# Opening the psychological black box in genetic counseling

Vos, J.

# Chapter 11

## Summary and discussion

# 1. The main thread of this thesis

*'Emery claimed that by 1984 there had been an evolution from what Kessler described as content-oriented to person-oriented genetic counseling. He based his claim on the acknowledgement in the literature that genetic information often has profound psychological effects, which may have long-term consequences that can extend to relatives. He asserted that a qualified genetic counselor had to be aware of the client's fears, hopes, defenses, and rationalizations in order to help him/her deal with his/her problems in a realistic manner. Many of the providers promoting psychological goals were trained in psychiatry or psychology and were well aware that clients do not necessarily make logical or rational choices (although they may be logical to the client). They recognized that scientific explanations are only one way to understand risk, allowing for personal interpretation and meaning. Genetic science does not necessarily alleviate guilt or anxiety in the client. In some cases, the information itself may actually raise anxiety or reinforce feelings of guilt or responsibility. A psychological goal of genetic counseling aims to help clients cope with such feelings and adapt to their circumstances. (37)*

Since many years, the practice of genetic-counselors in the Netherlands seems to have been dominated by a counselee-oriented approach. The development of genetic-counseling towards a counselee-oriented approach has been acknowledged and described by many authors, such as Kessler. He used the term 'person-orientation' which was in contrast with 'content-orientation', which means according to him 'that the focus of the session was overwhelmingly focused on the provision of medical information and genetic facts rather than on an attempt to explore personal meanings, attitudes, feelings, and dynamic issues' (419).

Thus, Kessler used his terms to describe how genetic-counselors communicate with counselees. To distinguish our focus from Kessler's, we have chosen to use different terms: information-oriented and counselee-oriented. Kessler has focused on the practice of genetic-counseling, but we have focused on the psychological processes that follows the genetic-counseling sessions and that may be described in psychological studies. The 'information orientation' and 'counselee orientation' describe how the communicated information and the communication process influence the counselees' lives in general in aftermath of the sessions.

On the basis of the current counselee-oriented practice of genetic-counseling in for instance the Netherlands, we had expected to find many counselee-oriented studies. In contrary, the literature seems to be dominated by studies that are mainly information-orientated (see chapter 1). For instance, many studies described the impact of DNA-test

result disclosure on risk-perception, medical decisions and distress. But it is not clear what a DNA-test result really *means* for a counselee, and how she embeds the result in her life.

In this chapter, I draw the main thread of this thesis by summarizing and discussing the results from previous chapters. I will do that by discussing five counselee-oriented themes. DNA-testing has a far-reaching impact on the lives of counselees (paragraph 2). The subjective interpretation of counselees is a complex but important phenomenon (3). This interpretation explains and mediates the impact of DNA-testing (4). The whole family is involved in the counseling process (5). Genetic-counseling is a complex procedure in which different pieces of information are communicated, and differences may exist between subgroups of counselees (6). Theoretical and clinical implications are not discussed in this chapter, but are presented in the addendum.

## 2. Conclusion 1: The far-reaching impact of DNA-test results

Many authors have described which factual consequences DNA-testing may have on the lives of counselees. For instance, the disclosure of BRCA1/2-test results – especially PMs (Pathogenic Mutations) - has shown to lead to a more frequent uptake of surveillance and prophylactic surgery of breasts and/or ovaries (e.g.221,247,397,420-423,255). In the period of waiting for the DNA-test result and shortly after that, many counselees seem to feel somewhat distressed, but these feelings seem to normalize over time (183). We also found that up to 50% of all counselees with a PM or UV-result (Unclassified-Variant) had undergone PBM (Prophylactic Bilateral Mastectomy) or PBSO (Prophylactic Bilateral Salpingo Oophorectomy) within 5 years after the DNA-test result (chapter 5), and that the majority of all counselees (PM, UV and UR/Uninformative-Results) underwent frequent surveillance of breasts and/or ovaries (chapters 5 and 6). Most counselees did not report significant distress or psychopathology in our study, but between 5% and 25% of them reported clinical levels of distress (chapters 5 and 6), especially counselees who had received a UV-result (chapters 3 and 6).

Thus, like previous studies, we have reported that DNA-testing is often followed by medical decisions and symptoms of distress and psychopathology. But this conclusion may not completely explain what counselees experience as really important after DNA-testing. The range of medical and psychopathological outcomes is relatively narrow, as a recent review concluded that 'new research is necessary to develop the array of outcome measures' by means of more sensitive and specific instruments (424). The reported medical facts and psychopathological symptoms do not seem to create a lively image of what is precisely going on in the experience of counselees, because they do not answer the questions: what do these medical facts and psychological symptoms really *mean* for the counselee, and how does she embed these in her life? To answer these questions, we

have developed new instruments, and studied new counselee-oriented aspects of the counselees' lives that were influenced by the DNA-test result. We call these aspects counselee-oriented because they focus on the personal meaning that a DNA-test result has on the counselees' lives.

