

# Rates of Endoscopy and Endoscopic Findings among People with Frequent Symptoms of Gastroesophageal Reflux in the Community

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**BACKGROUND:** Epidemiological studies have confirmed that gastroesophageal symptoms are highly prevalent. However, studies linking epidemiology with clinical or chart data are scarce. We aimed to determine the frequency of endoscopy and endoscopic findings, as well as predictors of health-care utilization, among people with reflux symptoms in the community.

**METHODS:** A previous survey of 2,118 Olmsted County, MN, residents in 1993 identified 242 subjects with frequent reflux symptoms (at least weekly) who received care at a medical center in the county. Data were abstracted from Mayo Clinic records between 1988 and 1998.

**RESULTS:** Overall, 130 of the 242 (54%, 95% CI 47–60%) had sought care for reflux. Twenty-five patients (10%) had visited a gastroenterologist; 47 (19%) had an upper endoscopy (EGD), 64 (26%) had an upper GI X-ray, and one had an ambulatory 24-h esophageal pH study. Long segment Barrett's esophagus was detected in 4 (9%) of those having an EGD and adenocarcinoma was found in one patient with Barrett's. Three patients had surgery for gastroesophageal reflux disease. Thirteen patients (5%) died, but no deaths were due to esophageal reflux or adenocarcinoma. Age, higher education, frequent heartburn, and dysphagia were all significant, independent predictors of consulting.

**CONCLUSIONS:** Although many people in the community have frequent reflux symptoms, few have investigations, and deaths were unrelated to reflux disease or its complications. Data from referral clinic or endoscopy series should not be extrapolated to the large numbers of people in the community with symptoms of reflux.

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## INTRODUCTION

Gastroesophageal reflux disease (GERD) is a highly prevalent condition: 44% of the U.S. population have monthly reflux symptoms and 20% report at least weekly reflux symptoms (1). When heartburn and acid regurgitation are dominant complaints, they are both highly specific for abnormal 24-h esophageal acid exposure (2). Acid exposure, in turn, is linked to the development of Barrett's esophagus and esophageal adenocarcinoma (3). The incidence of adenocarcinoma of the esophagus is rising (3). There has been increased interest in the association of symptomatic GERD with cancer following documentation of the striking risk of esophageal adenocarcinoma in a Swedish case-control study (4). Heartburn was associated with 8-fold increase in the risk of esophageal adenocarcinoma, and this increased to 44-fold in those with a duration of chronic symptoms longer than 20 yr (4). However, the incidence of esophageal adenocarcinoma remains low at 2 per 100,000 person-years (5, 6). The cancer incidence and

mortality rates in people with frequent reflux symptoms are not well known.

Health-care seeking in GERD has been formulated according to the "Iceberg" model of reflux proposed by Castell (7). Here, health-care seekers with GERD constitute only the tip of the iceberg; the majority of those with reflux do not seek health care, and hence a major portion of the GERD problem remains hidden from the view of physicians. In this model, chronic symptoms and complications are confined to the consultants. However, this iceberg model needs to be validated with clinical data from the community.

Likewise, a great deal has been written about the rates of findings of esophagitis, strictures and Barrett's esophagus among people having endoscopy, and the rate of cancer development in people with Barrett's esophagus (8–14). However, all of this literature only applies to people who have had an endoscopy. What is not known is how these endoscopy series apply to the population of people with reflux symptoms. Our concern is that risks identified in endoscopy series may not be

applicable to the general population. What has been missing are data on the rate at which people with reflux symptoms in the community sought endoscopy.

To address these issues, we aimed to estimate specific reflux-related health-care resource utilization in a subset of a randomly selected, population-based sample. Specifically, in subjects reporting frequent reflux symptoms, we aimed to estimate the proportion who sought care, had esophageal investigations (endoscopy, upper GI X-ray, 24-h esophageal pH study), died due to reflux-related complications, took antireflux medications (antacids, H<sub>2</sub> receptor antagonists, proton pump inhibitors), and had undergone surgery for reflux. We also aimed to identify predictors of health-care consulting among community subjects with frequent reflux symptoms.

