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Screening for Barrett's Esophagus: Results from a Population-Based Survey

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Abstract

Background—Screening for Barrett's esophagus (BE) and adenocarcinoma (EAC) is controversial, but interest remains in finding the optimal method. Attitudes on screening within the community are unknown. We aimed to assess these attitudes via a survey.

Study—A mixed-mode survey was conducted in adults <50 years to assess awareness regarding BE, willingness to participate in screening, and preferences regarding method of screening. Methods evaluated were sedated endoscopy (sEGD), unsedated transnasal endoscopy (uTNE) and video capsule (VCE).

Results—A total of 136 from 413 (33 %) adults responded [47 % males, mean (SD) age 63 (10.2) years], and 26 % of responders knew of BE at baseline. After reading the information on BE, 72 % were interested in screening. A history of undergoing screening tests and GI symptoms were predictive of interest. Unsedated techniques were preferred by 64 % (VCE: 56 % and uTNE: 8 %) versus sEGD (36 %).

Conclusions—The majority of adults were willing to undergo screening for BE/EAC, with a preference for unsedated techniques.

Keywords

Barrett's esophagus; Screening; Esophageal adenocarcinoma; Transnasal endoscopy; Capsule endoscopy; Survey

Introduction

Barrett's esophagus (BE) is a condition in which squamous epithelium, that normally lines the distal esophagus, is replaced by intestinalized columnar epithelium [1]. It is the strongest risk factor for, and the only known precursor of, esophageal adenocarcinoma (EAC). Due to the exponential rise in the incidence of EAC over the past few decades [2] and persistently poor survival when detected after the onset of symptoms, interest remains in early detection and surveillance of precursor conditions (such as BE). On the other hand, reports of lower than previously estimated rates of progression in large BE cohorts continue to appear [3]. This raises a clinically relevant conundrum of rising EAC rates with poor survival, in the background of decreasing progression rates in clinically diagnosed BE. One potential explanation for this phenomenon could be the continuing high prevalence of undiagnosed BE in the community. Population-based studies have shown that almost two-thirds of subjects with BE remain undiagnosed [4]. Recent data suggests that increasing use of endoscopy in the Western world only reveals a third of all prevalent BE in the community [4, 5].

There are several challenges to screening for BE. This includes lack of precise identification of a high risk target population given modest correlation of BE, particularly short segment BE with gastroesophageal reflux (GER) symptoms [6-8]. Current inability to adequately risk stratify BE subjects following diagnosis and the variable natural history of BE remain additional barriers to screening [9]. Sedated endoscopy (sEGD) remains the gold standard for BE screening despite limitations [10, 11]. However, sEGD is limited in use due to its direct and indirect cost, invasiveness, discomfort and potential complications [12, 13]. Retrospective studies show screening followed by surveillance confers a survival benefit with EAC being diagnosed at an earlier stage with less lymph node involvement [14-17]. Therefore, a tool that is widely accessible and acceptable in the general population is lacking in clinical practice [18-20].

Professional gastroenterology organizations offer weak support for BE screening [11]. The AGA [7] recommends screening individuals with multiple risk factors, such as obese male Caucasians over the age of 50 with a longstanding history of GERD, recognizing that a large proportion of patients will fall outside this group. More recently, targeting higher risk

subsets (e.g. men <50 years old with chronic GERD symptoms) has been proposed to render screening strategies cost effective [21]. Despite lack of a consensus, community gastroenterologists continue to screen patients for BE. Recent advances in esophageal endotherapy techniques (resection and ablation), which have the ability to decrease the incidence of adenocarcinoma in BE subjects and treat dysplasia effectively, has also enhanced interest in the early detection of precursors to esophageal adenocarcinoma.

Non-invasive and non-endoscopic (such as capsule sponge) tests have been identified as cost effective alternatives for screening, particularly when applied to high risk and high prevalence populations [22]. However, there is currently no data on the acceptability of these techniques in the target or general populations. Unsedated trans-nasal endoscopy (uTNE) [19, 23-27] and video capsule endoscopy (VCE) [28, 29-33] have been studied in BE patients, and show promise as potential screening tools for BE. Though VCE is only modestly accurate for detecting BE [30], multiple investigators have reported the accuracy and feasibility of uTNE in BE screening and diagnosis [19, 23, 24, 27, 34]. Both sedated and unsedated techniques were recently assessed in a prospective study [34]. It showed patients were willing to participate in screening using either technique. However, it remains to be determined how acceptable these tests are in the general community as a screening tool in comparison to sEGD.