We found that not only medical and psychopathological domains of the counselees' lives had been influenced by the disclosure of the DNA-test result. The Life Changes Questionnaire in chapters 3 and 6 showed that the counselees had experienced significant changes in their existential view on life, their experiences of their body, personality and emotional well-being, coping with uncertainty and relationships. There was a large variation in the extent that the DNA-test result influenced the lives of individual counselees; some reported small or no changes at all, and others reported very large changes. The counselees attributed most changes to the DNA-test result, but some counselees mentioned that the cancer had also contributed to these changes.

Despite the fact that psychopathology was absent in more than three-quarters of all participants, the majority of all counselees felt vulnerable, stigmatized, and felt low mastery over their cancer (chapters 5 and 6). Moreover, more than two-third of all counselees experienced an unfulfilled need for certainty regarding the DNA-test result, the heredity of cancer in the family, and their own cancer (chapter 10).

Thus, when we focused on information-oriented impact-measures, we did not find a very large impact of DNA-testing on the lives of counselees. But when we used counselee-oriented instruments, significant changes in life were found, especially regarding the experience of vulnerability, uncertainty, existential view on life, and the counselees' experience of themselves. These changes were described as the essence of being-at-risk and were associated with many other important psychological processes, such as distress (chapters 3 and 10). In summary, the disclosure of DNA-test results significantly influences the counselees' lives, ranging from practical and visible changes to deep and not primarily visible changes. Moreover, these deep changes seem to be an essential part of the counselees' experience of DNA-testing. This has also been suggested by previous qualitative and theoretical studies (59-61,425,426).

## 3. Conclusion 2: The subjective interpretations of DNA-test results

> *The genetic-counselor has provided me with all the certainties that she had regarding the possibility that I could carry a genetic mutation. But an uncertain factor always remains. I recall that she laughed when I said: 'You say that this pedigree is suspicious? Really? OK. I hear you. I know what you're really saying.' The genetic-counselor laughed, because we could not avoid the truth. You know, genetic-counselors are not saying that aloud –that is how science is- but they are actually telling this story, that I have the mutation.* (Based on interview RL-006)

One of the aims of genetic-counseling is to help counselees understand the genetic contributions to their disease (52). For that reason, researchers have asked counselees how they understand their DNA-test results. As we discussed in chapter 4, many studies used ambiguous questions, such as 'what are your risks to develop cancer?' It was unclear whether the answer to such a question reflected the counselees' recollections or interpretations of their cancer-risks or an unidentifiable mixture of both. Other authors have asked counselees about their understanding and their cognitions of the communicated risks. But few have studied what it *means* to be at risk to develop cancer or to carry a PM. Moreover, many studies have only discussed the counselees' perception of their own cancer-risks and not of other pieces of information communicated by the genetic-counselor.

For these reasons, we asked counselees to recall the communicated DNA-test result category, and to recall and interpret their own cancer-risks, their relatives' risks, and the likelihood that cancer is heritable in the family. All these aspects differed significantly from each other, suggesting that these different questions measure different aspects of the counselees' perception. This suggests that the counselees' perception indeed consists of multiple elements. Many aspects were also intercorrelated, which is understandable because they were about the same DNA-test result and about the same counselee in the same family (see chapter 1, 1.3.2.3.).

How accurate was the counselees' perception, that is: how much did their perception deviate from the actually communicated information? When we asked counselees, the large majority of them answered that they had understood the communicated information. When we asked them to identify which DNA-test result category (i.e. PM, UR or UV) had been communicated, the large majority answered accurately, except for women with UVs, who inaccurately regarded these as being either a PM or a UR in 25% (chapters 3-6). When we asked counselees about their recollections and interpretations of the *meaning* of the DNA-test result for cancer-risks and heredity-likelihood, their answers were most frequently inaccurate, i.e. they differed significantly from what actually had been communicated (chapters 4-6, 9). These results suggest that counselees accurately perceive the general meaning of the DNA-test result –such as the DNA-test result category-, but they do not accurately recall and interpret the precise meaning of the result for their life, that is for their own cancer-risks, their relatives' risks and the likelihood that cancer is heritable in the family.

After the DNA-test result disclosure session, the counselees' recollections and interpretations changed slightly 'in the right direction', that is they deviated less from the actually communicated genetic information, compared to the first measurement after the intake session (chapter 4-6). However, as described above, the recollections and interpretations differed significantly from the actually communicated information at all measurement moments. This seems to suggest that before genetic-counseling, counselees

already had developed strong ideas about their cancer-risks and heredity-likelihood which were only slightly adapted, as if they had a pre-set bandwidth within they subtly adjusted their perceptions.

In summary, we have confirmed previous studies that have suggested that genetic information is not simply 'taken up as value-neutral objective truth, but rather risk information is deeply subjective, interiorized against a pre-existing sense of self' (63). The counselees' perception of the communicated genetic information has also shown to be a broad complex process which cannot be examined by using a single, ambiguous question. The counselees' perception can be compared with a children's whisper game: the genetic-counselor communicates 'A', but the counselees recalls 'B' and interprets 'C' (chapter 7). Thus, the counselees' interpretation of facts are not similar to the communicated facts; some may say: the world of genetic-counseling does not consist of facts, but this world is constructed by the counselees (cf.427).

