

ARTICLE

Preferences for genetic testing for colorectal cancer within a population-based screening program: a discrete choice experiment

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This study explored individuals' preferences for genetic testing for colorectal cancer (CRC) in a screening situation and their willingness to participate in genetic testing for Lynch syndrome, familial adenomatous polyposis (FAP), and familial colorectal cancer (FCC). For that purpose, 532 respondents aged 55–65 years completed a Discrete Choice Experiment. Using panel latent class models, the preferences for two screening situation characteristics (the probability of being genetically predisposed and the probability of developing CRC) and screening test characteristics (the frequency of preventive colonoscopies and CRC survival) were estimated. Based on these preferences, respondents' willingness to participate in the three screening initiatives was estimated. Lower-educated respondents and respondents who express serious anxiety and worries found colonoscopy frequency and the probability of developing CRC relatively more important and survival relatively less important compared with higher-educated respondents and respondents who express no anxiety and worries. These differences in preferences resulted in opposite preferences for participation in FCC and FAP screening. In conclusion, the general population is willing to participate in genetic screening for CRC. If individuals are suspected of genetic or familial CRC, they should at least be informed about their increased risk of being genetically predisposed and about the importance of participating in all preventive follow-up colonoscopies in order to maximize survival.

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INTRODUCTION

Although genetic screening, in addition to population-based colorectal cancer (CRC) screening, may be beneficial for those who run a higher risk of developing CRC, there is a discussion about whether this additional form of screening is advisable and desirable.^{1–4} CRC is one of the most commonly diagnosed cancers and the leading cause of death among all cancer types worldwide.⁵ Prognosis, treatment intensity and the 5-year survival rate significantly improve if CRC is diagnosed at an early stage.^{6,7} Moreover, CRC can actually be prevented, because it is usually preceded by a slow progressive premalignant lesion (an adenomatous polyp), which may become cancer but can be detected and removed during colonoscopy.⁷ Therefore, population-based screening programs for CRC are recommended and widely implemented in Western countries. Within these programs, there is little attention for genetically predisposed individuals who run a higher risk of developing CRC. About 5% of all diagnosed CRCs is of genetic origin.^{8–10} This relatively small percentage actually reflects a substantial number of CRC patients given the high incidence of CRC in the general population. Offering genetic testing to participants in a population-based CRC screening program after a positive colonoscopy and/or with a familial cancer history (ie, screening situation) will identify genetically predisposed individuals and their families.^{11,12} By including genetic screening in current population-based CRC screening programs, CRC-related morbidity

and mortality may further decrease due to increased surveillance of cases and their relatives.^{11–13}

However, genetic testing raises several ethical and counseling challenges.^{14,15} For instance, knowing that one is at risk to develop cancer might induce fear of actually developing cancer, possibly with a negative impact on a person's quality of life.^{16,17} Positive test results may also have a severe impact on the family of the tested individual,^{16–18} as they themselves might run a higher risk of developing cancer as well. Moreover, the general population often holds unrealistic expectations about the accuracy with which genetic screening tests can predict future disease status.^{17,19}

Despite these potential negative consequences, the general population shows great interest in genetic screening and has a positive attitude towards such screening initiatives.^{16,20–22} Previous research shows that individuals are willing to take part in genetic screening when the test aims to identify an increased risk for a monogenic form of a common disease, when adequate treatment and/or prevention options are available and when clinicians recommend screening.^{21,23–25}

To date, no research has been conducted into studying the preferences of the general population for genetic testing for CRC specifically within a screening situation. Therefore, this study aims to explore individual preferences concerning genetic testing for CRC within a population-based CRC screening program. A further aim is to estimate whether individuals are willing to participate in genetic

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testing for (1) Lynch syndrome, (2) familial adenomatous polyposis (FAP) and (3) familial colorectal cancer (FCC) within a screening situation.

MATERIALS AND METHODS

Discrete choice experiment (DCE)

DCEs are increasingly being used to determine an individual's preferences regarding different characteristics of interventions or medical treatments.²⁶ This method is based on the Random Utility Theory. This theory assumes that any intervention or treatment can be described by its characteristics or 'attributes', such as the probability of a positive test outcome. The preferences of an individual for an intervention or treatment is determined on the basis of the 'levels' of the attributes, such as 1, 3 or 15% probability that the test outcome is positive.²⁶ Hypothetical situations are constructed by varying the levels of the attributes. Respondents are provided with a series of 'choice tasks' that consist of at least two situations. They are asked to choose the situation they prefer most within every choice task.

