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Preference-Based Assessments

Individuals' Preferences for Esophageal Cancer Screening: A Discrete Choice Experiment

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ABSTRACT

Objectives: The increasing incidence of esophageal adenocarcinoma (EAC) and the dismal prognosis has stimulated interest in the early detection of EAC. Our objective was to determine individuals' preferences for EAC screening and to assess to what extent procedural characteristics of EAC screening tests predict willingness for screening participation.

Methods: A discrete choice experiment questionnaire was sent by postal mail to 1000 subjects aged 50 to 75 years who were randomly selected from the municipal registry in the Netherlands. Each subject answered 12 discrete choice questions of 2 hypothetical screening tests comprising 5 attributes: EAC-related mortality risk reduction, procedure-related pain and discomfort, screening location, test specificity, and costs. A multinomial logit model was used to estimate individuals' preferences for each attribute level and to calculate expected rates of uptake.

Results: In total, 375 individuals (37.5%) completed the questionnaire. Test specificity, pain and discomfort, mortality reduction, and out-of-pocket costs all had a significant impact on respondents' preferences. The average expected uptake of EAC screening was 62.8% (95% confidence interval [CI] 61.1-64.5). Severe pain and discomfort had the largest impact on screening uptake (−22.8%; 95% CI −26.8 to −18.7). Male gender (β 2.81; $P < .001$), cancer worries (β 1.96; $P = .01$), endoscopy experience (β 1.46; $P = .05$), and upper gastrointestinal symptoms (β 1.50; $P = .05$) were significantly associated with screening participation.

Conclusions: EAC screening implementation should consider patient preferences to maximize screening attendance uptake. Based on our results, an optimal screening test should have high specificity, cause no or mild to moderate pain or discomfort, and result in a decrease in EAC-related mortality.

Keywords: Barrett's esophagus, discrete choice experiment, esophageal cancer, patient preferences, screening.

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Introduction

In the Western world, the incidence of esophageal adenocarcinoma (EAC) and its precursor Barrett's esophagus (BE) is increasing.[1] Because EAC is frequently detected at an advanced stage, patients with EAC have a dismal prognosis (5-year survival of <20%).[2] Patients with EAC in BE diagnosed through endoscopic surveillance programs have earlier-stage tumors and better survival than patients whose EAC is discovered after the onset of symptoms.[3] Nevertheless, up to now, only a minority (<10%) of patients have been diagnosed with BE before a cancer diagnosis, with the remaining staying undetected.[4]

Since the recent development of novel, less invasive (non) endoscopic techniques for BE screening in the community, there has been a renewed interest in the early detection of BE and related neoplasia.[5–7] Nevertheless, it remains to be seen how acceptable these less invasive screening tests will be in the general community compared with conventional upper endoscopy.

The important role of public preferences in cancer screening, and medical decision making in general, has gained increasing attention.[8] A key factor driving the success or failure of a screening program is the willingness of the target screening population to undergo the screening test. Individuals may be willing to undergo a screening test despite several drawbacks to maximize health benefit or they may accept a lower health benefit to avoid an invasive screening method.[9] Obtaining insights into people's preferences for EAC screening is relevant to informing clinicians and decision makers about how to design future screening programs.[10]

This study aimed to determine individuals' preferences regarding EAC screening programs using a discrete choice experiment (DCE) and to obtain quantitative insights as to what extent

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procedural characteristics of EAC screening tests predict willingness in screening participation.

Methods

Discrete Choice Experiment

A DCE is a form of tradeoff analysis that elucidates how people make complex decisions by balancing competing factors.[11,12] In a DCE, it is assumed that a medical intervention, such as a screening program, can be described by its characteristics (attributes) and that an individual's preference for undergoing a screening test is determined by predefined levels of those attributes.[13] Attribute levels are varied systematically in a series of questions and respondents choose the option they prefer most for each question. DCEs can determine which attributes lead to preferences for or against an EAC screening test. DCEs are now being used widely in healthcare research.[8,11]

Attributes and Attribute Levels

The attributes and levels were derived in a stepwise manner, which included literature review,[5] expert opinions (n = 8), interviews (n = 10), and a focus group with individuals of the target screening population (n = 8). In the interviews and focus group, individuals were asked to indicate which characteristics of EAC screening tests they would expect to be important and to rank them in order of importance in their decision to participate in a screening program. Using convenience sampling, local experts, including 4 clinicians (2 gastroenterologists and 2 surgeons with expertise in esophageal cancer), a registered nurse specialized in BE, an epidemiologist, a communication adviser, and a senior researcher with experience in qualitative research, were involved in instrument development. Fifteen potential attributes were selected for inclusion in the questionnaire. This list was further redefined based on clinical and methodological input that balanced the completeness of the test attribute description with questionnaire feasibility. Results were presented to experts in a multidisciplinary esophagus research meeting after pretest interviews, and their input was used to ensure that participants' hypothetical choices approached real-life choices. The final survey included 5 attributes with 4 levels each (Table 1): EAC-related mortality reduction, location of the screening test, pain and discomfort during the test, out-of-pocket costs, and test specificity, including the need for unnecessary follow-up testing. We did not include the actual labels of the screening procedures because screening tests for esophageal cancer are currently under development, and we were therefore interested in preferences regarding individual characteristics of screening tests.