## METHODS

### Subjects

The Olmsted County, MN, population comprises approximately 100,000 persons of whom 90% are white; socio-demographically, the community is similar to the U.S. white population (15). Eighty percent of the Olmsted County population resides within 5 miles of Rochester, and county residents receive their medical care almost exclusively from two group practices: Mayo Medical Center and Olmsted Medical Center. Mayo Clinic has maintained a common medical record system with its two affiliated hospitals (St. Mary's and Rochester Methodist) for over 95 yr. Migration into and out of the community by adults is relatively low. Recorded diagnoses and surgical procedures are indexed, including the diagnoses made for outpatients seen in office or clinic consultations, emergency room visits, or nursing home care, as well as the diagnoses recorded for hospital inpatients, at autopsy examination, or on death certificates (15). The system was further developed by the Rochester Epidemiology Project, which created similar indices for the records of other providers of medical care to local residents, most notably the Olmsted Medical Center and its affiliated Olmsted Community Hospital. Thus, details of the medical care provided to the residents of the county are available for study. Annually, over 80% of the entire population is attended by one or both of these two practices, and nearly everyone is seen at least once during any given 4-yr period. Therefore, the Rochester Epidemiology Project medical records linkage system also provides what is essentially an enumeration of the population from which samples can be drawn. After approval from the Mayo Clinic's Institutional Review Board, we used this system to draw a random sample of the population (Olmsted County residents attended in 1988–1991) stratified by sex, age (5-yr intervals between 25 and 74 yr), and health-care provider (Mayo and non-Mayo).

The complete (inpatient and outpatient) medical records of the individuals listed in the sample were reviewed, in the randomly selected order, until 100 subjects with Mayo Clinic registration numbers and 10 subjects without Mayo Clinic

registrations were found to be eligible in each of the 20 age and gender strata. Subjects were excluded if they died before they could be contacted ( $n = 5$ ), were unable to speak English ( $n = 6$ ), had a major psychotic episode ( $n = 42$ ), mental retardation ( $n = 15$ ), or dementia ( $n = 16$ ), had participated in a previous population survey by the authors ( $n = 8$ ), or had significant illnesses that might impair their ability to complete the questionnaire (*e.g.*, metastatic cancer, major stroke) ( $n = 17$ ).

The study questionnaire (see below) and an explanatory letter were mailed to this age-, sex-, and health-care provider-stratified sample of 2,277 residents of Olmsted County (1). Reminder letters were mailed at 2, 4, and 7 wk. Subjects who indicated at any point that they did not wish to complete the survey were not contacted further. Otherwise, nonresponders were contacted by telephone to request their participation and to verify their residence within the county. After mailing the survey to the people identified above, it was found that an additional five people had died and that another eight were unable to read the questionnaire, whereas 143 subjects had moved from the county and three more were assumed to have moved because they had no medical contacts in the previous 5 yr and could not be found by mail or telephone. Thus, a total of 2,118 eligible subjects received the survey (1).

### Questionnaire

The gastroesophageal reflux questionnaire (GERQ) was designed as a self-report instrument to measure symptoms experienced over the prior year and to collect past medical history (16). Previous testing has shown this instrument to be reliable, with a median kappa statistic for symptom items of 0.71 (interquartile range: 0.63–0.81) (16). In comparison with a physician interview, the questionnaire was also found to be a valid measure of symptoms (median kappa 0.62; interquartile range: 0.49–0.74). The GERQ contains 80 questions and a somatic symptom checklist (SSC), a measure of somatization. The first 32 questions examine the symptoms of heartburn, acid regurgitation, chest pain, and dysphagia in detail. The remaining 48 questions measure additional upper gut symptoms; respiratory complaints; physicians visits for GERD; total number of physician visits; medication use; health habits; past history of esophageal, gastric, cardiac, or pulmonary disease; and family history of heartburn or esophageal disease.

The following definitions were used to identify symptoms in the GERQ: heartburn, a burning pain or discomfort behind the breast bone in the chest; acid regurgitation, a bitter- or sour-tasting fluid coming into the throat or mouth; (3) chest pain, any pain or discomfort felt inside the chest but not including heartburn or any pain that is primarily in the abdomen; and (4) dysphagia (trouble swallowing), a feeling that food sticks in the throat or chest. Symptom frequency was measured on the following scale: 1, none in past year; 2, less than once a month; 3, about once a month; 4, about once a week; 5, several times a week; and 6, daily. Symptoms occurring once a week or more were defined as frequent. Symptom severity was assessed on a 4-point scale as follows: mild (can

be ignored), moderate (cannot be ignored but does not affect lifestyle), severe (affects lifestyle), and very severe (markedly affects lifestyle).

