

Public Preferences and Predicted Uptake for Esophageal Cancer Screening Strategies: A Labeled Discrete Choice Experiment

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INTRODUCTION: As novel, less invasive (non)endoscopic techniques for detection of Barrett's esophagus (BE) have been developed, there is now renewed interest in screening for BE and related neoplasia. We aimed to determine public preferences for esophageal adenocarcinoma screening to understand the potential of minimally invasive screening modalities.

METHODS: A discrete choice experiment was conducted in 1,500 individuals, aged 50–75 years, from the general population. Individuals were repeatedly asked to choose between screening scenarios based on conventional upper endoscopy, transnasal endoscopy, nonendoscopic cell collection devices, breath analysis, and a blood test, combined with various levels of test sensitivity and specificity, and no screening. A multinomial logit model was used to estimate individuals' preferences and to calculate expected participation rates.

RESULTS: In total, 554 respondents (36.9%) completed the survey. The average predicted uptake was 70.5% (95% confidence interval: 69.1%–71.8%). Test sensitivity (47.7%), screening technique (32.6%), and specificity (19.7%) affected screening participation (all $P < 0.05$). A low test sensitivity had the highest impact on screening participation, resulting in a 25.0% (95% confidence interval: 22.6%–27.7%) decrease. Respondents preferred noninvasive screening tests over endoscopic and capsule-based techniques, but only if sensitivity and specificity were above 80%.

DISCUSSION: Our study suggests that individuals generally prefer noninvasive BE screening tests. However, these tests would unlikely improve screening uptake when associated with a much lower accuracy for detecting BE and esophageal adenocarcinoma compared with conventional upper endoscopy. Improving accuracy of minimally invasive screening strategies and informing the target population about these accuracies is therefore essential to maximally stimulate screening participation.

SUPPLEMENTARY MATERIAL accompanies this paper at <http://links.lww.com/CTG/A428>.

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INTRODUCTION

The ongoing increasing incidence of esophageal adenocarcinoma (EAC) and its still dismal prognosis in most patients has stimulated interest in its early detection (1). Although Barrett's esophagus (BE) is a known precursor of EAC, only a minority of patients with EAC are known with a previous diagnosis of BE (2). As most cases of BE remain undiagnosed, identifying patients with undiagnosed BE and early-stage EAC will likely reduce cancer mortality (3). However, routinely screening of at-risk individuals with conventional upper endoscopy is unlikely to be feasible because of its direct and indirect costs, invasiveness, discomfort, and potential complications (4–6).

Several approaches to overcome limitations of current screening policies have been explored to identify individuals at highest risk of BE and EAC. Recently, alternative screening modalities, such as transnasal endoscopy (TNE), non-endoscopic cell collection devices, and circulating and exhaled biomarkers, are being developed for the detection of BE to improve effectiveness, reduce costs, and minimize invasiveness of screening techniques compared with upper endoscopy (7–9). Although screening with these minimally invasive screening techniques is not yet recommended by current guidelines, various studies have piloted EAC screening with these techniques and have shown promising results (6–8,10,11). Hence, these

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minimally invasive tests may be implemented in clinical practice in the near future.

In cancer screening and medical decision-making in general, the value of individuals' preferences is increasingly being recognized (12). As the population benefit of EAC screening is largely dependent on high participation rates, coordination with the population is needed to create support and confidence in a potential screening program. Involving the target screening population at an early stage is therefore of great importance. To date, little is known about public's perceptions regarding innovative minimally invasive screening techniques.

The aim of this discrete choice experiment (DCE) was to quantify population's preferences for various screening test characteristics and their relative importance in valuing the overall attractiveness of an EAC screening program. The second aim was to estimate the predicted participation rate of screening with various (minimally invasive) EAC screening modalities while taking into account different characteristics of each test.

METHODS

Study population and study setting

The study was conducted among the general population in the Netherlands. A survey was sent by postal mail to a total of 1,500 individuals aged 50–74 years who were randomly selected from the population registry of Nijmegen and surrounding towns. Respondents could return the survey in a postage-paid envelope. Individuals with a known history of BE or EAC were excluded. Ethical approval was waived by the medical ethical committee region Arnhem–Nijmegen.

Discrete choice experiment

A DCE is a form of trade-off analysis which has its theoretical grounds in the random utility theory and is increasingly being used in healthcare research (13,14). DCEs are able to establish preferences in controlled experimental conditions through responses to realistic and hypothetical screening scenarios, composed of their characteristics (attributes) which are specified by variants of those attributes (levels) (15). A DCE is constructed by systematically varying attribute levels to generate a set of screening modalities. In each choice task, respondents will choose between 2 competing screening modalities and will select the scenario that generates the highest personal utility. By changing these attribute levels repeatedly, preferences for different screening attributes can be estimated (13).

Survey

The survey was based on good research practices for conjoint analysis in health (15). In the first part, preferences regarding different EAC screening modalities were assessed using a DCE. The second part contained questions about patient demographic characteristics, upper endoscopy and screening experiences, health history, and a health literacy questionnaire (16). The survey further included information about BE and EAC screening and surveillance, a description of attributes and levels, and information on how to complete the choices tasks. Furthermore, participants were told that a (noninvasive) screening test does not give a definite result, but only indicates whether additional follow-up testing and surveillance are indicated.

