen's d and correlations.

3. Results

3.1. Sample

Table 2 shows sample information. We approached 89 probands, but were unable to contact 44 of them (mainly due to deceased, too ill to participate and moved to another address). Twenty-five (56%) out of the remaining 45 probands participated, and 20 (44%) probands did not want that we asked their relatives; the main reported reasons for decline were: 'I do not know whether my relatives would accept me providing you with their private addresses'; 'I do not have contact with relatives'; 'I do not want to burden them'; 'I have not communicated the result' and 'I want to keep the genetic-counseling process closed and completed'. We approached 157 of their relatives, of whom 60 (38%) did not react, mainly due to organizational issues such as inaccurate address. Seventy out of the remaining 97 (72%) agreed up participation. Twenty-seven relatives (28%) declined; the most frequently reported reason was wanting to keep the genetic counseling process psychologically closed and being afraid that participation could remind them of painful memories. Statistical analysis of participation/decline rates did not reveal other significant patterns. In sum: the large non-response in probands and relatives was due to the retrospective design which caused high rates of decease and inaccurate addresses of

eligible individuals; analyses of decliners showed that participation in this study was regarded as a sensitive theme, involving ethical issues and wanting to keep counseling psychologically closed.

Included relatives were mainly first-degree (64%), especially daughters (32%) or sisters (29%). Fifty-four (77%) relatives were women, 15 (21%) had had breast cancer, none ovarian cancer and 5 (7%) another kind of cancer. Six of the affected and none of the unaffected women had undergone prophylactic mastectomy, and one affected woman prophylactic bilateral salpingo-oophorectomy (BSO). Perception did not differ between affected and unaffected participants.

Thirteen (52%) probands had actually received a UV, 7 (28%) a PM and 5 (20%) an UR. Of the 70 relatives, 44 (63%) belonged to a family in which an unclassified-variant was communicated, 14 (20%) in a mutation-family and 12 (17%) in an uninformative-family.

Table 2. *Information about procedure and sample*

Variable	M(sd)	N(%)
Probands		
Total number of contacted probands		45(100%)
Probands declining		20(44%)
Probands agreeing to approach their relatives		25(56%)
Relatives		
Total number of contacted relatives		97(100%)
Relatives declining		27(28%)
Participating relatives		70(72%)
Relationship of relative to proband		
1st degree		45(64%)
2nd degree		12(17%)
3rd degree		12(17%)
4th degree		1(2%)
Sociodemographics of relatives		
women		54(77%)
high-school or higher		26(37%)
employed		50(71%)
Cancer-history of relatives		
breast cancer		15(21%)
ovarian cancer		0
another kind of cancer		5(7%)
year of cancer diagnosis	2002(4.0)	
mastectomy/affected women		6/15(40%)
mastectomy/unaffected women		0/55
bilateral salpingo-oophorectomy/unaffected women		1/70(1%)
Pedigree		
% affected 1st degree relatives/all relatives	37%(10%)	
% affected 2nd degree relatives/all relatives	7%(7%)	
% affected 3rd degree relatives/all relatives	7%(2%)	

Table 3. *Overview of variables*

Step	Description	actually communicated DNA-test result (means, sd)			
		overall	**unclassified-variant**	**pathogenic-mutation**	**uninformative-result**
I actually communicated	communicated to proband: unclassified-variant, pathogenic-mutation, uninformative (n,%)		13(1.0)	7(1.0)	5(1.0)
	cancer-risks (% rescaled to 1-7 scale)	4.9(1.2)	4.0(1.0)	6.0(0.0)	3.0(0.0)
III probands' recollections	recollection of unclassified-variant, pathogenic-mutation, uninformative (n,%)		11(.45)	11(.45)	2(.1)
	recalled own cancer-risks	4.7(1.4)	4.6 (1.5)	5.2 (.4)	3.5 (.6)
	recalled heredity-likelihood	4.6(1.9)	4.5 (.7)	6.2 (1.2)	2.3 (.8)
IV probands' interpretations	interpreted own cancer-risks	6.0(1.7)	6.5 (1.2)	4.1(1.7)	4.1(.9)
	interpreted heredity-likelihood	6.4(1.3)	5.5 (.7)	7.0 (.0)	4.7(2.3)
	interpreted relatives' cancer-risks	5.5(1.2)	5.3 (1.4)	6.7(.8)	5.3(.8)
VI relatives' recollections	recollection of: unclassified-variant, pathogenic-mutation, uninformative (n,%)		19(.3)	35(.5)	14(.2)
	recalled own cancer-risks	4.9(1.0)	4.9 (.9)	5.7(.7)	3.9 (1.1)
	recalled heredity-likelihood	3.4(1.4)	3.9(1.2)	5.0(.0)	2.4(1.2)
VII relatives' interpretations	interpreted own cancer-risks	3.8(1.4)	4.3(1.0)	5.0(.0)	2.9(1.3)
	interpreted heredity-likelihood	3.8(1.3)	4.0(1.4)	3.0(1.2)	4.1(.8)