DCE development

To construct the DCE used for this study, possible attributes were identified from previously published studies,^{21–24,27} six expert interviews (ie, a scientist with a specific interest in public health genomics, a scientist with a specific interest in ethics of genetics/genomics, a specialist in cancer genetics and three medical specialists in gastroenterology) and five group interviews ($n=38$) with the target population of men and women aged 55–65 years. These group interviews were conducted using the Nominal Group Technique.²⁸ During these interviews, participants were asked to rank a number of potential attributes from most to least important, and the mean group ranking of the attributes was then discussed in the group, after which participants could change their original individual ranking.²⁸ Finally, four attributes were selected for this DCE (Table 1). The levels that were used to describe the identified attributes were based on realistic numbers representing the three most common types of genetic and familial CRC: Lynch syndrome, FAP, and FCC. About 3% of all CRC patients are diagnosed with Lynch syndrome.^{4,29–31} Without surveillance, these patients have a 70% probability of developing CRC during their lifetime.^{4,29–31} Patients who are diagnosed with Lynch syndrome are offered a preventive colonoscopy every 2 years. On average, their 5-year survival rate is 92% if they are aware of their genetic predisposition and participate in biannual colonoscopies.^{4,29–31} FAP is present in 1% of all CRC patients.^{29–31} The probability of developing CRC among these patients is 99% without surveillance and therefore they are advised to undergo an annual colonoscopy.^{29–31} This results in a 5-year survival rate of 80% if CRC is discovered.^{29–31} Finally, FCC is considered to be present in 15% of all CRC patients.^{29–31} These patients have an at least 15% probability of developing CRC based on the number and age of relatives with CRC. They are offered screening

by means of a 5-yearly colonoscopy, which increases their 5-year survival rate to 98% if CRC is found.^{29–31}

NGene 1.0 (ChoiceMetrics Pty Ltd, 2011, St. Leonards, NSW, Australia) software was used to develop a D-efficient design.²⁶ The DCE consisted of nine unique choice tasks each containing two situations. Following each choice task, participants were asked whether they would actually participate in the chosen situation or not (ie, opt-out). Before participants were asked to complete the choice tasks, they received detailed information on the meaning of all attributes and levels as well as an explanation on how to complete a choice task, illustrated by an example (see Supplementary File). The draft questionnaire was pilot tested among a subgroup ($n=90$) of our target population. Four of these pilot tests were 'think aloud' tests, during which a researcher was present when the participant completed the questionnaire, reading out loud. It was tested by means of this pilot whether correct wording was used and whether the target population understood the attributes, levels and choice tasks. Additionally, the attribute-level estimates that were retrieved from the pilot study served as input for the design of the final DCE questionnaire.

Questionnaire

The final questionnaire consisted of three parts. The first section of the questionnaire comprised 25 questions on demographics, such as gender, age, educational level, health literacy and ethnicity. Educational level was dichotomized into higher (ie, tertiary education) or lower education (ie, all other educational levels). Health literacy was measured by three validated Dutch questions of the Set of Brief Screening Questions.³² Participants scored these questions on a five-point Likert scale, from zero to four. An average score of ≤ 2 indicates inadequate health literacy, while an average score > 2 indicates adequate health literacy.³² Furthermore, questions pertained to information on experience with other national cancer screening programs, experience with genetic screening and family cancer history. Respondents were asked to indicate to what extent they agreed or disagreed with several theorems about their attitude, social norm, self-efficacy and intention towards genetic screening for CRC. The second part of the questionnaire consisted of the actual DCE as explained above. The third part consisted of several theorems regarding the consequences of genetic testing, such as fear and worries, and on the possibility of incidental findings.

Study population

From 2014 onwards, all Dutch residents aged 55–75 years will receive a biannual invitation to participate in the national population-based screening program for CRC. Screening is carried out by means of the fecal immunochemical test. If the test result is positive, that is, blood is detected in the stool, a colonoscopy will be planned and participants are asked to complete a family cancer history questionnaire. At present, it is expected that genetic screening for CRC might only become part of the Dutch CRC screening program for individuals with a positive colonoscopy and/or a familial cancer history.