Table 1. Attributes and levels for esophageal cancer screening.

Attribute	Level
Mortality reduction:*	
Number of deaths that can be prevented by the screening test	5 deaths out of 1000 screened people 4 deaths out of 1000 screened people 3 deaths out of 1000 screened people 2 deaths out of 1000 screened people
Location of the test	At home Mobile unit General practitioner Hospital
Pain and discomfort during the screening test	No pain and discomfort (0 on a scale of 0 to 10) Mild pain and discomfort (2 on a scale of 0 to 10) Moderate pain and discomfort (5 on a scale of 0 to 10) Severe pain and discomfort (8 on a scale of 0 to 10)
Out-of-pocket costs of the test	€0 €25 €50 €75
Specificity:	
Accuracy of the test when you do not have (a precursor of) esophageal cancer	If you DO NOT have cancer, the test result will never say you have cancer (specificity: 100%) If you DO NOT have cancer, the test result will say you may have cancer 1 out of 10 times (specificity: 90%) If you DO NOT have cancer, the test result will say you may have cancer 3 out of 10 times (specificity: 70%) If you DO NOT have cancer, the test result will say you may have cancer 5 out of 10 times (specificity: 50%)

Note: Levels for each attribute incorporated the characteristics or possible test outcomes of different available screening methods.
*It was given that 6 out of 1000 people would be diagnosed with esophageal cancer if no screening program was provided.

DCE Design and Questionnaire Development

The DCE was designed, conducted, and analyzed using Sawtooth Software V9.5.3 (Sawtooth, North Orem, Utah). The International Society for Pharmacoeconomics Outcomes Research (ISPOR) Guidelines for Good Research Practices for Conjoint Analysis in Health were followed in the development of the DCE (see Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.03.013).[11]

To answer a discrete choice question, respondents needed to imagine themselves eligible for EAC screening (see Appendix Fig. 1 in Supplemental Materials). Respondents were asked to consider 2 screening tests in each choice set as realistic alternatives and to choose the screening test that appealed most to them. Subsequently, subjects were asked to choose between their preferred screening test and no screening (dual-response none). This "opt-out" question was necessary because EAC screening is a preventive intervention and, as in real life, respondents are not obliged to undertake EAC screening.

The questionnaire was administered in Dutch and consisted of 12 discrete choice questions of 2 (hypothetical) screening tests comprising the 5 attributes plus 2 common fixed tasks (1 warm-up choice task and a choice task with a dominant screening option). This dominance test, in which all attributes favored 1 alternative, was included to determine participants' understanding of the questionnaire, to ascertain respondents' (lack of) attention, and to test for rationality.[14] We ran the models both by including all respondents and by deleting respondents who failed this rationality test. The questionnaire further included a written description of the attributes and levels, questions on background variables, and a question assessing the level of certainty of the questionnaire (10-point scale).[15] An English translation of the information provided to respondents is included in the Supplemental Materials. Two pilot studies were performed to ascertain

respondents could manage the length of the questionnaire and to examine the intelligibility, acceptability, and validity of the questionnaire (see Supplemental Materials).

Study Setting and Population

The study was conducted in the general population. The questionnaire was sent to a total of 1000 individuals aged 50 to 74 years because EAC screening is not recommended in patients younger than 50 years and 75 years is the upper age limit for BE surveillance.[16] Individuals were randomly selected from the population registry of Nijmegen in the Netherlands, which harbors 48 500 individuals in the target age group. Eligible subjects without a history of BE or EAC were contacted by postal mail. They received the questionnaire and information about EAC and EAC screening. Respondents could return the questionnaire in a postage-paid envelope. In case of nonresponse, a reminder was sent after 4 weeks.

Previous studies have shown that a sample size of 300 respondents is sufficient for reliable statistical analysis.[11,17,18] Based on an expected response rate of 30%, we invited 1000 individuals to participate.

Statistical Analysis

The main outcomes are part-worth utilities for each attribute level. Part-worth utilities represent how much a respondent values each level of an attribute. A positive part-worth utility indicates that an attribute level is preferred over levels with negative values. Dual responses were analyzed by modeling the 2 choices within every choice task (a choice among 2 screening tests and a choice between this alternative and no screening) as independent choice tasks.[19] We examined rates of nonresponse, task nonattendance, attribute dominance, and self-reported evaluations of the choice tasks to ascertain there was an active trade-off between attributes and to assess the validity of the results.