3.2. Question 1: differences between steps

All variables differed significantly between steps I-III, III-IV, IV-VI, and VI-VII. Al p-values were smaller than .01, and Cohen's d's varied between 0.3 and 0.7, which is regarded as medium effects. (see figure 1)

3.3. Question 2: fading-out

Table 4 shows mean correlations between the steps. First, when we examined the four communicated aspects as depicted in the left columns of the geneticist, we found that the correlations decreased at every step downwards: correlations I-III>I-IV>I-VI>I-VII. Thus, the actually communicated information by the genetic-*counselor* faded out more and more in respectively the proband's recollections and interpretations and the relatives' recollections and interpretations. Second, we found that the correlations of the proband's recollections decreased at every step downwards in table 4: correlations III-VI>III-VI>III-VII. Thus, the proband's recollections faded out more and more in respectively the proband's

interpretations and the relatives' recollections and interpretations. Third, the correlations of the probands' interpretations with other variables decreased in each step: IV-VI>IV-VII. Thus, the proband's interpretations faded out more and more in the relatives' recollections and interpretations. Fourth, the relatives' recollections VI correlated only for .25 with interpretations. Thus, the relatives' recollections faded out in the relatives' interpretations.

The mean correlations between the main steps as depicted in figure 1 are: .40 between the information actually communicated by the genetic-*counselor* and the proband's recollections(I-III); .30 between the proband's recollections and interpretations(III-IV); .08 between the proband's interpretations and the relatives' recollections(IV-VI); and .25 between the relatives' recollections and interpretations.

3.4. Question 3: DNA-test results

We calculated all correlations of research questions 2 and 3 separately for three different DNA-test results. The number of participants for PMs was too small to calculate correlations in steps III, IV and VI. Similar to overall results, the genetic-information from the first communication steps faded out in each DNA-test result group. Exceptions were the high correlations of the information actually communicated by the genetic-*counselor* and the relatives' recollections of UVs and URs (R's=.44, .49). Unclassified-variants were recalled worse by probands compared to other results (R=.16), and the proband's interpretations of an unclassified-variant did not correlate with the relatives' recollections and interpretations.

3.5. Covariates

No significant effects of covariates were found, except for the proband's mothers who interpreted higher cancer-risks, and the probands' daughters who less often recalled having received PMs (R's=.25, -.29, -24, p's<.01).

Table 4. *Mean correlations between steps: overall and specified for different DNA-test results*

		From this step (e.g. I → III)												
		I. geneticist				***III. proband: recollections***			***IV. proband: interpretations***			***VI. relative: recollections***		
	DNA-test result	***overall***	*UV*	*UR*	*PM*	***overall***	*UV*	*UR*	***overall***	*UV*	*UR*	***overall***	*UV*	*UR*
To this step (e.g. I → III)	***III. proband: recollections***	**.40**	.16	.40	.58									
	IV. proband: interpretations	**.33**	.22	.33	.48	**.30**	.34	.64						
	VI. relative: Recollections	**.29**	.44	.49	.29	**.07**	.16	.09	**.08**	0	.06			
	VII. relative: Interpretations	**.15**	.20	.26	.05	**.03**	.09	.06	**0**	0	0	**.25**	.13	.07

All correlations: p<.01; UV=unclassified-variant, UR=uninformative-result, PM=pathogenic mutation; several cells contained too little pathogenic-mutation carriers to calculate mean correlations, therefore only correlations with step I are presented.

4. Discussion

4.1. Conclusion

This study is the first to examine the relatives' perception of genetic-counseling as part of the family communication timeline of genetic-counseling. We compared the communication of genetic-information between probands and relatives with a children's whisper game. Our expectation was confirmed that errors would accumulate in the communication of genetic-information from step to step: from information actually communicated by the genetic-*counselor* to the proband's recollection, and from that to the proband's interpretation, and from that to the relatives' recollection, and from that to the relatives' interpretation.

First, all steps differed significantly from each other, implying that noise occurred in all transfers of information between genetic-*counselor*, proband and relatives. This also means that the recollections and interpretations of both probands and relatives were inaccurate, when compared with the information that was actually communicated to them.

Second, the information originally communicated by the genetic-*counselor* faded out at every step in the communication timeline, like a whisper game. The final step, the relatives' interpretation, showed a correlation of no more than .15 with the originally communicated information.

4.2. Noise

The least noise (R=.40) had arisen in the communication between genetic-*counselor* and proband, and the largest noise (R=.08) between the proband's and relatives' perception. The correlations between recollections and interpretations were relatively low, both for probands and relatives (R's=.30, .25), which was comparable to previous studies (203,285).

Why did noise arise? First, probands and relatives may have difficulties understanding the meaning of DNA-test results and pedigree (277,285). Their inaccurate perceptions could also be caused by the time passed since communication of the DNA-test result, low education, innumeracy (299-301), and black-or-white thinking, i.e. 'either I get cancer or I do not get cancer' (83,88).