In this study, we aimed to assess the knowledge and attitudes regarding BE and screening for BE/EAC in subjects older than 50 in the population with reflux symptoms, who may be targeted for screening. The goal in this study was not to evaluate whether screening is appropriate, but to assess the knowledge and attitudes with respect to BE and comparative acceptability of sedated and unsedated techniques. By understanding patient preferences for screening tools, appropriate modalities and educational modules can hopefully be developed for future application.

Methods

Sample Selection

A population-based survey was undertaken in 2008 to randomly sample a community of adults aged 50 years and older within the seven county area of southeaster Minnesota (MN) surrounding Mayo Clinic Rochester. The geographic area sampled included Dodge, Fillmore, Goodhue, Mower, Olmsted, Wabasha and Winona counties. Addresses and telephone numbers of directory listed households were acquired through Genesys Marketing Systems Group, which works with ADVO, Inc., a company that maintains the residential address list for the US Postal Service (USPS). According to the latest USPS counts, there are a total of 107,943 households in the seven county areas. A separate list of individuals from these counties was obtained via appended random digit dialing (RDD). These two lists were linked via phone records, and individuals were then contacted for participation in the survey. The list was balanced on the gender distribution of residents in SE Minnesota and the selection stratified on gender.

Survey Design

The survey consisted of questions that assessed awareness of BE and its premalignant potential, willingness to participate in screening for BE/EAC, baseline acceptance of screening tests (such as colonoscopy, mammography, prostate cancer screening), preferences regarding optimal method of screening for BE, influence of a personal or family history of cancer on choosing to be screened, potential barriers to participation in population screening for BE/EAC, and demographic information (such as education and ethnicity). Educational information and description of sedated EGD (sEGD), unsedated transnasal endoscopy (uTNE) and video capsule endoscopy (VCE) was also included with the survey. A PhD level survey methodologist (TJB), with expertise in and experience conducting surveys of gastrointestinal related diseases reviewed this instrument. A copy of the survey is attached as “Appendix”.

Survey Administration

A mixed mode approach was used to contact chosen individuals. As previously described, individuals selected were asked to fill out a self-administered form that was sent to them via postal mail. If a completed questionnaire was not received 2 weeks after the mailing, telephone-interviewing staff at the Survey Research Center (SRC) initiated telephone contact and encouraged prospective respondents to mail in their completed questionnaires or to complete a telephone interview. Non-respondents at the end of the telephone reminder phase were sent another survey packet. This multi-method approach increases response by allowing responders to reply in a manner aligned with their preference [35-38].

Sample-Size Estimation

We hypothesized that 40 % of survey respondents would be willing to undergo VCE compared to 15 % willing to undergo any endoscopic procedure (uTNE and/or sEGD). These conservative estimates are based on our prior recruitment rates for VCE in Olmsted County [34], and rate of participation in a community colon cancer screening study reported in the literature [39]. Using a chi-square test to compare two independent proportions, a sample size of 100 patients responding to the survey was calculated to provide us with 80 % power (using a two-sided type 1 error of 5 %) to detect the difference in modality preference. We estimated sampling *approximately* 300 households in order to meet the sample size target of 100 responders for the proposed study.

Statistical Analysis

The association of age and gender with responding (i.e. returning a survey) was assessed using a logistic regression model with response (yes vs. no) as the dependent variable. The associations of willingness to participate in screening for BE, choice of screening test and participation in a focus group to identify the best approach to screening for BE/EAC (no/not sure/yes) was assessed using a multiple variable logistic regression model (with a generalized logit link function, the category, “not willing”, as the reference level). The variables studied were demographic characteristics [age, gender, education level, employment status, marital status], personal history [presence of upper GI symptoms, history of undergoing screening tests for breast or prostate, and colon cancer, history of

having a sEGD in the past] and family history [esophageal cancer, family history of any cancer]. Descriptive statistics (i.e. percentages) were also generated along with 95 % confidence intervals for these estimates.