Those who reported either heartburn at least weekly or acid regurgitation at least weekly were considered to have frequent reflux symptoms. Those who reported chest pain were asked if it was due to their heart. Those who indicated “no” on the GERQ were considered to have noncardiac chest pain.

### Response Rate

A total of 1,524 of the 2,118 eligible subjects (72%) returned the survey (1). The mean age was 50.5 yr and 52% were women. Overall, women tended to respond more frequently than men (76% vs 69%), and the response rate increased with age. A significant ( $p < 0.05$ ) interaction of age and sex was detected because older men were more likely to respond than older women.

Using the data from the questionnaire, 304 (20%) reported frequent reflux symptoms. Among these, 242 (80%) had received at least some portion of their care at Mayo Medical Center and were eligible for the chart review portion of this study.

### Data Abstraction

A detailed chart abstraction was performed by study personnel using a standardized written abstract form for the 242 subjects. The complete (inpatient and outpatient) Mayo Clinic medical records were abstracted for the five yr before and after the symptom survey (1988–1998). The abstract form collected data for each endoscopy performed at Mayo as well as clinic visits, esophageal tests, medication use, surgical treatment for GERD, mortality, and cause of death.

Change in medication use (from the 1988–1993 period to the 1994–1998 period) was defined as follows:

Upgrade—Drugs in the following direction of progression: nil → antacid → sucralfate → H<sub>2</sub> receptor antagonist (H<sub>2</sub>RA) or prokinetic → proton pump inhibitor (PPI) → PPI and a second drug (17).

Downgrade—Drugs in the following direction of progression: PPI and a second drug → PPI → H<sub>2</sub>RA or prokinetic → sucralfate → antacid → nil (17).

### Statistical Analysis

The distributions of variables were recorded as percentages for discrete data and as mean ( $\pm$  SD) or median (range) for continuous responses. Exact binomial confidence intervals were computed for proportions. Logistic regression was used to assess the association between subsequent GERD consulting status (y/n) and symptoms (individually) adjusted for age, gender, and education. Odds ratios (95% CI) were calculated from the resulting model regression coefficients.

## RESULTS

### Subjects

The mean age at the time of the survey of the 242 subjects with frequent reflux symptoms was 50 ( $\pm$  14) yr (median 50,

range: 25–74 yr); 50% were males. The proportion of subjects in each decade of age was similar in men and women (data not shown).

### Health-care Seeking

All patients but one had at least one medical encounter, but only 130 patients (54%, 95% CI 47–60%) had a visit specifically for GERD. We could not determine whether care was sought for reflux in one patient. These 130 patients averaged five visits each. Heartburn and acid regurgitation were reported in the medical record by 98% and 76% of consulters, respectively. However, only 25 (10%, 95% CI 7–15%) had a visit with a gastroenterologist.

Table 1 presents the percentage of consulters by demographic and symptom categorizations. In those with heartburn about once a week, 43% were consulters, while in those with heartburn several times a week or daily, 62% were consulters. Forty-seven percent of those who did not have acid regurgitation were consulters, while up to 65% of patients who did have acid regurgitation were consulters, depending on the frequency. In those with noncardiac chest pain, 50% were consulters compared to 57% in those without chest pain.

Table 1 also shows odds ratios measuring the association of symptom status with seeking health care for GERD. Older age and a higher education level were significantly associated with consulting for GERD. After adjusting for age, gender, and education, increased heartburn frequency and having dysphagia were significantly associated with an increased odds of being a consulter. Acid regurgitation, and the severity or duration of reflux symptoms were not significant predictors, and neither was chest pain.

### Investigations

Of the total sample of 242 subjects, 47 (19%, 95% CI 15–25%) had an EGD and 64 (26%, 95% CI 21–32%) had an upper GI X-ray examination; only one patient had a 24-h esophageal pH test. Long segment Barrett's esophagus was detected in four patients (2%, 95% CI < 1–4%), which was 9% of those having an EGD. Adenocarcinoma was diagnosed in one patient with Barrett's esophagus over the follow-up period.

Potential predictors of undergoing EGD amongst those with frequent reflux symptoms are shown in Table 2. The significant predictors were female gender, severe heartburn, frequent and severe acid regurgitation, and dysphagia.

