CLINICAL GUIDELINE

ACP American College of Physicians
Best Practice Advice

Upper Endoscopy for Gastroesophageal Reflux Disease: Best Practice Advice From the Clinical Guidelines Committee of the American College of Physicians

Nicholas J. Shaheen, MD, MPH; David S. Weinberg, MD, MSc; Thomas D. Denberg, MD, PhD; Roger Chou, MD; Amir Qaseem, MD, PhD, MHA; and Paul Shekelle, MD, PhD, for the Clinical Guidelines Committee of the American College of Physicians*

Background: Upper endoscopy is commonly used in the diagnosis and management of gastroesophageal reflux disease (GERD). Evidence demonstrates that it is indicated only in certain situations, and inappropriate use generates unnecessary costs and exposes patients to harms without improving outcomes.

Methods: The Clinical Guidelines Committee of the American College of Physicians reviewed evidence regarding the indications for, and yield of, upper endoscopy in the setting of GERD, and to highlight how clinicians can increase the delivery of high-value health care.

Best Practice Advice 1: Upper endoscopy is indicated in men and women with heartburn and alarm symptoms (dysphagia, bleeding, anemia, weight loss, and recurrent vomiting).

Best Practice Advice 2: Upper endoscopy is indicated in men and women with:

- Typical GERD symptoms that persist despite a therapeutic trial of 4 to 8 weeks of twice-daily proton-pump inhibitor therapy.
- Severe erosive esophagitis after a 2-month course of proton-pump inhibitor therapy to assess healing and rule out Barrett esophagus. Recurrent endoscopy after this follow-up examination is not indicated in the absence of Barrett esophagus.
- History of esophageal stricture who have recurrent symptoms of dysphagia.

Best Practice Advice 3: Upper endoscopy may be indicated:

- In men older than 50 years with chronic GERD symptoms (symptoms for more than 5 years) and additional risk factors (nocturnal reflux symptoms, hiatal hernia, elevated body mass index, tobacco use, and intra-abdominal distribution of fat) to detect esophageal adenocarcinoma and Barrett esophagus.
- For surveillance evaluation in men and women with a history of Barrett esophagus. In men and women with Barrett esophagus and no dysplasia, surveillance examinations should occur at intervals no more frequently than 3 to 5 years. More frequent intervals are indicated in patients with Barrett esophagus and dysplasia.

Ann Intern Med. 2012;157:808-816. www.annals.org
For author affiliations, see end of text.

Gastroesophageal reflux disease (GERD) is among the most common conditions encountered in primary care practice. Its effect on quality of life is substantial (1, 2). Upper endoscopy is widely available and routinely done for diagnosis and management of GERD and its complications (3). However, the indications for this procedure are incompletely defined. Overuse of upper endoscopy contributes to higher health care costs without improving patient outcomes. The purpose of this best practice advice article from the Clinical Guidelines Committee of the American College of Physicians (ACP) is to describe the indications for, and yield of, upper endoscopy in the setting of GERD and to help primary care physicians make high-value decisions about referral of patients for upper endoscopy. In formulating these recommendations, a team of general internists, gastroenterologists, and clinical epidemiologists reviewed the literature on use of upper endoscopy in the setting of GERD, as well as epidemiology of GERD and esophageal adenocarcinoma. Clinical guidelines from professional organizations recommending use of upper endoscopy in GERD were compared. This document is not based on a formal systematic review but instead seeks to provide practical advice based on the best available evidence.

See also:

Print
Editorial comment. 827
Summary for Patients. I-28

Web-Only
Consumer Reports Patient Resource on High-Value Care for GERD

GERD, Barrett Esophagus, and Esophageal Adenocarcinoma

Gastroesophageal reflux disease is a condition that develops when reflux of stomach contents into the esophagus

* This paper, written by Nicholas J. Shaheen, MD, MPH; David S. Weinberg, MD, MSc; Thomas D. Denberg, MD, PhD; Roger Chou, MD; Amir Qaseem, MD, PhD, MHA; and Paul Shekelle, MD, PhD, was developed for the Clinical Guidelines Committee of the American College of Physicians: Paul Shekelle, MD, PhD (Chair); Roger Chou, MD; Paul Dallas, MD; Thomas D. Denberg, MD, PhD; Nick Fitterman, MD; Mary Ann Forciea, MD; Robert H. Hopkins Jr., MD; Linda L. Humphrey, MD, MPH; Tanveer P. Mir, MD; Holger J. Schünemann, MD, PhD; Donna E. Sweet, MD; and David S. Weinberg, MD, MSc. Approved by the ACP Board of Regents on 28 July 2012.

causes troublesome symptoms, complications, or both (4). Implicit in this definition is that tissue injury is not necessary to fulfill disease criteria. Indeed, 50% to 85% of patients with GERD have nonerosive reflux disease (5). As many as 40% of U.S. adults report some symptoms of reflux disease (chiefly heartburn and regurgitation), and 10% to 20% have symptoms on a weekly or more frequent basis (6–8). At least 2 acid-suppressive medications have been in the top 10 list of most prescribed medications in the United States every year from 2003 to 2009 (9) and more than 110 million prescriptions for these agents are filled yearly (10). Many more patients purchase over-the-counter acid-suppressive medications.

Approximately 10% of patients with chronic heartburn symptoms have Barrett esophagus, a metaplastic change of the esophageal lining from the normal squamous to specialized columnar epithelium (11). Both GERD and Barrett esophagus are associated with an increased risk for esophageal adenocarcinoma (12, 13). Although the absolute risk for adenocarcinoma of the esophagus in the general population remains low (26 cases per 1 million in the U.S. population), its incidence has increased more than 5-fold in the past 40 years (14). Patients with adenocarcinoma of the esophagus continue to have a poor prognosis, with a 5-year survival rate less than 20% (15). Most cases of esophageal cancer presents symptomatically, usually at a stage too advanced to allow curative intervention (16).

