Opening the psychological black box in genetic counseling

Vos, J.

Chapter 3

The counselees' view of an Unclassified Variant in BRCA1/2: *recall, interpretation, and impact on life*

Joël Vos[1], Wilma Otten[2], Christi J. van Asperen[1], Anna M. Jansen[1], Fred H. Menko[3], Aad Tibben[1].

[1] Center for Human and Clinical Genetics, Department of Clinical Genetics, Leiden University Medical Center, Leiden, The Netherlands.

[2] Department of Medical Decision-Making, Leiden University Medical Center, Leiden, The Netherlands.

[3] Department of Clinical Genetics, VU University Medical Center, Amsterdam, The Netherlands.

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Abstract

Background

Unclassified Variants (UVs, variants of uncertain clinical significance) are found in 13% of all BRCA1/2 mutation analyses. Little is known about the counselees' recollections and interpretations of a UV, and its psychosocial/medical impact.

Method

Retrospective semi-structured interviews with open questions and five-point Likert scales were carried out in 24 counselees who received a UV-result 3 years before (sd=1.9).

Results

Sixty-seven percent (16/24) recalled the UV-result as a non-informative DNA-result; 29% recalled a pathogenic result. However, 79% of all counselees interpreted the UV-result as a genetic predisposition for cancer. Variation in recall and interpretation were unexplained by demographics, cancer history of themselves and relatives, and communication aspects of UV-disclosure. Sixty-seven percent perceived genetic counseling as completed, whereas 71% expected to receive new DNA-information. Although most counselees reported that UV-disclosure had changed their lives in general little, one in three counselees reported large changes in specific life domains, especially in surveillance behavior and medical decisions. Ten out of 19 participants who interpreted the UV as pathogenic had undergone preventive surgery, against none of the 5 counselees who interpreted the UV as non-informative.

Implications

Counselors and researchers need to address discrepancies between the counselees' factual recall and their subjective interpretation of non-informative BRCA1/2-test results.

1. Introduction

1.1. Background

After the identification of the BRCA1- and BRCA2-genes in hereditary breast and ovarian cancer, many mutation analyses have been carried out in women at increased risk (7,8). The lifetime cancer risk associated with a BRCA-mutation is 39 to 85% for breast and 11 to 63% for ovarian cancer. The risk for affected women to develop a second primary breast cancer is 40 to 60% (17,196-198).

1.2. Need for certainty

The prime motives for women at increased breast/ovarian cancer risk to apply for genetic counseling and DNA-testing, are reducing uncertainty and the need for information on surveillance and surgery (1,5). Therefore, many counselees expect to receive a clear-cut result, either a positive (pathogenic) or a negative (no-mutation) result (216,217). However, about 90% of the test-applicants receive a DNA-test result, which does *not* provide certainty: the communicated cancer risks and risk management options remain solely based on family history, and DNA-testing is not offered to relatives. There are two kinds of uncertain DNA-test results: uncertain negative results (often called 'inconclusive') and uncertain positive results ('Unclassified Variant', or 'Variant of Uncertain Clinical Significance' detected). In uncertain negative results, no mutations have been found in affected counselees at high risk of breast and/or ovarian cancer. This accounts for about 80% of all BRCA1/2-results, and includes the possibility of a still undetected BRCA1/2 mutation (false negative) or a mutation in a yet unknown gene (30). Uncertain positive variants (UVs) are mutations for which the effect on the protein function of the gene is still unknown. These account for 12.5% of all BRCA1/2-results, that is, 32% of all BRCA1 and 53% of all BRCA2-mutations (30).

1.3. The genetic-uncertainty-causes-distress hypothesis

Some authors hypothesize that disclosure of uncertain DNA-results evoke more psychological distress than certain DNA-results, because these results would maintain uncertainty about the genetic status (86,199,218,219,220).

Some studies confirmed that individuals with an uncertain negative result experience more distress than those who received a certain negative result (i.e. exclusion of a known familial mutation), but less distress than those who received a certain positive result (a pathogenic mutation) (163,200,204,221,222). In two studies, uncertain positive results (UV) did not seem to cause more psychological distress than a certain DNA-result (223,224).

Authors do not always explicate their hypothesis that uncertainty about the genetic status would cause distress. Two studies mentioned the continuation or rise of uncertainty after UV-disclosure compared to the pre-disclosure situation (224,225), and two studies reported uncertainty to be an important issue for UV-counselees (225,226).