A multinomial logit model was used to analyze the data and calculate part-worth utilities using effect coding.[20] It was assumed that individuals chose the screening option that yielded them the highest utility. We estimated the following model for the total utility for an EAC screening test.[21]

Equation 1:

$$U = V + \varepsilon = \beta_0 + \sum_{i=1}^{20} \beta_i \cdot x_i + \varepsilon$$

U represents individuals' preference for an EAC screening test. We assumed that a respondent would choose the EAC screening test that maximizes his utility. V is a systematic component specified as the observable total utility of an EAC screening test. β_0 indicates the general attitude of subjects toward EAC screening compared with no screening, regardless of attribute levels. $\beta_{1\text{-}20}$ represents part-worth utilities for all attribute levels. X_i has the value of 1 if an attribute level is present in a screening alternative, −1 if the reference level is present, and 0 otherwise. ε is the random error, accounting for unobserved components of choice. A 2-log likelihood test was used to test all 10 potential interaction effects one at a time. A Bonferroni corrected *P* value of <.005 was used to make sure that interaction effects between attributes were absent.

Importance scores for each attribute show the contribution of each attribute relative to other attributes in decision making. Scores were calculated by dividing the difference between the part-worth utilities for the most preferred and least preferred level of each attribute by the sum of all 5 part-worth utility ranges. This results in a rank order of the 5 attributes of a screening test from most to least important. An attribute with a 2-sided *P* value <.05 was considered to be important in the decision to participate in a certain EAC screening program.

To assess the expected uptake of an EAC screening program, we applied the model as shown in Equation 2.[22,23]

Equation 2:

$$P_{\text{participation}} = \frac{1}{1 + e^{-V}}$$

The average expected screening uptake was calculated by entering the constant term (β_0) into the model. The influence of the different attribute levels on expected uptake was calculated by entering part-worth utilities of every attribute level into the model.

The expected uptake of different screening tests was calculated by adding up the different levels corresponding with the screening test concerned and entering this value into the model. Because this subanalysis aimed to focus on uptake of EAC screening modalities, we deliberately did not include attributes of a screening program, such as the impact on cancer mortality. We therefore assumed that all screening tests would generate a reduction in EAC-related death of 3 per 1000 screened individuals and were free of out-of-pocket costs. For conventional endoscopy with conscious sedation, we further applied the levels severe discomfort, location at the hospital, and a specificity of 100%. For transnasal endoscopy, we used a mobile unit as location with moderate discomfort and a specificity of 95%.[24] The levels general practitioner, mild and no discomfort, and 90% and 80% test specificity were applicable to capsule sponge and breath testing, respectively.[7,25] We used linear interpolation between the levels 100% and 90%, and 90% and 70% to calculate the utility for 95% and 80% test specificity, respectively.

Trade-offs between the attributes were calculated by dividing the coefficients of the different levels of the attributes (harms) by the linear coefficient of the mortality reduction attribute (benefit: deaths avoided). This ratio indicates how many extra EAC-related deaths should be avoided to accept a test that will cause additional harm (ie, more pain, lower specificity, higher costs). We also calculated the willingness to pay for each of the different attribute levels as the ratio of the coefficients of the different attribute levels and the coefficient of the out-of-pocket costs.

Sociodemographic variables are presented as means ± standard deviations (SD) or median values with interquartile ranges (IQR) for continuous variables and frequencies or percentages for categorical variables and compared with those of the Dutch population. Aggregate data on socioeconomic status of both responders and nonresponders were available at the level of the area postal code of the subject, weighted by population size and classified into 3 groups (high, intermediate, and low).

Individual importance scores of each of the 5 attributes and each participant's most important attribute were estimated using hierarchical Bayes regression.[26] Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using multivariable logistic regression models to determine the influence of patient-level demographic variables on reporting an attribute as the most important factor in decision making. To determine the effects of patient characteristics on the likelihood of choosing "no screening," we conducted an exploratory multivariable linear regression analysis with the general attitude of subjects toward EAC screening (β_0) as dependent variable. We preselected variables based on literature review, expert opinions, and previous research on cancer screening. Subsequently, factors with a *P* value of <.2 in univariable analyses were included in the multivariable model with backward selection. Statistical analyses were

conducted using SPSS version 25.0 (IBM Corp, Armonk, NY). A 2-tailed P value $<.05$ was considered significant.