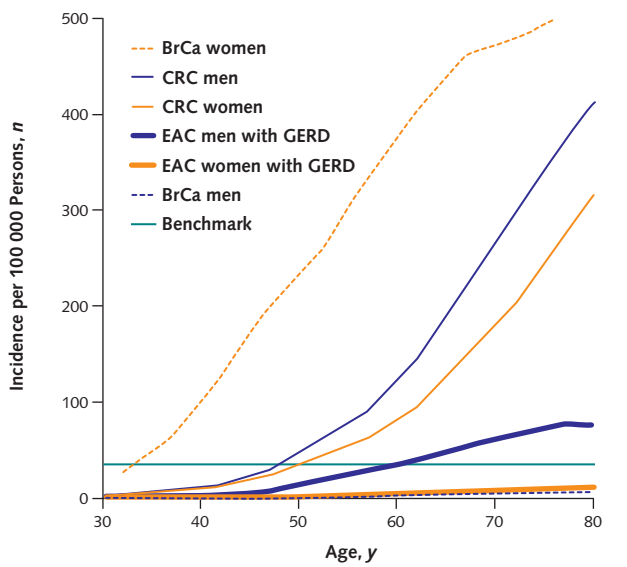
Adenocarcinoma of the esophagus is believed to develop from Barrett esophagus through progressive stages of dysplasia. Although progression is not inevitable, worsening dysplasia is associated with a greater risk for cancer. For example, whereas patients with Barrett esophagus and no dysplasia have a cancer risk of 0.1% to 0.5% per patient-year (13, 17), patients with Barrett esophagus and high-grade dysplasia have a cancer risk of 6% to 19% per patient-year (18–20).

Given the rising prevalence of chronic GERD symptoms (21), it is perhaps not surprising that the use of upper endoscopy for GERD indications is also rising. At present, GERD is the most common indication for upper endoscopy in the United States (3). Assessment of data from the Centers for Medicare & Medicaid Services show that although Medicare enrollment increased by 17% over the past decade, there was a concurrent increase of greater than 40% in use of upper endoscopy among Medicare beneficiaries (www.cms.gov/NonIdentifiableDataFiles). In addition, 13% of patients older than 50 years continuously covered by Independence Blue Cross (Pennsylvania) for 5 years had upper endoscopy during that period. Thirty-four percent of these examinations had a GERD indication. These data indicate that 4.4% of covered patients had upper endoscopy for GERD over a 5-year period, or nearly 1% each year (Snyder R. Personal communication.).

Endoscopy as a Screening Test for Adenocarcinoma of the Esophagus

In an effort to promote early detection and reduce the risk for death from adenocarcinoma of the esophagus, many clinicians perform screening upper endoscopy on patients with chronic GERD symptoms. Patients who are diagnosed with Barrett esophagus are then enrolled in endoscopic surveillance programs in which biopsies of the abnormal tissue are done to identify dysplastic changes (22). Although screening and surveillance programs should theoretically allow for the early detection of cancer, several factors limit the reach and effectiveness of such programs. First, GERD symptoms have poor sensitivity and specificity as predictors of cancer risk. Approximately 40% of patients who develop adenocarcinoma of the esophagus have no heartburn (12, 23, 24), and the yearly risk for cancer among persons aged 50 years or older who have heartburn has been estimated at 0.04% (25). Second, focusing on heartburn ignores other predictors of disease. There is a striking predominance of male sex in esophageal adenocarcinoma, with approximately 80% of cancer occurring in men (26, 27). In fact, men without GERD symptoms appear to have a higher risk for Barrett esophagus than women with GERD symptoms (28). Data suggest that the risk for esophageal adenocarcinoma in women with GERD is roughly equal to that of breast cancer in men (**Figure 1**) (29).

Figure 1. **Cancer incidence as a function of age.**



Estimated incidence of EAC in men and women with weekly GERD symptoms as a function of age, compared with other types of cancer, including BrCa in women and men and CRC in men and women. The green horizontal line represents incidence of CRC in women aged 50 years (an age at which endoscopic screening procedures are endorsed by many organizations) as a benchmark comparison. Note that the incidences of EAC in women with GERD and BrCa in men overlap (from reference 29). BrCa = breast cancer; CRC = colorectal cancer; EAC = esophageal adenocarcinoma; GERD = gastroesophageal reflux disease.

Endoscopy with random biopsies may not detect dysplasia or early cancer because the dysplastic lesion often involves only a small percentage of the total surface area of the Barrett segment (30). Histologic interpretation of endoscopic biopsy specimens is difficult because of small tissue samples and the somewhat subjective nature of grading dysplasia (31, 32). Another challenge associated with endoscopic surveillance is the requirement for patient adherence to serial endoscopy sessions. Data show that a substantial number of patients eligible for surveillance may not return for recommended examinations (33).

In addition, the utility of endoscopic surveillance is limited by the low incidence of adenocarcinoma in nondysplastic Barrett esophagus. Although patients with this disorder are at higher risk for cancer than the general public, the absolute risk for this cancer in patients with Barrett esophagus but no dysplasia is still low. A recent population-based study found that less than 2% of patients with nondysplastic Barrett esophagus followed for more than 5 years developed cancer (17). Finally and most important, no direct evidence shows that screening and surveillance endoscopy programs actually decrease death from adenocarcinoma of the esophagus. Cohort and case–control studies demonstrate that cancer discovered through endoscopic screening and surveillance do present at earlier stages, with less lymph node involvement, and are associated with longer survival than cancer presenting symptomatically (34–37). However, lead time and length bias limit the interpretability of such data (38). Given that 1% to 5% of the U.S. adult population may have Barrett esophagus (39, 40), the public health and financial implications of endoscopic screening and surveillance programs are substantial.

The 3 major U.S. gastroenterologic professional societies have all released guideline documents with differing recommendations, which may confuse clinicians about the most appropriate course. The American Society of Gastrointestinal Endoscopy recommends that screening upper endoscopy be considered "in selected patients with chronic, longstanding GERD" (41). They identify frequent GERD symptoms (several times per week), chronic GERD symptoms (symptoms for >5 years), age older than 50 years, white race, male sex, and nocturnal reflux symptoms as risk factors. American Gastroenterological Association guidelines recommend against screening the general population with GERD for Barrett esophagus and esophageal adenocarcinoma but say that it should be considered in patients with GERD who have several risk factors associated with esophageal adenocarcinoma (42, 43), including age 50 years or older, male sex, white race, hiatal hernia, elevated body mass index, and intra-abdominal distribution of fat. Neither the relative importance of these risk factors nor the number of risk factors necessary to trigger screening is stated. Lastly, the American College of Gastroenterology guidelines note that "screening for Barrett's esophagus in the general population cannot be recommended at this time. The use of screening in selective populations at higher risk remains to be established, and therefore should be individualized" (22). They, too, note GERD symptoms and body mass index as risk factors for Barrett esophagus. As acknowledged by the authors, formulation of these guidelines was hampered by the generally poor quality of data about the use of endoscopic screening and surveillance programs. In many cases, expert opinion formed the basis for specific recommendations.