The hypothesis that genetic uncertainty causes distress seems too general and unspecific (227,228) to find high distress levels due to uncertain DNA-results and the genetic counseling in general (74,229). *Firstly*, other variables should be included, such as: demographics, family history and cancer history (222,230,231), coping style and personality (232,230,233,234), illness perception (235,87), and family communication (236). *Secondly*, the question could be raised whether current general distress measures are sensitive enough to measure the subtle impact of DNA-results on the various life domains of the counselees. Moreover, the contextual meaning of these measures is not always clear, due to the absence of comparison with other relevant stressors and reference groups (74). *Third*, the hypothesized relationship between uncertain DNA-results and distress assumes that the counselees correctly understand and interpret these DNA-results as uncertain.

1.4. The distorted perception hypothesis

Several authors hypothesize (86,201,237,238) that counselees may incorrectly interpret uncertain results as certain results. Uncertain negative results may be interpreted as the certain absence and UVs as the certain presence of a genetic predisposition for cancer. The few studies available on this issue mainly operationalized distorted perception as perceived cancer risks. Some researchers found that counselees mentioned lower risks of developing cancer, a lower likelihood of being a mutation carrier or the absence of genetic predisposition at all, after disclosure of uncertain negative results (compared to pre-disclosure measures) (199-202), but others did not (86,204). Studies on UV-disclosure seem to indicate that counselees have a good comprehension of UVs (223), and perceive their cancer risks as unchanged, lower (223,225) or increased (226) compared to pre-disclosure.

These contradictory results may be caused by a too limited operationalization of distorted perception. For this reason, some researchers broadened their focus to both cognitive and affective risks (239,240). However, risk perception itself is just one part of a complex interpretation process in which several intertwined aspects of genetic counseling are perceived and interpreted. One of these aspects is the counselees' possibility to correctly understand and recall the DNA-test result. Rao et al. (226) reported that only 41% of the counselees correctly reproduced a UV-test result as an uncertain positive variant while 59% reproduced a certain negative result. However, it remains unclear whether this 59% did not correctly reproduce the factual UV-information counseled to them or whether they subjectively interpreted this UV-information differently. The present study will disentangle these two aspects of objective recollection and subjective interpretation.

1.5. Research questions

I. To examine the distorted perception hypothesis, our study focuses on possible differences between factual recall and subjective interpretation in a retrospective group of UV-counselees. II. To explore other clinical relevant aspects of the interpretation process, we measure: subjective understanding, perception of the completion of genetic counseling, expectation to receive a UV-result, and uncertainty about the familial occurrence and possible genetic cause of cancer. To study the genetic-uncertainty-causes-distress hypothesis, we measure: (III) the impact of UV-disclosure upon life in general and upon several specific life domains, and (IV) the influence of other variables on the recall, interpretation, impact and distress: sociodemographics, *counselor*'s communication, family history, cancer history.

These questions are relevant because communication of DNA-results that do not provide complete certainty will be more common in the future, due to the proliferation of humane disease data bases (241). Moreover, the question is raised by clinicians whether low penetrance genes should be communicated to counselees or not.

2. Methods

2.1. Participants

The current retrospective study is part of a larger Dutch multicenter study on UVs, approved by the Medical Ethical Committees of the participating centers. Participants were adult women with breast and/or ovarian cancer who had received a UV-test result in the BRCA1 or BRCA2 gene at the Department of Clinical Genetics of the Leiden University Medical Center (LUMC) or the VU University Medical Center Amsterdam (VUMC) in the period 1998-2006. For reasons of relational nature, genetic testing was incidentally offered to unaffected relatives of counselees with a UV-test result.

2.2. Genetic counseling

Genetic counseling for breast/ovarian cancer consists of two or three sessions: intake, disclosure of the DNA-test result, and sometimes disclosure of new genetic information. In the intake session, moderate risks (20-30%) or high risks (>30%) for developing recurrent breast and ovarian cancer were communicated based on pedigree information, and corresponding surveillance options were discussed. Prophylactic surgery of breasts and/or ovaries was discussed, given that a PM would be found. A counselee was tested for BRCA1/2 in case of clinically presumed hereditary breast and/or ovarian cancer, when the mutation detection rate was about 10%, or if cancer was diagnosed at a relatively young age (242,29). Although figures are unavailable, some *counselor*s discussed the possibility of finding a UV-result. UV-test results were communicated face-to-face in the DNA-disclosure

session and afterwards summarized in a letter. In a third session, some counselees received information on the pathogenic (4/24) or non-pathogenic (5/24) meaning of their UV based on the latest scientific developments.

