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AGA Institute Rapid Review and Recommendations on the Role of Pre-Procedure SARS-CoV-2 Testing and Endoscopy

Shahnaz Sultan,[1,*] **Shazia M. Siddique**,[2,*] Osama Altayar,[3] Angela M. Caliendo,[4] Perica Davitkov,[5] Joseph D. Feuerstein,[6] Dawn Francis,[7] John M. Inadomi,[8] Joseph K. Lim,[9] Yngve Falck-Ytter,[5] and Reem A. Mustafa,[10] on behalf of the American Gastroenterological Association*

[1]Division of Gastroenterology, Hepatology, and Nutrition, University of Minnesota, Minneapolis Veterans Affairs Healthcare System, Minneapolis, Minnesota; [2]Division of Gastroenterology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania; [3]Division of Gastroenterology, Washington University School of Medicine, St Louis, Missouri; [4]Department of Medicine, Warren Alpert Medical School of Brown University, Providence, Rhode Island; [5]Division of Gastroenterology, Northeast Ohio Veterans Affairs Healthcare System, Case Western Reserve University School of Medicine, Cleveland, Ohio; [6]Division of Gastroenterology and Center for Inflammatory Bowel Diseases, Beth Israel Deaconess Medical Center, Boston, Massachusetts; [7]Mayo Clinic College of Medicine, Division of Gastroenterology and Hepatology, Jacksonville, Florida; [8]Department of Internal Medicine, University of Utah School of Medicine, Salt Lake City, Utah; [9]Yale Liver Center and Section of Digestive Diseases, Yale University School of Medicine, New Haven, Connecticut; and [10]Division of Nephrology and Hypertension, Department of Internal Medicine, University of Kansas Medical Center, Kansas City, Kansas

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The genome of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), the cause of coronavirus disease 2019 (COVID-19), was first identified on January 12, 2020. This was a critical first step that allowed for the development of molecular diagnostic tests to identify the presence of virus.[1–3] At the individual patient level, testing for SARS-CoV-2 infection in symptomatic patients helps to identify individuals who can be isolated to prevent the spread of disease and can inform treatment decisions aimed at reducing morbidity and mortality.[4] At the population level, widespread testing of individuals (symptomatic and asymptomatic) is critical to understanding the true prevalence of disease. This information can then inform local decisions regarding the economy and the provision of health care services, including the re-introduction of endoscopy across health care systems and ambulatory care centers.[5]

Tests fall under 2 broad categories: tests that detect virus and tests that detect the presence of antibodies associated with the virus (serology tests). Direct detection of viral RNA is most commonly performed via nucleic acid amplification testing of specific known targets in the genome of the virus using reverse transcription polymerase chain reaction (RT-PCR).[6] The most common sample types (or sources) are swabs that are taken from the nasopharynx and/or oropharynx, lower respiratory tract, or saliva by a trained health care worker or self-collection. It is important to recognize that the quality of sample collection, as well as the source, influence test results. Development of an antibody response to SARS-CoV-2 infection through the identification of antibodies indicates recent or past infection.

The predictive value of a test refers to the probability of having a condition or disease in an individual with a positive test result (positive predictive value) and the probability of not having a condition or disease in an individual with a negative test result (negative predictive value). A pretesting strategy in asymptomatic individuals before endoscopy can be informative in distinguishing people with SARS-CoV-2 infection and those without SARS-CoV-2 infection, but it is affected by the prevalence of the disease in asymptomatic individuals.

This rapid review and rapid guideline address the role of implementing a SARS-CoV-2 pretesting strategy before endoscopy. An earlier American Gastroenterological Association (AGA) guideline examined the role of personal protective equipment (PPE) (including extended use and reuse of N95/N99 respirators or powered air purifying respirators [PAPRs] in resource-constrained settings) when testing was not readily available; the aim of this guideline was to determine the role of testing in endoscopy center reopening.[7] To inform the recommendations, a systematic review of the diagnostic performance of currently available tests for SARS-CoV-2 infection was conducted. A survey was conducted to gather information about the threshold of risk that endoscopists were willing to accept during endoscopy and an overview of strategies to estimate prevalence of infection among asymptomatic individuals is provided. Finally, the panel drafted recommendations for the role of a pretesting strategy for low-, intermediate-, and high-prevalence settings and a recommendation for serology testing (Table 1).

***Authors share co-first authorship.**

Abbreviations used in this paper: **AGA, American Gastroenterological Association; CDC, Centers for Disease Control and Prevention; CI, confidence interval; COVID-19, coronavirus disease 2019; GRADE, Grading of Recommendations Assessment, Development and Evaluation; PAPR, powered air purifying respirator; PPE, personal protective equipment; RT-PCR, reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2.**

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AGA SECTION

Table 1. Executive Summary of Recommendations[a]

What is the role of a pretesting strategy in asymptomatic individuals 48–72 h before endoscopy (including a self-quarantine between testing and endoscopy)? Benefits: Triage and PPE use to reduce the risk of infection. Downsides: Patient burden, limited testing capacity, testing logistics, and cost.

