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ARTICLE

A randomized experimental study to test the effects of discussing uncertainty during cancer genetic counseling: different strategies, different outcomes?

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Abstract

Uncertainty is increasingly discussed during genetic counseling due to innovative techniques, e.g., multigene panel testing. Discussions about uncertainty may impact counselees variably, depending on counselors' communication styles. Ideally, the discussion of uncertainty enables counselees to cope with uncertainty and make well-informed decisions about testing. We examined the impact of how counselors convey uncertainty and address counselees' uncertainty, and explored the role of individual characteristics. Therefore, a randomized controlled experiment using videos was conducted. Former counselees ($N = 224$) viewed one video depicting a genetic consultation about multigene panel testing. The extent of counselors' communication of uncertainty (comprehensive vs. the essence) and their response to counselees' uncertainty expressions (providing information vs. providing space for emotions vs. normalizing and counterbalancing uncertainty) were systematically manipulated. Individual characteristics, e.g., uncertainty tolerance, were assessed, as well as outcome variables (primary outcomes: feelings of uncertainty and information recall). No effects were found on primary outcomes. Participants were most satisfied when the essence was communicated, combined with providing information or providing space responses ($p = 0.002$). Comprehensive information resulted in less perceived steering toward testing ($p = 0.005$). Participants with lower uncertainty tolerance or higher trait anxiety were less confident about their understanding when receiving comprehensive information ($p = 0.025$). Participants seeking information experienced less uncertainty ($p = 0.003$), and trusted their counselor more ($p = 0.028$), when the counselor used information providing responses. In sum, the impact of discussing uncertainty primarily depends on individual characteristics. Practical guidelines should address how to tailor the discussion of uncertainty.

Introduction

Genetic counselors are increasingly required to discuss the possibility of highly complex genetic testing with counselees, such as multigene panel tests [1]. These tests may

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involve the sequencing of high numbers of genes which increases the diagnostic yield [2]. However, the resulting large amount of genetic information increases uncertainty. Finding a clear answer about a genetic predisposition causing cancer is therefore more complicated compared to single-gene tests [3].

Informing counselees adequately about panel test-related uncertainties during pre-test counseling is essential for several reasons. First, most counselees seek genetic counseling to receive certainty about their medical situation [4], and creating awareness about potential uncertainties may alter their expectations and prepare them for possible uncertain test outcomes [5]. Furthermore, being aware about potential uncertainty enables counselees to make a well-informed and autonomous decision about whether or not to pursue multigene panel testing, in line with their own situation, values, and preferences [6]. Finally, explicitly discussing uncertainty may also benefit the relationship between counselors and counselees as it shows honesty and openness [7].

The importance of communicating about uncertainty is not limited to the genetic setting, but is widely recognized [8]. Communicating uncertainty is generally seen as a moral duty of physicians [9], and may have various beneficial effects [10]. Still, communicating uncertainty may also impact patients negatively. Physicians' communication of uncertainty was found to decrease decision satisfaction in patients [11]. Moreover, uncertainty potentially overwhelms patients and stimulates negative affect, such as feelings of uncertainty and anxiety [12].

Variable effects of discussing uncertainty may result from a lack of guidelines on how and when to discuss uncertainty with patients [6]. Evidence indicates that in the setting of clinical genetics, counselors particularly struggle with these questions in the specific case of sequencing high numbers of genes [2]. Although many recommendations have been proposed on how to communicate uncertainty, empirical evidence to substantiate these is often lacking [13]. A recent study identified a wide variety of communication strategies that counselors use to discuss uncertainty [14]. Differences between counselors in their use of different strategies may result in wide practice variation. Also, we have found that if counselors discuss uncertainty with counselees, they tend to focus on scientific uncertainty (i.e., about the evidence on diagnosis and implications for prevention, treatment, and prognosis), rather than the practical and/or personal impact of that uncertainty on people's life and future [15]. As counselees mainly experience and express personal uncertainties, focusing primarily on scientific uncertainty does not match their needs and may eventually limit their ability to decide about testing [16]. High amounts of complex scientific information can moreover evoke uncertainty and distress in counselees, which may hamper their information recall and decision making [17]. Hence, counselors need to strike a balance between sufficiently informing counselees about uncertainties and avoiding an overload of information. To do so, a possible strategy may be to limit information provision to the most essential uncertainties. For example, counselors could explain that an uncertain test result is a possible outcome rather than providing an extensive explanation of the complexities and unknowns associated with an uncertain test result. Being told only the essence of panel test-related uncertainties, excluding any complex details, may increase counselees' information recall and thereby their ability to make a decision [18].