Discrete choice experiment development

Selection of attributes and levels. Attributes and levels were selected by applying a framework for instrument development of a DCE, consisting of 6 stages including literature review, expert consultation, stakeholder engagement, a focus group, pretest interviews, and pilot testing (17). This approach combines the use of the current evidence and expert opinions, in addition to patient input and quantitative preference assessment. Contrary to a previously conducted unlabeled DCE, we included a direct measure of invasiveness, i.e., the actual screening tests, instead of a generic pain and discomfort attribute to take into account all essential elements of the burden of various screening tests (18). Conventional endoscopy, TNE, nonendoscopic cell collection devices, a breath test, and a blood test have until now most commonly studied as EAC screening tests and were included as attribute levels (2). All participants were informed regarding the incorporated test characteristics of these 5 screening tests, including direct and indirect consequences of the tests. A literature review concerning the sensitivity and specificity of these screening techniques was conducted to set up the test accuracy levels (2). Figure 1 presents the levels of the 3 attributes of the final survey. See Supplementary Materials, <http://links.lww.com/CTG/A428> for further details of the selection process of attributes and levels.

Experimental design and choice task development. We created a D-efficient, labeled, fractional factorial design using Sawtooth Software V9.5.3 (Sawtooth, North Orem, UT). All attribute levels were represented in the same frequency, and a modest degree of overlap was included to improve response efficiency (19). The experimental design aimed to develop a set of choice tasks that would provide maximum information to describe trade-offs among attributes while limiting respondent burden. Test sensitivity and specificity were not interconnected, and no prohibitions and dependencies between attribute levels were added to maintain level balance and design efficiency. The final design consisted of 130 pairs of hypothetical screening modalities, divided into 10 versions of 13 choice tasks.

In each choice task, participants were asked to consider 2 screening modalities in each choice set as realistic alternatives and to choose the screening test that appealed most to them (Figure 2). A dual-response opt-out was included in each choice task because EAC screening is a preventive intervention and to maximize information about trade-offs (20).

Respondents were randomly assigned to 1 of the 10 survey versions each containing 13 different choice sets and a warm-up question. Two pilot studies were performed to examine the intelligibility, acceptability, and validity of the survey (Supplementary Methods, <http://links.lww.com/CTG/A428>).

Validity. We assessed rates of nonresponse, task nonattendance, attribute dominance, and self-reported evaluations to determine validity of the results. Furthermore, a dominance test, in which one of the screening tests was superior given the levels of all test characteristics, was included to examine participants' understanding and attention. Analyses were performed by both including and excluding respondents who failed this dominance test.

Sample size

Sample size calculations in stated-preference methods often rely on rules of thumb, which recommend having a minimum sample







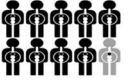
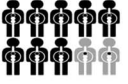

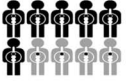





Attributes	Level 1	Level 2	Level 3	Level 4	Level 5
Screening modality	Upper endoscopy 	Transnasal endoscopy 	Pill on a string 	Breath test 	Blood test 
Accuracy of the test if you DO have (a precursor of) esophageal cancer	 <i>The test will never miss cancer.</i>	 <i>The test will miss cancer 1 out of 10 times.</i>	 <i>The test will miss cancer 2 out of 10 times.</i>	 <i>The test will miss cancer 3 out of 10 times.</i>	 <i>The test will miss cancer 4 out of 10 times.</i>
Accuracy of the test if you DO NOT have (a precursor of) esophageal cancer	 <i>If you DO NOT have cancer, the test will never say you may have cancer.</i>	 <i>If you DO NOT have cancer, the test will say you may have cancer 1 out of 10 times.</i>	 <i>If you DO NOT have cancer, the test will say you may have cancer 2 out of 10 times.</i>	 <i>If you DO NOT have cancer, the test will say you may have cancer 3 out of 10 times.</i>	 <i>If you DO NOT have cancer, the test will say you may have cancer 4 out of 10 times.</i>

Figure 1. Overview of attributes and levels for esophageal cancer screening and related visualizations.

size of 300 (21). We targeted a sample size of 500 to ensure sufficient power and assess preference differences across subgroups. To anticipate on a potentially large nonresponse, 1,500 individuals were invited to participate.

Study outcomes

The main outcomes are part-worth utilities for each attribute level. Part-worth utilities represent the relative desirability of the levels within each attribute in numerical form. Secondary outcomes include expected uptake of different screening tests, trade-offs, and importance scores for each attribute showing the contribution of each attribute relative to other attributes in decision-making.

Statistical analysis

Sociodemographic variables are shown as mean values with SDs or medians with interquartile ranges for continuous variables and frequencies for categorical variables. Statistical analyses were conducted using SPSS version 25 (IBM Corp, Armonk, NY). A two-tailed P value <0.05 was considered significant.

A multinomial logit model was used to analyze collected choice data and to estimate part-worth utilities for each attribute level (22). Importance scores were calculated by dividing the differences between the part-worth utilities for the most preferred and the least preferred level of each attribute by the sum of all 3 utility ranges.