Recommendation	Remarks
Recommendation 1 For most endoscopy centers where the prevalence of asymptomatic SARS-CoV-2 infection is intermediate (0.5%–2%), the AGA suggests implementing a pretesting strategy using information about prevalence and test performance (sensitivity/specificity) in combination with considerations about the benefits and downsides of the strategy. *Conditional recommendation, low certainty evidence*	In settings where testing is feasible and there is less perceived burden on patients, and when the benefits outweigh the downsides (eg, false positives do not significantly outnumber the true positives), an endoscopy center may reasonably choose to implement a pretesting strategy. Among individuals that test negative, endoscopists and staff should use surgical masks[b] for all upper and lower endoscopies. Endoscopists and staff who are unwilling to accept the potential small risk of infection (from false negatives) may use N95/N99[b] respirators or PAPRs for upper and/or lower endoscopies. In settings where the logistics of testing are challenging and the downsides outweigh the benefits (eg, the false positives outnumber the true positives) and endoscopy units are unwilling to accept the potential (albeit small) risk of infection then an endoscopy center may reasonably choose not to implement a pretesting strategy and proceed with using higher PPE (N95/N99 respirators or PAPRs) for all procedures.
Recommendation 2 For endoscopy centers where the prevalence of asymptomatic SARS-CoV-2 infection is low (<0.5%), the AGA suggests against implementing a pretesting strategy. *Conditional recommendation, very low certainty evidence*	In low-prevalence settings, a pretesting strategy may not be informative for triage due to the high number of false positives, thus PPE availability may drive decision-making. If PPE is available, the majority of gastroenterologists may reasonably select to use N95/N99[b] respirator or PAPRs. However, a small minority, with a low risk-aversion threshold, may reasonably choose to use surgical masks.[b]
Recommendation 3 For a small number of endoscopy centers in high-prevalence areas, the AGA suggests against implementing a pretesting strategy. In "hotspots," endoscopy may be reserved for emergency or time-sensitive procedures with use of N95/N99[b] respirators or PAPRs for all procedures. *Conditional recommendation, very low certainty evidence*	In high-prevalence areas, a pretesting strategy may not be informative for decisions about PPE use because of the unacceptable number of false negatives and PPE availability may drive decision-making. If PPE is available, N95/N99[b] respirators or PAPRs may be used for all upper and lower endoscopies, regardless of time sensitivity. A *hotspot* is defined by a surge in COVID-19 cases with an acute burden on hospital capacity. In hotspots, resumption of outpatient endoscopy may depend on availability of PPE.
Recommendation 4 For all endoscopy centers, the AGA recommends against serologic testing as part of a pretesting strategy for patients or endoscopy staff. *Strong recommendation, low certainty evidence*	Serology testing for the presence of antibodies indicates past infection and has no role in diagnosing SARS-CoV-2 infection in asymptomatic individuals before endoscopy. The evidence supporting the role of seroconversion for return to work or hospital staffing policies is also lacking.

[a]These recommendations assume that all patients are systematically screened for COVID-19 symptoms using the CDC screening checklist and are required to wear masks while in the endoscopy unit. The strength of a recommendation is expressed as strong or conditional and has the following interpretation: strong recommendation—for clinicians: most individuals should follow the recommended course of action, and only a small proportion should not; conditional recommendation—for clinicians: the majority of individuals in this situation would want the suggested course of action but many would not; different choices will be appropriate.
[b]Appropriate PPE includes a face shield over the surgical mask and face shield over the N95/N99 respirator (to allow for reuse/extended use in limited PPE availability settings).[7]

Scope and Purpose

We sought to provide an overview of the considerations of diagnostic testing in the decision to reopen or expand endoscopy operations in the setting of a pandemic. We summarized the available data on the diagnostic test characteristics of tests for SARS-CoV-2 infection and provided evidence-based clinical guidance on the role of pretesting before endoscopic procedures. This rapid review and guideline was commissioned and approved by the AGA Governing Board to provide timely, methodologically

rigorous guidance on a topic of high clinical importance to the AGA members and the public.

Panel Composition and Conflict of Interest Management

The guideline panel included gastroenterologists, an infectious disease expert, a member of the Practice Management and Economics Committee, and guideline methodologists from the Clinical Guideline Committee and Clinical Practice Updates Committee. Panel members disclosed all potential conflicts of interest according to the AGA Institute policy. All members were required to disclose financial, intellectual, or other potential conflicts.

Target Audience

The target audience for these guidelines includes gastroenterologists, advanced practice providers, nurses, and other health care professionals in academic centers and in private practice settings across various geographic locations. Patients as well as policy-makers can also benefit from these guidelines. These guidelines are not intended to impose a standard of care for individual institutions, health care systems, or countries. They provide the basis for rational informed decision-making for clinicians, patients, and other health care professionals in the setting of a pandemic.

How to Use These Guidelines

This rapid guideline is intended to help clinicians make decisions about pre-procedural testing before endoscopy; however, decisions may be constrained by local health system or state-level policies, as well as availability of resources, specifically RT-PCR tests and PPE. Recommendations are accompanied by qualifying remarks, which serve to facilitate more accurate implementation. They should never be omitted when recommendations from these guidelines are quoted or translated. A summary of the recommendations is provided in Table 1, with a more detailed rationale for each recommendation in the Discussion section. The Implementation Considerations section in this guideline will help clinicians implement these recommendations. This section includes a checklist for endoscopy center reopening, instructions for an online interactive tool, and a matrix to facilitate pretesting strategy considerations in low- and high-prevalence areas accounting for testing and PPE availability.

Methods

The evidence base to support this recommendation included the following: a systematic review and meta-analysis of diagnostic test performance (sensitivity and specificity) of currently available tests in the United States; a survey of gastroenterologists to understand the acceptable threshold of risk; and available data on prevalence of infection among asymptomatic individuals. Recommendations were developed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework.[8]

Systematic Review and Meta-Analysis of Diagnostic Test Performance

Information sources and literature search. We conducted a systematic literature search to identify all published and unpublished studies that could be considered eligible for our review, with no restrictions on languages. To capture relevant published articles, we electronically searched OVID Medline and EmBase from inception to May 16, 2020 using the Medical Subject Heading term developed for COVID-19. For additional unpublished or preprint studies, we searched medRxiv, LitCovid, Biorxiv, and SSRN on May 16, 2020 and May 17, 2020 (a Preferred Reporting Items for Systematic Reviews and Meta-Analyses Flow Diagram is provided in Supplementary Figure 1).