Results

Surveys were sent to 413 subjects in SE Minnesota, and 136 surveys were returned (33 % response rate). The likelihood of response (i.e. returning a survey) was associated with age (OR per 10 years = 0.79 [95 % CI 0.65–0.96], $p = 0.02$, i.e. decreasing odds for response with increasing age), but not gender (OR [female: male] = 1.3 [95 % CI 0.8–1.9], $p = 0.27$).

Table 1 lists the baseline characteristics of the responders. In summary, 97 % (132/136) of responders were Caucasian, and 47 % males with a mean (SD) age of 63 (10.2) years. The ethnicity of the remaining 3 % is unknown. Within the non-responder group, 47 % of nonresponders were female, with a mean (SD) age of 65 (11) years. Approximately 85 % of the responders were married, 52 % were working full time and 40 % had a college degree or higher education. Of responders not working (34 % of the group), 30 % were homemakers. The age group recorded here is older than the GERD literature [40, 41], but in keeping with the general US population [42]. A substantial proportion of responders experienced esophageal symptoms within the last year: 45 % reported heartburn, 58 % reported reflux and regurgitation, and 26 % reported dysphagia. Additional details were not collected in the survey to decrease burden for responders. Females complained more frequently of acid regurgitation and heartburn than males (heartburn: 47 vs. 41 %; acid reflux: 61 vs. 55 %, respectively). Definitions of heartburn, reflux, regurgitation, and dysphagia were included in the survey (“Appendix”).

As a measure of acceptance of other screening tools, responders were asked about their history of obtaining a colonoscopy (all responders), mammography/pap smear (women) or prostate screening antigen (PSA) blood test (men). As described in the methods section, not all 136 responders answered this question. A high percentage of responders underwent colonoscopy [88 % (118/134)], mammography/pap smears [98 % (64/65)] and PSA testing [81 % (51/63)]. Of the responders, 16 % (21/134) had a prior diagnosis of cancer. Specifically, five patients had a history of breast cancer, three prostate cancer, two colon cancer, six skin cancer, one lung cancer and the remaining four were not disclosed on the survey and remain unlisted. Overall, 63 % had at least one first or second degree relative with cancer, and 2 % (3/136) of responders had either a father (1) or brother (2) with esophageal cancer.

To assess the baseline perception of cancer risk, subjects were asked to rate their perception of their individual risk of developing a cancer in the next 10 years, in comparison to individuals who were of similar age, gender and race. This was done qualitatively. Approximately 29 % (38/133) believed themselves to be at a higher risk of developing any cancer at 10 years. Specifically, 21 % believed they were at higher risk of developing esophageal cancer, 32 % colon or rectal cancer, 23 % breast cancer, 22 % prostate cancer, 11 % lung cancer and 9 % stomach cancer. Responders were allowed to choose multiple cancers when reporting their perceived risk.

Prior to reading the information provided on BE, baseline knowledge was assessed. Only 26 % (35/136) of responders had heard of BE prior to the survey. Regarding potential methods of detection, 57 % (78/136) were aware of sEGD, 18 % (24/136) of uTNE and 17 % (23/136) of VCE. Of those responders aware of sEGD, 36 % (28/78) had undergone sEGD for GI symptoms (such as reflux symptoms, abdominal pain, GI bleeding and diarrhea). The remaining 50 patients aware of sEGD did not disclose how they knew about sEGDs. For those previously aware of uTNE, 30 % (7/23) had undergone this test for reflux, abdominal pain and other reasons. Of those aware of VCE prior to the survey (23 responders), only one had the test for obscure GI bleeding.

After reading the survey and accompanying educational information ("Appendix"), 71 % (95/133) [95 % CI 65, 81] were moderately to extremely interested in obtaining a screening test for BE. The most common reason for having the test was to detect risk factors implicated for EAC. When asked for modality preference, 64 % (85/131) chose unsedated techniques (VCE: 56 % (74/131) [95 % CI 48, 65] or uTNE: 8 % (11/131) [95 % CI 4, 15]) and 36 % (46/131) chose sEGD [95 % CI 27, 44].

For those that chose to be screened with any modality, the most common reason was the safe, minimal risk profile of the test (67 % of responders). Other reasons were low cost (50 %) and lack of sedation (37 %). Conversely, the most common reason to decline screening was the lack of physician recommendation (47 %). Other reasons for declining screening were the lack of current symptoms (33 %), and insufficient information about the screening modalities (27 %).