Subgroup analyses were conducted among individuals at higher risk of EAC (i.e., men and respondents with upper gastrointestinal symptoms) and with upper endoscopy experience to examine whether preferences differed systematically. Latent class analysis was used to assess heterogeneity effects on choices across groups of respondents (22). The model aims to identify 2 classes

of respondents based on unobserved or latent heterogeneity in preferences.

To determine the effects of respondent characteristics on the likelihood of choosing “no screening,” we conducted multivariable linear regression analysis with the general attitude toward EAC screening as dependent variable. Factors with a P value of <0.2 in univariable analyses were included in the multivariable model with backward selection.

We examined the predicted uptake of EAC screening by applying a previously developed model (23). We investigated the effects of changing the screening characteristics on the expected uptake by entering part-worth utilities of each attribute level into the model. Maximum acceptable risks of missing EAC and unnecessary follow-up testing were calculated by dividing the coefficients of the different attribute levels by the linear coefficients of the risk attributes. See Supplementary Materials, <http://links.lww.com/CTG/A428> for additional details of model development.

Ethics approval and consent to participate

Ethical approval for this study was waived by the CMO region Arnhem–Nijmegen. The study was performed in accordance with the Declaration of Helsinki. All study participants provided written informed consent.

RESULTS

Respondents

Of the 1,500 surveys sent, 561 were returned (response rate: 37.4%). Seven participants were excluded (6 did not answer any choice task, and 1 had a history of EAC). Mean age (SD) of 554 included participants was 61.9 (6.9) years, and 53% were men (Table 1). Reflux symptoms at least once a week were reported by

Suppose the Dutch government has introduced screening for esophageal cancer. Imagine that you are eligible to participate in esophageal cancer screening. Please look at the two screening tests below. Do you prefer screening test 1 or screening test 2? And would you actually participate in this screening program?



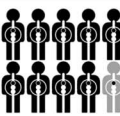

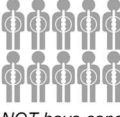

	Screening test 1	Screening test 2
How is the test done?	<p>Transnasal endoscopy</p>  <p>A small camera is introduced through the nose into your esophagus. No sedation is needed.</p>	<p>Breath test</p>  <p>Breathing into a mouthpiece for 5 minutes.</p>
Accuracy of the test if you DO have (a precursor of) esophageal cancer	 <p>If you DO have cancer, the test will miss cancer 1 out of 10 times.</p>	 <p>If you DO have cancer, the test will miss cancer 3 out of 10 times.</p>
Accuracy of the test if you DO NOT have (a precursor of) esophageal cancer	 <p>If you DO NOT have cancer, the test will never say you may have cancer.</p>	 <p>If you DO NOT have cancer, the test will say you may have cancer 2 out of 10 times.</p>
Which screening test do you prefer?		
	Screening test 1 <input type="radio"/>	Screening test 2 <input type="radio"/>
Suppose you receive an invitation for a screening program with the test you chose. Would you actually participate in this screening program?		
	Yes <input type="radio"/>	No <input type="radio"/>

Figure 2. Example of a discrete choice question (translated from Dutch).

113 respondents (20%), and 20% had undergone upper endoscopy in the past.

Validity and comprehensibility

Only 34 respondents (6.1%) failed the dominance test and selected the screening alternative with less favorable characteristics. Sixty-six individuals (11.9%) showed attribute dominance by always selecting the screening test with a better level of 1 attribute. Only 1 respondent (0.2%) always chose “screening test 2” across all choice tasks indicating task nonattendance. Seventy-five percent of participants were confident about their choices (agree or strongly agree on a 5-point Likert scale), and only 3.4% felt unsure. Self-reported confidence did not significantly influence passing the dominance test ($P = 0.54$). Respondents with high health literacy more often passed the dominance test than respondents with lower health literacy ($P = 0.046$). Sensitivity analyses, excluding respondents who failed the rationality task,

did not substantially change the results of the analyses. Hence, all respondents were included in our further analyses.

DCE results

In total, 6,929 choice tasks were completed by the respondents (median [interquartile range]: 13 [13–13]). The estimated part-worth utilities for the attribute levels were ordered as expected (Figure 3 and see Table S1, Supplementary Digital Content 1, <http://links.lww.com/CTG/A428>). In general, individuals prefer a noninvasive screening test with maximal sensitivity and specificity. All assessed attributes proved to be important determinants in the decision to participate in EAC screening (all $P < 0.05$). Breath analysis and blood testing had positive part-worth utilities, indicating that respondents preferred noninvasive screening tests above invasive screening tests. Part-worth utilities of all 5 screening techniques were higher than the utility of the none option (-0.87 [95% confidence interval [CI] -0.94 to -0.80]),