Second, probands and relatives may have selectively listened to the communicated information, and may have used heuristics, such as representativeness and availability biases and illusion of control (328). They may have been stuck in specific family communication patterns (329), and have developed their own opinion about cancer-risks and heredity-likelihood on the basis of their experiences with cancer in the family (304-307).

Third, probands may only have disclosed information which they perceived as most likely to be true and as most relevant for their relatives. Particularly in situations of personal threat, an individual may trust their own interpretations most (81-84).

Fourth, the largest part of the noise remained unexplained by the variables in this study. This suggests involvement of other variables.

4.3. Actually communicated information

The information communicated by the genetic-*counselor* did not completely fade-out, because it correlated with the relatives' recollections and interpretations (I-VI/VII). However, these remaining correlations were small (R's=.29, .15).This suggests that the largest part of the relatives' perception was not directly predicted by the actually communicated information, which confirms the whisper-game phenomenon.

Analyses yielded two results: 1.the actually communicated information predicted the relatives' perception to some extent; 2.the relatives' perception differed significantly from the actually communicated information. This is comparable with the results of a children's whisper-game: 1.the first and the last communicated words may be somewhat related; 2.there may be a difference between the first and last words. Thus, the relatives' perception was inaccurate/different compared to what was actually communicated by genetic-*counselor*s, but was also somewhat related. Finding significant correlations between the first and last steps suggest that the first step (slightly) predicts the last step; this suggests that the actually communicated information consistently predicted the counselees' inaccurate perception.

We hypothesize that the influence from the actually communicated information on the relatives' perception is completely explained/mediated by the way how probands communicate DNA-test results to relatives (321).

4.4. DNA-test results

We found large correlations between the genetic-*counselor* communication and the relatives' recollection in families with unclassified-variants and uninformatives. The genetic-*counselor*'s information predicted the relatives' recollections even better than the proband's recollections. Probands with these DNA-test results largely overestimated the cancer-risks and heredity-likelihood in their recollections and interpretations (277,285), but relatives reduced the extent of this overestimation, so that the relatives' perception was more in line with what the genetic-*counselor* had actually communicated.

Possibly, relatives understood the actual meaning of the DNA-test result better. Or they deduced from nonverbal communication that their proband was exaggerating. Or the answers of the relatives showed a tendency towards the mean. Or the relatives had read the summary letter that probands had received from their genetic-*counselor*; we have no

information whether relatives have read this letter, but only less than 20% of the letters included explicit risk-information for relatives.

Compared to other DNA-test results, unclassified-variants were recalled and interpreted the most inaccurate, and the probands' perception also correlated the worst with the relatives' perception.

4.5. Implications

Large noise occured in the family communication timeline of genetic counseling. Therefore, genetic-*counselor*s should not only be aware of the proband in their consultation room, but also of the absent relatives to whom the proband will disclose the DNA-test result.

Genetic-*counselor*s should explicitly help probands in disclosing DNA-test results to their relatives (108,330), especially regarding unclassified-variants and possible medical consequences for relatives (331). Probands often perceive the disclosure process as difficult and stressful (106,108,332), especially when children are involved (110,333-335) or when DNA-test results are negative (336). This could be achieved by improving the summary letters for probands, especially by including more explicit information for relatives (cf.337).

Direct communication between *counselor* and relatives may contribute in improving family communication (cf.338). For instance, genetic-*counselor*s might send letters to relatives, summarizing the DNA-test result and providing the possibility for private consultation by phone or face-to-face. This raises ethical questions. Are genetic-*counselor*s obliged to inform high-risk relatives? Are they allowed to inform a non-patient population who has not requested for genetic-information? Are they allowed to violate the proband's privacy? Is communication beneficial, when relatives do not receive risk-management options, but may feel 'alarmed'? Guidelines should be developed for genetic-*counselor*s if, when and how they should communicate DNA-test results to relatives (339).

4.6. Methodological issues

This study is limited by its small sample size and retrospective design. Therefore, causal relationships remain theoretically assumed. There may have been sampling bias, because probands decided which relatives we could ask to participate, and the relatives' participation percentage was low. The communication timeline assumes a linear feed-forward process, but feedback loops may have been present. All variables were assumed to be linear, to enable calculating mean correlations and t-tests. Non-presented analyses showed identical results with Spearman-correlations, Fisher-exact-tests and corrections for family-dynamics, second/changed DNA-test result, DNA-test-request by relatives, mastectomy and adnexextirpation/BSO. Mediation analyses including communication

processes are described elsewhere (321). Future studies should be prospective and include more variables.

Despite these limitations, this study 'taps from the richness of family responses to create a more complete picture of the effects of genetic testing' (64). It underlines studies on risk-perception in probands (203,277,285), and suggests a broader focus on the family domain, which is both 'critical and relatively neglected' in the science and practice of genetic-counseling (65).