Predictors of participation in screening were assessed using the responses from those returning the survey (Table 2). When asked if responders would be interested in a BE screening test, responses were not predicted by age, gender, prior upper endoscopy, personal and family history of cancer. However, responders with a prior history of colonoscopy [OR 4.95, 95 % CI (1.58, 15.51); $p = 0.006$] or GI symptoms in the past year [OR 3.37, 95 % CI (1.49, 7.63); $p = 0.004$] were more interested in screening, after adjusting for age and gender (Table 2). We also studied predictors of preference for unsedated versus sedated screening techniques (Table 3). A higher odds ratio value implies patient preference of a sedated technique. There were no predictors of response for sedated versus unsedated modality (uTNE or VCE vs. sEGD) when adjusted for age and gender (Table 3). Patients who had previously undergone sEGD showed a trend to preferring sedated techniques of screening, though this was not statistically significant [OR 3.94, 95 % CI (0.73, 21.28); $p = 0.11$] (Table 3).

Discussion

The population surveyed in this study is broadly representative of the population in SE Minnesota [43]. The purpose of this study was to assess acceptability of potential screening tests for BE/EAC in a community population, which may be at a higher risk of harboring BE. We specifically evaluated subjects thought to be at increased risk of developing BE/EAC (Caucasian subjects over the age of 50 with reflux symptoms) [44], and found that a majority of responders were willing to undergo screening with unsedated techniques (VCE

[uTNE). To our knowledge, this is the first report of its kind showing patient preference on screening modality when offered various choices, and also the baseline level of awareness of BE and esophageal adenocarcinoma in the community. While the at-risk population is predominantly male, our study had a slightly higher female response rate, which is in keeping with other cancer screening studies reported in the literature [42, 45, 46]. Females and patients between the ages of 50 and 59 are the most likely to respond to cancer-related questionnaires [45, 46]. There was limited representation of ethnic groups in our study, with 97 % responders being Caucasian. However, this is a reflection of the demographics of the SE Minnesota population. When we looked at the individual surveys, we were unable to elicit the ethnicity of the remaining 3 %. Caucasians do constitute the highest risk group for developing BE/EAC [47], and hence this study sheds light on the attitudes and preferences in this high-risk population.

The rates of GERD in this study are comparable to those reported in the literature. This study showed 45 % of responders with symptoms of heartburn, compared to 33–44 % in the GERD literature [48-50]. Similar high values for combination GERD symptoms, such as 58 % for acid reflux and regurgitation, have also been documented in the literature [41]. Unfortunately, the frequency of these symptoms was not collected in the survey. Approximately 26 % reported presence of any dysphagia within the last year. Non-obstructive dysphagia has previously been reported in 48 % of older GERD patients [50].

A higher perceived risk of cancer has been associated with an increased likelihood of undergoing a screening test [51, 52]. The percent of perceived risk by subjects in this study was comparable to the literature [46]. After providing the study group with information on BE and EAC, the percentage of responders concerned with developing EAC (21 %) was similar to that for breast (23 %) and colorectal (29 %) cancers. This suggests the perceived risk of developing EAC in the general population is similar to other cancers, despite the actual incidence being substantially lower. This discrepancy may be due to the prevalence of esophageal symptoms in this population. Demographic variables may account for some of this as well. Our study also reports a similar percentage of responders undergoing cancer screening to that in the general population, with breast cancer being most common (90 % in literature vs. 98 %), followed by prostate (86 % in literature vs. 81 %) and colorectal cancer (75 % in literature vs. 88 %) [46].

This survey suggests substantial interest in the community setting for BE/EAC screening, with 71 % of responders agreeing to be screened with any modality. However, practice of screening for BE/EAC in the community remains an issue with a lack of consensus. These non-invasive modalities have been prospectively studied in the BE/GERD literature, and have been found to be effective for detection [27, 53]. Thus, evaluating the acceptability of these technologies in the community setting is an important question to address. Cytosponge, a capsule sponge associated with biomarker testing [18, 51], was recently studied in the community setting in the UK [18], and showed promising sensitivity and specificity in detection of BE. However there was limited acceptance in the community, with only 18 % of the participants willing to have this done. The low acceptance could be a reflection of abnormal Cytosponge tests needing a conventional endoscopy as follow up in the study. Currently, this technology is only available in Europe. It is unclear if similar

acceptability will be demonstrated in the North American population. We did not identify patient factors that increased the likelihood of choosing unsedated versus sedated techniques, although those who chose unsedated were more likely to have had a prior sEGD ($p = 0.11$). This reflects the need for better screening modalities to be found and implemented.