## 4. Conclusion 3: Models explaining the impact of genetic-counseling

As reported, we have found that the communication of a BRCA1/2-result had influenced a broad range of outcomes in the counselees' lives (1.2.1.), and that many counselees perceived the DNA-test result differently than their genetic-counselor (1.2.2.). This raises the question: how did the actually communicated genetic-information influence the outcomes, and how is this related to the counselees' own perception?

Few previous studies have answered the question *how* the disclosure of DNA-test results has influenced the counselees' lives. Most studies described the impact of testing on the counselees' lives, and they simply showed differences between the outcomes of PM, UR and UV-results (e.g.183). Other studies assumed that the communication of genetic-information directly predicts the outcomes.

This simple model of genetic-counseling has only been confirmed in our retrospective study: the communication of a PM or a UR directly correlated with the counselees' decision to (not) undergo PBSO and/or PBM (chapter 5). This finding need not tell that the communication of a DNA-test result directly causes counselees to opt for prophylactic surgery and undergo surveillance, but it may simply reflect the general guidelines. Because surgery options are more strongly suggested in case of PM and not strongly in case of UR, and for surgeons it is not common policy to perform PBSO and/or PBM in case of UR. Thus, this result seems to show that the guidelines are being followed. It does not mean that in general, the communication of a DNA-test result directly causes other outcomes such as psychological well-being and changes in life. This finding should also be nuanced by the fact that in our prospective study, none of the pieces of

communicated genetic-information (including the PM and UR-categories) was directly related with any outcomes (chapter 6); this result may be explained by the fact that the measurement-moment was shortly after the disclosure of the DNA-test result.

In contrast to this simple model, we have found that the counselees' perception of the communicated cancer-risks and heredity-likelihood correlated with and/or mediated their medical decisions and distress. All reported effects sizes were moderate to large (chapters 5 and 6). The outcome-measures correlated especially strongly with the counselees' interpretations of their own cancer-risks. Thus, how counselees subjectively think and feel about their DNA-test result had strongly influenced their lives, regardless of their recollections and the actually communicated DNA-test result.

Moreover, the accuracy of the counselees' perception of cancer-risks correlated as strongly with information-oriented as with counselee-oriented variables, but the latter also explained/mediated the influence of the information-oriented variables (chapter 9). This means that the information-oriented variables did *not directly* correlate with the accuracy but it did correlate with the accuracy only *via* the complete mediation of the counselee-oriented variables. Thus, information-oriented variables, such as the communication of a pathogenic DNA-test result, influenced the counselees' perception *because* they seemed to evoke a personal and existential process in the counselee. The counselees' risk-perception was not determined by merely rationally knowing 'I am at risk' (i.e. information-oriented), but by the personal and existential meaning of knowing this (i.e. counselee-oriented).

These findings confirm qualitative studies indicating that when counselees are confronted with risk-information, they 'translate the probabilistic statements into terms with personal meaning' (62), and try to 'embed this information in the general story of their lives' (59). By subjectively translating and embedding this information, the counselees seemed to have distorted the originally communicated cancer-risks, creating their own perception of the DNA-test result that deviates from what the genetic-counselor had actually communicated. Subsequently, counselees made medical decisions and experienced distress on the basis of this inaccurate interpretation, and not on the basis of the actually communicated information or on the basis of their recollections. Moreover, the medical, psychological and existential impact of genetic-counseling was explained by these personal and existential processes, such as the counselees' unfulfilled need for certainty about the DNA-test result, heredity-likelihood and cancer (chapter 10).

In summary, we have shown that counselee-oriented variables correlated equally strong or stronger with the impact of DNA-testing compared to information-oriented variables, and they also mediated the influence of information-oriented variables. This is in line with other qualitative or theoretical studies that have suggested that the counselees' perception should be used as a main predictor or mediator of the impact of genetic-counseling (e.g.77,79,90). These results may be exemplified by Emma's following remark:

*'The genetic-counselor has communicated many 'facts'. But when I reflect on what this result really means for my life, and when I have to make medical decisions, I do not use figures and facts. I simply follow my own feelings. And they tell me something completely different than the genetic-counselor.'*

## 5. Conclusion 4: DNA-testing involves untested relatives

Previous studies have shown that counselees often inform their untested relatives about the DNA-test result, and they have described the impact of DNA-testing on the relatives' lives from the perspective of the counselee and/or from a merely qualitative point of view.

Previous studies suggested that the counselees' experiences with cancer in their family influence their perception of the communicated information (e.g.164,166-168). Like many studies, we have examined whether the counselees' perception was influenced by the number and percentage of relatives with cancer and/or who has deceased due to cancer (chapters 3, 5, 6, 9, 10). These pedigree-variables did not influence the results, and neither did the openness to discuss hereditary cancer in the family (chapters 8, 9). Why did these 'familial facts' not influence the counselees' perception and outcomes?