2.3. Instruments

Information on age, children, marital status, educational level, employment, time elapsed since UV-disclosure, and cancer history was collected in a questionnaire. The number and percentage of affected relatives were extracted from the medical files.

Information about the counselor's communication was derived from the *counselor*'s summary letter by means of content analysis: relevant aspects about DNA-disclosure were identified and coded as variables, and scored per letter; only variables mentioned in more than 10% of all letters (n≥3) were included.

Interview: In addition to an interview with open questions, 5-point Likert scales were used. Independently from heredity information about the familial occurrence and possible genetic cause of cancer, we asked specific questions about the UV-result and its meaning.

Firstly, the participants were asked to recall what the *counselor* had communicated about the UV-result (*'factual recall'*). *Secondly*, they were asked to describe their thoughts and feelings about the UV-result (*'subjective interpretation'*). Their perceived level of understanding of the UV-result was measured with a 5-point Likert scale, ranging from 1, no understanding, to 5, very good. Another item measured their perceived level of uncertainty about the heritability of cancer in general,i.e. familial occurrence and possible genetic cause of the cancer, based on both the DNA-result and the pedigree information (range from 1, 'very uncertain', to 5, 'very certain').

Three yes/no-questions were asked: 'before receiving the DNA-test result, had you taken into account the possibility of receiving this DNA-test result?', 'do you expect to receive more information about this DNA-test result?' and 'is the genetic counseling process completed in your opinion?'

The relative amount of *general* changes in life due to genetic counseling was studied by three questions: 'how much has your life changed due to (a) genetic counseling, (b) having cancer, and (c) other life events?' The level of life changes was rated on a scale ranging from 1 ('no change') to 5 ('complete change'). Similarly, the changes in eight *specific life domains* after UV-disclosure were assessed. The domains, constructed on the basis of our clinical experience, were: preventive risk management (surveillance and preventive mastectomy and/or oophorectomy), general physical complaints, body experience, emotional well-being, social relationships, personality, coping with uncertainty, and existential view on life (e.g. meaning of life, values, religion). *Finally*, participants were asked to attribute the changes in each domain on a scale ranging from 'completely due to genetic counseling' ('1') to 'completely due to the development of cancer' ('5').

2.4. Categorization and statistical analyses

Two psychologists (JV, AJ) categorized the answers on factual recall and subjective interpretation after UV-disclosure independently. Three categories emerged: non-informative, the DNA-test result is uncertain, meaning that no information can be given about cancer risks; pathogenic, a PM is found, implicating high cancer risks; and non-pathogenic, no mutation is found, implicating no/low cancer risks. Interrater reliability was good (Cohen's Kappa: .84, $p<.001$). Categorization of differences was discussed until agreement was reached.

Frequencies and t-tests were calculated. The influence of covariates (*counselor*'s letter, cancer history, family history, demographics) on outcome variables (factual recall, subjective interpretation, general impact, impact on life domains) was calculated. Because of the small n, non-parametric test statistics (Fisher's/X^2 exact, Mann Whitney U, Kruskal Wallis) were used for analysis.

3. Results

3.1. Patient characteristics

Forty-nine out of 64 eligible women who had received a UV-result were asked to participate in this study. Reasons for exclusion were: 6 had died due to cancer, 6 had received comorbid cancer diagnoses, and 3 were psychologically too stressed. Twenty-four out of the 49 women consented and completed participation; 19 persons declined, 4 did not respond, one died before having the interview, and one withdrew because of unresolved feelings (response rate: 51%).

Nineteen out of 24 participants (75%) had cancer, and five were unaffected. Seventeen had breast cancer, 5 had ovarian cancer, and 10 of them had recurrent cancer. Mean time between UV-disclosure and participation was 3.0 years (sd: 1.9 years)(see Table 1). Relevant communication aspects in the *counselor*'s summary letter were identified (see Table 2). Fifteen women were only communicated a UV-result, but four women later learned about the definitive pathogenic meaning of their UV and 5 about the non-pathogenic meaning. On all outcome measures, no significant differences were found between these groups.