A prior history of colonoscopy and GI symptoms were significant predictors of willingness to undergo screening for BE (Table 2). In the colon cancer literature, subjects with frequent office visits or history of cancer screening tests are more likely to undergo cancer screening [54, 55]. Our findings show a similar association for BE and EAC. It is unclear if the presence of symptoms results in heavier use of health care, as it has not been well studied in the literature [44]. There is conflicting data on whether responders who take more sick leaves due to digestive diseases are more likely to respond [56-58]. More studies are needed to evaluate the effects of active symptoms on screening behavior.

We acknowledge the limitations of this study. Since the survey was performed with the assistance of appended RDD and telephone follow-up, the population surveyed consisted of English speaking, US residents with access to a telephone. However, using two methodologies (mail and phone) to select patients allowed for random sampling of the population. Second, the population sampled was overwhelmingly (97 %) non-Hispanic whites. Thus, the data may not be generalizable to the other ethnic groups. In a survey study, non-responder bias may influence validity of study results [59], as our survey response rate was 33 %. A recent study reviewed the demographic, socioeconomic and medical histories between non-responders and responders to two GI surveys administered in Olmsted county, Minnesota [43]. Comparison of both groups showed higher BMI and single/unmarried status to be a predictor of non-response, with no association to medical comorbidities or presence of GI symptoms. We found older age predicted lower rates of response, but other demographic, socioeconomic and cancer history between responder and non-responder groups were non-contributory.

The diagnosis of BE is known to be associated with increased insurance costs [60], increased participation in surveillance visits, and associated endoscopic procedures [61, 62]. Currently, a surveillance program for BE/EAC is also controversial as there is no level 1 evidence to document a survival benefit from surveillance. However, surveillance to detect BE has been found to be cost effective [63]. VCE and uTNE have been studied in the BE population, and are considered potential alternatives to sEGD for screening. The willingness to undergo screening is influenced by the perception of the risk of the procedure and associated financial costs. Our survey did not describe these aspects in detail, and we did not ascertain whether such variables would affect the acceptance of these tests, as these variables would be difficult to assess in an unsupervised survey study.

In summary, though a minority of responders in SE Minnesota was initially aware of BE, following education about BE and EAC, a majority of responders with risk factors for BE/EAC expressed a willingness to undergo screening. Responders appear to be more willing to undergo screening by unsedated techniques, with VCE being the most acceptable.

Further studies on which populations should be targeted for screening are needed to make screening feasible and cost effective.

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Abbreviations

BE	Barrett's esophagus
EAC	Esophageal adenocarcinoma
GER	Gastroesophageal reflux
GERD	Gastroesophageal reflux disease
RDD	Random digit dialing
SEGD	Sedated endoscopy
SRC	Survey Research Center
USPS	United States Postal Service
uTNE	Unsedated transnasal endoscopy
VCE	Video capsule endoscopy

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Table 1Baseline characteristics of group that responded to the survey ($N = 136$)

Variable	Data
Mean age, years [SD]	63 (10.2)
Male gender [N , (%)]	64 (47)
Level of education: N , (%) [128 responders]	
High school graduate or less	29 (22)
Vocational school	13 (10)
Associate degree	32 (24)
College degree	31 (23)
Graduate or professional school	23 (17)
Marital status: N , (%) [132 responders]	
Married	112 (85)
Separated/divorced	9 (8)
Widowed	11 (10)
Employment status: N , (%) [129 responders]	
Working full time	67 (52)
Working part time	18 (14)
Not working for pay	44 (34)
Ethnicity: N , (%) [132 responders]	
Caucasian	132 (97)
African American	0
Asian	0
Native American	0
Prevalence of any gastrointestinal symptoms: N , (%) [182 responses]	
Prevalence of heartburn	69 (45)
Prevalence of acid regurgitation	78 (58)
Prevalence of dysphagia	35 (26)
History of cancer screening tests: N , (%) [233 responses]	
Prior history of pap smear (women)	64 (90)
Prior history of colonoscopy	118 (88)
Prior history of PSA screening	51 (80)