Results

Respondents

The questionnaire was returned by 384 of the 1000 invited individuals (for a response rate of 38.4%), from which 9 were excluded (see Appendix Fig. 2 in Supplemental Materials). Demographic characteristics are presented in Appendix Table 1 (in Supplemental Materials). Mean age (SD) was 61.7 (7.5) years, and 48% of the respondents were men. Upper gastrointestinal symptoms were reported by 23% of the respondents, and 21% had previous upper endoscopy experience. No difference in socioeconomic status was found between responders and nonresponders (P = .43).

DCE Results

In total, 4290 choice tasks were completed by the 375 respondents (median [IQR]: 12 [12-12]). Seventy-five percent of respondents agreed that the choice tasks were easy to understand, and 62% agreed that the choice tasks were easy to answer (≥6 on a 10-point scale). Eighty-eight percent of the participants were confident about their choices. Twenty individuals (5.3%) failed the rationality test. Three participants (0.8%) always selected "screening test 1" or "screening test 2" across all choice tasks indicating task nonattendance. Sixteen participants (4.3%) displayed attribute dominance by always choosing the alternative with the better level of 1 attribute. Sensitivity analyses, removing those respondents, did not considerably change the outcome of the analyses. We, therefore, included them in further analyses.

Figure 1 and Appendix Table 2 (in Supplemental Materials) show the results of the final preference model. From the estimated part-worth utilities, it can be concluded that the most preferred screening method is a highly specific test with low costs and low pain and discomfort, which generates a high reduction of EAC-related death. A positive linear relationship was seen between part-worth utility and EAC-related mortality reduction (β = 0.2948) and a negative linear relationship between utility and out-of-pocket costs ($\beta = -0.0088$).

All assessed EAC screening attributes proved to be important determinants of preferences, except for screening location. Test specificity was the most important item for EAC screening, accounting for 27.2% of decision making, followed by pain and discomfort (importance score of 26.8%), and mortality reduction (importance score of 24.6%). Eight individuals (2.1%) selected screening location as the most important attribute. All of them showed highest preferences for screening tests performed at the general practitioner office or in the hospital.

Male respondents demanded less accuracy from an EAC screening test and were more willing to undergo unnecessary follow-up testing than females (P = .03) (see Appendix Table 3 in Supplemental Materials). Women more often preferred a test causing less pain than men did ($P < .01$).

Expected EAC Screening Uptake

A total of 17 (4.5%) respondents consequently chose never to be tested. On the contrary, 200 (53.3%) respondents consistently selected screening. In a subgroup analysis for of the remaining 158 (42.1%) respondents who did not consistently select screening, the effect of the attribute mortality reduction was much smaller compared with the group as a whole. In contrast, the attribute test specificity was by far the most important attribute, as 53.2% of individuals in this group selected specificity as most important compared with 32.3% of individuals who consistently chose (not) to be screened.

Using Equation 2, the average expected uptake of EAC screening was 62.8% (95% CI 61.1%-64.5%); In a subgroup analysis that analyzed male respondents separately, the average predicted expected uptake was 68.7% (95% CI 66.2%-71.1%), which increased to 91.6% (95% CI 88.0%-94.2%) for men with upper gastrointestinal symptoms.

With the most preferred screening test, the probability of screening participation increased to 88.9% (95% CI 87.1%-90.4%). An increase in mortality reduction especially seemed to increase the expected uptake. On the other hand, an increase in pain and discomfort from moderate to severe resulted in a relatively large decrease in the expected screening uptake (20.9%) (Fig. 2).

Comparing different screening tests, uptake was 63% for upper endoscopy screening, 77% for transnasal endoscopy, 76% for capsule sponge testing, and 70% for breath testing, with a test specificity of 80%.

The multivariable linear regression model showed that male gender ($P < .001$), population screening (P = .001) or upper endoscopy (P = .048) experience, cancer worries (P = .010), and upper gastrointestinal symptoms (P = .046) significantly interacted with the general attitude toward EAC screening (Table 2). This implies that men with upper gastrointestinal symptoms who worry about their own risk of developing cancer, have already participated in another population-based screening program, or have previously undergone upper endoscopy are more likely to participate in a screening program.

Trade-offs

Based on the expressed preferences, respondents required 32 additional avoided deaths of EAC per 10 000 screened individuals for participation in a screening program using a test with a specificity of 70% instead of a test with a specificity of 100% (Table 3). Individuals were willing to give up 29 avoided EAC-related deaths per 10 000 screened individuals if the test caused only moderate instead of severe pain. Respondents were willing to pay between €93 and €106 for a screening test causing no pain and discomfort or a test with the highest specificity or mortality reduction.