### Treatment and Outcomes

Between 1988 and 1993, 33% of the 242 subjects were taking medications for GERD including antacids (24%), H<sub>2</sub>RA (23%), PPI (4%), and miscellaneous (2%). By 1998, this had increased to 48% as follows: antacids (33%), H<sub>2</sub>RA (33%), PPI (17%), and miscellaneous (2%). Among those on medications in 1993, 35% upgraded and 32% downgraded their medications by 1998. Only three patients had fundoplication surgery for GERD. Overall, 13 (5%, 95% CI 3–9%) subjects

**Table 1.** Predictors of Consulting for Frequent Gastroesophageal Reflux Symptoms

Questionnaire Responses	n	% Consulters	OR (95% CI)*
Age			
<50	113	41%	1.57 (1.27, 1.95)†
≥50	127	65%	
Gender			
Female	120	58%	1.00 (referent)
Male	121	50%	0.72 (0.42, 1.23)
Education level			
Professional training or college graduate	68	51%	5.24 (1.49, 18.45)
Some college or high school graduate	155	56%	4.91 (1.52, 15.85)
Not high school graduate	16	31%	1.00 (referent)
Heartburn duration			
≤1 yr ago	32	34%	1.00 (referent)
>1–5 yr ago	61	54%	1.55 (0.60, 4.04)
>5 yr ago	145	57%	1.84 (0.76, 4.42)
Heartburn frequency			
About once a week	107	43%	1.00 (referent)
Several times a week or daily	133	62%	2.01 (1.16, 3.47)
Heartburn severity			
Mild	38	55%	1.00 (referent)
Moderate	179	52%	0.79 (0.37, 1.69)
Severe or very severe	23	61%	1.46 (0.48, 4.45)
Acid regurgitation duration			
None	58	47%	1.00 (referent)
≤1 yr ago	28	39%	0.92 (0.34, 2.46)
>1–5 yr ago	59	58%	1.48 (0.68, 3.24)
>5 yr ago	88	60%	1.75 (0.85, 3.61)
Acid regurgitation frequency			
None	58	47%	1.00 (referent)
<About once a month	117	53%	1.28 (0.65, 2.53)
About once a week	32	59%	1.76 (0.69, 4.45)
Several times a week or daily	26	65%	2.26 (0.81, 6.29)
Acid regurgitation severity			
None	58	47%	1.00 (referent)
Mild	50	58%	1.81 (0.80, 4.10)
Moderate	111	54%	1.27 (0.64, 2.54)
Severe or very severe	14	64%	2.24 (0.64, 7.92)
Chest pain			
No	118	57%	1.00 (referent)
Yes	121	50%	0.74 (0.43, 1.28)
Dysphagia			
No	162	48%	1.00 (referent)
Yes	74	65%	2.15 (1.17, 3.95)

\*Odds ratios (95% CI) for the demographic variables are from a logistic regression model that only includes the demographic variables as predictors. Odds ratios for the symptom variables are from models that only include the symptom of interest and the demographic variables as predictors.

†Odds ratio corresponding to a 10 yr increase in age.

died; no deaths were due to esophageal reflux or adenocarcinoma.

## DISCUSSION

In this study, we have linked epidemiologic and clinic data to try and better understand the community impact of GERD. As reported previously, reflux symptoms were common in the community with 20% of adults having heartburn or acid regurgitation at least once a week (1). The numbers of people receiving care were much smaller. We found that only about half of those with frequent reflux symptoms in a community seek health care over a 10-yr period, and just 10%

seek consultation with a gastroenterologist; only 19% had an endoscopy. Therefore, the study quantifies the “iceberg” concept of reflux (see Fig. 1) and provides community data in terms of the number with GERD likely to have serious underlying disease.

Predictors of consulting behavior for GERD remain poorly described, and the findings have been inconsistent. We found that heartburn frequency predicted consultation, as did the alarm feature, dysphagia. These findings are consistent with our previous population-based study, where 869 subjects reported an episode of heartburn or acid regurgitation, but only 47 (5%) reported a physician visit for heartburn or acid regurgitation in the past year; physician visits were associated with reflux symptom frequency (OR = 6.2; 95% CI 3.6–10.7) (1).