Table 1 Attributes and levels that were included in this DCE

Attributes	Level 1	Level 2	Level 3
Probability of being genetically predisposed (genetic predisposition): the likelihood that you are genetically predisposed to develop colorectal cancer	1%, 1 out of every 100	3%, 3 out of every 100	15%, 15 out of every 100
Probability of developing CRC (CRC risk): 5 out of every 100 (5%) Dutch individuals develop colorectal cancer. If you have a genetic predisposition to develop colorectal cancer and you do not participate in preventive colonoscopies, the likelihood that you will develop colorectal cancer is higher and varies between:	15%, 15 out of every 100	70%, 70 out of every 100	99%, 99 out of every 100
Frequency of preventive colonoscopies (colonoscopy frequency): If the genetic test shows that you are genetically predisposed to develop colorectal cancer, you will be invited to participate in preventive colonoscopies. These colonoscopies are performed to prevent cancer from developing or to diagnose cancer in an early stage. These colonoscopies will be scheduled on a regular basis varying between:	Every year	Every 2 years	Every 5 years
Probability of surviving CRC (survival): 60 out of every 100 (60%) Dutch individuals with colorectal cancer survive over the next 5 years. If you know you are genetically predisposed to develop colorectal cancer and if you participate in the preventive colonoscopies, the likelihood that you will survive colorectal cancer over the next 5 years will increase and varies between:	80%, 80 out of every 100	92%, 92 out of every 100	98%, 98 out of every 100

Abbreviation: CRC, colorectal cancer.

As it was expected that preferences for genetic screening for CRC are highly dependent on age and experience with CRC screening, individuals were eligible to participate in our study if they were aged 55–65 years and had not yet participated in the CRC screening program or one of the extensive pilot studies that preceded the decision to implement the Dutch population-based CRC screening. Respondents were recruited via an existing online panel of the general Dutch population. Respondents were selected to be representative for the entire target population with respect to age, gender and educational level. In total, 5500 individuals were invited to participate in this study and recruitment continued until at least 500 questionnaires were fully completed by a representative sample of the target population.

The Dutch Central Committee on Research involving Human Subjects concluded that formal testing by an Institutional Review Board was not necessary, as respondents were only required to complete an anonymous and non-invasive questionnaire once, which is in accordance with the Dutch legislation and guidelines laid down in the Declaration of Helsinki.

Statistical analysis

All results were considered statistically significant when $P < 0.05$. All attributes were considered to be non-linear and were recoded using effect codes.²⁶ This coding procedure codes the reference category as -1 and the sum of the effect-coded attribute levels is always 0.

Preferences for genetic screening for CRC. Nlogit 5.0 (Econometric Software Inc, 2012, Plainview, NY, USA) was used to conduct the panel latent class models for this study. Such models account for the multilevel structure of our data (ie, every respondent answered nine choice tasks). Moreover, by means of such models, it can be determined whether preferences differ across unobserved subgroups of the population. This modelling procedure identifies whether there are ‘classes’ within the data based on respondents’ answering patterns. Which respondents belong to what class is not assigned by researchers but is latent. Each respondent has a certain probability to belong to one of the identified classes. However, demographic characteristics can be incorporated into the modelling procedure, which provides insight into which respondents are more likely to belong to a certain class.

Based on model fit tests (AIC, Log likelihood), it was tested which model was most suitable for our data and how many classes could be identified within the data. This resulted in a two-class model based on the utility equation displayed below. The utility component (V) describes the utility that respondent ‘ r ’ belonging to class ‘ c ’ reported for alternative ‘ a ’ in choice task ‘ t ’. β_0 represents the constant of the model. The attribute-level estimates that indicate the relative importance of each attribute level are represented by $\beta_1 - \beta_8$. A significant attribute estimate within a certain class indicates that this attribute contributes to the decision-making process of respondents who belong to that class.

$$V_{rtalc} = \beta_0_{lc} + \beta_1_{lc} \text{ genetic predisposition}_{3\%} + \beta_2_{lc} \text{ genetic predisposition}_{15\%} + \beta_3_{lc} \text{ CRC risk}_{70\%} + \beta_4_{lc} \text{ CRC risk}_{99\%} + \beta_5_{lc} \text{ colonoscopy frequency}_{2\text{years}} + \beta_6_{lc} \text{ colonoscopy frequency}_{5\text{years}} + \beta_7_{lc} \text{ survival}_{92\%} + \beta_8_{lc} \text{ survival}_{98\%}$$

After fitting the above-specified utility function, a class assignment model was fitted. All demographic variables and all theorems were tested for a significant contribution to the class assignment model, and the final class assignment utility function was:

$$V_{rc} = \beta_0_{lc} + \beta_1_{lc} \text{ high educational level}_r + \beta_2_{lc} \text{ experience with genetic screening}_r + \beta_3_{lc} \text{ being anxious and worried about CRC predisposition}_r$$

A significant estimate in this function indicates that this variable contributes to the class assignment (eg, if the higher education variable is positive and significant for class 1, this indicates that respondents with a higher educational level are more likely to belong to class 1).