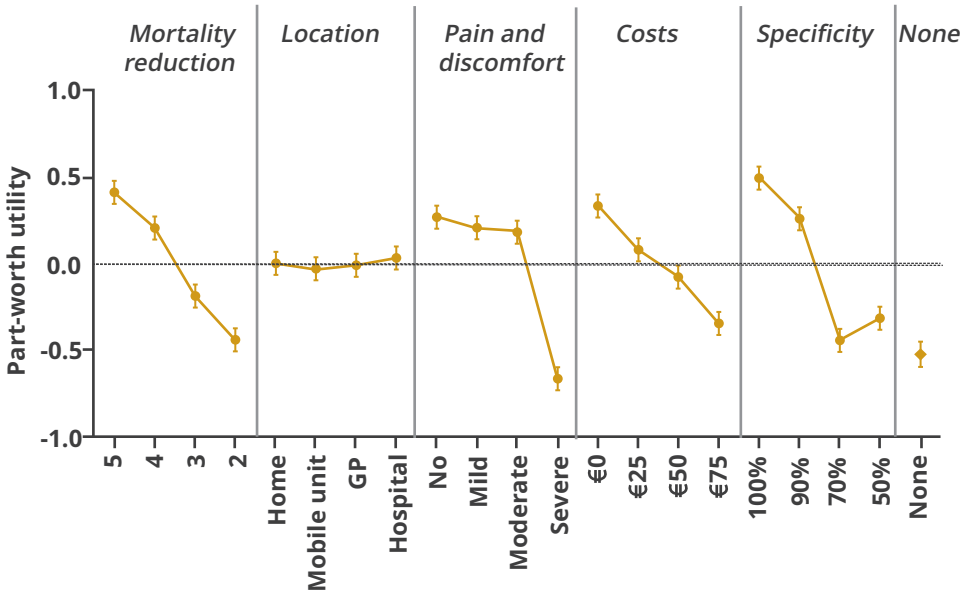
Predictors of Decision Making

The results of univariable and multivariable logistic regression analysis for independent predictors of patient preference are presented in Appendix Table 4 (in Supplemental Materials) and Table 4. Women were twice as likely as men to value pain and discomfort as the most important attribute category (OR 2.08; 95% CI 1.28-3.33). In contrast, men were more likely to report mortality reduction as the primary determinant (OR 1.83; 95% CI 1.08-3.11). Individuals who worry about their own risk of developing cancer considered pain and discomfort to be most important (OR 2.17; 95% CI 1.25-3.75) and worried less about test specificity (OR 0.45; 95% CI 0.25-0.82). Lower household income and participation in other screening programs were associated with decreased odds for valuing test specificity as the most important attribute.

Discussion

This DCE showed that mortality reduction, pain and discomfort, out-of-pocket costs, and test specificity influenced individuals' preferences for EAC screening. When deciding whether

Figure 1. Preferences of individuals for esophageal cancer screening. Higher values indicate that the attribute level was preferred to levels with lower values. The wider the range, the more critical the attribute was in the decision making of screening participation. The negative value of the part-worth utility of no screening indicates that respondents preferred screening over no screening.



to participate in EAC screening, respondents were mostly driven by high levels of test specificity. Thereafter they preferred low levels of pain and discomfort and low out-of-pocket costs and a decrease in EAC-related mortality. The average expected screening uptake of 63% shows that the majority of responders expressed a willingness to undergo screening for EAC. Participation rates were considerably higher with the most preferred screening test and in certain subgroups (eg, men with upper gastrointestinal symptoms). Individuals were willing to trade some mortality reduction to gain improvement in the levels of the other attributes, indicating that individuals are prepared to undergo more burdensome tests if this results in sufficient risk reduction of EAC-related mortality.

No previous DCEs have assessed how characteristics of EAC screening tests determine individuals' preferences for participation, but our results are consistent with other screening DCEs. Previous studies on preferences for colorectal cancer screening concluded that attributes related to accuracy (sensitivity and specificity) appear to be more important than attributes related to the screening procedure.[10] Another review of 15 studies, which focused on preferences of screening tests for breast, cervical, and colorectal cancer, highlighted the importance of efficacy/sensitivity, the screening procedure, and costs in determining the choice of a screening test.[27] We showed that participants found test specificity more important than EAC-related mortality reduction or the pain and discomfort of the procedure. This indicates that individuals may not be willing to undergo unnecessary follow-up testing, even though this could mean that more lesions are missed. Test specificity was included in 47% of previously published studies as an attribute, which was significant in all studies except one.[27] In contrast, specificity was not reported as the most influential attribute in those studies.[10,27] This may be due to the relatively low incidence of EAC compared with other cancer types, such as colorectal and breast cancer.

In this study, participants were generally positive about EAC screening. The participation rates for the existing cancer-screening programs in the Netherlands (ie, colorectal cancer, breast cancer, and cervical cancer screening) have also been high so far (ie, 71.3%, 80.0%, and 61.4%, respectively),[28–30] which is also reflected by the fact that 77% of the respondents had already participated in 1 or more of the population-based cancer screening programs. This suggests an overall positive attitude toward cancer screening.