**Table 2.** Predictors of Esophagogastroduodenoscopy (EGD) for Frequent Gastroesophageal Reflux Symptoms.

Questionnaire Responses	N	% EGD	OR (95% CI)*
Age			
< 50	113	18%	1.27 (0.99, 1.63) <sup>†</sup>
≥ 50	127	21%	
Gender			
Female	120	28%	1.00 (referent)
Male	121	12%	0.33 (0.16, 0.68)
Education level			
Professional training or college graduate	68	19%	6.36 (0.73, 55.64)
Some college or high school graduate	155	21%	5.15 (0.64, 41.84)
Not high school graduate	16	6%	1.00 (referent)
Heartburn duration			
≤1 yr ago	32	9%	1.00 (referent)
> 1–5 yr ago	61	26%	3.53 (0.86, 14.45)
> 5 yr ago	145	19%	2.60 (0.67, 10.02)
Heartburn frequency			
About once a week	107	17%	1.00 (referent)
Several times a week or daily	133	22%	1.26 (0.64, 2.49)
Heartburn severity			
Mild	38	11%	1.00 (referent)
Moderate	179	20%	1.95 (0.61, 6.23)
Severe or very severe	23	35%	5.93 (1.44, 24.47)
Acid regurgitation duration			
None	58	14%	1.00 (referent)
≤1 yr ago	28	11%	0.65 (0.15, 2.84)
> 1–5 yr ago	59	25%	1.87 (0.68, 5.14)
> 5 yr ago	88	22%	1.94 (0.73, 5.11)
Acid regurgitation frequency			
None	58	14%	1.00 (referent)
< About once a month	117	16%	1.16 (0.45, 2.97)
About once a week	32	34%	3.36 (1.11, 10.16)
Several times a week or daily	26	27%	2.08 (0.62, 7.00)
Acid regurgitation severity			
None	58	14%	1.00 (referent)
Mild	50	16%	1.25 (0.41, 3.81)
Moderate	111	21%	1.41 (0.56, 3.59)
Severe or very severe	14	43%	6.41 (1.59, 25.81)
Chest pain			
No	118	17%	1.00 (referent)
Yes	121	22%	1.55 (0.79, 3.07)
Dysphagia			
No	162	13%	1.00 (referent)
Yes	74	34%	3.44 (1.71, 6.95)
Sought care for GERD			
No	111	8%	1.00 (referent)
Yes	130	29%	4.03 (1.77, 9.15)

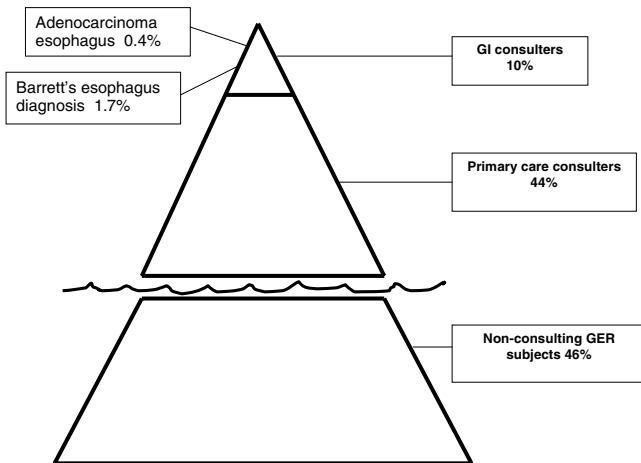
\*Odds ratios (95% CI) for the demographic variables are from a logistic regression model that only includes the demographic variables as predictors. Odds ratios for the symptom and care variables are from models that only include the variable of interest and the demographic variables as predictors.

<sup>†</sup>Odds ratio corresponding to a 10 yr increase in age.

Ho *et al.* found that heartburn consulters in Singapore were more likely to have severe heartburn and to have complained of nocturnal awakening due to heartburn than those who did not present to medical attention (18). Psychosocial factors may also be important in driving health-care seeking in GERD, but limited data are available and we could not assess the issue. Lydeard and Jones in the UK case-control study observed that consulters with dyspepsia (which included heartburn) were more likely to be worried about cancer and heart disease and to have experienced more disruptive or threatening life events than nonconsulters (19). In Hong Kong, Wong *et al.* reported that female gender, degree of depression, and

social morbidity as well as the frequency of heartburn were independent factors associated with health-care seeking behavior in ethnic Chinese contacted by a telephone survey (20). In a population study from Singapore, ethnic origin did not influence the consultation pattern (18).