Relative importance of the attributes. The relative importance of the attributes was estimated separately for both classes of the panel latent class models. The difference between the highest and lowest attribute-level estimate was calculated for each attribute. The largest difference value received an importance score of 1, representing the attribute that was deemed most important by respondents. The other difference values were divided by the largest difference value resulting

in a relative distance between all other attributes and the most important attribute.

Utility scores for Lynch syndrome, FAP and FCC screening. For each of the three realistic screening scenarios, specific utility scores were calculated for both classes separately. The attribute levels that correspond with each of the three screening scenarios were entered into the utility function. The outcome (V) represents individuals’ willingness to participate in one screening initiative compared with the other initiatives.

RESULTS

Respondents’ characteristics

Of the individuals initially invited ($n = 5500$), 798 (14.5%) respondents started the questionnaire within the first 4 weeks of data collection. Complete data was gathered for 532 eligible respondents (66.7% of those who started the questionnaire) and data collection was closed.

Table 2 describes the demographic characteristics of the study population. The majority of the respondents reported that genetic screening for CRC is important for themselves as well as for their family (Table 3). Although about half of the respondents expect to become seriously anxious and worried about developing CRC due to a suspected genetic predisposition, 89.0% reported that they would participate in genetic screening for CRC if such a program would become available (Table 3).

Preferences for genetic screening for CRC

The average probability of respondents belonging to either of the two latent classes was 65% and 35%, respectively, but this depended on educational level, experience with genetic screening tests and being worried and anxious about being predisposed to develop CRC (Table 4). Respondents with a higher educational level, respondents who had no experience with genetic screening tests and respondents who were less worried and anxious about their predisposition to develop CRC were more likely to belong to class 1. The probability of belonging to class 2 increased when respondents had a lower

Table 2 Demographic characteristics of the study population ($n = 532$)

	Mean (SD)	Percentage
Age, years	59.5 (3.1)	
Gender		
Female		50.9
Educational level		
Low		26.3
Average		37.1
High		36.6
Health literacy		
Inadequate		3.4
Ethnicity		
Dutch		96.6
Previously participated in another cancer screening program		48.9
Previously diagnosed with cancer		14.0
Family member previously diagnosed with cancer		24.6
Previously participated in genetic screening		7.7

Table 3 Proportion of respondents who agree with the provided theorems concerning genetic screening for CRC ($n=532$)

	Percentage
I think genetic testing for CRC is useful	89.1
I think it is important to take part in genetic testing for CRC	86.9
I consider it self-evident to take part in CRC	77.4
It would not be difficult for me to take part in genetic testing for CRC	76.7
It is important that my family takes part in genetic screening for CRC	70.3
My family would take part in genetic screening for CRC	69.1
My family would consider it important that I take part in genetic screening for CRC	71.2
It is important to know whether I am genetically predisposed so my family can take precautions	87.4
I would inform my family if I was genetically predisposed to develop CRC	89.1
I would be seriously anxious if I was genetically predisposed to develop CRC	43.7
I would find it seriously worrying if I was genetically predisposed to develop CRC	65.2
I always want to know about incidental findings	75.9
I never want to know about incidental findings	3.2
I only want to know about incidental findings concerning diseases that can be prevented	8.3
I only want to know about incidental findings concerning diseases that can be treated	12.6
I would take part in genetic screening for CRC	89.1

Abbreviation: CRC, colorectal cancer.

educational level, when they had experience with genetic screening tests and when they were worried and anxious about being predisposed to develop CRC.

In both classes, respondents preferred a genetic screening test when their probability of being genetically predisposed to develop CRC was high and their survival rate due to screening would increase the most. Respondents in class 1 preferred a genetic screening when the probability that they would develop CRC due to their genetic predisposition was highest, while respondents in class 2 preferred a genetic screening test if the probability that they would develop CRC due to their genetic predisposition was lowest. Respondents in class 1 preferred to have a biannual colonoscopy, while respondents in class 2 preferred to have an annual preventive colonoscopy.