What Is the Appropriate Use of Upper Endoscopy in the Setting of Chronic GERD?

Because of its high prevalence in the general population, care of patients with GERD is largely within the domain of primary care providers. In many health care systems, primary care providers refer patients for "open-access" upper endoscopy (endoscopy without antecedent specialist consultation). Given the dearth of data substantiating the clinical effectiveness of endoscopy in patients with chronic GERD symptoms and no alarm symptoms, what should the primary care provider do?

In most patients with typical GERD symptoms, such as heartburn or regurgitation, an initial trial of empirical acid-suppressive therapy with once-daily proton-pump inhibitors (PPIs) is warranted and endoscopy is not indicated. This may be escalated to twice-daily therapy if once-daily therapy is unsuccessful. If 4 to 8 weeks of twice-daily empirical PPI therapy is unsuccessful, further investigation with endoscopy is recommended (42). Any PPI (dexlansoprazole, esomeprazole, lansoprazole, omeprazole, pantoprazole, or rabeprazole) may be used because absolute differences in efficacy for symptom control and tissue healing are small (44–46). For most PPIs, dosing 30 to 60 minutes before a meal may provide optimal efficacy.

In contrast to issues surrounding endoscopic screening for esophageal cancer, the value of endoscopy is well-substantiated in several clinical settings. Gastroesophageal reflux disease associated with the alarm symptoms of dysphagia, bleeding, anemia, weight loss, or recurrent vomiting merits investigation with upper endoscopy because of its yield of potentially clinically actionable findings, such as cancer of the esophagus or stomach, bleeding lesions in the foregut, or stenosis of the esophagus or pylorus. In a recent analysis of approximately 30 000 patients with dysphagia who had endoscopy, greater than 50% had important clinical findings (most commonly, esophageal stricture) (47). Also, patients with a documented history of severe erosive esophagitis (grade B or worse on a validated A-to-D scoring system [48]) treated with PPIs have a substantial rate of incomplete healing with medical therapy (44, 49, 50) and may have Barrett esophagus in the areas of previously denuded esophageal epithelium (51–53). For these reasons, follow-up upper endoscopy is recommended after 8 weeks of PPI therapy for severe esophagitis to ensure healing and to rule out Barrett esophagus. If this examination is nor-

mal, further routine upper endoscopy is not indicated. The use of upper endoscopy in patients with esophageal stricture secondary to GERD is largely symptom-based. Because recurrence of strictures is common (54, 55), repeated upper endoscopy with dilatation may be required. However, in patients with a history of stricture who remain asymptomatic, routine endoscopy is not necessary.

In patients with well-controlled symptoms, should screening endoscopy be done to assess for Barrett esophagus or adenocarcinoma? Although current data and the published guidelines do not allow a definitive assessment of the value of endoscopic screening, several conclusions may be drawn. First, because of the difference in cancer incidence between men and women and the low absolute risk for this cancer in women (26, 27), routine screening of women, regardless of GERD symptoms, cannot be recommended. Similarly, given the very low incidence of esophageal adenocarcinoma in younger patients (56), routine screening of those younger than 50 years, regardless of GERD symptoms, does not seem to be warranted. If endoscopic screening of patients with GERD symptoms is to be pursued, men older than 50 years will provide the highest yield of both Barrett esophagus and early adenocarcinoma. Decision making in men older than 50 years with GERD symptoms should be individualized, but the low quality of the evidence in support of screening must be recognized. The decision making should also include an assessment of the patient's life-limiting comorbid conditions.

Among patients who have endoscopy and are found to have Barrett esophagus, many organizations recommend endoscopic surveillance (22, 41, 57). Again, these recommendations rest on observational data from surveillance programs showing improved outcomes in cancer found as part of surveillance programs, compared with those presenting symptomatically (36, 37). Although no studies have evaluated comparative benefits of various screening intervals for patients with Barrett esophagus without dysplasia, upper endoscopy at 3- to 5-year intervals has been recommended on the basis of natural history data and expert opinion (22, 41, 57). More frequent endoscopy is reserved for the subset of patients who develop low- or high-grade dysplasia, as they face a higher risk for progression to cancer.

Patients with chronic GERD symptoms whose screening upper endoscopy showed no Barrett esophagus may wonder about the utility of recurrent examinations. Because patients are accustomed to the paradigm of periodic cancer screening examinations, the question, "When will I need it again?" is common. In patients with chronic GERD (symptoms for more than 5 years or medical therapy for more than 5 years to avert symptoms) whose initial endoscopic screening results were negative, no additional endoscopic screening is necessary, even if the patient continues medical therapy. Observational data show that the likelihood of development of Barrett esophagus in the 5 years after a negative result in such patients is less than 2% (58), making the yield of serial examinations after an initial negative result very low. Therefore, routine serial endoscopy in patients with initially negative results for Barrett esophagus is not recommended.

Does Practice Follow the Evidence?

Limited data suggest that clinicians who care for patients with GERD symptoms often do not follow suggested practice. Using liberal criteria defined by the American Society of Gastrointestinal Endoscopy for appropriateness of upper endoscopy (59), studies demonstrate that 10% to 40% of upper endoscopies are not "generally indicated" (60–64). Common errors include serial upper endoscopies for patients with GERD and no Barrett esophagus, examinations for Barrett surveillance at intervals that are too short, and early endoscopy in patients without alarm symptoms or factors associated with elevated risk for Barrett esophagus or esophageal cancer. Surveys of endoscopists demonstrate that they often would do screening upper endoscopy in situations where it would be extremely low yield (65). In addition, endoscopists often recommend surveillance intervals in patients with known Barrett esophagus shorter than those merited based on the natural history (65–68).

What Factors May Promote Overuse of Upper Endoscopy?

An oft-cited factor that promotes overuse of upper endoscopy is fear of medicolegal liability in the event that endoscopy is not done and esophageal adenocarcinoma subsequently develops. Indeed, in 1 survey of endoscopists, a primary predictor of use of upper endoscopy in low-yield situations was previous identification as a defendant in a malpractice suit (65). Financial incentives may also play a role, given that upper endoscopy constitutes approximately one third of the case load for the average endoscopist (3). Patient and primary caregiver expectations may also promote overuse. Because patients and primary care providers anticipate serial cancer screening, they may inappropriately view no screening or a once-in-a-lifetime screening upper endoscopy for GERD symptoms as inadequate on the basis of an inflated estimate of the risk for precancerous or cancerous lesions. Similarly, patients who have Barrett esophagus and no dysplasia may be dissatisfied with a 3- to 5-year interval of surveillance examinations. Once they are given the diagnosis of a "precancerous condition," patients (and their primary care providers) may prefer more frequent endoscopic surveillance. Patients with Barrett esophagus may grossly overestimate their risk for esophageal cancer (69).