*Firstly*, unpublished analyses on the prospective study suggested that not the numbers of affected relatives and the factual openness influenced the counselees' perception, but the meaning of these family characteristics did. For instance, not the communication openness per se mattered, but the experienced social support and equality and trust in the familial relationships did. The moral support that the counselees had received and their experiences of their relationships with relatives, nuclear family and friends influenced the counselees' interpretations of the DNA-test result. Other studies also suggest that the most important predictor is not the mere sum of affected and deceased relatives, but it is the personal meaning that a counselee attaches to her experience of being a member of a family with many cancer patients, such as the extent to which she identifies with a deceased relative (355,328).

*Secondly*, the familial facts may influence the counselees' perception and outcomes not directly but only *indirectly*. Because a counselee who grows up in a family with many cancer-patients may develop a feeling of vulnerability to develop cancer, and may even start to expect the occurrence of cancer. Counselees from high risk families may feel fundamentally insecure (428), and feelings of being-at-risk may become a part of their identity (61) (see also 2.1.5.). Subsequently, this vulnerability or identity may have determined their interpretation of cancer-risks and heredity before genetic-counseling, which has shown to be difficult to change during counseling (1.2.2.) and which influences the outcomes (1.2.3.). Thus, family-experiences may have formed the counselees' identity,

which may subsequently have influenced their risk-perception and the outcomes of genetic-counseling.

We found that the untested relatives in our family study felt 'much involved' during the genetic-counseling process (chapter 7). Ten percent would even have preferred being involved more in the genetic-counseling process, 25% would have liked receiving direct information from the genetic-counselor – e.g. a letter -, and 15% would have preferred to have had a face-to-face conversation with the genetic-counselor (unpresented data; no differences between PM/UV/UR). These low percentages may reflect the fact that the untested relatives participating in our study were already well informed by the tested counselee, and that they were much involved during the genetic-counseling process; thisfinding that relatives were well informed and strongly involved may also be due to sample biases (chapters 7-8).

The relatives' perception of their own risk to develop cancer had been influenced by the actual DNA-test result like in a children's whisper game: noise had occurred in the recollection, interpretation, and communication by the probands before the relatives created their own recollections and interpretations of the DNA-test result. The lives of relatives had somewhat changed after DNA-test result disclosure, both regarding medical and psychological aspects. These changes were only directly correlated with the relatives' recollections and interpretations of the DNA-test result.

Probably, the untested relatives' interpretations and consequences also deviated from what the proband/counselee had communicated because these relatives had used their own experiences with cancer as well as their own experiences with the specific messenger of 'the genetic news'. For instance, one relative said about the counselee who had told the genetic news: 'She always exaggerates information; therefore, I do not think that the genetic problem is as big as she says that it is'.

In summary: Relatives felt much involved in genetic-counseling, but some would have preferred more involvement. DNA-test result disclosure had an indirect, significant impact on the lives of untested relatives. We have shown that the family history may have indirectly influenced the counselees' perception, like in a children's whisper game. The counselee had communicated message 'C', this information was subsequently filtered by the indirect, non-reassuring and closed communication process, and the relative recalled having received 'D', interpreted this as 'D' and the impact on his/her life was only related with 'D'. Thus, DNA-testing seems to be a social event, in which relatives are involved. Giving a personal meaning to a DNA-test result may inherently be a social process (cf.90,375,376).

# 6. Conclusion 5: De-simplifying the models of genetic-counseling

> *'I have to admit,'* Emma said, *'that I did not know beforehand what it really meant to request for genetic-counseling. I had expected that they would just ask a few questions about my family and about my own cancer history. Immediately after that, they would prick me with a needle to get a blood sample. I would just have to wait for a month or so, and then I would hear that I either have the gene, or that I do not. The first result would imply that I had to have my unaffected breast and ovaries removed. The second result would imply that I could open a bottle of champagne. But the real DNA-test result was neither black nor white, it was gray. There are no rules for what I have to think and to do.'*

Like Emma, many counselees seemed to simplify the genetic-information, and think in terms of black-or-white, i.e.: 'either I get cancer or I do not get cancer' (216,217). Not only counselees seem to simplify genetic-counseling. Despite the complexity of genetic-counseling (e.g. tables 1 and 3 in chapter 6), many psychological researchers have only included a relatively small number of predictors, outcomes and moderators. For instance, few studies have used mediation, moderation, or structural equation models. This tendency towards simplification may reflect the researchers' own need for certainty and non-ambiguity (345-386). Or they followed the scientific rule of parsimony, that is: using the simplest or most frugal route of explanation available.

Recently, the literature seems to show a trend of de-simplifying the models of genetic-counseling. More recently published psychological studies on genetic-counseling use more extended models, and include many predictors and covariates. A reason for this trend may be that previous studies only reported small or moderate effect sizes, and showed different results for different groups of counselees. For instance, reviews suggested that simple models of DNA-test results rarely directly predict the psychological impact of DNA-testing (66,68,76,70,71), and that counselees with different DNA-test results experience different levels of distress (183).

To render justice to the complexity of genetic-counseling, and to avoid too hastily excluding hypotheses, we have included many variables in our studies. In this paragraph, we discuss how the results of our studies were influenced by the variation in the actually communicated genetic information, and by the variation between the counselees.