How well counselees understand and deal with uncertainties inherent to panel testing also depends on how counselors address uncertainties put forward by counselees [19]. Previous studies have shown that a common response to patients' expressions of uncertainty is further explaining or providing additional information, rather than exploring patients' uncertainties [20]. This response may confront patients with additional uncertainty instead of reducing it. Contrary, providing space to discuss the uncertainties put forth by counselees may help reduce their feelings of uncertainty and anxiety [21]. In addition, exploring counselees' emotions may facilitate their emotion management, which may subsequently improve their information recall and promote their involvement in deciding about panel testing [22]. Another strategy that has been used by counselors to discuss uncertainty is normalizing and/or counterbalancing uncertainty [14]. Normalizing uncertainty as being part of life may enable patients to accept and manage information about uncertainty [23]. Furthermore, counterbalancing the negative aspects of uncertainty with positive aspects, i.e., emphasizing that it entails both a positive (e.g., not necessarily carrying a cancer-associated variant) and negative side (e.g., no reassurance of not being a carrier), may help counselees put uncertainty in perspective [24].

Hence, the extent to which counselors discuss uncertainty related to multigene panel testing and address uncertainty expressed by counselees may influence how counselees are affected. We aimed to test the effects of different strategies to discuss uncertainty during pre-test consultations about multigene panel testing on counselees. We additionally explored the role of individual characteristics, e.g., uncertainty tolerance, in this relationship. The following research questions were addressed:

RQ1: How does the extent to which uncertainties are introduced by counselors (i.e., comprehensive vs. the essence) affect counselees affectively and cognitively?

RQ2: How does the response of the counselor to the uncertainties put forward by the counselee (providing

information vs. providing space vs. normalizing and counterbalancing uncertainty) affect counselees affectively and cognitively?

RQ3: Is there an interaction between the extent of counselors' communication of uncertainties and their response to uncertainties put forward by the counselee on counselees' outcomes?

RQ4: Do counselees' individual characteristics, such as their uncertainty tolerance, moderate the effects of counselors' discussion of uncertainty on counselees' outcomes?

Materials and methods

Study design

A randomized controlled experimental study was conducted using video vignettes, i.e., recordings of a simulated consultation [25]. We systematically manipulated the extent of counselors' uncertainty communication, and their responses to counselees' uncertainty expressions in a 2 (comprehensive vs. essence) x3 (providing information vs. providing space vs. normalizing and counterbalancing uncertainty) design. Effects of these manipulations were tested among analog patients, i.e., former counselees who were asked to imagine themselves being the patient in the video. The validity of this design has previously been demonstrated [25], and has previously been used to test effects of communication within the genetic setting [26]. The Medical Ethics Review Board of the Amsterdam UMC granted permission for this study (W2018-338).

Development of the video vignettes

Based on previous recordings of genetic consultations [15], a baseline script was developed involving a pretest genetic counseling session about multigene panel testing for suspected hereditary cancer. To minimize video length, the script only comprised the counselor providing (uncertain) information concerning the panel test and responding to the counselee's expressions of uncertainty. Information about family and medical history was provided in the introduction using a voice-over.

Script variations regarding counselors' communication and responses were subsequently developed. Regarding the extent of counselors' uncertainty communication, the baseline script involved a comprehensive communication of the uncertainties surrounding panel testing, consistent with current practice [15]. An alternative version involving the communication of only the essence of uncertain information was developed based on previous research. For this condition, the script was modified in five places (see Box 1 for

Box 1 Script segments displaying one example of the manipulations on (A) the extent of counselors' communication of uncertainty, and (B) counselors' responses to uncertainty expressions of the counselee

(A) The extent of counselors' communication of uncertainty (2 versions)[a]

1: *Comprehensive*

If we perform such a panel test we **do not know** which test result **we'll get**, on forehand. **Most probably** no predisposition **will be** found, so no cancer-associated variant. That **does not guarantee** that there is no genetic predisposition, but indicates nothing is found in the genes we've sequenced **so far**. So, **for now**, **we'll conclude** that there is none. It is also **possible** that […].

2: *Essence*

If we perform such a panel test it is **most likely** that we don't find a genetic predisposition. That means that, **for now**, we conclude that there is none. It is also **possible** that […].

(B) Counselors' responses to uncertainty expressions of the counselee (3 versions)[a]

Counselee's expression of uncertainty: Okay, so what you're basically saying is that there is a possibility that I will not receive certainty about carrying a variant that has caused the cancers I've had.