Potential Harms of Endoscopy Overuse

Upper endoscopy is a low-risk procedure, carrying a 1-in-1000 to 1-in-10 000 risk for complications, which include perforation, cardiovascular events, or death (70, 71).

Other rare, but real, risks inherent in upper endoscopy include aspiration pneumonia, respiratory failure, hypotension, dysrhythmia, or other reactions to the anesthetic agents. Despite the uncommon nature of endoscopy complications, given the large number of patients with chronic GERD symptoms, overuse of upper endoscopy in patients with GERD symptoms implies the potential for thousands of complications (25). Costs and complications are also associated with downstream diagnostic tests or unnecessary treatment due to erroneous findings on upper endoscopy. For example, some patients with Barrett esophagus may have esophagectomy for low-grade dysplasia misdiagnosed as high-grade dysplasia or cancer. Similarly, many patients labeled as having Barrett esophagus, when examined retrospectively, do not fulfill the criteria for diagnosis and are incorrectly labeled as having the disease (72).

In addition to potential physical risks to patients' health, overuse of upper endoscopy has substantial negative financial implications for both patients and society. On average, upper endoscopy costs more than $800 per examination (73). Even insured patients may have to bear a substantial portion of this cost in the form of copays and deductibles. The indirect costs to the patients and their families are also substantial. Because conscious sedation is generally used for these examinations, both the patient and a guardian are generally absent from work or other activities on the day of the examination. Because many patients who have upper endoscopy for GERD symptoms are aged 65 years or older, much of the direct cost of endoscopic screening and surveillance is sustained by the Medicare program.

How Can Primary Care Physicians Promote Rational Use of Upper Endoscopy in the Setting of GERD?

Figure 2 summarizes ways in which the primary care provider can promote appropriate use of upper endoscopy. Primary care providers increasingly act as the source for endoscopic referral. Once an open-access referral has been generated, it is highly likely that the examination will be done because of patient expectations and the gastroenterologist's desire to provide the requested service.

In patients being referred to a gastroenterologist or surgeon for consultation about upper gastrointestinal symptoms, as opposed to referral for the technical service of endoscopy, both the patient and the consultant should clearly understand that a cognitive service to aid in medical management, not a "referral for upper endoscopy," is the goal of the evaluation. In addition, understanding the epidemiology and risk factors for Barrett esophagus, adenocarcinoma of the esophagus, and other complications of GERD can help primary care physicians make more rational decisions about referral for endoscopy.

ACP Best Practice Advice

Best Practice Advice 1

Upper endoscopy is indicated in men and women with heartburn and alarm symptoms (dysphagia, bleeding, anemia, weight loss, and recurrent vomiting).

Best Practice Advice 2

Upper endoscopy is indicated in men and women with:

- *Typical GERD symptoms that persist despite a therapeutic trial of 4 to 8 weeks of twice-daily PPI therapy.*
- *Severe erosive esophagitis after a 2-month course of PPI therapy to assess healing and rule out Barrett esophagus. Recurrent endoscopy after this follow-up examination is not indicated in the absence of Barrett esophagus.*
- *History of esophageal stricture who have recurrent symptoms of dysphagia.*

Best Practice Advice 3

Upper endoscopy may be indicated:

- *In men older than 50 years with chronic GERD symptoms (symptoms for more than 5 years) and additional risk factors (nocturnal reflux symptoms, hiatal hernia, elevated body mass index, tobacco use, and intra-abdominal distribution of fat) to detect esophageal adenocarcinoma and Barrett esophagus.*
- *For surveillance evaluation in men and women with a history of Barrett esophagus. In men and women with Barrett esophagus and no dysplasia, surveillance examinations should occur at intervals no more frequently than 3 to 5 years. More frequent intervals are indicated in patients with Barrett esophagus and dysplasia.*

The ACP has found evidence that upper endoscopy is indicated in patients with heartburn and alarm symptoms, such as dysphagia, bleeding, anemia, weight loss, and recurrent vomiting. However, upper endoscopy is not an appropriate first step in most patients with GERD symptoms and is indicated only when empirical PPI therapy for 4 to 8 weeks is unsuccessful. Upper endoscopy is not indicated in asymptomatic patients with a history of esophageal stricture but is appropriate in patients with recurrent symptoms of dysphagia.

Screening upper endoscopy should not be routinely done in women of any age or in men younger than 50 years regardless of GERD symptoms because the incidence of cancer is very low in these populations. Screening endoscopy may be indicated in men older than 50 years with several risk factors for Barrett esophagus. This screening decision should include an assessment of the patient's life-limiting comorbid conditions. Risk factors include chronic GERD symptoms (symptoms of >5 years' duration), nocturnal reflux symptoms, hiatal hernia, elevated body mass index, tobacco use, and intra-abdominal distribution of fat. If an initial screening examination is negative for Barrett esophagus or esophageal adenocarcinoma, recurrent peri-

Figure 2. **Summary of the ACP best practice advice: upper endoscopy in the setting of GERD.**

ACP
American College of Physicians
Best Practice Advice

Upper Endoscopy for GERD: Best Practice Advice From the Clinical Guidelines Committee of the American College of Physicians