### 6.1. The variation of communicated genetic information

This paragraph summarizes how the study results have (not) been influenced by variation in the information actually communicated by the genetic-counselor. We describe the variation in the DNA-test result nomenclature, in the communicated genetic-information,

between the individual genetic-counselors and the participating departments of genetic-counseling.

*Firstly*, the whisper game of genetic-counseling may have started among the genetic-counselors, who use many different terms to refer to non-pathogenic DNA-test results. Our literature study showed that different authors may use the same term to express a different meaning; thus, many terms seemed to have been used unreliably. Many terms also showed to be non-valid, because the term did not express what it was intended to do. Some words seemed to disclose a particular value –intended or unintended-, such as the word 'non-informative' seemed to imply the non-usefulness of this result (cf.429). Therefore, we suggested developing a new nomenclature. We did not systematically study whether this Babylonian speech confusion about the BRCA1/2-terminology had also influenced the counselees. However, the following quote suggests that the choice of words may have influenced the counselees' perception of an unclassified variant:

> *'The genetic-counselor told me that something… unqualified was found. It is called that way, isn't it? This means that… It was not qualified, so that must not be right then. Yes, that is it. They found a deviation in my genes. That's why my relatives and I have developed cancer.'*

*Secondly*, we found that the communicated information was very diverse (chapters 6 and 9). Previous studies only examined a small range of information, but we included a larger one. In chapter 4, we summarized six pieces of information that we regarded as being the most important: the DNA-test result category (PM, UR, UR), the heredity-likelihood, the counselees' cancer-risks, her untested relatives' risks, medical options for risk management, and options for relatives to undergo DNA-testing. In chapters 6 and 9, we reported that many genetic-counselors frequently add explanations to these six main pieces of information, which may be due to the tailoring of information to the counselee (430).

We found that different DNA-test results had led to somewhat different perceptions. Counselees perceived a PM-result more accurately than UR/UV-results, possibly because of its relatively clear meaning and unequivocal medical consequences. PM-counselees seemed to benefit from mirroring the cancer-risks (e.g. 80% at risk also implies 20% not at risk), possibly because this communication format counteracted the counselees' inclination to misinterpret a PM-result as implying 100% risk (216,217).

Counselees perceived a UR or UV as less accurate, possibly because they mixed the meaning of the DNA-test result and the pedigree (chapter 4), or because the result was not like they had expected. This counselees' confusion over the meaning of the DNA-test result became even larger when other genetic-counselors added extra explanations, such as

using multiple formats or mirroring risks, when counseling was by phone and/or letter instead of face-to-face, and hwen  a flyer explaining genetic-counseling was provided.

Different DNA-test results had also led to somewhat different outcomes. Long after having received the DNA-test result, PM-counselees had more often undergone surgery than UR-counselees, and UV-counselees experienced more symptoms of depression (chapter 4). Shortly after DNA-testing, the communication of the counselees' cancer-risks, the PM- and UV-results indirectly correlated with medical intentions and feeling vulnerable (chapters 5 and 6).

However, all these differential effects of the actually communicated genetic-information on the impact on the counselees' lives were completely mediated by the counselee-oriented variables, such as the counselees' interpretations. The mediation effects were somewhat different for the different DNA-test results (i.e. moderated mediation), but the general results were similar for all DNA-test results.

*Third*, we found differences between individual genetic-counselors. For instance, some genetic-counselors always mirrored the communicated risks but others did not, and some communicated during the intake session that a UV-result may be found and others did not. Some genetic-counselors evaluated most of their counseling sessions as to-the-point, and others evaluated their sessions as emotional. Unfortunately, we could not study the effects of individual counselors on the results of our study, because our sample was too small to perform multilevel analysis.

*Fourth*, there were also slight differences between the five participating medical centers. These results have not been reported in the previous chapters because these are only trends (all p-values>.05, p<.10). These effects were mediated by a consistent use of counseling-related factors in the centers, such as communicating risks in words, communicating the a priori detection rate of a PM during the intake session, and having face to face counseling. The extent to which the summary letter was clear also differed per center, which may also have contributed to different study outcomes for different centers. We also found differences in the personality variables of counselees between the different centers, which seem to confirm stereotypes in the Netherlands. Counselees in Groningen showed relatively few emotions and reported not thinking frequently about existential issues. Counselees in the Randstad (Leiden, Rotterdam, Amsterdam) had a more independent personality, and less frequently asked friends and relatives to support them in their genetic-counseling process. Counselees in Maastricht were more emotional and social in coping with their DNA-test result.

In summary, many different pieces of communicated genetic-information have shown to influence the counselees' perception and the impact on their lives. But all these aspects

were mediated/explained by counselee-oriented variables. In the end, a relatively simple model remained: the communicated information influenced the counselees' interpretations which subsequently influenced the counselees' medical decisions and well-being (i.e. mediation).