1: *Providing information response*

Counselor: We will try to figure it out as much as possible, but sometimes it will still be unclear whether you carry a genetic predisposition and there is an increased risk to develop cancer. In that case, you will be in the same uncertain situation as you are in right now.

2: *Providing space response*

Counselor: Yes… How do you feel about that?

Counselee: Well, I was hoping for some clear answers. I would not like it if it remains unclear.

Counselor: And how come certainty so important to you?

Counselee: Because of my children. I want to know whether they are at risk. I don't want them to get cancer and need to deal with everything I've been going through.

3: *Normalizing and counterbalancing uncertainty response*

Counselor: That is correct. Some things will remain uncertain simply because we are not yet able to figure out everything. On forehand, we don't know what the test will bring us. If something uncertain is found, I cannot reassure you that there is no increased risk of cancer. On the other hand, it also means that you or your relatives do not necessarily carry a genetic predisposition.

[a]*Versions are combined to create six video vignettes: A1B1 (7.40 min); A1B2 (8.40 min); A1B3 (8.40 min); A2B1 (5.50 min); A2B2 (6.50 min); A2B3 (7 min).*

one example). Regarding counselor's responses to uncertainty expressed by the counselee, the baseline script involved providing information responses (i.e., the repeating and/or further explanation of uncertainties), consistent with current practice [15]. Two alternative versions were created by manipulating counselors' responses, modifying the script in four places (see Box 1 for one example). Based on previous research those versions involved providing space responses, i.e., inviting further sharing of uncertainty by asking questions, and normalizing and counterbalancing uncertainty responses. The two communication versions and the three response versions were combined to create six scripts. A first draft of all manipulations was adapted after discussion among the research team. Next, clinical geneticists ($n = 2$) and communication experts ($n = 4$) provided input for the scripts and the manipulations. Finally, former counselees ($n = 4$) reviewed the scripts and manipulations with regard to the level of realism of the counselee's behavior, resulting in the final scripts. Scripts were video-recorded with two trained actors portraying a female counselor and a male counselee, respectively. The six videos were identical except for the manipulations. Duration of the final video vignettes varied between 5.50 and 8.40 minutes.

Participants and procedure

Former counselees, i.e., patients with cancer or their relatives who received genetic counseling for suspected hereditary cancer, were recruited retrospectively and prospectively for this study via three genetic centers. Retrospectively, individuals who had received genetic counseling within the last 12 months were invited for this study via a letter sent by their counselor. Interested counselees could then self-register and provide contact details to the researcher. Prospectively, counselees visiting for genetic counseling between June 2019 and January 2020 were informed about the study by their counselor at the end of their consultation. The researcher subsequently received contact details of interested counselees. Next, the researcher informed potential participants telephonically about the study and answered any questions. After written informed consent was obtained, participants received a web link to the online questionnaire in which one randomly selected video was embedded. First, they completed the first part of the questionnaire (T0) assessing their individual characteristics. Next, they viewed the video after being instructed to imagine themselves in the situation of the counselee in the video. Afterwards, they completed the second part of the questionnaire (T1) assessing outcomes and their evaluation of the counseling. All participants received a gift card worth €20, after participation. Study procedures were pilot tested among 31 former counselees comparable to the study participants. The pilot results yielded minor suggestions for improvement in questionnaire structure and syntax, and indicated that study procedures were feasible.

Measurements

Individual characteristics

We assessed participants' age, gender, educational level, and medical characteristics, i.e., time since counseling, cancer patient or relative, own/relative's cancer diagnosis, and, if tested, carrier status. Moreover, the following personality characteristics were assessed: (i) trait anxiety, using the 20-item validated Dutch translation of the State-Trait Anxiety Inventory [27]; (ii) uncertainty tolerance, using the validated Dutch translation of the 12-item Intolerance of Uncertainty Scale [28]; and (iii) coping style (i.e., monitoring (information seeking) vs. blunting (information avoidance)), using the validated 6-item Dutch Threatening Medical Situations Inventory questionnaire [29].

Primary and secondary affective and cognitive outcomes

In Table 1, a detailed overview of outcomes and their measures is presented. As primary affective outcome, we assessed feelings of uncertainty. Secondary affective outcomes were: feelings of control, anxiety, hope, satisfaction with the consultation, satisfaction with the provided information, perceived steering, and trust in the video counselor. As primary cognitive outcome, we assessed information recall. Secondary cognitive outcomes were: understanding of uncertainty, confidence in understanding, ability to decide, and intention for decision.