Study selection and data extraction. Two reviewers were assigned to each database (S.M.S. and P.D. to SSRN; O.A. and J.F. to Medrxiv and Biorxiv; and S.S. and R.M. to LitCovid) and independently screened titles and abstracts, as well as eligible full-text studies. Disagreements were resolved by discussion to reach consensus. Studies were included if they reported data on diagnostic test accuracy (cohort studies, cross-sectional studies, and case-control studies). All studies compared an index test with a reference standard test. Reviewers extracted relevant information into a standardized data extraction form (Supplementary Table 1). Data extracted included study characteristics (authors, publication year, country, and study design), index test and reference standard, and sensitivity and specificity of the index test. In addition, studies that reported on prevalence of SARS-CoV-2 infection were also identified and reviewed.

Assessment of risk of bias. Risk of bias for studies on diagnostic test accuracy was assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 revised tool.[9] This tool assesses the risk of bias in the following domains: patient selection, index test, reference standard, and flow and timing of study. Studies were categorized as being higher quality if they had a cross-sectional or cohort design as opposed to case-control design; included a reference standard that is not a laboratory-developed test; and if there were 2 reference standards or at least 1 reference standard with a second test for discordant results.

Data synthesis and analysis. We used the bivariate normal model to pool sensitivity and specificity using the logit transformation.[10] We performed sensitivity analyses by limiting the analysis to studies at low risk of bias based on the patient selection and reference test domains of the Quality Assessment of Diagnostic Accuracy Studies-2 tool. We used the package *mada*, version 0.5.8, in R software, version 3.6.3, to conduct the analysis and produce the forest plots.[11,12]

Certainty of evidence and evidence to recommendations. The GRADE framework was used to assess overall certainty by evaluating the evidence for each outcome on the following domains: risk of bias, imprecision, inconsistency, indirectness, and publication bias.[13,14] The GRADE interactive summary of findings table was generated using the GRADEpro Guideline Development Tool.[15] In developing recommendations, the panel considered the certainty of evidence, the balance between the desirable and undesirable effects (ie, the benefits and downsides of a pretesting strategy), and additional domains were acknowledged where applicable (eg,

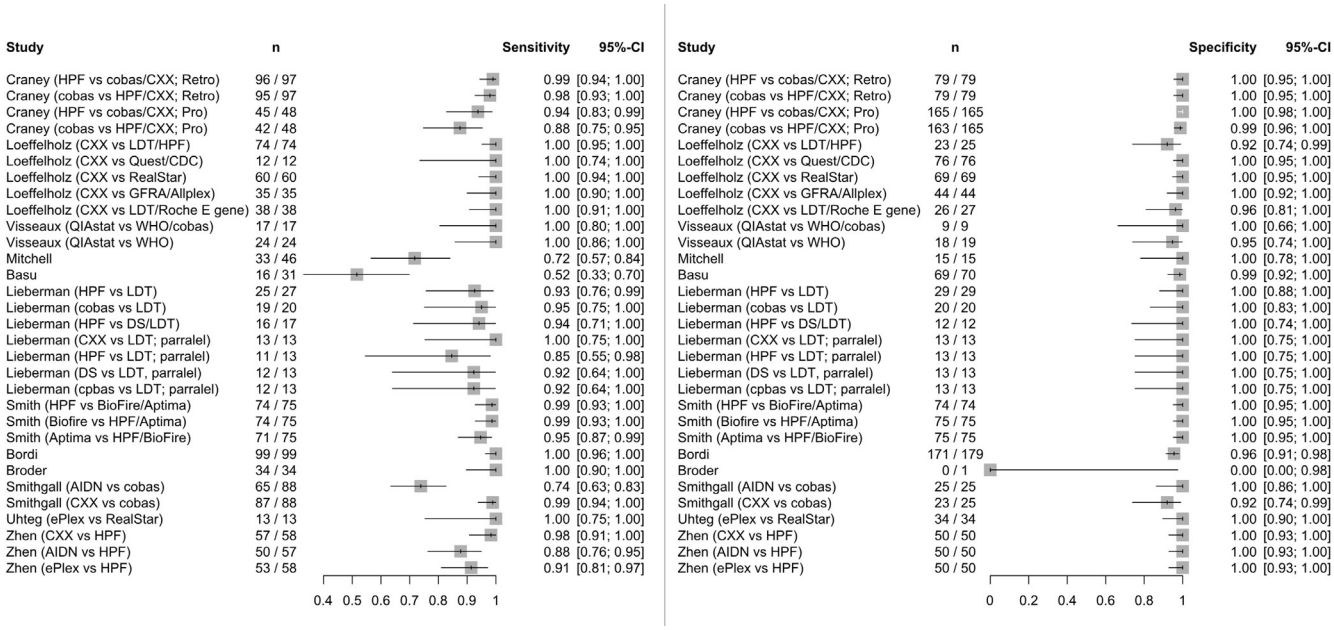

Figure 1. Forest plot of test accuracy (pooled sensitivity and specificity).

feasibility, resource use, and acceptability). For all recommendations, the expert panelists reached consensus. As per GRADE methodology, recommendations are labeled as "strong" or "conditional" (Supplementary Tables 2 and 3). The phrase *we recommend* indicates strong recommendations and *we suggest* indicates conditional recommendations.