Disease or condition	GERD
Target audience	Internists, family physicians, and other clinicians
Target patient population	Men and women with GERD
Intervention	Upper gastrointestinal endoscopy
Evidence that using upper endoscopy in patients without appropriate indications does not improve outcomes	Multiple cohort studies demonstrate low yield of serial upper endoscopy for either Barrett esophagus or esophageal adenocarcinoma in patients not found to have Barrett esophagus on initial evaluation. Frequent endoscopic evaluation of patients with nondysplastic Barrett demonstrates a low rate of malignant transformation. Cost-effectiveness analyses demonstrate poor cost-effectiveness of frequent endoscopic surveillance sessions in patients with Barrett esophagus.
Harms of upper endoscopy	Complications related to sedation for the examination, perforation, bleeding, and pulmonary aspiration Misdiagnosis leading to inappropriately aggressive therapy Financial implications related to insurance due to labeling with Barrett
Approaches to overcome barriers to evidence-based practice	Appropriate setting of expectations regarding management of GERD Address patient uncertainty: Discuss the low likelihood of esophageal cancer in the setting of uncomplicated GERD symptoms and the limited role of endoscopy in guiding therapy in GERD Clarify the purpose of consultation with subspecialists in communication with the patient and the subspecialist Limit referral to open-access endoscopy units to the best practice advice listed below
Talking points for clinicians when discussing the use of upper endoscopy in the setting of GERD	The likelihood of esophageal cancer in people with heartburn is very low. Even in cases of severe irritation of the esophagus, the preferred first treatment will be acid-suppressive therapy. In most cases, early endoscopy does not change treatment plans. Unlike other chronic diseases, patients do not need to be evaluated for GERD on regular intervals. Frequent endoscopy in most patients with Barrett esophagus has not been shown to be better at preventing cancer than endoscopy on 3- to 5-y intervals.
Best practice advice	*Best practice advice 1: Upper endoscopy is indicated in men and women with heartburn and alarm symptoms (dysphagia, bleeding, anemia, weight loss, and recurrent vomiting).* *Best practice advice 2: Upper endoscopy is indicated in men and women with:* *Typical GERD symptoms that persist despite a therapeutic trial of 4–8 wk of twice-daily PPI therapy.* *Severe erosive esophagitis after a 2-mo course of PPI therapy to assess healing and rule out Barrett esophagus. Recurrent endoscopy after this follow-up examination is not indicated in the absence of Barrett esophagus.* *History of esophageal stricture who have recurrent symptoms of dysphagia.* *Best practice advice 3: Upper endoscopy may be indicated:* *In men older than 50 y with chronic GERD symptoms (symptoms for more than 5 y) and additional risk factors (nocturnal reflux symptoms, hiatal hernia, elevated BMI, tobacco use, and intra-abdominal distribution of fat) to detect esophageal adenocarcinoma and Barrett esophagus.* *For surveillance evaluation in men and women with a history of Barrett esophagus. In men and women with Barrett esophagus and no dysplasia, surveillance examinations should occur at intervals no more frequently than 3–5 y. More frequent intervals are indicated in patients with Barrett esophagus and dysplasia.*

BMI = body mass index; GERD = gastroesophageal reflux disease; PPI = proton-pump inhibitor.

odic endoscopy is not indicated. Among patients found to have Barrett esophagus on screening upper endoscopy, endoscopic surveillance may be indicated at 3- to 5-year intervals. More frequent endoscopic examinations are reserved for patients with low- or high-grade dysplasia because of their higher risk for progression to cancer.

Unnecessary endoscopy exposes patients to preventable harms, may lead to additional unnecessary interventions, and results in unnecessary costs. Patient education strategies should be used to inform patients about current and effective standards of care.

Figure 2 summarizes ACP's best practice advice for the upper endoscopy in the setting of GERD.

Conclusion

Endoscopy has revolutionized the diagnosis and management of gastrointestinal illness. However, inappropriate

use has the potential to add cost with no benefit. Data suggest that upper endoscopy in the setting of GERD symptoms is useful only in a few, well-circumscribed situations, as previously reviewed. Avoidance of repetitive, low-yield endoscopy that has little effect on clinical management or health outcomes will improve patient care and reduce costs.

From the University of North Carolina School of Medicine, Chapel Hill, North Carolina; Fox Chase Cancer Center and American College of Physicians, Philadelphia, Pennsylvania; Harvard Vanguard Medical Associates, Auburndale, Massachusetts; Oregon Health & Science University, Portland, Oregon; and West Los Angeles Veterans Affairs Medical Center, Los Angeles, California.

Note: Best practice advice papers are "guides" only and may not apply to all patients and all clinical situations. Thus, they are not intended to override clinicians' judgment. All ACP best practice advice papers are considered automatically withdrawn or invalid 5 years after publication or once an update has been issued.

Disclaimer: The authors of this best practice advice paper are responsible for its contents, including any clinical or treatment recommendations. No statement in this article should be construed as an official position of Veterans Affairs.

Financial Support: Financial support for the development of this best practice advice paper comes exclusively from the ACP's operating budget. Dr. Shaheen is supported by the National Cancer Institute (grant U54CA163060 and U54CA156733).

Potential Conflicts of Interest: Any financial and nonfinancial conflicts of interest of the group members were declared, discussed, and resolved according to ACP's conflicts of interest policy. A record of conflicts of interest is kept for each Clinical Guidelines Committee meeting and conference call and can be viewed at www.acponline.org/clinical_information/guidelines/guidelines/conflicts_cgc.htm. Disclosures can also be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M12-0618.

Requests for Single Reprints: Amir Qaseem, MD, PhD, MHA, American College of Physicians, 190 N. Independence Mall West, Philadelphia, PA 19106.

Current author addresses and author contributions are available at www.annals.org.

References

1. **Havelund T, Lind T, Wiklund I, Glise H, Hernqvist H, Lauritsen K, et al.** Quality of life in patients with heartburn but without esophagitis: effects of treatment with omeprazole. Am J Gastroenterol. 1999;94:1782-9. [PMID: 10406235]

2. **Eloubeidi MA, Provenzale D.** Health-related quality of life and severity of symptoms in patients with Barrett's esophagus and gastroesophageal reflux disease patients without Barrett's esophagus. Am J Gastroenterol. 2000;95:1881-7. [PMID: 10950030]

3. **Sonnenberg A, Amorosi SL, Lacey MJ, Lieberman DA.** Patterns of endoscopy in the United States: analysis of data from the Centers for Medicare and Medicaid Services and the National Endoscopic Database. Gastrointest Endosc. 2008;67:489-96. [PMID: 18179793]

4. **Vakil N, van Zanten SV, Kahrilas P, Dent J, Jones R; Global Consensus Group.** The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. Am J Gastroenterol. 2006;101:1900-20. [PMID: 16928254]

5. **El-Serag HB.** Epidemiology of non-erosive reflux disease. Digestion. 2008;78(Suppl 1):6-10. [PMID: 18832834]

6. **Dent J, El-Serag HB, Wallander MA, Johansson S.** Epidemiology of gastro-oesophageal reflux disease: a systematic review. Gut. 2005;54:710-7. [PMID: 15831922]

7. **Locke GR 3rd, Talley NJ, Fett SL, Zinsmeister AR, Melton LJ 3rd.** Prevalence and clinical spectrum of gastroesophageal reflux: a population-based study in Olmsted County, Minnesota. Gastroenterology. 1997;112:1448-56. [PMID: 9136821]

8. **Nebel OT, Fornes MF, Castell DO.** Symptomatic gastroesophageal reflux: incidence and precipitating factors. Am J Dig Dis. 1976;21:953-6. [PMID: 984016]

9. Pharmaceutical Sales 2009. Verispan, VONA; 2009. Accessed at www.drugs.com/top200_2009.html on 10 May 2012.

10. **Pallarito K.** How safe are popular reflux drugs? Experts debate evidence linking acid-blockers to possible bone, heart problems. US News World Rep. 4 November 2009. Accessed at http://health.usnews.com/health-news/family-health/bones-joints-and-muscles/articles/2009/11/04/how-safe-are-popular-reflux-drugs on 10 May 2012.