Perceptions of the video counseling and video engagement

To check whether manipulations were perceived by participants as intended, two items were used to assess participants' perceptions of the extent of counselors' communication of uncertainty (e.g., "The doctor informed the counselee in detail about the panel test.", 5-point Likert scale; range: 1 = not at all to 5 = very much), and three items assessed perceptions of providing uncertain information, providing space, and normalizing and balancing uncertainty responses (e.g., "The doctor responded to the counselee's expressions by asking further about these expressions.", 5-point Likert scale; range: 1 = not at all to 5 = very much). Engagement with the video was measured using a 4-item short version of the validated 15-item Dutch Video Engagement Scale [30]. Finally, perceived realism of the video was measured with three previously used items assessing whether participants thought the video was realistic, credible, and likely to have happened in real life

Table 1 Overview of all outcome variables and their used instruments, scoring methods, and example items.

Outcome variables	Instrument	Scoring method[a]	Example item[a]
Affective			
Feelings of uncertainty [primary outcome]	A self-developed questionnaire based on previous measures [42], involving: –a single item measured on a visual analog scale (VAS; range 0–100); –9 items using a 5-point Likert scale (range: 1 = completely disagree and 5 = completely agree).	Single VAS-item and 9-items questionnaire were analyzed separately. A mean score was calculated for the 9 items scale, with higher scores indicating higher feelings of uncertainty (Cronbach's alpha = 0.78).	VAS-item: "How uncertain do you feel at the moment?" Likert scale item: "It is uncertain what will happen in the future"
Feelings of control	The validated Dutch Perceived Personal Control questionnaire [43], slightly adapted and involving 6 of the original 9 items.		
State anxiety	The 6-item validated Dutch State-Trait Anxiety Inventory [44].		
Hope	A self-developed questionnaire based on previous measures [45], involving 10 items on a 4-point Likert scale (range: 1 = strongly disagree and 4 = strongly agree).	A mean score was calculated, with higher scores indicating greater hope (Cronbach's alpha = 0.90).	"I have faith in the future"
Satisfaction with the video consultation	The validated 5-item Patient Satisfaction Questionnaire [46]		
Satisfaction with the provided information	One item of the EORTC QLQ-INFO 25 [47], measured on a visual analog scale (0–100).		
Perceived steering	A self-developed 3-item questionnaire on a 5-point Likert scale (range: 1 = not at all and 5 = very much).	A mean score was calculated, with higher scores indicating more perceived steering (Cronbach's alpha = 0.67).	"To what extent did you feel that the doctor had a preference as to whether or not to perform the genetic test?"
Trust	The Dutch Wake Forest Trust in Physician Scale [48], slightly adapted and involving 8 of the original 10 items.		
Cognitive			
Information recall [primary outcome]	A self-developed questionnaire consisting of 5 open-ended questions about on the content of the videos.	Using a code sheet, items were scored as fully correct (2 points), partly correct (1 point) and incorrect (0 points), independently by two researchers (Cohen's kappa κ = 0.92). A sum score was calculated based on consensus scores, with higher scores indicating higher recall.	"Which result is most likely be generated by the test?"
Understanding of uncertainty	A self-developed questionnaire with 2 items, based on the content of the videos, measured on a visual analog scale (range: 0–100).	A mean score was calculated, with higher scores indicating more understanding of uncertainty (Cronbach's alpha = 0.59).	"How likely is it that this test will provide clarity about carriership?"
Confidence in understanding	A single item that has been used in a previous study [49] on a 5-point Likert scale (range: 1 = not at all and 5 = very much).		"How confident are you that you correctly understood the information the doctor gave in the video?"
Ability to make a decision	A self-developed single item with three answer categories: "Yes," "No," and "I don't know."		"Would you be able to make a decision about testing based on the information provided in the video?"
Intention for decision	A self-developed single item with three answer categories: "Performing this panel test," "Not performing this panel test," and "I don't know."		"What would you decide based on this information?"

Self-developed questionnaires were developed within the research group after which eight think-aloud interviews were conducted with former counselees to increase validity of questionnaires by gaining insight into understanding and interpretation of items [50].

[a]*Only presented for self-developed questionnaires as scoring guidelines and items for validated questionnaires can be found in the original articles.*

(7-point Likert scale; range: 1 = totally not agree and 7 = totally agree; Cronbach's alpha = 0.84) [31].

Analyses

Power analyses

A priori power analyses using G*Power 3.1.9.2 indicated that a sample size ranging from 162 (for ANOVAs with main effects on primary outcomes) to 196 (for ANOVAs with main and interaction effects on primary outcomes) was required to detect medium effects (0.25) with an alpha of 0.05 and 80% power [32].