Risk-Aversion Threshold Survey

Guideline panels often conduct internal surveys among panel members to determine values and preferences of providers. In order to gain a better understanding of a broader population of endoscopists, the panel developed a survey open to all AGA members. The goal was to understand the endoscopists' threshold to accept risks associated with pretesting to inform PPE use (surgical mask vs N95/N99 or PAPR). We developed a short online survey that was piloted and modified before dissemination. Earlier data have shown that endoscopy centers in North America are adopting pretesting strategies.[16] The purpose of our survey was to better understand risk-aversion thresholds based on false-negative results, which drive decision-making for triage and PPE. A false-negative result can provide false reassurance to an individual who has SARS-CoV-2 infection, could be shedding virus, and may transmit the infection to others. The survey presented a clinical scenario of an asymptomatic patient undergoing elective endoscopy who tested negative for SARS-CoV-2 72 hours before the endoscopy. Respondents were given 5 options for acceptable levels of risk of transmission of SARS-CoV-2. The first option was 1 in 1000, with a comment stating that selecting this option would indicate willingness to open the endoscopy center using a surgical mask only. The last option was 1 in 40,000, with a comment stating that selecting that option would indicate willingness to open the endoscopy center only once N95s are available, despite a negative test result. The range of options were based on the following assumptions: local prevalence of 1% (intermediate), baseline risk of SARS-CoV-2 transmission without PPE of 50%, and reduction of risk of COVID-19 transmission with PPE to 20% with surgical mask and 5% with N95 respirators.

We collected responses from US-based gastroenterologists using the "AGA Community" platform. The "AGA Community" is a nonpublic community for members of the AGA through which gastroenterologists connect with colleagues and have conversations about relevant issues in their field.

Prevalence of SARS-CoV-2 in Asymptomatic Individuals

A pretesting strategy in asymptomatic individuals before endoscopy can be informative in distinguishing people with SARS-CoV-2 infection and those without, but it is affected by the prevalence of the disease in asymptomatic individuals. To identify sources of data that provide information about the prevalence of infection in asymptomatic individuals, we searched the published and unpublished literature and also reviewed public health websites. We also queried panel members regarding data from their local institutions.

Results

Systematic Review and Meta-Analysis of Diagnostic Test Performance

We identified 12 studies that provided information for 31 comparisons about test accuracy for the various nucleic acid amplification testing tests.[17–28] The risk of bias was rated using the Quality Assessment of Diagnostic Accuracy Studies-2 (Supplementary Table 4). The pooled sensitivity was 0.941 (95% confidence interval [CI], 0.908–0.963) and pooled specificity was 0.971 (95% CI, 0.958–0.980) (Figure 1). We performed a sensitivity analysis for studies with low risk of bias and found similar results: pooled sensitivity of 0.929 (95% CI, 0.847–0.968) and pooled specificity of 0.968 (95% CI, 0.942–0.983) (Supplementary Figure 2). An important caveat of these studies is that

tests were validated in samples from symptomatic individuals, and it is likely that in asymptomatic individuals the tests may not perform as well and would have lower sensitivity and specificity.

Risk-Aversion Threshold Survey Results

We received 74 responses to the survey (Table 2). There was a wide distribution of answer selections: 37.8% (28 of 74) selected willingness to accept a risk of 1 in 40,000, indicating that they would not be willing to open their endoscopy center unless N95s are available for all cases, including those with a negative SARS-CoV-2 test. On the other hand, 19 of 74 (25.7%) selected 1 in 1000, indicating that they were willing to open their endoscopy units and use surgical masks regardless of testing. The remainder of the participants (27 of 74 [36.5%]) were willing to accept risks between 1 in 2500 and 1 in 10,000. Survey respondents included gastroenterologists practicing in academic institutions (23 of 74 [31.1%]), in nonacademic hospitals (15 of 74 [20.3%]), in independent practice (34 of 74 [45.9%]), and in other institutions (2 of 74 [2.8%]). Gastroenterologists performing procedures in private practice ambulatory centers were willing to accept higher infection risk compared with gastroenterologists in academic centers and nonacademic hospitals. Of 19 participants choosing the 1 in 1000 risk, 12 (63.2%) were in private practice.

Prevalence of SARS-CoV-2 in Asymptomatic Individuals

For diagnostic tests to inform decision-making, it is essential to determine the pretest probability (eg, prevalence) of disease in asymptomatic individuals. We searched for studies that evaluated the prevalence of SARS-CoV-2 among asymptomatic individuals, but only identified studies reporting on seroprevalence, which were noninformative. Public websites reporting on numbers of positive cases (predominantly in symptomatic patients) and deaths were reviewed but, due to limitations of nonrandom testing; variability in availability of testing; and delays in reporting, these estimates cannot directly inform prevalence estimates in asymptomatic individuals. Acknowledging the limited publicly available evidence for accurate estimates of prevalence of SARS-CoV-2 infection in asymptomatic individuals, we relied on information from panel members' experiences within their health systems (based on rates of positive cases in asymptomatic individuals undergoing testing before any elective procedure) and modeling studies trying to estimate prevalence of SARS-CoV-2 infection in the general population.