Relative importance of the attributes

Respondents in both classes reported different preferences with respect to genetic screening for CRC, which indicates preference heterogeneity. Respondents in class 1 found survival to be most important, followed by colonoscopy frequency, CRC risk and genetic predisposition (Table 4). For respondents in class 2, colonoscopy frequency was most important (relative importance score of 1) followed by CRC risk, survival and genetic predisposition (Table 4). Figure 1 shows these results in more detail, here the values of the attributes display the relative distance of all attributes to the most important attribute on a scale of 0–1. The range in those distances is large in class 2, while for respondents in class 1 most attributes were approximately equally important.

Utility scores for Lynch syndrome, FAP and FCC screening

Respondents in class 1 (higher education, no experience with genetic testing and who are less anxious and worried about CRC predisposition) preferred Lynch syndrome screening ($V=0.62$) over FAP

Table 4 Preferences for genetic testing for colorectal cancer based on latent class analysis^a

	Class 1			Class 2		
	Estimate	SE	RI	Estimate	SE	RI
Constant	0.21***	0.04		0.14	0.12	
<i>Genetic predisposition</i>						
1% (ref.)	-0.20***	0.04	4	0.18*	0.11	4
3%	-0.07*	0.04		-0.31***	0.10	
15%	0.27***	0.04		0.13	0.10	
<i>CRC risk</i>						
15% (ref.)	-0.37***	0.04	3	0.63***	0.11	2
70%	0.20***	0.04		-0.22**	0.10	
99%	0.17***	0.04		-0.41***	0.11	
<i>Colonoscopy frequency</i>						
Every year (ref.)	-0.29***	0.04	2	1.13***	0.12	1
Every 2 years	0.29***	0.04		0.61***	0.11	
Every 5 years	-0.00	0.05		-1.74***	0.18	
<i>Survival</i>						
80% (ref.)	-0.57***	0.04	1	-0.51***	0.16	3
92%	-0.01	0.04		0.10	0.08	
98%	0.58***	0.05		0.41**	0.16	
<i>Class probability model</i>						
Constant	0.78***	0.18				
Higher education	1.02***	0.24				
Experience with genetic screening	-0.87**	0.39				
Being worried and anxious	-0.88***	0.22				
<i>Average class probability</i>		0.65			0.35	

Abbreviations: CRC=colorectal cancer; RI=relative importance. * $P<0.10$; ** $P<0.05$; *** $P<0.01$.^aThe attribute-level estimate of the reference categories can be calculated as: $-1 \times (\text{sum of the other attribute-level estimates})$.

screening ($V=-0.68$) and preferred FCC screening ($V=0.69$) over both the other screening initiatives. Respondents in class 2 (respondents with a lower education, experience with genetic screening tests and respondents who are anxious and worried about CRC predisposition) preferred Lynch syndrome screening ($V=0.32$) over FCC screening ($V=-0.43$) and preferred FAP screening ($V=0.53$) over both the other screening initiatives.

DISCUSSION

This study shows that the probability of being genetically predisposed, the probability of developing CRC, the frequency of preventive follow-up colonoscopies and the probability of surviving CRC, all influence respondents' preferences for genetic testing for CRC. However, results also show heterogeneity in these preferences. Respondents with a lower education found colonoscopy frequency and the probability of developing CRC relatively more important and survival relatively less important than higher-educated respondents. These differences in preferences were also found among respondents who had some *versus* no experience with genetic screening tests and among respondents with serious or little anxiety and worries about being genetically predisposed to develop CRC. Because of the differences in preferences among subgroups in the population, their willingness to participate in

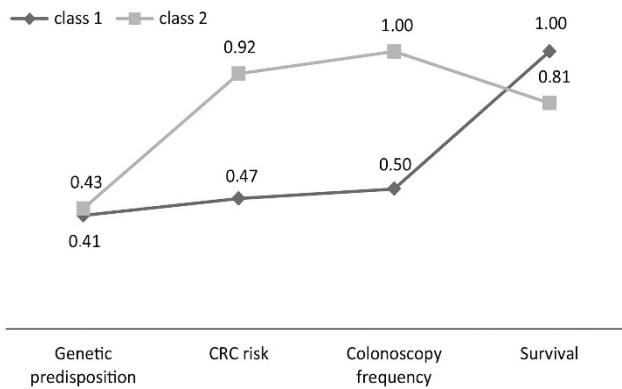


Figure 1 Relative importance of the attributes stratified by class. Values reflect the relative distance of all attributes to the most important attribute on a scale from 0 to 1 (1 indicating the most important attribute).

specific genetic screening initiatives also differed. Respondents in class 1 preferred FCC screening most and FAP screening least, while the respondents in class 2 showed complete opposite preferences for the screening initiatives.