11. **Taylor JB, Rubenstein JH.** Meta-analyses of the effect of symptoms of gastroesophageal reflux on the risk of Barrett's esophagus. Am J Gastroenterol. 2010;105:1729, 1730-7. [PMID: 20485283]

12. **Lagergren J, Bergström R, Lindgren A, Nyrén O.** Symptomatic gastroesophageal reflux as a risk factor for esophageal adenocarcinoma. N Engl J Med. 1999;340:825-31. [PMID: 10080844]

13. **Sikkema M, de Jonge PJ, Steyerberg EW, Kuipers EJ.** Risk of esophageal adenocarcinoma and mortality in patients with Barrett's esophagus: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2010;8:235-44. [PMID: 19850156]

14. **Pohl H, Sirovich B, Welch HG.** Esophageal adenocarcinoma incidence: are we reaching the peak? Cancer Epidemiol Biomarkers Prev. 2010;19:1468-70. [PMID: 20501776]

15. **Eloubeidi MA, Mason AC, Desmond RA, El-Serag HB.** Temporal trends (1973-1997) in survival of patients with esophageal adenocarcinoma in the United States: a glimmer of hope? Am J Gastroenterol. 2003;98:1627-33. [PMID: 12873590]

16. **Dulai GS, Guha S, Kahn KL, Gornbein J, Weinstein WM.** Preoperative prevalence of Barrett's esophagus in esophageal adenocarcinoma: a systematic review. Gastroenterology. 2002;122:26-33. [PMID: 11781277]

17. **Hvid-Jensen F, Pedersen L, Drewes AM, Sørensen HT, Funch-Jensen P.** Incidence of adenocarcinoma among patients with Barrett's esophagus. N Engl J Med. 2011;365:1375-83. [PMID: 21995385]

18. **Overholt BF, Lightdale CJ, Wang KK, Canto MI, Burdick S, Haggitt RC, et al; International Photodynamic Group for High-Grade Dysplasia in Barrett's Esophagus.** Photodynamic therapy with porfimer sodium for ablation of high-grade dysplasia in Barrett's esophagus: international, partially blinded, randomized phase III trial. Gastrointest Endosc. 2005;62:488-98. [PMID: 16185958]

19. **Shaheen NJ, Sharma P, Overholt BF, Wolfsen HC, Sampliner RE, Wang KK, et al.** Radiofrequency ablation in Barrett's esophagus with dysplasia. N Engl J Med. 2009;360:2277-88. [PMID: 19474425]

20. **Wani S, Puli SR, Shaheen NJ, Westhoff B, Slehria S, Bansal A, et al.** Esophageal adenocarcinoma in Barrett's esophagus after endoscopic ablative therapy: a meta-analysis and systematic review. Am J Gastroenterol. 2009;104:502-13. [PMID: 19174812]

21. **El-Serag HB, Sonnenberg A.** Opposing time trends of peptic ulcer and reflux disease. Gut. 1998;43:327-33. [PMID: 9863476]

22. **Wang KK, Sampliner RE; Practice Parameters Committee of the American College of Gastroenterology.** Updated guidelines 2008 for the diagnosis, surveillance and therapy of Barrett's esophagus. Am J Gastroenterol. 2008;103:788-97. [PMID: 18341497]

23. **Chow WH, Finkle WD, McLaughlin JK, Frankl H, Ziel HK, Fraumeni JF Jr.** The relation of gastroesophageal reflux disease and its treatment to adenocarcinomas of the esophagus and gastric cardia. JAMA. 1995;274:474-7. [PMID: 7629956]

24. **Farrow DC, Vaughan TL, Sweeney C, Gammon MD, Chow WH, Risch HA, et al.** Gastroesophageal reflux disease, use of H2 receptor antagonists, and