We defined *low-prevalence* areas as areas where the prevalence of asymptomatic infection is <0.5%, *intermediate prevalence* areas as areas where the prevalence is between 0.5 and 2%, and *high prevalence* as areas where the prevalence is >2%. We defined *hotspots* as areas where there is a sudden surge in the number of daily cases with an acute burden on hospital capacity. The prevalence of exclusively asymptomatic infections is believed to be significantly lower than the commonly reported county or state estimates of positive cases and estimated to be approximately 1/10 of the rates of positive cases. This is supported by a modeling study of state-level data, which estimated that for each diagnosed symptomatic patient there may be 10 asymptomatic or undiagnosed individuals in that population.[29] Furthermore, based on a study conducted between April 13 and May 15, 2020 in Miami, FL, the prevalence in an asymptomatic pre-endoscopy population was 0.25% compared with prevalence ranges from 5.4% to 12.7% in neighboring regions.[30] Similarly, another study from Stanford University found 2 of 999 total positives (0.2% prevalence).[31] Members of our panel provided some information regarding local data for positive test results in their health systems. At University of Washington Medical Center and Harborview Medical Center from March 27 to June 28, 2020, there were 2 asymptomatic (no fever, cough, or shortness of breath) patients among 1437 who tested positive. Prevalence in asymptomatic patients was 0.14% (B. Teng, MD, personal communication; July 30, 2020).

Table 2. Survey Respondent Characteristics by Risk-Aversion Threshold

Characteristic	All respondents	Characteristics by response selection				
		1 in 1000	1 in 2500	1 in 5000	1 in 10,000	1 in 40,000
Total, n	74	19	10	10	7	28
Sex, male, n (%)	51 (68.9)	12 (63.2)	9 (90.0)	10 (100.0)	5 (71.4)	15 (53.6)
Settings, n (%)						
Academic medical center	23 (31.1)	4 (21.1)	5 (50.0)	1 (10.0)	4 (57.1)	9 (32.1)
Independent practice	34 (45.9)	12 (63.2)	3 (30.0)	4 (40.0)	3 (42.9)	12 (42.9)
Nonacademic hospital	15 (20.3)	2 (10.5)	1 (10.0)	5 (50.0)	0 (0.0)	7 (25.0)
Other	1 (1.4)	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)	0 (0.0)
Veterans Affairs hospital	1 (1.4)	1 (5.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Group size, median (IQR)	7.0 (4.0–20.0)	9.0 (5.0–24.0)	8.5 (4.5–18.8)	4.0 (4.0–8.3)	8.0 (5.5–37.0)	8.0 (4.0–14.5)
Clinical experience						
Procedures per year, median (IQR)	500 (300–1000)	493 (213–1075)	400 (263–1000)	800 (325–950)	450 (325–500)	500 (300–1000)
Years of practice, median (IQR)	20 (12–30)	22.5 (15.5–30)	17.5 (6.5–25.5)	31 (30–33.5)	20 (9–25)	17.5 (11.3–27.5)

Discussion

The guideline panel acknowledges that local, state, and health system policies may dictate requirements for pre-procedural testing of asymptomatic patients as well as decisions about PPE use. The following recommendations are based on the assumption that gastroenterologists have decision-making power over implementing a pretesting strategy.

Outcomes for Decision-Making

Triage and personal protective equipment use. A pretesting strategy can inform endoscopy operations by helping with decisions regarding triage and PPE use. Using an estimate for the prevalence of asymptomatic SARS-CoV-2 infection and test performance (sensitivity and specificity), the number of true positives, true negatives, false positives, and false negatives can be calculated. All patients who test positive for SARS-CoV-2 infection will have their elective procedure canceled and be advised to self-quarantine for 14 days. A positive test result, however, includes asymptomatic individuals with SARS-CoV-2 infection (true positive), as well as individuals who test positive but do not have infection (false positive). All patients who test negative for SARS-CoV-2 infection can proceed with endoscopy and a surgical mask can be used by endoscopists and staff for upper and lower endoscopies. A negative test result, however, includes individuals who do not have infection (true negative) and those individuals who have SARS-CoV-2 infection but test negative (false negative).

The 2 main concerns with a pretesting strategy are the false positives (ie, individuals who test positive for SARS-CoV-2 but do not have the infection) and false negatives (ie, individuals who test negative for SARS-CoV-2 but do have the infection). In a patient who tests negative for SARS-CoV-2 infection (false negative) and a surgical mask is used for upper endoscopy, there can be a potential (albeit small) increased risk of infection to the endoscopy staff and false reassurance to the individual. In a patient who tests positive for SARS-CoV-2 who does not have infection (false positive), implications for the patient include cancellation of the procedure, self-quarantine for 14 days, apprehension, and loss of work. Below we summarize the evidence, weigh the benefits and downsides and provide the rationale for each recommendation.

Recommendation 1: For most endoscopy centers where the prevalence of asymptomatic SARS-CoV-2 infection is intermediate (0.5%–2%), the AGA suggests implementing a pretesting strategy using information about prevalence and test performance (sensitivity/specificity) in combination with considerations about the benefits and downsides of the strategy.

Conditional recommendation, low certainty evidence

Remarks: In settings where testing is feasible and there is less perceived burden on patients, and when the benefits outweigh the downsides (eg, false positives do not significantly outnumber the true positives), an endoscopy center may reasonably choose to implement a pretesting strategy. Among individuals that test negative, endoscopists and staff should use surgical masks for all upper and lower endoscopies. Endoscopists and staff who are unwilling to accept the potential small risk of infection (from false negatives) may use N95/N99 respirators or PAPRs for upper and/or lower endoscopies.

In settings where the logistics of testing are challenging and the downsides outweigh the benefits (eg, the false positives outnumber the true positives) and endoscopy units are unwilling to accept the potential (albeit small) risk of infection then an endoscopy center may reasonably choose not to implement a pretesting strategy and proceed with using higher PPE (N95/N99 respirators or PAPRs) for all procedures.