Statistical analyses

All statistics were performed using IBM SPSS Statistics 25. Normality of data distributions was explored by visual inspection and values of skewness and kurtosis. Descriptive statistics were calculated to summarize characteristics for the total sample. To test whether we needed to control for possible covariates, *t*-tests, Chi-squared tests, and one-way ANOVAs were first performed to assess differences in participants' individual characteristics, perception of manipulations, level of engagement, and perceived realism between video variants. Second, participants' individual characteristics, perception of manipulations, engagement,

and realism were tested for associations with the primary outcomes using Pearson's correlation or regression analyses.

Effects of counselors' communication (RQ1), their responses to uncertainty (RQ2), and interaction effects (RQ3) on primary and secondary outcomes were tested using one-way ANOVAs and ANCOVAs. Interaction effects on outcomes were interpreted before main effects to avoid misinterpretations of (non-)significant effects [33]. Finally, we tested whether personality characteristics (i.e., anxiety, uncertainty tolerance, and coping style) acted as moderators using multiple linear regression analyses (RQ4), following the steps of Baron and Kenny [34].

Results

Sample characteristics

Of all former counselees who were invited to participate in this study ($N = 307$), 224 completed the questionnaire (response rate 73%). The majority was female (159; 71%), and mean age was 51 years (range 21–84). Most participants had received genetic counseling in the past 3 months (45%), and were either waiting for their test result (36%) or were confirmed not to be a carrier (30%). Table 2 presents all sample characteristics.

Randomization for the two communication of uncertainty conditions was successful as participants did not differ in background characteristics. Regarding the response to uncertainty conditions, participants only differed in gender ($\chi^2 = 6.093$; $p = 0.047$): participants in the providing information condition were less often male (19%) compared to the providing space (32%), and normalizing/balancing condition (36%). Gender was therefore added as covariate to ANOVAs testing differences between the three response conditions.

Table 2 Background characteristics of the total sample ($N = 224$).

	n (%)	Mean ± SD (range)
Sociodemographic and medical characteristics		
Age		51 ± 13.9 (21–84)
Gender		
Female	159 (71)	
Male	65 (29)	
Educational level		
Low: none/primary school	18 (8)	
Intermediate: secondary/intermediate voc. education	96 (43)	
High: higher education/university	110 (49)	
Time since counseling		
Less than week	1 (1)	
1 week−1 month	57 (25)	
1–3 months	100 (45)	
4–6 months	36 (16)	
7–12 month	30 (13)	
Cancer status		
Affected with cancer	99 (44)	
Healthy; relative with cancer	125 (56)	
Cancer diagnosis		
Breast	64 (28)	
Colon	38 (17)	
Ovarian	25 (11)	
Lung	17 (8)	
Melanoma	15 (7)	
Prostate	13 (6)	
Other	52 (23)	
Carrier status		
Carrier of a cancer-associated variant	39 (17)	
Waiting for result	80 (36)	
Not a carrier	68 (30)	
Not tested (yet)	37 (17)	
Personality characteristics		
Trait anxiety (potential range:1–4)		1.1 ± 0.4 (1–3)
Uncertainty tolerance (potential range:1–5)		1.8 ± 0.6 (1–4)
Monitoring coping style (potential range:1–5)		2.4 ± 0.8 (1–5)
Blunting coping style (potential range:1–5)		2.6 ± 0.6 (1–5)

Perceptions of the video counseling and video engagement

As intended, participants in the comprehensive condition perceived the information as significantly more extensive than participants in the essence condition ($M = 4.1$ vs. $M = 3.3$, $t = 3.33$; $p = 0.001$). Manipulation of the response versions was partly perceived as intended. Participants in the providing space, and the normalizing/counterbalancing uncertainty condition perceived the counselor's responses as significantly more space providing and as normalizing and counterbalancing uncertainty ($F(2,221) = 4.65$; $p = 0.011$ and $F(2,221) = 3.44$; $p = 0.034$, respectively), but participants in the providing information condition did not perceive more information providing responses ($F(2,221) = 1.56$, $p = 0.212$). The two communication versions were assessed as equally realistic ($M = 4.9$ vs. $M = 4.9$, $t = 0.69$; $p = 0.489$), as were the three response versions ($F(2,215) = 1.05$; $p = 0.353$). Scores of video engagement were moderate; $M = 4.4$, SD = 1.1 (range: 2–7), and did not differ between conditions ($F(5,218) = 0.26$; $p = 0.933$).