Table 1. Respondent characteristics

Characteristics	Total (n = 554)
Gender—male	295 (53.4%)
Age (yr)	61.9 ± 6.9
Municipality—city	286 (51.1%)
Cultural background—white	522 (94.9%)
Civil status—with a partner	421 (76.5%)
Highest level of education	
Primary school	95 (17.3%)
High school	126 (23%)
Vocational college	94 (17.2%)
College/university	233 (42.5%)
Current employment status	
Employed full-time	135 (24.7%)
Employed part-time	149 (27.2%)
Retired	175 (32.0%)
Unemployed	88 (16.1%)
Health literacy (confident with forms)	
Extremely	241 (44.0%)
Quite a bit	267 (48.7%)
Somewhat	29 (5.2%)
A little bit	5 (0.9%)
Not at all	6 (1.1%)
Household	
Single, no living in children	61 (11.2%)
Single, 1 or more living in children	64 (11.7%)
With partner/family, no living in children	107 (19.6%)
With partner/family, 1 or more living in children	315 (57.6%)
Family history of esophageal cancer	21 (3.8%)
Knowing someone affected by esophageal cancer	90 (16.2%)
Generic health status (EQ-5D) summary score	0.80 ± 0.13
Body mass index	25.1 (23.3–27.8)
Previous diagnosis of cancer	104 (18.8%)
Worries about the own risk of developing cancer	
Sometimes, often, almost all the time	104 (19.0%)
Not at all	444 (81.0%)
Participated in population-based cancer screening programs	415 (74.9%)
Upper endoscopy experience	108 (19.5%)
Upper gastrointestinal symptoms	
Current	110 (19.9%)
Previous	44 (7.9%)

Table 1. (continued)

Characteristics	Total (n = 554)
Heartburn ^a	80 (15.1%)
Regurgitation ^a	70 (13.6%)
Values presented as n (%), mean ± SD, median (interquartile range).	
^a Symptoms at least once a week.	

indicating that screening with any screening test is preferred above no screening.

We found that individuals who had undergone upper endoscopy before were more likely to undergo endoscopic screening again than individuals who had not undergone upper endoscopy before. Preferences of male respondents and individuals with upper gastrointestinal symptoms and upper endoscopy experience are displayed in Table S3, Supplementary Digital Content 1, <http://links.lww.com/CTG/A428>. No differences in preferences between male and female responders were found.

Preferences in subgroups

Latent class analysis revealed that 2 distinct subgroups with similar decision-making profiles could be identified (see Table S3A, Supplementary Digital Content 1, <http://links.lww.com/CTG/A428>). Unlike class 2 (n = 199), respondents in class 1 (n = 355) were unwilling to trade-off test accuracy to undergo a less invasive screening test and more willing to undergo EAC screening in general. Respondents in class 1 more often worried about their own risk of developing cancer ($P < 0.001$), more likely had undergone upper endoscopy ($P = 0.05$), and less frequently had a history of cancer ($P = 0.05$) (see Table S3B, Supplementary Digital Content 1, <http://links.lww.com/CTG/A428>).

Expected EAC screening uptake

Only 15 respondents (2.7%) consequently chose never to be screened, whereas 280 participants (50.5%) always selected screening regardless of attribute levels. This resulted in an expected average participation rate of EAC screening of 70.5% (95% CI: 69.1%–71.8%). The participation rate was 73.0% (95% CI: 71.1%–74.8%) for male respondents and 78.1% (95% CI: 75.1%–80.9%) for individuals with upper gastrointestinal symptoms. The participation rate among individuals who have undergone upper endoscopy before increased to 79.6% (95% CI: 76.5%–82.3%).

The effects of changing the EAC screening program characteristics on the participation rate are shown in Figure 4. A low sensitivity would result in a 25.0% (95% CI: 22.6%–27.7%) decrease in expected uptake. Figure 5 shows the predicted uptake for all 5 screening techniques. Predicted uptake of upper endoscopy was 78.5% (95% CI: 76.0%–80.8%). A breath test should have at least 80% sensitivity and specificity to be equally attractive to participants as upper endoscopy. Nonendoscopic cell collection devices require a higher accuracy with a sensitivity of 100% and specificity of 70%. TNE as first screening test should at least have a 100% sensitivity and 80% specificity.

The multivariable linear regression model showed that individuals who had a lower education level (i.e., lower or equal to high school), were younger, and had previous upper endoscopy experience were more likely to participate in either screening test