Not all questions asked were answered by survey responders

Table 2

Predictors of participation in BE/EAC screening

Predictor	Moderately/quite/ extremely interested (N = 95): n, (%)	Not at all/a little interested (N = 38): n, (%)	OR (95 % CI)	P value
Female	55 (77.5 %)	16 (22.5 %)	1.0 ref	0.26
Male	40 (62.5 %)	21 (32.8 %)	1.00 (0.96,1.04) ^a	
Age <60	49 (71.0 %)	20 (29.0 %)		0.84
Age ≥ 60	46 (68.7 %)	18 (26.9 %)	0.64 (0.29,1.39) ^a	
Have not had endoscopy	70 (68.6 %)	29 (28.4.0 %)	1.0 (ref)	0.88
Have had an endoscopy	24 (75.0. %)	8 (25.0 %)	1.08 (0.42,2.74) ^b	
Lower chance of cancer	64 (67.4 %)	30 (31.6 %)	1.0 (ref)	0.13
Same or higher chance of cancer	30 (79.0 %)	7 (18.4 %)	2.11 (0.81,5.51) ^b	
Not had a colonoscopy	6 (37.5 %)	10 (62.5 %)	1.0 (ref)	0.006
Had a colonoscopy	88 (74.6 %)	27 (22.9 %)	4.95 (1.58,15.51) ^b	
No personal history of cancer	77 (68.1 %)	34 (30.1 %)	1.0 (ref)	0.18
Personal history of cancer	18 (85.7 %)	3 (14.3 %)	2.47 (0.66,9.23) ^b	
No family history of cancer	29 (64.4 %)	15 (33.3 %)	1.0 (ref)	0.45
Family history of cancer	57 (73.1 %)	20 (25.6 %)	1.38 (0.60,3.17) ^b	
No GI symptoms	28 (56.0 %)	21 (42.0 %)	1.0 (ref)	0.004
GI symptoms	67 (78.8 %)	16 (18.8 %)	3.37 (1.49,7.63) ^b	
Less than college	27 (62.8 %)	15 (34.9 %)	1.0 (ref)	0.11
College or more	63 (73.3 %)	21 (24.4 %)	2.01 (0.86,4.67) ^b	
Not married	12 (63.2 %)	7 (36.8 %)	1.0 (ref)	0.22
Married	81 (71.7 %)	29 (25.7 %)	1.97 (0.67,5.81) ^b	
Not employed	28 (63.6 %)	13 (29.6 %)	1.0 (ref)	0.24
Employed	62 (72.9 %)	23 (27.1 %)	1.94 (0.64,5.92) ^b	

Bold values indicate statistical significance

^aLogistic model with age (continuous) and gender variables only^bLogistic model adjusted for age (continuous) and gender

Table 3

Predictors of participation in screening with sedated and unsedated techniques

Variable	Sedated (<i>n</i> = 14) versus unsedated (<i>n</i> = 38), OR (95 % CI)	<i>P</i> value
Female	1.0 (ref)	0.24
Male	2.20 (0.59, 8.18) ^a	
Age	1.03 (0.97, 1.10) ^a	0.33
Have not had endoscopy (sedated EGD)	1.0 (ref)	0.11
Have had an endoscopy (sedated EGD)	3.94 (0.73, 21.28) ^b	
Less than college	1.0 (ref)	0.43
College or more	0.59 (0.16, 2.21) ^b	
Not married	1.0 (ref)	0.45
Married	0.52 (0.10, 2.82) ^b	
Not employed	1.0 (ref)	0.15
Employed	0.24 (0.04, 1.67) ^b	

The logistic models used “sedated” as the corresponding event response, and thus increased odds (patient preference) for the sedated technique is indicated by odds ratio values >1.0, while odds ratio values <1.0 suggest a preference for the unsedated technique

^a Logistic model with age (continuous) and gender variables only

^b Logistic model adjusted for age (continuous) and gender