Table 1. *Demographic variables and cancer history (n=24)*

Variable	N (%)	Mean (Sd)
Medical center		
LUMC	18 (75)	
VUMC	6 (25)	
Demographic variables		
High school or higher	13 (54)	
Being married	21 (88)	
Having children	21 (88)	
Having daughters	18 (75)	
Age (years)		54.4 (11.8)
Time since counseling (years)		3.0 (1.9)
Development of first cancer		
before counseling	18 (75)	
after counseling	1 (4)	
Kind of cancer, time since diagnosis (years)		
Breast cancer	17 (71)	9.5 (8.5)
Ovarian cancer	5 (21)	5.5 (6.4)
Recurrent breast cancer	4 (17)	11.7 (8.5)
Recurrent ovarian cancer	1 (4)	2.0 (--)
Metastatic cancer	5 (21)	9.3 (7.9)
Pedigree characteristics: mean number of relatives (% of all relatives who is affected); mean number of affected relatives (sd)		
1st degree relatives	6.8 (.21)	1.42 (1.1)
2nd degree relatives	17.2 (.15)	2.58 (2.1)
3rd degree relatives	10.7 (.07)	0.75 (1.2)

Figure 1. *The counselees' recollections and the subjective interpretations of the UV-disclosure*

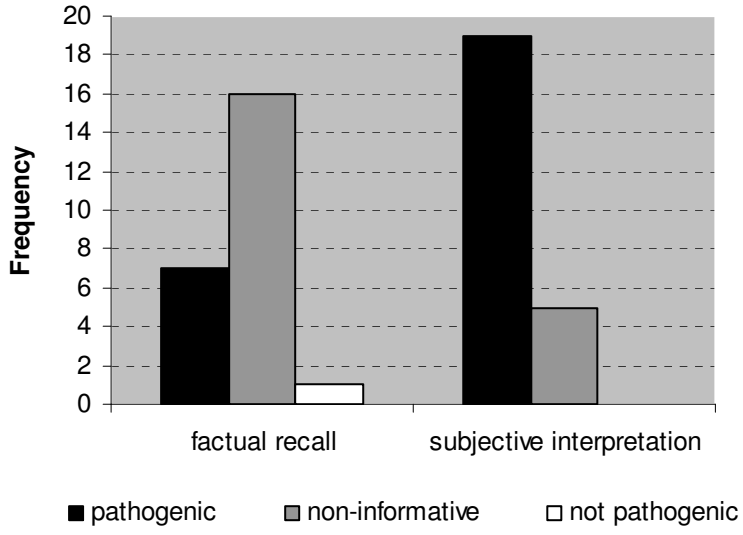

Table 2. *Communication variables in the counselor's letter; scored if mentioned in more than three (10%) of all letters*

Variables	N (%) of letters
Heredity information based on family history	7 (29.2)
Meaning of UV	
non-pathogenic	1 (4.2)
non-informative	20 (83.3)
possibly pathogenic	3 (12.5)
Meaning of family history	
not suspicious for hereditable cancer	2 (8.3)
hereditable cancer not mentioned	12 (50)
suspicious for hereditable cancer	10 (41.7)
This UV has been found before	3 (12.5)
Formulation of UV	
mutation	13 (54.2)
deviation	9 (37.5)
change	1 (4.2)
variant	1 (4.2)
Risk management options as if pathogenic BRCA results	21 (87.5)
Continuation of DNA-research	20 (83.3)

3.2. Question 1: factual recall and subjective interpretation of UV-disclosure

Factual recall - Sixteen participants (67%) recalled that the *counselor* had communicated the UV as a 'non-informative mutation', 7 (29%) recalled that a PM was communicated, and 1 (4%) recalled that she had received a non-pathogenic test result. (see Figure 1, Table 3)

Subjective interpretation - Nineteen women (79%) interpreted the UV-test result as carrying a PM, and only 5 women (21%) interpreted this as being non-informative.

Associations - The subjective interpretation of most women (17/24) was different from their factual recall about the UV-disclosure session; recall and interpretation were only identical in 7/24 persons, and were not associated with each other (X^2=4.02, df=2, p=.013).