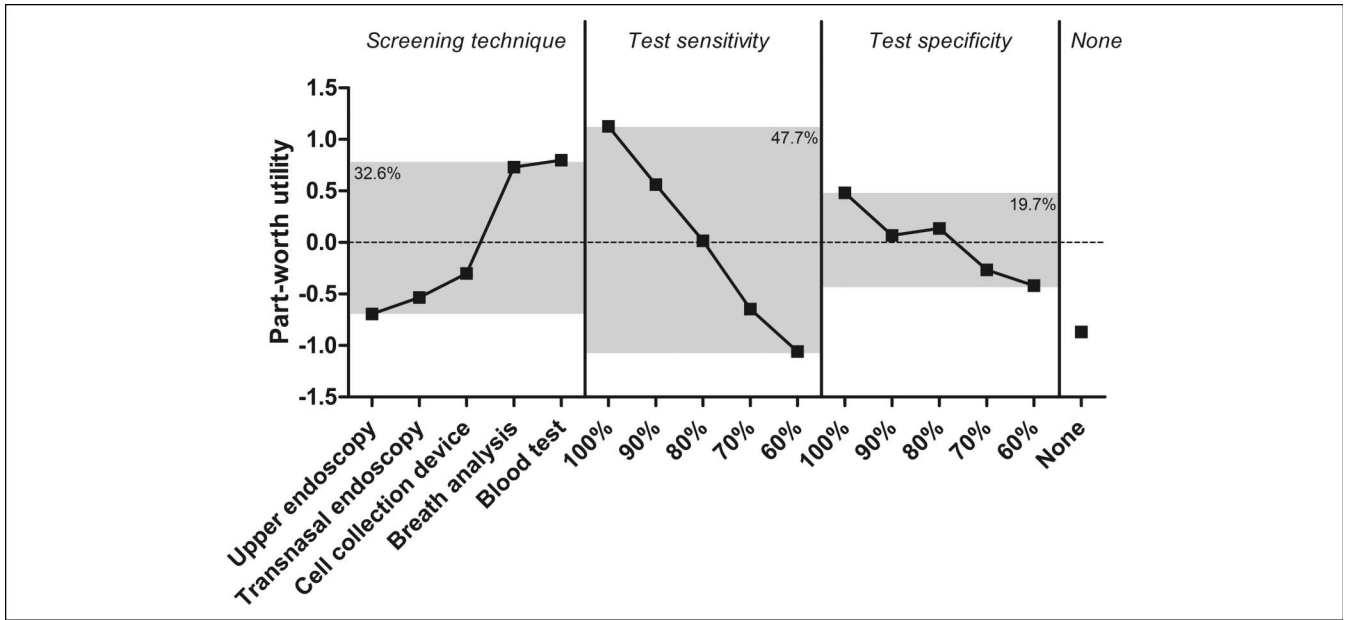


Figure 3. Part-worth utilities and importance scores for screening test attributes. Test sensitivity, screening technique, and test specificity accounted for 47.7%, 32.6%, and 19.7% of decision-making, respectively.

than individuals who had a higher education level, were older, and had not undergone upper endoscopy (Table 2).

Maximum acceptable risks

Respondents were willing to accept a 67%–70% additional risk of unnecessary follow-up testing to undergo a less invasive screening test (i.e., breath analysis or blood test) instead of conventional upper endoscopy (Table 3). Furthermore, participants were

willing to give up 26% test sensitivity to undergo a minimally invasive screening test.

DISCUSSION

In this population-based DCE, screening technique, test sensitivity, and specificity all significantly affect preferences for EAC screening. Individuals were mostly driven by high levels of test sensitivity followed by screening technique. Noninvasive

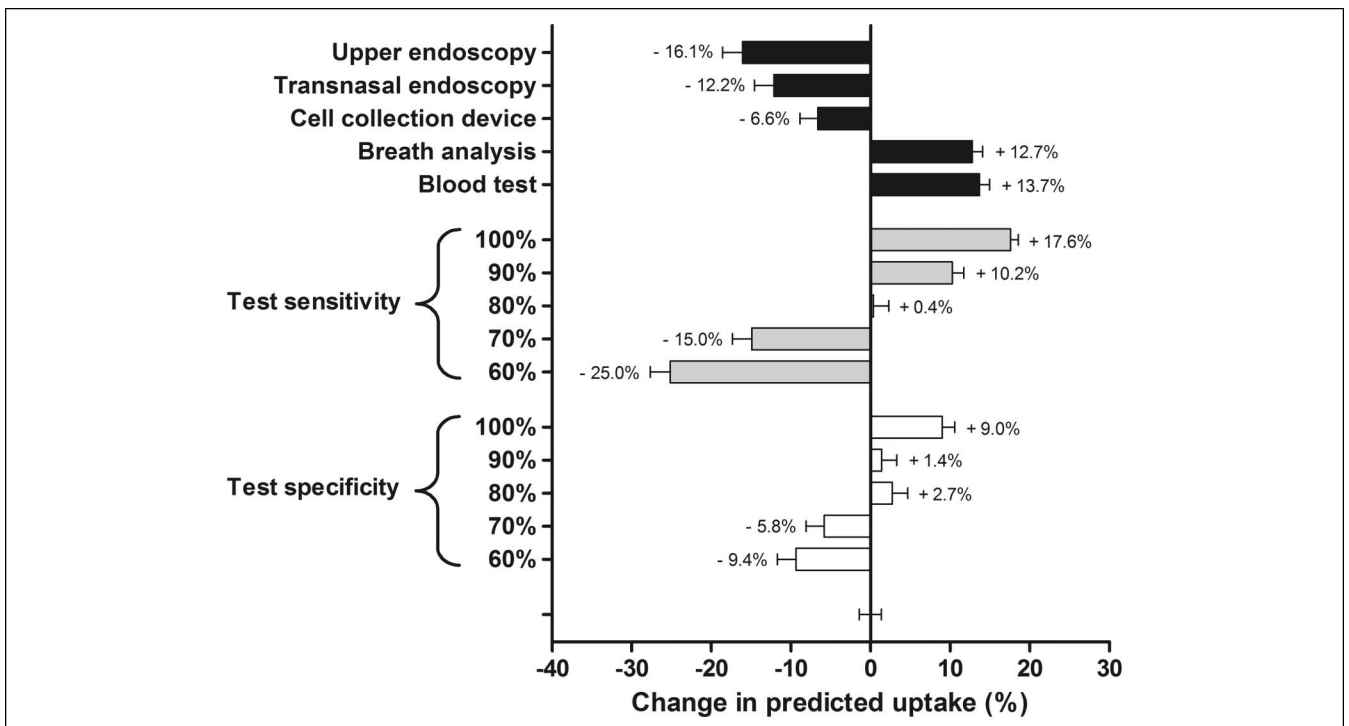


Figure 4. Effects of changing the screening program characteristics on the probability of participation (70.1%) in esophageal cancer screening.