Figure 2. Effects of changing the screening program characteristics on the probability of participation in esophageal cancer screening.

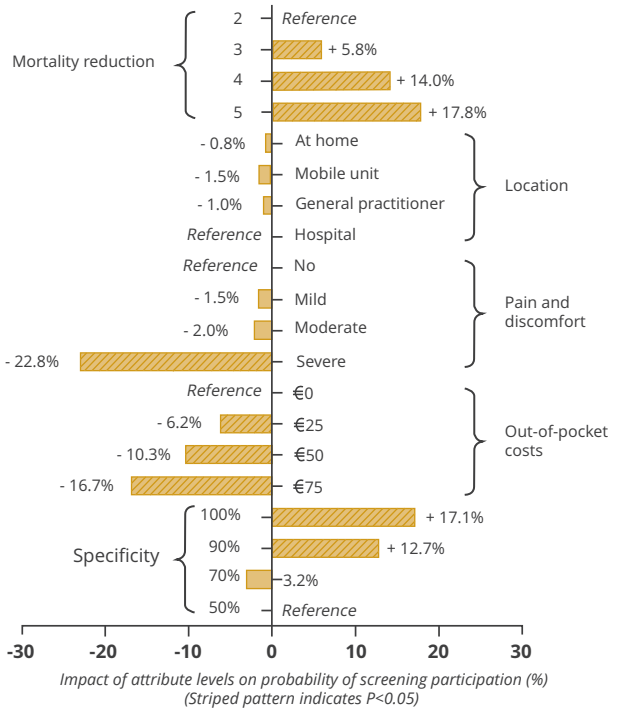


Table 2. Multivariable linear regression model to identify predictors for screening participation.

Characteristics	Univariable linear regression model before backward elimination of nonsignificant variables		Final multivariable linear regression model after backward elimination of nonsignificant variables	
	β coefficient (95% CI)	*P* value	β coefficient (95% CI)	*P* value
Gender				
Male	1.63 (0.50-2.75)	.005	2.81 (1.56-4.06)	<.001
Female	Reference		Reference	
Age (years)	0.02 (−0.05 to 0.10)	.54		
Cultural background				
White/Caucasian	Reference			
Other	−0.41 (−3.76 to 2.94)	.81		
Civil status				
With a partner	1.07 (−0.27 to 2.40)			
Without a partner	Reference	.12		
Highest level of education				
High school or less	Reference			
Vocational college	−0.84 (−2.48 to 0.80)	.32		
College / university	−1.68 (−3.0 to −0.41)	.01		
Current employment status				
Employed full-time	−0.08 (−2.09 to 1.94)	.94		
Employed part-time	0.07 (−1.89 to 2.03)	.94		
Retired	0.35 (−1.56 to 2.26)	.72		
Unemployed	Reference			
Annual household income in Euros (€)				
<25 000	Reference			
25 001-50 000	−0.13 (−1.73 to 1.46)	.87		
> 50 001	−0.60 (−2.30 to 1.10)	.49		
Do not know or prefer not to say	−0.49 (−2.25 to 1.38)	.61		
Family history of esophageal cancer	−0.24 (−3.06 to 2.58)	.87		
Knowing someone affected by esophageal cancer	0.47 (−1.10 to 2.05)	.56		
Generic health status (EQ-5D) summary score	−3.44 (−7.48 to 0.61)	.10		
Prior diagnosis of cancer	1.10 (−0.52 to 2.72)	.18		
Worries about own risk of developing cancer				
Sometimes, often, almost all the time	2.5 (1.07-3.93)	.001	1.96 (0.47-3.45)	.010
Not at all	Reference		Reference	
Participated in population-based cancer screening programs	0.95 (−0.41 to 2.31)	.17	2.47 (0.98-3.95)	.001
Upper endoscopy experience	2.12 (0.71-3.54)	.003	1.46 (0.02-2.91)	.048
Current upper gastrointestinal symptoms	2.66 (1.32-3.99)	.000	1.50 (0.03-2.97)	.046
Socioeconomic status				
High	2.19 (−0.31 to 4.68)	.09		
Intermediate	0.88 (−0.30 to 3.18)	.14		
Low	Reference			

Signs of estimated parameters of attribute levels were consistent with a priori preference expectations and showed face validity, except for 50% and 70% test specificity.[31] In addition to the difference between these levels not being statistically significant, these levels may be considered as unacceptable trade-offs and therefore may not influence individuals' choices. Another explanation may be that respondents simply did not understand the concept and meaning of the attribute test specificity. Nevertheless, the majority indicated that the choice tasks were easy to understand and felt confident about their choices and only a small minority (5.3%) of respondents failed the rationality test, suggesting that the majority understood the discrete choice questions.