Table 3. *Table of outcome variables regarding counseling sessions: n (%)*

Variables	Intake	UV-disclosure	Disclosure of new information about the UV-test result	
			pathogenic	non-pathogenic
total	24	24	3 (1 missing)	5
factual recall of genetic counseling	0 (0)	7 (29)	2 (67)	0 (0)
pathogenic	3 (13)	16 (67)	0 (0)	1 (20)
non-informative	0 (0)	1 (4)	0 (0)	5 (100)
not pathogenic	21 (87)	0 (0)	0 (0)	0 (0)
not mentioned				
subjective interpretation of genetic counseling	15 (63)	19 (79)	2 (67)	1 (20)
pathogenic	5 (21)	5 (21)	0 (0)	5 (100)
non-informative	3 (12)	0 (0)	0 (0)	0 (0)
not pathogenic	1 (4)	0 (0)	0 (0)	0 (0)
not mentioned				
subjective understanding of genetic counseling †	4.37 (71)	4.37 (82)	5.00 (0)	3.33 (1.21) *
subjective uncertainty about the heredity ‡	3.21 (1.18)	2.92 (1.39)	5.00 (.00) *	2.67 (1.5)

** Significant Kruskal-Wallis tests between columns at .05-level. † Means and sd. of scores on a 5-point scale ranging from 1 (no understanding) to 5 (complete understanding). ‡ Means/ sd. on a 5-point scale ranging from 1 (complete uncertainty) to 5 (complete certainty)*

3.3. Question 2: subjective level of understanding, expectations, completion of genetic counseling, and uncertainty

Participants reported to understand the UV-result well (m=4.37, sd=0.82). Fifteen participants (64%) reported to have realized beforehand that they might receive a UV-test result. Seventeen participants (71%) perceived genetic counseling as completed. However, 16 (67%) expected to receive new genetic information in the future (with the inclusion of 9 women who perceived the counseling as completed). Participants reported that UV-disclosure neither provided certainty nor uncertainty about the heredity, i.e. familial occurrence and possible genetic cause, of the cancer (mean=2.92, sd=1.39).

These outcome measures were unrelated with recall and interpretation, except for expectations and uncertainty. Those who *recalled* UV-disclosure as pathogenic instead of non-informative, less often expected to receive new information (n=17, n=4; t=2.58, df=16.00, p<.05). Participants who *interpreted* UV-disclosure as pathogenic instead of non-informative, perceived more uncertainty about the heredity (t=3.33,df=19.81, p<.005).

3.4. Question 3: the impact of disclosure of test results

Most participants reported that disclosure of the DNA-test result had changed their lives 'little' (m=2.48, sd=1.1.6), but 25% mentioned large life changes. Other life events, like change of work, cancer diagnosis or death of relatives, had changed their lives 'little' (m=2.95, sd=1.5), but having cancer had changed their lives significantly the most (m=3.95, sd=.97; respectively t=4.86, df=20. p<.001; t=2.96, df=20, p<.01). (see table 4)

The counselees who *recalled* the UV-test result as pathogenic instead of non-informative, reported significant less life changes due to cancer (respectively m=2.80, sd=.84; m=4.40, sd=.63; t=-4.64, df=18, p<.001) and did *not* report differences between life changes due to cancer and due to other life events (respectively m=2.75, sd=0.96; m=2.50, sd=1.05; m=3.10, sd=1.50). No association was found between the interpretation of the UV-test result and life changes due to DNA-disclosure.

All life domains had changed little after UV-disclosure, and these little changes were not related with recall and interpretation. Existential view on life and risk management changed the most (means = 3). However, in all life domains, about one in three counselees reported large changes (i.e., score higher than 3), especially in existential view on life (46%) and risk management (42%). All changes were attributed to having cancer and not to DNA-test results (i.e., attribution scores lower than 3), with exception of 'preventive risk management' (m=4.33, sd=.98) and 'body experience' (m=3.14, sd=2.38); changes in 'physical complaints' were as much attributed to the development of the cancer as to the DNA-result (m=3.0,sd=2.5).

Ten participants (41.7%) had undergone prophylactic surgery within one year after UV-disclosure, and before receiving new genetic information. Seven persons completely attributed this decision to UV-disclosure, and three attributed this to cancer developments

as well. Regarding recall of UV-disclosure, no differences in surgical decisions were found between those recalling pathogenic or non-informative information. However, ten out of 19 participants (53%) who *interpreted* the UV as pathogenic had undergone preventive surgery, against none of the 5 counselees who interpreted this as non-informative (X^2=4.51, df=1, p<.05; Fisher's p <.05).