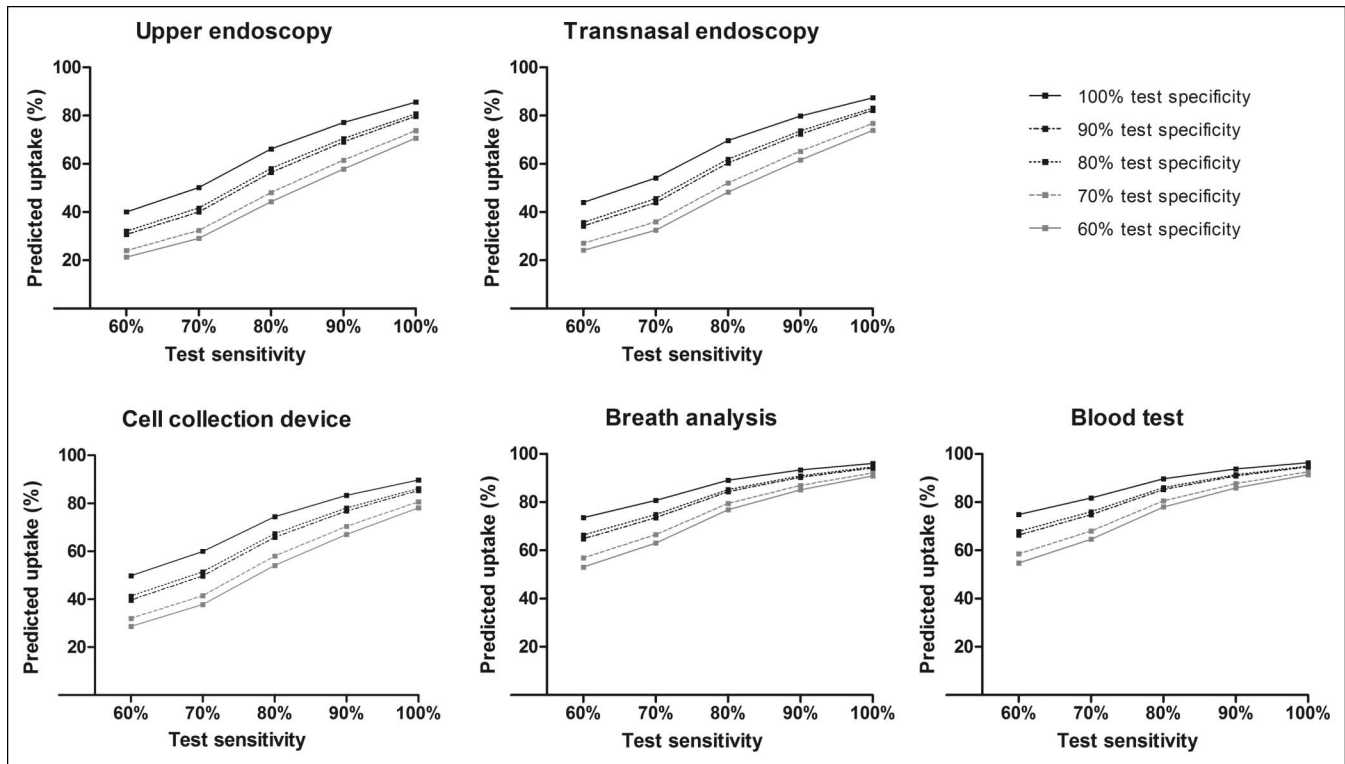


Figure 5. Predicted uptake for the different screening strategies at different levels of test sensitivity and specificity. (a) Conventional upper endoscopy. (b) Transnasal endoscopy. (c) Nonendoscopic cell collection devices. (d) Breath analysis. (e) A blood test.

screening methods were generally preferred above capsule cell collection devices and endoscopic techniques. However, to undergo a noninvasive screening test instead of endoscopic screening, test sensitivity and specificity had to be at least 80%. In this study, the predicted participation rate to be screened with any modality was 70%. This is comparable with that of other population-based screening programs in the Netherlands, with participation rates of 71%, 80%, and 61%, for colorectal, breast, and cervical cancer screening, respectively (24–26).

Since screening for EAC with minimally invasive screening modalities is still an innovative concept, the available literature on the support for EAC screening in the population is limited. An unlabeled DCE assessing attributes of an optimal EAC screening test found that test accuracy generally outweighs the importance of potential pain and discomfort (18). Various DCEs evaluating preferences for breast, cervical, and colorectal cancer screening reported, consistent with our results, that attributes related to test accuracy were more important than attributes related to the screening procedure (12,27). Although these studies targeted different cancer types and populations, their results provide face validity to the results of the current study.