NOTE. Appropriate PPE includes a face shield over the surgical mask and face shield over the N95/N99 respirator to allow for reuse or extended use in limited PPE availability settings.

Summary of the Evidence

We did not identify any comparative studies that directly assessed a strategy of pre-procedural testing vs no testing in asymptomatic individuals before endoscopy. The overall body of evidence was limited by small numbers, poorly defined and inconsistent reference standards, and test accuracy from case–control studies (which can lead to inflated estimates of test accuracy). In addition, there were missing data in the studies regarding timing of specimen collection in relationship to onset of clinical symptoms and specimen type used for testing. Given all of these concerns, the overall certainty was low.

Also, there were no test accuracy studies that evaluated the performance of RT-PCR tests in asymptomatic individuals. Based on evidence demonstrating similar viral shedding in presymptomatic individuals compared with symptomatic individuals, we applied the test accuracy for symptomatic patients, however, we assumed that the lower boundary of the 95% CI more accurately reflected test performance in the asymptomatic population. We display the summary of findings table for an intermediate prevalence setting (0.5% to 2%) in Figure 2.

Benefits and Downsides

The benefits and downsides (or pros and cons of a pretesting strategy are summarized in Figure 3. The major benefits include reassurance for endoscopy staff and other patients, potential reduction in transmission by deferring procedures in patients who test positive for SARS-CoV-2, and informed decisions regarding use of PPE. Risk of transmission among health care workers, including in an endoscopy setting, has been reported to range from 4.3% to 21%.[32–34] Addressing safety concerns is an important aspect to resuming endoscopy operations for both endoscopists and patients.[35,36]

The downsides include perceived patient burden and limited availability of testing, logistics and bottleneck of testing for providers, and false-positive and false-negative results. For patients, false-positive cases may lead to unnecessary case delay, self-quarantine, and consequences for

patients and families, and ability to work; and false-negative cases can lead to false reassurance and potential for increased transmission. For providers, false-negative cases can lead to a potential increased risk for infection.

Rationale

The panel made a conditional recommendation for pre-procedural testing in areas where the asymptomatic prevalence of infection ranges between 0.5% and 2%. A conditional recommendation implies that most clinicians would follow the recommended course of action but many would not, and that different approaches would be reasonable. The panel considered the number of false positives and false negatives, the downstream consequences of these test results, the net benefits and downsides of testing, and resource considerations.

In developing this recommendation, the panel evaluated the hypothetical impact of a pretesting strategy in an intermediate prevalence setting in which the prevalence of SARS-CoV-2 infection is between 0.5% and 2%. Based on our meta-analysis of studies that were at low risk of bias, the commercially available tests in the United States have an estimated pooled sensitivity of 93% and specificity of 97% in symptomatic individuals. The panel assumed a sensitivity of 85% and specificity of 94% (these estimates were derived from our pooled meta-analysis of currently available commercial tests and represent the lower boundary of the 95% CI, which more likely reflects test accuracy in asymptomatic individuals).

At a prevalence of 0.5%, in a sample of 1000 asymptomatic individuals who undergo the test, 64 will have a positive test result; of the 64 individuals with a positive result and 4 will be true positives but 60 will be false positives. At a prevalence of 2%, in 1000 asymptomatic individuals, 76 individuals will have a positive test result and 17 will be true positives but 59 will be false positives. With respect to the number of false negatives, in a sample of 1000 asymptomatic individuals, at a prevalence of 0.5%, 1 individual out of 1000 will have a false-negative result and at a prevalence of 2%, 3 individuals out of 1000 will have a false-negative result (Figure 4). As the prevalence increases, the proportion of false positives decreases. In our hypothetical example, the percentage of asymptomatic individuals who would test positive ranges from 6% to 22%.

Individual endoscopy practices may use an interactive tool and input the local prevalence of infection in asymptomatic individuals (see Implementation Consideration section), input the sensitivity and specificity of the test used in their local setting, and determine the number of false-positive and false-negative results.

In settings in which testing is feasible and there is less perceived burden on patients, when the benefits outweigh the downsides, an endoscopy center may reasonably choose to implement a pretesting strategy. Among individuals that test negative, endoscopists should use surgical masks for all upper and lower endoscopies. Endoscopists who are willing to accept the potential (albeit small) risk of infection from false positives (in an intermediate prevalence with a hypothetical sample of 1000 individuals, the number of false negatives would range from 1 in 1000 to 3 in 1000). Endoscopists who are unwilling to accept the small risk of infection may use N95/N99 respirator or PAPRs for upper and lower endoscopies.

Alternatively, an endoscopy center may reasonably choose not to implement a pretesting strategy and proceed with using higher PPE (ie, N95/N99 respirators or PAPRs) for all procedures.

Recommendation 2: For endoscopy centers where the prevalence of asymptomatic SARS-CoV-2 infection is low (<0.5%), the AGA suggests against implementing a pretesting strategy.
Conditional recommendation, very low certainty evidence
Remarks: In low-prevalence settings, a pretesting strategy may not be informative for triage due to the high number of false positives, thus PPE availability may drive decision-making. If PPE is available, the majority of gastroenterologists may reasonably select to use N95/N99 respirator or PAPRs. However, a small minority, with a low risk-aversion threshold, may reasonably choose to use surgical masks.