Table 4. *Table of outcome variables: completion, expectations, impact on life*

Variable	N (%)	Mean (sd)
genetic counseling feels as being completed	17 (71)	
expectation of new genetic information	16 (67)	
changes in life *		
due to cancer		2.48 (1.16)
due to genetic counseling		3.95 (.97)
due to other life events		2.95 (1.50)
mean changes of life domains, number of counselees reporting changes larger than 3 *		
existential view on life	11 (46)	3.00 (1.53)
risk management (surveillance, operations)	10 (42)	2.75 (.156)
body experience	8 (33)	2.43 (1.41)
personality	8 (33)	2.46 (1.41)
emotional well-being	8 (33)	2.42 (1.44)
coping with uncertainty	7 (29)	2.21 (1.41)
relationships	6 (25)	2.21 (1.38)
physical complaints	4 (16)	1.67 (1.17)

** Means/sd. on a 5-point scale ranging from 1 (no changes in life) to 5 (complete change of life)*

3.5. Question 4: cancer history, family history and summary letter

Neither significant associations nor significant moderation effects were found between covariates and outcome measures. Only one aspect of the summary letter was associated with the outcome measures: the seven persons who received heredity information (familial occurrence/possible genetic cause of the cancer) on the basis of the pedigree during the UV-disclosure session, reported a higher certainty about the heredity of the cancer (m=3.86, sd=.69; m=2.38, sd=1.26; t=-2.91, df=21, p=<.01), interpreted the UV more often as non-informative (71% instead of 10.5%; X^2=15.34, df=1, p<.001, Fisher's p<.001), and did less often choose for BSO (46.6% instead of 100%; X^2=5.93, df=1, p<.05, Fisher's p<.05).

4. Discussion

4.1. Conclusions

The results from our study suggest the existence of two parallel processes in reaction to the disclosure of uncertain positive DNA-test results, Unclassified Variants, in BRCA1/2: factual recall and subjective interpretation. These processes are not associated with each other, and differences could not be explained by the counselee's cancer history, family history or sociodemographics. Medical decisions seem to be more associated with subjective interpretation than with factual recall.

4.2. The distorted perception hypothesis

This study gives evidence for and against the hypothesis that the perception of many counselees of uncertain DNA-test results is distorted. On the one hand, most counselees correctly *recalled* a UV-test result as non-informative. They also understood correctly that UV-disclosure does neither provide certainty nor uncertainty about the familial occurrence and possible genetic cause of cancer. On the other hand, perception was sometimes distorted: a minority incorrectly *recalled* UV-disclosure as disclosure of a pathogenic result, and most counselees *interpreted* the UV-test result as a genetic predisposition for cancer.

The most striking result was that the majority of the participants recalled UV-disclosure as non-informative, but interpreted this as pathogenic at the same time. When confronted with this paradox, some participants said that they 'knew better' than the *counselor*. Question is whether this interpretation has to be judged as distorted perception? If the medical meaning of the UV-result is the gold standard, then the answer is 'yes'. However, if one focuses on other elements in the counseling and the psychological coping process of the counselee, the answer may be 'no'.

The counselees' interpretation may be influenced by information, textual and framing effects (243), or accentuation of certainties in genetic counseling (31).
For instance, some counselees seem to base their interpretation of the DNA-result on their family history, because counselees interpreted the UV more often as non-informative when the *counselor* also communicated heredity information based on the pedigree during the UV-disclosure session.

Interpreting the UV-result as a pathogenic result could be a functional way to cope with uncertain information. *Firstly*, it lowers the cognitive load by transforming the grey colour of the DNA-test result into black or white. However, this does not explain the direction of the dichotomy, i.e. the main interpretation of a UV as pathogenic. This direction may be explained by a mental strategy of 'playing safe' by assuming the worst-case scenario. Another explanation is that many counselees have a strong wish for certainty and control (1,5,244,245). Recalling and interpreting the UV-test result as pathogenic, and undergoing prophylactic surgery, do fulfil this need.

These findings contradict previous studies, also from our center, showing that counselees have a good understanding of uncertain DNA-test results (196,85,223), but confirm one study which showed that many counselees recalled the UV-result as a pathogenic result (226). Further research should examine whether the 'distortion' in the interpretation of a UV-result stems from additional counseling elements, or from motives to cope with uncertain information.