Effects on primary outcomes

Feelings of uncertainty

No interaction effects between the counselor's communication and responses were found on participants' feelings of uncertainty ($p = 0.213$ for single item; $p = 0.300$ for 9-item scale). After further exploration, no main effects were found of the extent of the counselor's uncertainty communication

($p = 0.809$ for single item; $p = 0.102$ for 9-item scale), nor of the counselor's responses on participants feelings of uncertainty ($p = 0.388$ for single item; $p = 0.374$ for 9-item scale; see Supplementary Table 3 for complete results).

Information recall

No interaction effects between the counselor's communication and responses were found on participants' information recall ($p = 0.648$). In addition, no main effects of the extent of the counselor's uncertainty communication ($p = 0.899$), nor of the counselor's responses were found ($p = 0.804$; see Supplementary Table 3).

Effects on secondary outcomes

Affective outcomes

Participants in the comprehensive communication condition combined with normalizing/counterbalancing uncertainty responses (A1B3) were significantly *less* satisfied with the provided information compared to those in the essence condition combined with providing information responses (A2B1), and to those in the essence condition combined with providing space responses (A2B2) ($F(5,214) = 3.87$; $p = 0.002$). In addition, significant main effects were found for the counselor's communication and responses on satisfaction. Participants who watched the comprehensive version were significantly *less* satisfied with the provided information ($M = 61.8$, $SD = 17.7$) than those watching the essence version ($M = 69.5$, $SD = 20.8$; $p = 0.002$). Furthermore, participants watching the providing space responses version were significantly more satisfied ($M = 74.3$, $SD = 18.8$) than those who watched the normalizing and counterbalancing uncertainty version ($M = 60.3$, $SD = 20.1$; $p = 0.025$).

Regarding perceived steering, no interaction effect was found ($p = 0.066$). However, a significant main effect of the counselor's communication of uncertainty was found; participants who watched the comprehensive version perceived *less* steering by the counselor about pursuing testing ($M = 1.3$, $SD = 0.6$), than those watching the essence version ($M = 1.6$, $SD = 0.6$; $p = 0.005$). No main effect of the counselor's responses was found ($p = 0.974$).

No interaction and main effects were found regarding the other secondary *affective* outcomes, i.e., participants' feelings of control, anxiety, hope, satisfaction with the video consultation, and trust in the video counselor (all $p > 0.4$; see Supplementary Table 4 for complete results).

Cognitive outcomes

No interaction and main effects were found on secondary *cognitive* outcomes, i.e., participants' understanding of uncertainty, confidence in understanding, ability to make a decision about testing, and intention for decision about testing (all $p > 0.18$; see Supplementary Table 5 for complete results).

Moderating role of counselees' personality characteristics

We found that counselees' uncertainty tolerance and trait anxiety moderated the main effect of the extent of counselors' uncertainty communication on counselees' confidence in understanding ($\Delta R^2 = 0.022$, $\Delta F(3, 217) = 2.636$, $p = 0.025$; and $\Delta R^2 = 0.021$, $\Delta F(3, 215) = 2.552$, $p = 0.029$, respectively). In participants with a lower uncertainty tolerance or higher trait anxiety, receiving comprehensive information resulted in *less* confidence in their understanding of uncertainty (see Fig. 1a, b). Moreover, counselees' coping style moderated the main effects of counselors' responses on participants' feelings of uncertainty ($\Delta R^2 = 0.029$, $\Delta F(3, 207) = 3.091$, $p = 0.003$), and trust in the video counselor ($\Delta R^2 = 0.011$, $\Delta F(3, 212) = 1.825$, $p = 0.028$). In participants with a monitoring coping style (i.e., seeking for information), information providing responses of the counselor resulted in *less* feelings of uncertainty (see Fig. 1c), and more trust in the counselor (see Fig. 1d).

Discussion

In this randomized controlled experimental study, we examined the effects of the extent of counselors' communication of uncertainty and their responses to uncertainty expressed by counselees during cancer genetic counseling about multigene panel testing on counselees. No effects were found on the primary outcomes, i.e., feelings of uncertainty and information recall. Regarding secondary outcomes, we found that counselees' satisfaction with the information was beneficially affected by concise communication about uncertainty combined with providing information or providing space responses toward uncertainty expressed by the counselee. Concise communication did however also increase counselees' perception of the counselor steering toward pursuing testing. Furthermore, we found some moderating effects of counselees' characteristics; comprehensive communication led to less confidence in understanding among more anxious people and those who are less tolerant of uncertainty. Also, providing information in response to counselees' expressions of uncertainty beneficially affected feelings of uncertainty and trust among people with a monitoring coping style (i.e., seeking information).