Many variables showed to be not significant in our studies. This does not imply that these variables may not be clinically relevant. For instance, some of these variables may have become non-significant because they have not frequently been communicated; we did not report their effects because we only described effects with $p<.01$ and $R>.20$. Another possibility is that these variables overlapped and/or interacted with other variables, which we have not studied. These infrequently communicated pieces of information may also reflect our small sample sizes and the possibility that the genetic-counselors have adjusted the information to the counselees' skills and situation (i.e. tailoring). We have not examined such effects of tailoring. See more methodic comments in paragraph 4 of the addendum.

### 6.2. The variation of counselees

Several studies have suggested that counselees with and those without cancer differ in their experience of the DNA-test result (249,5,71). Because a DNA-test result may tell an unaffected counselee whether she will develop cancer, and the DNA-test result mainly tells an affected counselee what the risks of her relatives are. In the retrospective study (chapters 3-5, 7-8), we have included both affected and unaffected counselees, but we did not find any differences between both groups. We have also included the counselees' medical history in all our studies, but these did not significantly influence the results.

This does not necessarily mean that different counselees with different cancer histories do not experience genetic-counseling differently, but this only means that our core measures were *not directly* influenced by these cancer history variables, i.e. the recollections and interpretations of risks, the accuracy of these recollections and interpretations, distress and medical decisions. The cancer history may have influenced the result *indirectly* or in interaction with other variables, but we have not studied this.

In summary, having had cancer has shown to be less important than the counselees' own interpretations and uncertainty regarding the DNA-test result. Thus, not the facts, but the counselees' interpretation of these facts had influenced their decisions and distress.

We have also added questions about sociodemographics, personality and family variables (chapters 3-10), but these did not directly correlate with the core variables in our study, with two exceptions. The more autonomous a counselee was, the more her perception deviated from the originally communicated genetic-information (chapters 4-6). This is understandable, because the more autonomous an individual is, the more likely it is that she creates her own opinion because she relies relatively more on her own opinion.

Family characteristics, such as the openness to discuss cancer in the family, influenced the way in which the counselee had communicated the DNA-test result to her untested relatives (chapter 8). For instance, counselees communicated DNA-test results more indirectly and more reassuring in families with a closed communication style.

### 6.3. Summary of the variation

Together with other authors, we have criticized previous studies for their simple underlying model of genetic-counseling which seems to have caused small effect sizes (68,66,76). Therefore, we have added a larger number of variables in our studies. Many pieces of communicated information and many personal characteristics of the counselee did not strongly influence the results. We have presented these non significant results in our studies, to show that our hypothesized counselee-oriented model was not influenced by these. Despite the inclusion of many variables, our model remained relatively simple, because all studies confirmed the mediating role of counselee-oriented variables. In paragraph 4 of the addendum, we describe how our model has over-simplified the situation of genetic-counseling, and we do suggestions for elaborations of our model in future research.

## 7. Limitations and implications for future research

### 7.1. Limitations

In 1.2.5., we argued that genetic-counseling is a complex process which involves many variables and many interactions. Compared with previous studies, we have extended the theoretical model of genetic-counseling with many new elements. Unfortunately, our model was also limited. These limitations were mostly due to practical reasons. For instance, our decisions for the type of statistical tests and the number of included variables were bound by our relatively small sample –which was the largest possible sample that we could collect in the Netherlands in this time period. Below, we summarize the most important limitations.

*Firstly*, the number of included variables was limited. We have included a small range of instruments to measure personality, coping styles, illness representations and other instruments based on cognitive theory. We have not examined the role of relatives, friends and other sources of information such as the Internet (cf.1.2.4.). All information was subjective, because we did not videotape the counseling sessions, and only used the counselees' questionnaire, summary letters, medical files and checklists. A real baseline-measurement was not possible in our studies due to practical reasons; thus, we do not know how the counselees' perception was before the genetic-counseling: we only know their perceptions after the intake and after the DNA-test result disclosure. We have not

examined whether the counselees' perception three months after the DNA-test result was predictive of their perception and outcomes later in time (i.e. longitudinal). We have not asked counselees whether they had read the summary letter sent by the counselor, and whether they had understood this letter; it can be expected that having read the letter (or not) has influenced the counselees' perception.

*Secondly*, we have not presented all results because of the limited length of the articles/chapters. For instance, we have only presented the influence of the counselees' perception of breast cancer risks, because 96% of all counselees reported that their breast cancer risk influenced their lives more than their ovarian cancer risk (chapters 3-10). We have separately analyzed the 4% of counselees who had reported that their ovarian cancer risks were most influential; these analyses did not lead to different conclusions, but this was probably due to the small sample.

*Third*, we have assumed that mediation was present in our studies, but we have not *proven* its presence (see chapter 1, 1.3.3.4.), because the results may also be explained by confounding. However, mediation was strongly indicated by the study design and our theoretical framework (188). By assuming that mediation was present, we also assumed that the DNA-test result caused the perception. It seems more likely that counselees already had certain perceptions before DNA-testing, which influenced their decision to request for genetic-counseling. We have categorized all data into three groups in our mediation models: predictors, mediators and outcomes. Interactions between variables have not been studied, such as the interactions between recollections and interpretations.