4.3. The genetic-uncertainty-causes-distress-hypothesis

Some authors suggested that disclosure of uncertain DNA-test results might evoke uncertainty and distress (86,199,218,237). However, we found no associations between UV-disclosure, uncertainty and distress.

Disclosure of a UV-test result was neither associated with the feeling of certainty nor with the feeling of uncertainty about the heredity of the cancer. Several counselees explained this feeling of being in the middle of certainty and uncertainty as the balanced sum of the uncertainty of their factual recall and the certainty of their subjective interpretation.

The *general* impact of UV-disclosure on the counselee's life is limited; the cancer history has a much greater impact. This underlines Coyne's suggestion to frame the impact of genetic counseling in the context of other stressors and reference groups (74). However, this does not imply that the psychological impact of UV-disclosure can be ignored. About one in three counselees reported large changes in all *specific* life domains. Moreover, the interpretation of UV-results as pathogenic explains the decision for preventive surgery of breasts and/or ovari. These results emphasize that genetic counseling and scientific research about uncertain DNA-results should focus on identifying vulnerable subgroups that experience a strong impact of uncertain DNA-results.

4.4. Medical consequences

Factual recall and subjective interpretation of UV-disclosure were not equally important for medical decision making. Recall was not associated with preventive options and surgical decisions, but interpretation was. Participants interpreting the UV as pathogenic more often decided in favour of prophylactic surgery, without *counselor*'s advice. They opted for this operation to minimize their risk of developing a second primary breast and/or ovarian cancer. This decision could not be explained by cancer history, family history or sociodemographics, except for the communication of heredity information based on family history which was associated with more frequent adnectomy. The participants mainly attributed their decision for prophylactic surgery to UV-disclosure, meaning that the UV-result and not their family/cancer history motivated this decision.

The decision for prophylactic surgery is medically not completely unjustified because these women have cancer and belong to a high risk family. Their pedigree seems to suggest that either the UV-result will turn out to be pathogenic or that a PM exists in a yet unknown gene. On the other hand, it is medically incorrect to attribute surgery decisions to a non-informative DNA-result: a UV-result is itself not a medical indication for prophylactic surgery of healthy tissue. These medical decisions should be based on family history and personal cancer history. However, variation in the participants' medical decisions were not explained by family history and cancer history, but were explained by the subjective interpretation of the UV-result as pathogenic.

Other studies confirm that counselees opt for prophylactic surgery after UV-disclosure (163,246,247), and that surgery decisions after genetic counseling are not only determined by factual information (248). Studies in other fields also suggest that people react to risk information using two conceptually different processes: a more cognitive-deliberational system and a more intuitive-emotional system (82-84). The latter system seems to signal whether an individual is OK or in danger, and if the risk is interpreted as dangerous, the individual is motivated to behaviourally protect himself or herself.

UV-dislosure might be a difficult process for *counselor*s. On the one hand, the laboratory report does not indicate a certain genetic predisposition for cancer. On the other hand, the pedigree suggests heredity, and many counselees expect or ask for genetic certainty. Consequently, *counselor*s should be aware of transferring their own ambivalence toward the test results to the counselees.

We suggest some communication guidelines. In addition to the explanation that the family history of cancer may for instance be caused by coincidence or by a mutation in yet unknown genes, *counselor*s should help counselees to assimilate this information at a cognitive level in order to prevent incorrect understanding and interpretation. *Counselor*s could ask counselees to summarize the information, and to verbalize their interpretation, like 'how do you feel about your cancer risk?' Subsequently, medical decisions should not be based on a UV-test result, but on the total context. *Counselor*s should also keep in track

with the counselees' understanding and interpretation in follow-up sessions, to make corrections if necessary.

4.5. Limitations and conclusions

Before-mentioned interpretations should be read cautiously, because this study is limited by the small number of participants, the retrospective design, and the absence of validated questionnaires, e.g. about psychological distress. Mean age and mean education level seem to be a little higher than in previous studies in our center (222). We have addressed these limitations in an ongoing nation-wide prospective and retrospective study with control groups, validated measures and the inclusion of relatives.

This study shows that UV-results might evoke a factual recollection of an uncertain result, and a subjective interpretation that implies a genetic predisposition. Although a UV-result has a relatively small impact on their lives compared to cancer, counselees report that they base their risk management decisions mainly on their interpretation of the UV-test result.