Changes in medication use in GERD have not been well described in the literature. In a recent metaanalysis, van Pinxteren *et al.* concluded that antisecretory drugs are effective in the empirical treatment of GERD, including endoscopy negative reflux disease, but PPIs are not superior to H<sub>2</sub>RAs in the latter (17). We noted that only a third of the study population with clinically relevant reflux symptoms



**Figure 1.** “Iceberg” of frequent heartburn or acid regurgitation: Proportion at each level based on the current study findings of people with frequent reflux symptoms.

were using medications in 1993, although this had increased to 50% by 1998. Our results accord with Frank *et al.* who conducted in-person interviews with 2,056 United States and Canadian residents selected at random; less than a fifth with frequent reflux had undergone an endoscopy, medications were used by less than 50% (with antacids still accounting for the majority), and the uptake of surgery was very infrequent (21). Ho *et al.* in Singapore found similarly that 34% of the 53 heartburn sufferers received pharmacological therapy for their symptoms (18). Isolauri and Laippala mailed to a random sample of 2,500 people 20 yr and older in Norway; of the 1,700 responders, 10% had daily heartburn and/or regurgitation as dominant symptoms, but medication (most commonly antacids) was used by only 16% of those with symptoms (22).

Engel *et al.* calculated that a history of gastroesophageal reflux accounted for 30% of esophageal adenocarcinomas in a multicenter population-based case-control study (6). It has been suggested, based on endoscopic studies that a substantial minority with frequent GERD have Barrett's esophagus. Gerson *et al.* prospectively screened for the presence of Barrett's esophagus in asymptomatic subjects older than 50 yr of age undergoing screening sigmoidoscopy for colorectal cancer; Barrett's esophagus was identified in 25% of asymptomatic male veterans older than 50 yr of age (23). Other studies have reported similarly high rates of Barrett's esophagus of approximately 20%, although these reports may be skewed by serious selection biases (9,10). Nonetheless, this has led to calls for screening of those with frequent reflux symptoms by EGD to detect Barrett's and hopefully prevent the development of cancer although this is controversial (8,24). Of note, most subjects were not referred for endoscopy in the present study. We found that the prevalence of Barrett's esophagus among people with frequent reflux symptoms in the community that were endoscoped was 9%. These findings may reflect referral bias, as the rate of Barrett's esophagus was higher than

expected, based on the calculated population prevalence of clinically diagnosed Barrett's esophagus in Olmsted County in 1998 (12). El-Serag *et al.* found among 215 employees in a VA Medical Center who volunteered for upper endoscopy that only one person had Barrett's esophagus (0.4%), suggesting this may be rarer in the community than has been supposed (25). However, the prevalence of Barrett's esophagus in the U.S. community currently is unknown. The rate of adenocarcinoma in our GERD population with Barrett's was one in 242 patients with frequent reflux symptoms, although 10 yr of follow-up in a predominantly middle-aged population may have been insufficient to identify more cancers. In our study, deaths, however, were unrelated to GERD or its complications.

The strength of this study was the ability to link population-based data on symptoms to the clinical record. Thus, we are able to apply proportions to the population at large. We chose to review the time period of 5 yr before and after the questionnaire. Conceivably, health-care seeking might have changed since 1998 and thus further investigation is warranted. Moreover, we only abstracted data about care delivered at Mayo Clinic. Patients could have sought care at other providers and had endoscopy there. General surgeons elsewhere in Olmsted County perform endoscopy and reflux surgery. However, there are no other gastroenterologists in Olmsted County and all pH testing is done at the Mayo Clinic. Migration into and out of the county is limited; only 6% over a 4-yr period had migrated, indicating Olmsted County is a relatively stable population. Thus, our results are likely applicable to other GI practices. Finally, we did not abstract the records of those with infrequent or no reflux symptoms. Some of them may have had symptoms or they may have undergone clinical investigation, but the proportions are likely to be much less than those reported here among the symptomatic patients. The study has weaknesses. The Olmsted County population is not representative of non-Caucasians, and our findings cannot be generalized to other ethnic groups. The lack of endoscopy being undertaken in the whole population with frequent reflux symptoms limits the interpretability of the data on Barrett's esophagus.

In conclusion, about 50% with frequent reflux symptoms in the community seek care; a minority undergo investigation, with only one in five having an EGD and one in 10 consulting a gastroenterologist. Gastroenterologists need to be cautious in extrapolating their experience in endoscopy to the millions of adults in the United States with frequent reflux symptoms. Gastroenterologists must remember that they probably only see the “tip of the iceberg” and cannot assume that everyone with reflux symptoms has the same rate of findings as those who seek consultation and have an endoscopy.

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