Rationale

In settings where the prevalence of asymptomatic infection is low (<0.5%), the downsides of a pretesting strategy may outweigh the benefits. The downsides include the burden of testing before endoscopy and the high number of false positives (approximately 90% of the asymptomatic individuals who test positive for SARS-CoV-2 will be false positives). Consequently, these individuals will have to cancel their procedure and be required to self-quarantine for 14 days.

The survey conducted by our team (Table 2) found a wide distribution of risk-aversion thresholds in the gastroenterology community. A minority of gastroenterologists (25.7%) had a low risk-aversion threshold and were willing to accept a 1 in 1000 risk of transmission. For this subset of gastroenterologists, surgical masks may be an acceptable option. For the remaining and therefore majority of gastroenterologists, N95/N99 respirators or PAPRs should be used for all upper and lower endoscopies.

Recommendation 3: For a small number of endoscopy centers in high-prevalence areas, the AGA suggests against implementing a pretesting strategy. In "hotspots," endoscopy may be reserved for emergency or time-sensitive procedures with use of N95/N99 respirators or PAPRs for all procedures.
Conditional recommendation, very low certainty evidence
Remarks: In high-prevalence areas, a pretesting strategy may not be informative for decisions about PPE use because of the unacceptable number of false negatives and PPE availability may drive decision-making. If PPE is available, N95/N99 respirators or PAPRs may be used for all upper and lower endoscopies, regardless of time sensitivity. A *hotspot* is defined by a surge in COVID-19

Sensitivity	0.85 (95% CI: 0.85 to 0.97)										
Specificity	0.94 (95% CI: 0.94 to 0.98)										
Outcome	№ of studies	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 0.5%	pre-test probability of 1%	pre-test probability of 2%	
True positives (patients without SARS-CoV2 infection)	12 studies	cohort & case-control type studies [1]	not serious	serious [2]	serious [3]	not serious	none	4 (4 to 5)	9 (9 to 10)	17 (17 to 19)	⊕⊕◯◯ LOW
False negatives (patients incorrectly classified as not having SARS-CoV2 infection)								1 (0 to 1)	1 (0 to 1)	3 (1 to 3)	
True negatives (patients without SARS-CoV2 infection)	12 studies	cohort & case-control type studies [1]	not serious	serious [2]	serious [3]	not serious	none	935 (935 to 975)	931 (931 to 970)	921 (921 to 960)	⊕⊕◯◯ LOW
False positives (patients incorrectly classified as having SARS-CoV2 infection)								60 (20 to 60)	59 (20 to 59)	59 (20 to 59)	

- This table is based on applying the sensitivity and specificity estimates to calculate true positives, false positives, true negatives, and false negatives in a hypothetical population of 1000 individuals.
- Explanations of Judgments:
1. The majority of studies were of case-control design, which may lead to an overestimation of sensitivity, but we did not rate down for risk of bias.
2. We rated down for indirectness because all of the studies were conducted in symptomatic patients
3. We rated down for inconsistency because of unexplained heterogeneity across comparisons

Figure 2. GRADE summary of findings table of test accuracy results for prevalence of 0.5%, 1%, and 2% of SARS-CoV-2 infection in asymptomatic individuals.

cases with an acute burden on hospital capacity. In hotspots, resumption of outpatient endoscopy may depend on availability of PPE.

Rationale

In settings where the prevalence of asymptomatic infection is high (>2%), the downsides of a pretesting strategy may outweigh the benefits. The downsides include the unacceptable rate of false negatives (asymptomatic individuals who test negative for SARS-CoV-2 who actually have infection). Consequently, these individuals will be given false reassurance. Based on our survey results for thresholds for risk aversion, endoscopists were unwilling to accept the small risk of increased infection due to false negatives and thus may opt to use higher PPE. Furthermore, in high-risk settings, testing may be limited and allocated to symptomatic individuals as opposed to asymptomatic individuals. However, if testing is available, a pretesting strategy may be implemented for triaging asymptomatic individuals undergoing outpatient elective procedures.

Recommendation 4: For all endoscopy centers, the AGA recommends against serologic testing as part of a pretesting strategy for patients or endoscopy staff.
Strong recommendation, low certainty evidence
Remarks: Serology testing for the presence of antibodies indicates past infection and has no role in diagnosing SARS-CoV-2 infection in asymptomatic individuals before endoscopy. The evidence supporting the role of seroconversion for return to work or hospital staffing policies is also lacking.

Rationale

A recently published systematic review from the Cochrane Collaboration showed that serologic tests to identify different immunoglobulins (IgM, IgG, and/or IgA) against SARS-CoV-2 may identify individuals who had prior or recent infections.[37] However, the conclusion was informed by studies of symptomatic hospitalized patients and it is not clear how the tests will perform in asymptomatic individuals, which is the case when we are assessing individuals before endoscopy. In addition, the presence of specific immunoglobulins does not necessarily indicate acute vs recent infections; IgM antibodies were identified in about 55% of patients after 35 days of disease onset, while IgG antibodies were identified in 30% of patients within the first week after disease onset. Finally, it is still not clear whether prior SARS-CoV-2 infection or harboring antibodies against SARS-CoV-2 will lead to protection against future infections.

Strengths and Limitations

The limitations of this guideline are outlined below. The data about the prevalence of asymptomatic individuals were limited, and our prevalence estimates were informed by small clinical studies and indirect evidence from statistical models.[29–31] Similarly, our search strategy did not identify studies that assessed the diagnostic accuracy of the available tests in asymptomatic individuals. We used indirect evidence from symptomatic individuals and assumed that the tests will like underperform in those individuals. In addition, the field is rapidly evolving and additional studies on the diagnostic accuracy of the available tests may have been published after our search strategy deadline. Furthermore, the currently available tests were all authorized by the US Food and Drug Administration under Emergency Use Authorization and may become unavailable in the future. With respect to our estimates of diagnostic test accuracy, the included studies were all case-control studies, which are associated with overestimation of diagnostic performance measures. Finally, our recommendations do not take into account cost or economic impact of pretesting strategies, as we did not perform formal economic analyses.