risk of esophageal and gastric cancer. Cancer Causes Control. 2000;11:231-8. [PMID: 10782657]
25. **Shaheen N, Ransohoff DF.** Gastroesophageal reflux, barrett esophagus, and esophageal cancer: scientific review. JAMA. 2002;287:1972-81. [PMID: 11960540]
26. **Cook MB, Dawsey SM, Freedman ND, Inskip PD, Wichner SM, Quraishi SM, et al.** Sex disparities in cancer incidence by period and age. Cancer Epidemiol Biomarkers Prev. 2009;18:1174-82. [PMID: 19293308]
27. **Vizcaino AP, Moreno V, Lambert R, Parkin DM.** Time trends incidence of both major histologic types of esophageal carcinomas in selected countries, 1973-1995. Int J Cancer. 2002;99:860-8. [PMID: 12115489]
28. **Rubenstein JH, Mattek N, Eisen G.** Age- and sex-specific yield of Barrett's esophagus by endoscopy indication. Gastrointest Endosc. 2010;71:21-7. [PMID: 19748616]
29. **Rubenstein JH, Scheiman JM, Sadeghi S, Whiteman D, Inadomi JM.** Esophageal adenocarcinoma incidence in individuals with gastroesophageal reflux: synthesis and estimates from population studies. Am J Gastroenterol. 2011; 106:254-60. [PMID: 21139576]
30. **Eisen GM, Montgomery EA, Azumi N, Hartmann DP, Bhargava P, Lippman M, et al.** Qualitative mapping of Barrett's metaplasia: a prerequisite for intervention trials. Gastrointest Endosc. 1999;50:814-8. [PMID: 10570342]
31. **Montgomery E, Bronner MP, Goldblum JR, Greenson JK, Haber MM, Hart J, et al.** Reproducibility of the diagnosis of dysplasia in Barrett esophagus: a reaffirmation. Hum Pathol. 2001;32:368-78. [PMID: 11331953]
32. **Alikhan M, Rex D, Khan A, Rahmani E, Cummings O, Ulbright TM.** Variable pathologic interpretation of columnar lined esophagus by general pathologists in community practice. Gastrointest Endosc. 1999;50:23-6. [PMID: 10385717]
33. **Ajumobi A, Bahjri K, Jackson C, Griffin R.** Surveillance in Barrett's esophagus: an audit of practice. Dig Dis Sci. 2010;55:1615-21. [PMID: 19669878]
34. **Peters JH, Clark GW, Ireland AP, Chandrasoma P, Smyrk TC, DeMeester TR.** Outcome of adenocarcinoma arising in Barrett's esophagus in endoscopically surveyed and nonsurveyed patients. J Thorac Cardiovasc Surg. 1994;108:813-21. [PMID: 7967662]
35. **Streitz JM Jr, Andrews CW Jr, Ellis FH Jr.** Endoscopic surveillance of Barrett's esophagus. Does it help? J Thorac Cardiovasc Surg. 1993;105:383-7. [PMID: 8445916]
36. **van Sandick JW, van Lanschot JJ, Kuiken BW, Tytgat GN, Offerhaus GJ, Obertop H.** Impact of endoscopic biopsy surveillance of Barrett's oesophagus on pathological stage and clinical outcome of Barrett's carcinoma. Gut. 1998;43: 216-22. [PMID: 10189847]
37. **Corley DA, Levin TR, Habel LA, Weiss NS, Buffler PA.** Surveillance and survival in Barrett's adenocarcinomas: a population-based study. Gastroenterology. 2002;122:633-40. [PMID: 11874995]
38. **Shaheen NJ, Provenzale D, Sandler RS.** Upper endoscopy as a screening and surveillance tool in esophageal adenocarcinoma: a review of the evidence. Am J Gastroenterol. 2002;97:1319-27. [PMID: 12094844]
39. **Ronkainen J, Aro P, Storskrubb T, Johansson SE, Lind T, Bolling-Sternevald E, et al.** Prevalence of Barrett's esophagus in the general population: an endoscopic study. Gastroenterology. 2005;129:1825-31. [PMID: 16344051]
40. **Rex DK, Cummings OW, Shaw M, Cumings MD, Wong RK, Vasudeva RS, et al.** Screening for Barrett's esophagus in colonoscopy patients with and without heartburn. Gastroenterology. 2003;125:1670-7. [PMID: 14724819]
41. **Hirota WK, Zuckerman MJ, Adler DG, Davila RE, Egan J, Leighton JA, et al; Standards of Practice Committee, American Society for Gastrointestinal Endoscopy.** ASGE guideline: the role of endoscopy in the surveillance of premalignant conditions of the upper GI tract. Gastrointest Endosc. 2006;63:570-80. [PMID: 16564854]
42. **Kahrilas PJ, Shaheen NJ, Vaezi MF; American Gastroenterological Association Institute.** American Gastroenterological Association Institute technical review on the management of gastroesophageal reflux disease. Gastroenterology. 2008;135:1392-1413, 1413.e1-5. [PMID: 18801365]
43. **Spechler SJ, Sharma P, Souza RF, Inadomi JM, Shaheen NJ; American Gastroenterological Association.** American Gastroenterological Association medical position statement on the management of Barrett's esophagus. Gastroenterology. 2011;140:1084-91. [PMID: 21376940]
44. **Castell DO, Kahrilas PJ, Richter JE, Vakil NB, Johnson DA, Zuckerman S, et al.** Esomeprazole (40 mg) compared with lansoprazole (30 mg) in the treatment of erosive esophagitis. Am J Gastroenterol. 2002;97:575-83. [PMID: 11922549]
45. **Dean BB, Gano AD Jr, Knight K, Ofman JJ, Fass R.** Effectiveness of proton pump inhibitors in nonerosive reflux disease. Clin Gastroenterol Hepatol. 2004; 2:656-64. [PMID: 15290657]
46. **Khan M, Santana J, Donnellan C, Preston C, Moayyedi P.** Medical treatments in the short term management of reflux oesophagitis. Cochrane Database Syst Rev. 2007:CD003244. [PMID: 17443524]
47. **Krishnamurthy C, Hilden K, Peterson KA, Mattek N, Adler DG, Fang JC.** Endoscopic findings in patients presenting with dysphagia: analysis of a national endoscopy database. Dysphagia. 2012;27:101-5. [PMID: 21674194]
48. **Lundell LR, Dent J, Bennett JR, Blum AL, Armstrong D, Galmiche JP, et al.** Endoscopic assessment of oesophagitis: clinical and functional correlates and further validation of the Los Angeles classification. Gut. 1999;45:172-80. [PMID: 10403727]
49. **Labenz J, Armstrong D, Lauritsen K, Katelaris P, Schmidt S, Schütze K, et al; Expo Study Investigators.** A randomized comparative study of esomeprazole 40 mg versus pantoprazole 40 mg for healing erosive oesophagitis: the EXPO study. Aliment Pharmacol Ther. 2005;21:739-46. [PMID: 15771760]
50. **Laine L, Katz PO, Johnson DA, Ibegbu I, Goldstein MJ, Chou C, et al.** Randomised clinical trial: a novel rabeprazole extended release 50 mg formulation vs. esomeprazole 40 mg in healing of moderate-to-severe erosive oesophagitis - the results of two double-blind studies. Aliment Pharmacol Ther. 2011;33:203-12. [PMID: 21114792]
51. **Modiano N, Gerson LB.** Risk factors for the detection of Barrett's esophagus in patients with erosive esophagitis. Gastrointest Endosc. 2009;69:1014-20. [PMID: 19152902]
52. **Gilani N, Gerkin RD, Ramirez FC, Hakim S, Randolph AC.** Prevalence of Barrett's esophagus in patients with moderate to severe erosive esophagitis. World J Gastroenterol. 2008;14:3518-22. [PMID: 18567080]
53. **Hanna S, Rastogi A, Weston AP, Totta F, Schmitz R, Mathur S, et al.** Detection of Barrett's esophagus after endoscopic healing of erosive esophagitis. Am J Gastroenterol. 2006;101:1416-20. [PMID: 16863541]
54. **Ruigómez A, García Rodríguez LA, Wallander MA, Johansson S, Eklund S.** Esophageal stricture: incidence, treatment patterns, and recurrence rate. Am J Gastroenterol. 2006;101:2685-92. [PMID: 17227515]
55. **Said A, Brust DJ, Gaumnitz EA, Reichelderfer M.** Predictors of early recurrence of benign esophageal strictures. Am J Gastroenterol. 2003;98:1252-6. [PMID: 12818265]
56. **El-Serag HB, Mason AC, Petersen N, Key CR.** Epidemiological differences between adenocarcinoma of the oesophagus and adenocarcinoma of the gastric cardia in the USA. Gut. 2002;50:368-72. [PMID: 11839716]
57. **Spechler SJ, Sharma P, Souza RF, Inadomi JM, Shaheen NJ; American Gastroenterological Association.** American Gastroenterological Association technical review on the management of Barrett's esophagus. Gastroenterology. 2011; 140:e18-52. [PMID: 21376939]
58. **Rodriguez S, Mattek N, Lieberman D, Fennerty B, Eisen G.** Barrett's esophagus on repeat endoscopy: should we look more than once? Am J Gastroenterol. 2008;103:1892-7. [PMID: 18564120]
59. Appropriate use of gastrointestinal endoscopy. American Society for Gastrointestinal Endoscopy. Gastrointest Endosc. 2000;52:831-7. [PMID: 11203479]
60. **Hassan C, Bersani G, Buri L, Zullo A, Anti M, Bianco MA, et al.** Appropriateness of upper-GI endoscopy: an Italian survey on behalf of the Italian Society of Digestive Endoscopy. Gastrointest Endosc. 2007;65:767-74. [PMID: 17466196]
61. **Keren D, Rainis T, Stermer E, Lavy A.** A nine-year audit of open-access upper gastrointestinal endoscopic procedures: results and experience of a single centre. Can J Gastroenterol. 2011;25:83-8. [PMID: 21321679]
62. **Rossi A, Bersani G, Ricci G, Defabritiis G, Pollino V, Suzzi A, et al.** ASGE guidelines for the appropriate use of upper endoscopy: association with endoscopic findings. Gastrointest Endosc. 2002;56:714-9. [PMID: 12397281]
63. **Charles RJ, Cooper GS, Wong RC, Sivak MV Jr, Chak A.** Effectiveness of open-access endoscopy in routine primary-care practice. Gastrointest Endosc. 2003;57:183-6. [PMID: 12556781]
64. **Gonvers JJ, Burnand B, Froehlich F, Pache I, Thorens J, Fried M, et al.** Appropriateness and diagnostic yield of upper gastrointestinal endoscopy in an open-access endoscopy unit. Endoscopy. 1996;28:661-6. [PMID: 8934082]
65. **Rubenstein JH, Saini SD, Kuhn L, McMahon L, Sharma P, Pardi DS, et al.** Influence of malpractice history on the practice of screening and surveillance for Barrett's esophagus. Am J Gastroenterol. 2008;103:842-9. [PMID: 18076733]