Overall, different strategies to discuss uncertainty did not affect counselees' feelings of uncertainty and information recall differently. These findings are in line with previous

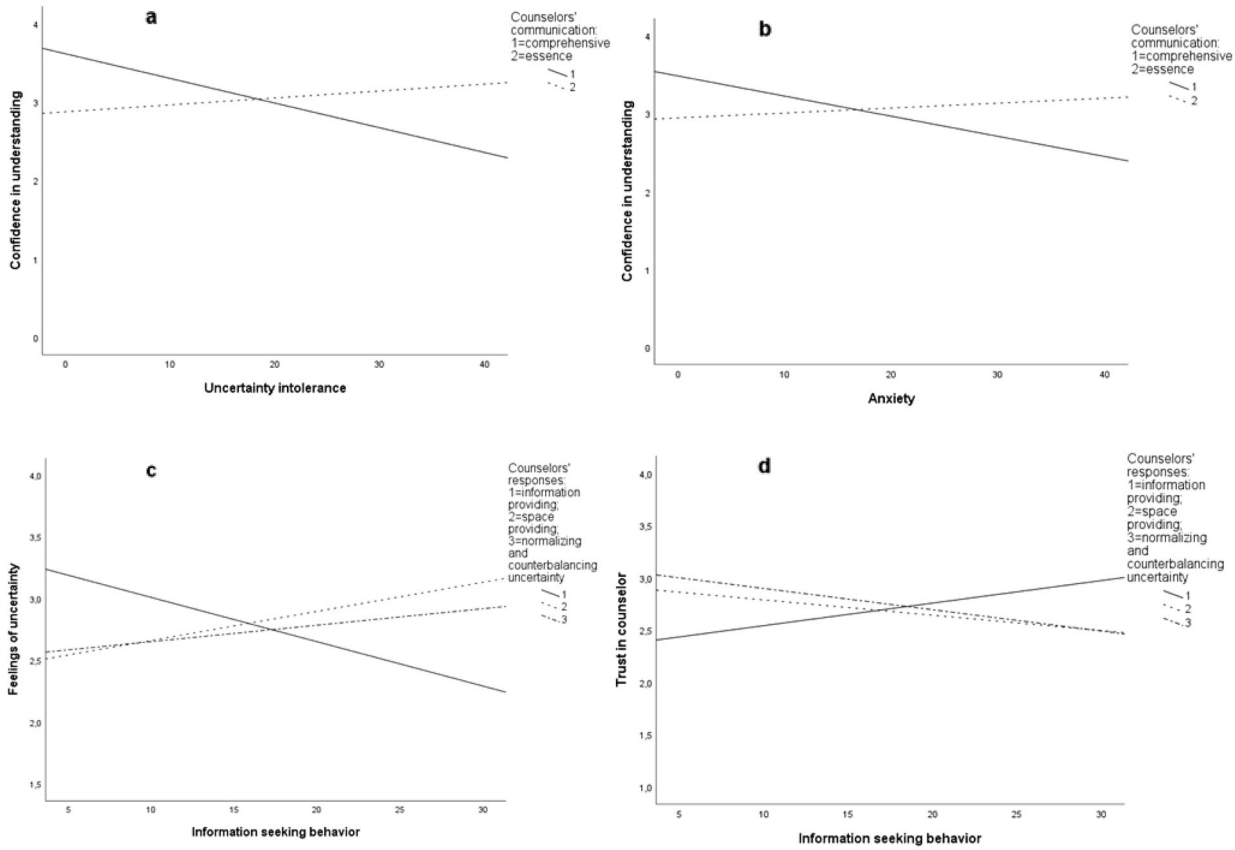

Fig. 1 Moderation of participants' personality characteristics on main effects. a, **b** The moderation of uncertainty tolerance and anxiety, respectively, on the main effect of counselors' communication on counselees' confidence in understanding. **c**, **d** The moderation of information seeking behavior on the main effect of counselors' responses on counselees' feelings of uncertainty and trust, respectively.