Moreover, we have assumed that causal directions were present in our studies, that is: the risk-information changed the risk-perception which changed the psychological and medical outcomes. These assumptions were suggested by the qualitative data in our pilot interview study (chapter 3), and by the Life Changes Questionnaire in which we explicitly asked counselees about changes in life *caused by* genetic-counseling. However, we could not determine the presence of causality due to the design of the studies. For instance in the retrospective studies (chapters 4-5, 7), there was only one measurement-moment after the DNA-test result disclosure, but the statistical model that we tested in these chapters/articles assumed causality over time (i.e. risk-information had changed the perception). In the prospective study (chapters 6, 9-10) we have only presented results for measurement-moment 2 (T2); inclusion of T1 did not significantly change the results/effect sizes. Hence, causality has to be confirmed in intervention studies.

*Fourth,* we have translated risks that were communicated in percentages into categorical risks on a 1-7 scale, and we have used these translations in our subsequent calculations (chapters 4-7, 9). Genetic-counselors usually communicated genetic-risks in percentages and in words. However, which risk was verbally communicated, was not always reported in the retrospective medical files (chapters 4-5, 7) and was also not always reported in the checklist filled-in by the genetic-counselor (chapters 6, 9). Therefore, we

had to use the communicated risks in percentage. However, we could not ask the counselees which percentage they recalled to have been communicated, because the majority had forgotten which percentage was mentioned by the counselor (chapter 4, 6); this finding has not been reported in previous studies in which the counselees were simply asked 'what is your risk to develop cancer?' (cf. chapter 4). Thus, we had to combine the communicated risks in percentages with the recalled risks in categories. For that reason, we translated the percentage-risks into the 1-7 scale. As reported in the chapters, the results did not change when we checked the translation with the verbal information that we could find in some summary letters and checklists, and when we did subgroup analyses with percentage-risks only or categorical-risks only.

*Fifth,* we had decided to present only statistical relationships with small, moderate or large effect sizes with a p-value smaller than .20 (see chapter 1, 1.3.3.4.). On the one hand, this may have excluded clinically relevant results (i.e. type II statistical error). On the other hand, the large number of tests in combination with not performing a Bonferroni correction increased the likelihood of finding relationships that are not actually true (i.e. type I statistical error). We do not expect that these statistical errors have caused us to overlook relevant results, because we have confirmed our findings in multiple samples.

*Sixth*, we have only examined the general relationships of the communicated genetic-information with the counselees' perception and outcomes. We did not study the specific effects of tailoring of information to the counselees' needs, as genetic-counselors frequently do (430) (see discussion of chapter 6).

*Seventh*, our studies were limited by the samples. Only female BRCA1/2-counselees – most of whom had already had cancer - were included, because these counselees belong to the most frequently tested group of counselees in genetic-counseling in the Netherlands. The counselees' sociodemographic characteristics were comparable with other studies in BRCA1/2-counselees, which for instance shows that they were relatively highly educated (e.g.169,482). The sample sizes were relatively small compared to the large number of subgroups and variables that we studied. Due to this small sample size we were not able to use more complex statistical models such as multilevel modeling in which the different genetic-counselors and the different departments of clinical genetics are analyzed as separate levels.

*Seventh*, our studies have only been performed in the Netherlands, which may have influence the results. For instance in other countries, both the counseling procedure and distress of counselees may differ (183,477). In the Netherlands, it is common practice that the genetic-counselor draws an extensive pedigree and communicates cancer-risks for both the counselee and her relatives on the basis of this pedigree, which may not always be done in for instance the United States. It is likely that this common practice in the Netherlands has influenced the counselees' perception of the DNA-test result, for instance

because they mixed the meaning of the DNA-test result and the meaning of the pedigree (chapter 4).

### 7.2. Implications for future research

We have kept our models relatively simple, to avoid deduction bias –i.e. applying large theories/models to the empirical reality-, and to start with the counselees' experience as a consequence of a counselee-oriented approach. We have extended the simple input-output-model that has been used frequently in genetic-counseling, and have added the mediation model (chapters 5, 6). On the basis of the detected importance of the counselees' interpretation we have suggested a shift from an information-oriented approach towards a counselee-oriented approach in the fields of genetic-counseling and risk-perception. These themes are relatively new – especially in the field of clinical genetics - but more studies are required to create and test more complex models. Knowledge from other fields such as risk-perception may be included in future models (90).

Of course, we suggest that future research should replicate our findings, while overcoming the limitations of our studies. We advise building new instruments to measure more elements of the counselee-oriented perception and outcomes. The hypothetical explanations in paragraph 2 should be examined in depth, such as the relationships between information-oriented and counselee-oriented variables (2.1.), the importance of the counselees' need for certainty (2.2.), and the counselees' skills to live with dual realities such as the unfulfilled need for certainty (2.3.).

It has been suggested that the best way to examine such counselee-oriented topics is by means of qualitative or phenomenological studies (e.g.6,483). We recommend performing studies with a mixed qualitative and quantitative design, so that the significance level of the results can be determined.