This is the first DCE that studied the preferences of the general population for genetic testing for CRC within a screening situation. However, previous studies did measure preferences for population-based CRC screening program characteristics (without genetic screening)^{33–36} or preferences for genetic screening test characteristics in general (not specifically applied to CRC).²⁴ Although these studies focused on different topics and different target populations, their results do provide face validity for the results of the current study.

Insights into the preferences of the target population for genetic screening for CRC provide clear recommendations for effective communication between counselors and counselees about genetic testing specifically within a screening situation.^{22,37} Optimal communication may improve knowledge among the general population and may facilitate informed decision making among individuals who are offered genetic screening. First, respondents deemed survival probability as a highly important test characteristic of genetic screening. Although increased survival rates as a result of participation in genetic screening should be communicated to those eligible for screening, counselors should bear in mind to ensure that individuals understand that their survival rates will only increase if they participate consistently in preventive colonoscopies. Second, the current study shows that some of the respondents preferred annual preventive colonoscopies, in particular those who had a lower educational level and who expressed serious anxiety and worries about a genetic predisposition for CRC. These respondents might have reasoned that frequent screening will increase the likelihood of early cancer detection and therefore will increase their probability of surviving CRC. However, annual colonoscopies are, at present, only recommended for surveillance of individuals diagnosed with FAP;^{29–31} individuals with Lynch syndrome or FCC are usually screened less often (biannually and every 5 or 6 years, respectively) based on solid clinical evidence.^{4,29–31} For respondents with a lower educational level or those who are anxious and worried, effective communication and counseling are necessary to reduce their anxiety and to explain that screening frequency depends on the specific type of genetic or familial CRC. Third, respondents preferred a genetic screening test when their probability of being genetically predisposed increased. This result supports the fact that participation in screening will increase if all individuals suspected of genetic or familial CRC are actively informed about their personal risk

of being predisposed to develop CRC. As relative occurrence of FAP within all genetic or familial CRC is relatively small (about 1%), some participants appeared less interested in FAP screening. However, this is the most aggressive and severe genetic variant of CRC for which active screening is of utmost importance.^{38,39} Fortunately, most FAP patients are aware of their predisposition from a young age due to a family history resulting in an acceptable surveillance compliance.⁴⁰ However, when clinicians suspect individuals may have FAP without a clear family history, they are advised to (continue to) stress the importance of active screening once genetic predisposition is confirmed.

This study is subject to some limitations. First, generalizability of our results to non-Dutch individuals may be limited because the number of non-Dutch respondents in our study population is relatively low compared with Dutch national population figures. Second, some respondents probably perceived the choice tasks to be difficult. Respondents with a lower educational level preferred to participate in a genetic screening test for CRC if their risk of actually developing CRC as a result of their genetic predisposition would be lowest. They might have mistakenly interpreted this attribute as their probability of developing CRC in general. Third, in this study we used an unlabeled design and respondents were not informed about the different genetic or familial CRC diagnoses (FAP, Lynch syndrome, FCC). Therefore, we did not include any diagnosis-specific attributes or information. Future DCE studies should be conducted to determine whether preferences differ per diagnosis.

In conclusion, the current study suggests that the general population is willing to participate in genetic testing for CRC. Both screening situation characteristics and screening test characteristics influenced respondents' preferences for genetic screening for CRC. The increased survival rates as a result of genetic screening and preventive follow-up colonoscopies were the most important screening test characteristics for respondents with a higher educational level, respondents who have no experience with genetic testing and who are less anxious and worried about CRC predisposition. The frequency of colonoscopies was the most important screening test characteristic for respondents with a lower educational level, experience with genetic testing and who were anxious and worried about CRC predisposition. If individuals are suspected of genetic or familial CRC, counsellors should provide information about their increased risk of being genetically predisposed and about the importance of participating in all the preventive follow-up colonoscopies in order to maximize their survival. Specifically, individuals with a lower educational level and those who express worries or anxiety should be informed about the frequency of preventive colonoscopies that is appropriate for the genetic or familial CRC they are diagnosed with.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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