Existing data about the preferences of individuals toward EAC screening in literature are based on rating scales, which have multiple limitations.[32] In a questionnaire study using 5-point Likert scales, 71% of participants were moderately to extremely interested in undergoing screening for EAC with any modality.[33] Similar to our study, a prior endoscopy and upper gastrointestinal symptoms were significant predictors of willingness to undergo EAC screening. Individuals preferred less invasive screening techniques above conventional endoscopy. The most common reasons for choosing the test were the safe and minimal risk profile of the test, low costs, and lack of sedation.[33] These results are in line with our findings, which showed that especially severe pain and discomfort had a large impact on respondents' willingness to undergo EAC screening, suggesting conventional endoscopy with or without conscious sedation would be the least preferred screening method.

Understanding how individuals value the attributes of healthcare interventions is important for the design,

Table 3. Trade-offs between EAC-related mortality reduction and out-of-pocket costs (willingness to pay) and different aspects of esophageal cancer screening tests.

Attribute levels	Number of extra avoided EAC-related deaths (per 10 000 screened individuals) a test should provide	Willingness to pay
Pain and discomfort		
No (0/10)	Reference	€106.24 (€104.55-€107.94)[†,‡]
Mild (2/10)	2.0 (1.3-2.8)	€99.37 (€97.60-101.14)[‡]
Moderate (5/10)	2.8 (2.1-3.5)	€96.86 (€95.15-€98.56)[‡]
Severe (8/10)	31.6 (30.8-32.3)*	Reference
Test specificity		
100%	Reference	€92.78 (€91.08-€94.48)[‡]
90%	8.0 (7.3-8.7)	€65.80 (€64.11-€67.49)
70%	32.0 (31.3-32.8)	−€15.06 (−€16.91 to −€13.21)
50%	27.6 (26.9-28.3)	Reference
Mortality reduction		
5 deaths out of 1000		€97.21 (€95.55-€98.88)[‡]
4 deaths out of 1000	Not applicable	€73.58 (€71.87-€75.29)
3 deaths out of 1000		€28.67 (€26.98-€30.37)
2 deaths out of 1000		Reference
Out-of-pocket costs		
€0	Reference	
€25	8.6 (7.9-9.3)	Not applicable
€50	14.1 (13.4-14.8)	
€75	22.9 (22.2-23.6)	

Note: Trade-offs are presented as number of avoided deaths per 10 000 screened individuals and willingness to pay (€) with 95% confidence intervals.
EAC indicates esophageal adenocarcinoma.
*Interpretation note: Individuals think a test should avoid 31.6 extra EAC-related deaths per 10 000 screened individuals to undergo a test that causes severe pain instead of a test that causes no pain.
[†]Interpretation note: Individuals are willing to pay €106.24 to undergo a test that causes no pain instead of a test that causes severe pain.
[‡]Willingness to pay estimates are outside the range of the cost attribute used in the discrete choice experiment design (i.e. >€75). In such cases, linear extrapolation was used to calculate willingness to pay.

development, and implementation of effective screening programs. Screening for EAC will only be beneficial at the population level if the screening program and the information given connect with the preferences of the target population, resulting in high participation rates. Current guidelines recommend considering EAC screening with conventional upper endoscopy in patients with chronic and frequent gastroesophageal reflux symptoms and multiple risk factors (age ≥ 50 years, white race, male sex, obesity, first-degree relative with BE or EAC).[16,34–36] To date, however, it is not proven that screening with upper endoscopy is beneficial. Furthermore, our study showed that the most preferred test should be accurate and cause no discomfort. At present, no such test is universally offered for EAC screening, but newer tests such as nonendoscopic cell collection devices and exhaled biomarkers are currently under development with promising results.[5,6] These may become viable options once their clinical effectiveness has been established. This DCE could guide future research on minimally invasive screening techniques. Furthermore, these results could be particularly useful for estimating the participation rates of a screening program, especially in the absence of observational data from clinical trials of a screening test and for screening modalities that are currently not available.

This study has several strengths. First, a DCE is more effective in approximating the real-world scenario compared with other methods investigating decision making, such as self-report or absolute ranking of factors.[37] In contrast to the often used Likert-scale questionnaires, respondents of a DCE are required to choose between different sets of program characteristics rather than just rank or rate a single characteristic.[13] Hence respondents of a DCE show no tendency to provide socially desirable answers and to agree with the provided statements. Furthermore, DCEs enable us to determine preferred program characteristics of both existing and nonexisting programs and to quantify the importance of the assessed screening program characteristics relative to each other. In contrast to other DCEs, a dual-response none question was included, since it better reflects actual screening participation and prevents overestimation of screening uptake.[38] Additionally, this DCE explicitly quantified the trade-offs between benefits and the downsides of EAC screening that individuals are willing to accept.