Our studies had an observational, non-interfering nature. Intervention studies are required to determine whether the counselee-oriented phenomena can be changed. For instance, a specific counselee-oriented skills training for genetic-counselors may be developed, or standardized interview questions may be created for use during the counseling sessions (cf. paragraph 5). Psychologists may study the effects of using improved flyers explaining genetic-counseling (cf.5.3.), medical and psychological follow-up sessions for instance by means of an Internet intervention (cf.5.5.), and individual or group psychotherapy (cf.6.4.). *Finally*, the role of the genetic-counselor may be examined. In our studies, we have only focused on the information-oriented and counselee-oriented processes, but not at counselor-oriented processes and how these may be related to the other processes. It may be relevant to study which characteristics of individual counselors predict the outcomes of genetic-counseling, and for what reasons.

## 8. Summary by means of Emma's example

Emma's quest for explanations of the genetic contributions to the occurrence of cancer in her family did neither start with the communication of information. Nor did it start when she visited the department of genetic-counseling. It started when she grew up in a family in which many relatives had cancer, which alerted her about the possibility that she could also develop cancer. Feeling vulnerable to develop cancer has always been a fundamental part of her identity. For many years already, her perception of her future had been marked by uncertainties regarding the development of her cancer, the possibility of developing a secondary tumor and her relatives' risks. Her uncertainties grew over time, and she felt especially uncertain about her daughter who may develop cancer one day. Like many other counselees, she finally asked for genetic-counseling, not to develop 'an accurate perception of her and of her relatives' cancer risks', but to fulfill her need for certainty.

Unfortunately, Emma's need for certainty would not actually be fulfilled. Emma had expected to receive clear-cut genetic-information: 'either I have the gene or I do not have the gene'. But the genetic-counselor had communicated nuanced information both during the intake session and the session in which the DNA-test result was disclosed. Emma was explained that a UV-result was found, and intermediate cancer-risks had been communicated on the basis of the pedigree. Additionally, the genetic-counselor provided her with many extra explanations and information, which eventually did not directly influence her perception, but may have added to her experience of the communicated information as being complex, and to feeling confused.

The actually communicated information is important to understand Emma's inner processes. Without first orienting ourselves, as researchers and clinicians, on the actually communicated genetic-information, we cannot understand the processes that occurred at the same time inside this counselee and that will significantly influence her life. Both information-oriented and counselee-oriented processes are needed to understand how a counselee experiences a DNA-test result, interprets it, and embeds it in her life.

In her perception, Emma mixed the meaning of the DNA-test result with the meaning of the pedigree. Because she recalled and interpreted that the UV-result *meant* that she and her relatives had high cancer-risks. Her recollection differed from what had actually been communicated. She was not convinced of what the genetic-counselor had communicated, and she believed more in her own interpretation of the UV-test result as being a PM. Emma told her interpretation to her relatives, and possibly due to the indirect and non-reassuring way in which she had communicated this result, her relatives also created their own recollections and interpretations that were dissimilar to hers.

Emma's perception of the UV-result was influenced by both the actually communicated information and by her ideas about her cancer, such as its duration and

severity. These information-oriented processes could be explained by the personal and existential meaning that this DNA-test result had for her. The actually communicated cancer-risks triggered her need for certainty; she experienced this unfulfilled need for certainty as unbearable and in reaction to that, she created her own interpretation that deviated from what the genetic-counselor had actually communicated. Emma had many ideas about her illness, for instance, she expected that she would be ill for many years; these cognitions were mediated/explained by her feelings of vulnerability and having an uncertain future which she had developed many years ago, and that had been triggered/increased by the UV-result; these fundamental feelings of vulnerability made her feel that this UV-result meant that she carries a PM. Of course, these are Emma's examples of mediation processes, and each counselee may experience her own individual mediation processes.

Emma experienced the impact of the UV-result as far-reaching. For instance, she decided to undergo PBM because of her (mis)interpretation of the UV-result as implying that she has a large risk to develop cancer again. The DNA-test result had also triggered and increased her awareness of her feelings of vulnerability and uncertainty. Her body started to feel 'even more differently than before DNA-testing, like a time bomb'. She worried much, and she experienced her uncertainties as the essence of these worries.

In summary, both the information-oriented and counselee-oriented approaches are needed to explain the experiences of a counselee like Emma. Of course, the difference between the information-oriented and the counselee-oriented approaches is not always clear-cut, and elements of both may overlap. For instance, we have categorized the counselee's cognitions and coping styles such as denial and avoidance as information-oriented, because the instruments that we used to measure cognitions and coping styles were applied to one specific situation, i.e. the DNA-test result, and the questions were mostly formulated in terms of cognitions. For instance, denial and avoidance may also be described from an existential, counselee-oriented level as a fundamental mechanism of a counselee.

It is obvious that an absolute, purely Counselee-Oriented Approach does not exist. In practice, all genetic-counselors use both information-oriented and counselee-oriented elements in their sessions. We hope that our study provides further support for the development of such an integrated approach, with a better understanding of the counselee-oriented processes.