Qualitative (survey) studies have determined the extent to which patients prefer minimally invasive screening tests compared with upper endoscopy. Nonsurprisingly, consistent with our findings, these studies showed that minimally invasive screening methods were preferred over upper endoscopy (28–30). Quantitative data on the acceptability of novel screening modalities have been obtained in EAC screening studies. The predicted uptake of screening with nonendoscopic cell collection devices (50%) and TNE (72%) based on our model, considering realistic attribute

levels, was higher than the uptake observed in screening trials (8,31). A study piloting screening with the Cytosponge in a primary care setting had a response rate of 19% (31). The participation rate in a population-based randomized screening trial for TNE was 46% (8). Besides targeting other populations and potential hypothetical bias, participants in these trials were likely not specifically informed on test accuracy. This underlines the importance of adequately informing the potential screening population about the accuracy of EAC screening tests to achieve informed decision-making, prevent unrealistic expectations, and above all to enhance uptake.

Both qualitative and quantitative studies were, however, limited by not determining underlying utilities and trade-offs and by comparing only 2 screening tests. Furthermore, participants were frequently recruited using market research or were already participating in pilot screening studies; hence, these results represent the views of a small group of most likely motivated individuals.

Interestingly, individuals with upper endoscopy experience had a more positive attitude toward upper endoscopy and EAC screening in general. There may have been an expose effect, where respondents tended to prefer screening tests merely because they are familiar with it. Also, an experience effect may have been present, in which anticipated discomfort is higher than actually experienced. Hence, anticipated discomfort may be reduced for successive endoscopies. This suggests that individuals who underwent endoscopic screening are willing to return for a subsequent upper endoscopy, which is important for the efficacy of screening and BE surveillance programs. This is supported by previous studies, which concluded that the overall burden of endoscopy was lower in patients undergoing regular endoscopic surveillance (4,32).

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		0.17		
Male	0.57 (−0.24 to 1.38)			
Female	Reference			
Age (yr)	−0.04 (−0.10 to 0.02)	0.15	−0.08 (−0.14 to −0.02)	0.02
Cultural background		0.30		
White	Reference			
Other	0.12 (−0.86 to 2.81)			
Civil status		0.10		
With a partner	1.07 (−0.83 to 1.08)			
Without a partner	Reference			
Highest level of education				
High school or less	Reference		Reference	
Vocational college	−0.55 (−1.72 to 0.62)	0.36	−0.58 (−1.90 to 0.73)	0.39
College/university	−0.97 (−1.86 to −0.08)	0.03	−1.11 (−2.10 to −0.11)	0.03
Current employment status				
Employed full-time	0.77 (−0.53 to 2.07)	0.24		
Employed part-time	0.63 (−0.64 to 1.90)	0.33		
Retired	0.01 (−1.23 to 1.25)	0.99		
Unemployed	Reference			
Family history of esophageal cancer	0.13 (−2.00 to 2.24)	0.91		
Knowing someone affected by esophageal cancer	0.34 (−0.75 to 1.46)	0.54		
Generic health status (EQ-5D) summary score	0.16 (−2.96 to 3.28)	0.92		
Previous diagnosis of cancer	−0.74 (−1.77 to 0.29)	0.16		
Worries about the own risk of developing cancer				
Sometimes, often, almost all the time	1.93 (0.91 to 2.96)	<0.001		
Not at all	Reference			
Participated in population-based cancer screening programs	0.39 (−0.56 to 1.34)	0.42		
Upper endoscopy experience	1.52 (0.51 to 2.54)	0.003	2.06 (0.51 to 3.61)	0.01
Current upper gastrointestinal symptoms	1.05 (0.03 to 2.06)	0.04		

CI, confidence interval.

Early detection and prevention of BE and EAC may be the best strategy to reduce the increasing incidence of EAC (3,6,33). Screening for EAC can only be successfully implemented if there is sufficient support among the target screening population. Information about trade-offs regarding EAC screening modalities and participation rates is valuable for the design, development, and potential implementation of effective EAC screening programs. Understanding individuals' preferences may assist healthcare providers and policymakers in their decision whether or not to implement minimally invasive screening tests in practice when they

become available for use. The results of this study are also relevant to predict participation rates for newer screening modalities with similar profiles or improved versions of a screening test, which can be used in modeling studies. Our findings illustrate a clear preference for noninvasive screening tests such as blood and breath tests. This supports further research on improving accuracy of circulating or exhaled biomarker-based tests for use in future EAC screening programs to meet priorities of the target screening population.