Some limitations warrant consideration as well. First, in a DCE, individuals are required to make trade-offs between hypothetical screening options. Although extensive pretesting had been performed, rigorous stated preferences designs and analysis methods were used, and answers on the evaluation questions were mostly positive, it cannot be ruled out that individuals may behave differently than if they were making real-world decisions, resulting in hypothetical bias. Nevertheless, a meta-analysis, assessing the external validity of DCEs by comparing DCE data to real-life health choices, indicated that DCEs can produce reasonable predictions of health-related behaviour.[39]

A second limitation of our study is that the outcomes of a DCE depend on the choice of attributes and attribute levels.[40] Only a limited number of attributes could be included to reduce the complexity of the choice tasks. Thus not all aspects of an EAC screening test can be captured in this DCE. To address these limitations, we used input from the literature, interviews, and focus

Table 4. Predictors for reporting mortality reduction, pain and discomfort, or specificity as the most important attribute in decision making. Final logistic regression model after backward elimination of nonsignificant variables.

Characteristics	Mortality reduction (n = 70)		Pain and discomfort (n = 101)		Specificity (n = 154)	
	OR (95% CI)*	*P* value	OR (95% CI)*	*P* value	OR (95% CI)*	*P* value
Gender						
Male	1.83 (1.08-3.11)	.019	0.48 (0.30-0.78)	.003		
Female	Reference		Reference			
Annual household income in Euros (€)						
< 25 000					Reference	
25 001-50 000					1.96 (1.06-3.60)	.031
> 50 001					1.77 (0.92-3.38)	.086
Do not know or prefer not to say					0.84 (0.40-1.78)	.649
Cancer worries						
Sometimes, often, almost all the time			2.17 (1.25-3.75)	.006	0.45 (0.25-0.82)	.009
Not at all			Reference		Reference	
Participated in cancer screening programs						
Yes					0.58 (0.35-0.98)	.040
No					Reference	

Note: Data presented as odds ratios with 95% confidence intervals.
CI indicates confidence interval; OR, odds ratio.
*The multivariable logistic regression model included all covariates with a *P* value <.2 of Appendix Table 4 (in Supplemental Materials).

groups to ensure content coverage of factors related to individuals' biologic decision making. Nevertheless, the range of the out-of-pocket costs attribute might be too small because the willingness-to-pay estimates exceed the maximum cost level. The invasiveness of a screening procedure was indirectly described by the levels "location of the test" and "pain and discomfort." Although a labeled DCE describes choice sets more realistically and individual feelings regarding screening tests can be taken into account, an unlabeled DCE provides more insights into which characteristics of a screening modality are most important for the respondents and the trade-offs respondents made between those characteristics.[41] Thus acquired data can be used for the development of new EAC screening tests not assessed in this DCE.

Third, this DCE specifically focused on the uptake of a single EAC screening test, not a series of screening tests implemented over time and endoscopic surveillance of patients with BE. Nevertheless, as the risk of developing BE after an initial negative endoscopy is low, once-in-a-lifetime screening should be sufficient to detect BE.[42] Furthermore, progress has been made to identify patients with BE at low risk of neoplastic progression in whom surveillance can be discontinued.[43,44]

Fourth, the way we framed the information on mortality reduction and specificity could be difficult for respondents to interpret. Nonetheless, this is comparable to how individuals currently make decisions in a clinical setting. To minimize framing effects, we attempted to frame our information according to the literature.[1,45,46]

Finally, our questionnaire response rate was 37.5%, resulting in potential selective nonresponse. We were not able to collect demographic information on nonresponders to determine whether there were systematic differences between responders and nonresponders. Although the response rate was similar to other population-based surveys, our sample may not be representative of the general population.[33,47–49] Respondents were more educated than the general Dutch population. Also, the number of non-Dutch respondents was relatively low, which may limit generalizability. This may be because of language difficulties, as good understanding of the Dutch language was needed to complete the questionnaire. Nevertheless, this is a reflection of the general population in Southeast Holland. Furthermore, the at-risk population for EAC is predominantly Caucasian and, hence, this study elucidates on the preferences in this high-risk population.

Conclusion

This study suggests a substantial interest in EAC screening in the general population, particularly in individuals at higher risk for EAC (ie, men with upper gastrointestinal symptoms). Based on our results, an optimal screening test should have high specificity, cause no or mild to moderate pain or discomfort, and result in a decrease in EAC-related mortality. Understanding individuals' preferences for EAC screening tests may help when further designing the optimal screening modality by selecting the attributes that maximize attendance and further reduce morbidity and mortality from EAC.

Supplemental Material

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.jval.2020.03.013.

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