66. **Falk GW, Ours TM, Richter JE.** Practice patterns for surveillance of Barrett's esophagus in the United States. Gastrointest Endosc. 2000;52:197-203. [PMID: 10922091]

67. **Harewood GC, Rathore O, Patchett S, Murray F.** Assessment of adherence to published surveillance guidelines—opportunity to enhance efficiency of endoscopic practice. Ir Med J. 2008;101:248-50. [PMID: 18990956]

68. **Crockett SD, Lipkus IM, Bright SD, Sampliner RE, Wang KK, Boolchand V, et al.** Overutilization of endoscopic surveillance in nondysplastic Barrett's esophagus: a multicenter study. Gastrointest Endosc. 2012;75:23-31.e2. [PMID: 22100301]

69. **Shaheen NJ, Green B, Medapalli RK, Mitchell KL, Wei JT, Schmitz SM, et al.** The perception of cancer risk in patients with prevalent Barrett's esophagus enrolled in an endoscopic surveillance program. Gastroenterology. 2005;129:429-36. [PMID: 16083700]

70. **Arrowsmith JB, Gerstman BB, Fleischer DE, Benjamin SB.** Results from the American Society for Gastrointestinal Endoscopy/U.S. Food and Drug Administration collaborative study on complication rates and drug use during gastrointestinal endoscopy. Gastrointest Endosc. 1991;37:421-7. [PMID: 1833259]

71. **Chan MF.** Complications of upper gastrointestinal endoscopy. Gastrointest Endosc Clin N Am. 1996;6:287-303. [PMID: 8673329]

72. **Corley DA, Kubo A, DeBoer J, Rumore GJ.** Diagnosing Barrett's esophagus: reliability of clinical and pathologic diagnoses. Gastrointest Endosc. 2009;69:1004-10. [PMID: 19152897]

73. **Inadomi JM, Somsouk M, Madanick RD, Thomas JP, Shaheen NJ.** A cost-utility analysis of ablative therapy for Barrett's esophagus. Gastroenterology. 2009;136:2101-2114.e1-6. [PMID: 19272389]

Current Author Addresses: Dr. Shaheen: University of North Carolina School of Medicine, CB#7080, Room 4150, 130 Mason Farm Road, Chapel Hill, NC 27599-7080.
Dr. Weinberg: Department of Medicine, Fox Chase Cancer Center, 333 Cottman Avenue, Philadelphia, PA 19111.
Dr. Denberg: Harvard Vanguard Medical Associates, 275 Grove Street, Auburndale, MA 02466.
Dr. Chou: Oregon Health & Science University, 3181 Southwest Sam Jackson Park Road, Mail Code: BICC, Portland, OR 97239.
Dr. Qaseem: American College of Physicians, 190 N. Independence Mall West, Philadelphia, PA 19106.
Dr. Shekelle: RAND Corporation, 1776 Main Street, Santa Monica, CA 90401.

Author Contributions: Conception and design: N.J. Shaheen, D.S. Weinberg, T.D. Denberg, R. Chou, A. Qaseem, P. Shekelle.
Analysis and interpretation of the data: N.J. Shaheen, D.S. Weinberg, T.D. Denberg, R. Chou, A. Qaseem.
Drafting of the article: N.J. Shaheen, D.S. Weinberg, T.D. Denberg, R. Chou, A. Qaseem.
Critical revision of the article for important intellectual content: N.J. Shaheen, D.S. Weinberg, T.D. Denberg, R. Chou, A. Qaseem, P. Shekelle.
Final approval of the article: N.J. Shaheen, D.S. Weinberg, T.D. Denberg, R. Chou, A. Qaseem, P. Shekelle.
Statistical expertise: A. Qaseem.
Obtaining of funding: D.S. Weinberg.
Administrative, technical, or logistic support: D.S. Weinberg, A. Qaseem.
Collection and assembly of data: N.J. Shaheen, D.S. Weinberg.