This current study has several strengths. First, preference data were obtained using stated-preference methodology. This is more

Table 3. Maximum acceptable risk calculations

Benefit attribute levels	Additional risk of missing esophageal cancer (%)	Additional risk of unnecessary follow-up testing (%)
Screening test		
From upper endoscopy to ...	Reference	Reference
Transnasal endoscopy	2.87	7.49
Cell collection device	7.05	18.39
Breath analysis	25.56 ^a	66.64 ^a
Blood test	26.76 ^a	69.78 ^a
Sensitivity	Not applicable	
From 60% sensitivity to ...		Reference
70% sensitivity		19.19
80% sensitivity		50.23
90% sensitivity		75.67
100% sensitivity		100
Test specificity		Not applicable
From 60% specificity to ...	Reference	
70% specificity	2.73	
80% specificity	9.94	
90% specificity	8.73	
100% specificity	16.14	

^aInterpretation: for a less invasive screening test (i.e., breath analysis or blood test) instead of conventional upper endoscopy, respondents were willing to accept, on average, a 26% additional risk of missing esophageal cancer and a 67%–70% risk of unnecessary follow-up testing.

effective in approximating real-world decisions than other survey methods because respondents choose between different sets of EAC screening characteristics rather than just ranking or rating single characteristics (34). Also, there is a lower tendency to provide socially desirable answers. DCEs provide information on trade-offs respondents are making and enable researchers to evaluate new screening options. In contrast to previous DCEs, we used a labeled design, in which the name of the screening test is mentioned in each choice option. A labeled DCE takes into account individual feelings and knowledge regarding EAC screening tests that cannot be described in an unlabeled DCE (35). This makes choice sets more realistic and less abstract which may add to the validity of the results. In addition, a patient-centered approach was followed to construct the choice tasks and the survey was extensively pretested and piloted in the target population. Task complexity and response burden were limited by including only 3 attributes and 14 choice tasks per respondent. Finally, comprehensibility was high because only 6.1% of respondents failed the dominance test and only 3.4% felt unsure about their choices made.

Although this study attempted to follow good research practices, limitations are also present. First, the sample may not be representative for the total Dutch general population. Our response rate was 37%, resulting in potential selective non-response. As nonresponders may have a more negative attitude toward screening than responders, our results may reflect a more positive attitude. Furthermore, participants were higher educated than the general population aged between 50 and 75 years. Our response rate was, however, comparable with other

published studies using surveys that recruited participants from the general population (28,36–38). In addition, this study reflects public preferences in the Netherlands, where the national population cancer screening programs are coordinated by the government. Costs of population screening and follow-up investigation are covered by the government and healthcare insurances, respectively. Preferences may be different in populations with other healthcare systems. Furthermore, limitations common to DCEs are ordering effects, hypothetical bias, and framing effects. First, ordering effects were minimized by randomizing participants to one of the survey versions because randomizing the order of choice tasks and attributes for each participant was not possible in a paper-based survey (39). Second, the predicted uptake of upper endoscopy was high. Although participants were informed on both direct and indirect consequences of endoscopy (e.g., missing a day from work and inability to operate a motor vehicle for 24 hours), hypothetical bias may exist and stated preferences may differ from the actual decision to participate in screening. Hypothetical bias was limited by using clinically relevant decision scenarios, the inclusion of labels of actual screening tests, and an opt-out option to resemble real-world screening practices (13,40). In addition, previous studies have shown good external validity of DCE results (41). Third, framing effects could have been present because the outcomes of a DCE depend on the choice of attribute levels, but were limited by extensive pretesting and framing information according to evidence from the literature (42,43).

In conclusion, this study suggests a substantial interest in EAC screening in the general population. Based on the

developed preference model, the predicted uptake was considerably higher for noninvasive screening tests than for capsule cell collection devices and endoscopic techniques. However, as sensitivity was more important than screening technique, a less burdensome alternative would unlikely improve screening uptake when associated with much lower accuracy for detecting BE or EAC. Hence, improving accuracy of minimally invasive screening strategies and increasing the knowledge of the potential screening population regarding this accuracy are important to increase screening participation. This explicit view of the public's interpretation of EAC screening may enhance the confidence of clinicians to take steps in undertaking a screening program with accurate minimally invasive screening techniques at its core.

CONFLICTS OF INTEREST

Guarantor of the article: Yonne Peters, MD.

Specific author contributions: Y.P.: study concept and design, data acquisition, quality control of data and algorithms, data analysis and interpretation, statistical analysis, manuscript preparation, editing, and review; P.D.S.: study concept and design, data interpretation, manuscript editing, and review, and study supervision.

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Study Highlights

WHAT IS KNOWN

- ✓ The future of esophageal cancer prevention relies on early detection of BE followed by effective endoscopic treatment when neoplastic changes are detected.
- ✓ Screening for EAC will only be beneficial if the screening program and the information provided connect with the preferences of the target screening population.
- ✓ Insight into barriers and facilitators for possible implementation is vital to a potential shift in the screening paradigm with minimally invasive screening modalities at its core.

WHAT IS NEW HERE

- ✓ Using a DCE, which is an established method to determine how individuals make complex decisions, we assessed individuals' preferences regarding innovative minimally invasive screening modalities.
- ✓ Improving the accuracy of noninvasive screening strategies and increasing awareness in the target population about their accuracies is essential to optimize informed choice and enhance screening participation.

TRANSLATIONAL IMPACT

- ✓ The developed preference model can be used to decide whether or not to implement EAC screening with minimally invasive tests in future guidelines.

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