studies assessing direct effects of communication on outcomes [35, 36]. Possibly, we were unable to capture indirect or slowly evolving effects of communication about uncertainty through our assessment of patient-reported outcomes directly after the communication took place [21]. Based on the effects on secondary outcomes and moderating effects, we may however conclude that concise communication about uncertainty is not necessarily inferior to a comprehensive approach to communicating uncertainty, and that it may even be more beneficial for counselees. When receiving only the essence, counselees may perceive the information as less complex and more clear cut. Consequently, they may feel less overloaded with information that may enhance their satisfaction with the information and confidence in understanding. This finding may help counselors in feeling less obliged to provide extensive and highly detailed information, as counselees do not necessarily benefit from it [37]. Concise communication about uncertainty also caused counselees to perceive more steering from their counselor toward pursuing testing, however. This may have resulted from an imbalance between uncertain and certain information. Counselees receiving the concise information could have perceived an emphasis on certain information that favors pursuing testing. For example, summarizing the possible test results without explaining their uncertainties and complexities in detail limits the discussion of difficulties and drawbacks of panel testing. In this study, counselees in the "essence" condition were provided with only the most prominent uncertainties associated with panel testing, based on the tiered-binned model of Bradbury et al. [38]. This model allows them to have realistic expectations and enable informed decision making without providing many detailed information items. However, when only concise information is provided about uncertainty, counselees may only be minimally prepared for potential uncertainties afterwards. Although participants in both conditions indicated to be well able to decide whether to pursue panel testing (see Supplementary Table 5), future research should assess how well counselees are able to deal with unexpected uncertainties afterwards if not having been extensively prepared for them beforehand.

We saw that different strategies to discuss uncertainty generally did not affect counselees directly, but that effects were moderated by counselees' personality characteristics, as

shown before [39]. For example, counselees with a monitoring coping style who tend to seek instead of avoid information may benefit more from increased information about uncertainty, whereas such extensive information may be harmful for information avoidant, uncertainty intolerant, or highly anxious counselees. Thus, no overall, single optimal strategy to discuss uncertainty during genetic counseling may exist. To determine optimal communication styles in line with the individual counselee, it is important for counselors to assess counselees' characteristics, needs, and preferences regarding receiving uncertain information. For example, the QUOTE-gene, an instrument to measure needs and preferences prior to genetic counseling [40], could be adapted to the current situation and used to elicit counselees' needs and preferences as a preparatory tool for consultations about panel testing, and to help counselors to tailor their communication of and responses to uncertainty accordingly.

This study has some strengths and limitations. A strength of this study is that we used a randomized design with analog patients. This design enabled us to manipulate counselors' communication and responses in a standardized setting allowing us to draw conclusions about causality. Moreover, we were able to successfully manipulate the discussion of uncertainty such that participants assessed the video as a realistic depiction of clinical practice. This design however also has some limitations. First, it limits ecological validity of this study as viewing a video is not equal to receiving this information in real clinical practice. We might wonder whether analog patients are able to experience emotions comparable to those in clinical practice, by watching a videotaped consultation. Particularly, regarding a complex emotion such as uncertainty that is potentially influenced by aspects beyond communication, such as nonverbal behavior [41]. Second, videos differed in length, causing video duration to be a potential confounder. As differences in length are however inherent to the manipulations we examined in this study, we did not control for duration. Third, all participants had had genetic counseling within the last 12 months. Their experience with genetic counseling could have biased measurements such as information recall and understanding, as it may be based on their previous counseling instead of the video counseling. Moreover, a substantial number of participants were confirmed not to carry a cancer-associated variant or had not undergone genetic testing (yet). They may have experienced a certain reassurance that the depicted consultation did not apply to their situation and have felt less affected by the uncertain information. However, we corrected for individual characteristics such as their experiences to minimize possible biases. Fourth, participants' engagement with the video was relatively low compared to previous studies using a similar design (e.g., [41]). As only a small part of a genetic consultation was shown, participants' ability to imagine themselves being in the situation of the video counselee may have somewhat been impaired. This could subsequently have resulted in counselees being less affected by the strategy that was used to discuss uncertainty. Finally, several questionnaire items, such as feelings of uncertainty (i.e., the primary affective outcome), were developed for this specific study as validated instruments did not exist.

In conclusion, our results primarily showed beneficial effects of a concise vs. extensive discussion of panel test-related uncertainties on counselees' outcomes. Effects were however shown to primarily depend on counselees' characteristics such as their uncertainty tolerance and information seeking coping style. These findings invalidate the idea of one exclusive optimal strategy to discuss uncertainty with counselees during pre-test counseling. Therefore, counselors should be encouraged to explore and talk about the extent and way in which counselees want to discuss uncertainty during genetic counseling, in order to match counselees' individual characteristics, needs, and preferences. Clinical practice on multigene panel testing for hereditary cancer could benefit from practice guidelines on how to tailor the communication of uncertainty to the individual counselee. Communication skills training aimed at improving counselors' skills in communicating uncertainty may therefore contribute to optimizing genetic counseling about multigene panel testing.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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