We would also like to highlight the strengths of our guidelines. We used rigorous methodology to systematically pool

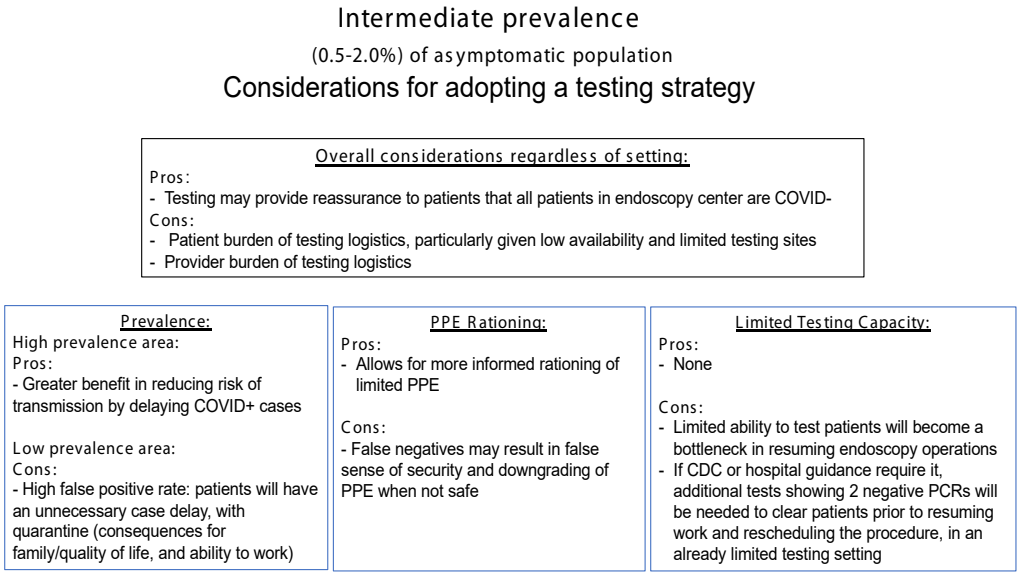

Figure 3. Considerations for adopting a pretesting strategy in intermediate-prevalence settings.

diagnostic accuracy results for commercially available tests in the United States. We also relied on gastroenterologists' reporting of risk aversion to help inform recommendations about the use of PPE based on survey results. Although the survey included only 75 responses, it was valuable in informing the panel's understanding of the variability in thresholds for risk aversion. In the absence of such data, judgments about risk acceptance would have been based on inferences made by panel members of their own individual risk thresholds. Our recommendations account for geographic variability in prevalence of SARS-CoV-2 infection (specifically focusing on the asymptomatic population), which directly impacts test performance and allows for more informed decision-making. Finally, we developed an interactive online tool for gastroenterologists to assist groups in making an individualized decision for their local setting based on their local prevalence and locally available test, and provide a framework for how test results can inform decisions regarding triage and PPE use.

Our guidelines align with recommendations from other gastroenterology societies with the following distinctions: first, we emphasize the importance of determining the prevalence of asymptomatic SARS-CoV-2 infection and second, we highlight the uncertainty around test performance in asymptomatic individuals, as clinical validation studies of currently available tests were conducted only in symptomatic patients with known or suspected COVID-19).[38–40] Furthermore, an economic analysis showed that RT-PCR testing is an effective strategy to restart endoscopic practice and, similar to our guideline, highlighted the importance of accounting for local availability of testing, disease prevalence, and the downstream consequences of false-positive and false-negative results.[5]

Implementation Considerations

Universal Preparations for Endoscopy

Regardless of whether a pretesting strategy is adopted, several measures are essential to establishing a safe working environment for endoscopy. A checklist was created using recommendations from the Centers for Disease Control and Prevention (CDC), with modifications relevant for an endoscopy center (Table 3).[41]

One important consideration is that the CDC screening checklist includes several gastrointestinal symptoms, such as diarrhea. Prior AGA meta-analysis and guideline found that isolated gastrointestinal symptoms (in the absence of other COVID-19 upper respiratory infection symptoms) are rare.[43] Furthermore, when they do occur as an atypical manifestation of COVID-19, other symptoms typically follow within 1 to 5 days. If a patient presenting for endoscopy has nausea, vomiting, or diarrhea for more than 5 days without the development of other COVID-19 symptoms, it is reasonable to consider them as "negative" per the CDC's screening checklist.

Use of an Online Interactive Tool to Determine Whether or Not to Adopt a Pretesting Strategy for Endoscopy

In order to determine whether a testing strategy should be used, our team has created a new online tool available on AGA's website to tailor decision-making to your local setting (https://gastro.org/practice-guidance/practice-updates/covid-19). This resource uses input prevalence data, along with diagnostic test accuracy data, to determine the downstream consequences of testing, such as false-positive and false-negative rates.

First, determine local prevalence in your area. There are several approaches that can be used. We present them here in order of preference after acknowledging the limitation of each method:

1. Use of locally available data from health systems that have been conducting screening for asymptomatic individuals in outpatient settings using nucleic acid amplification tests. This is likely the most accurate estimation of the prevalence of asymptomatic individuals. For example, if your endoscopy center has already employed a pretesting strategy, obtaining

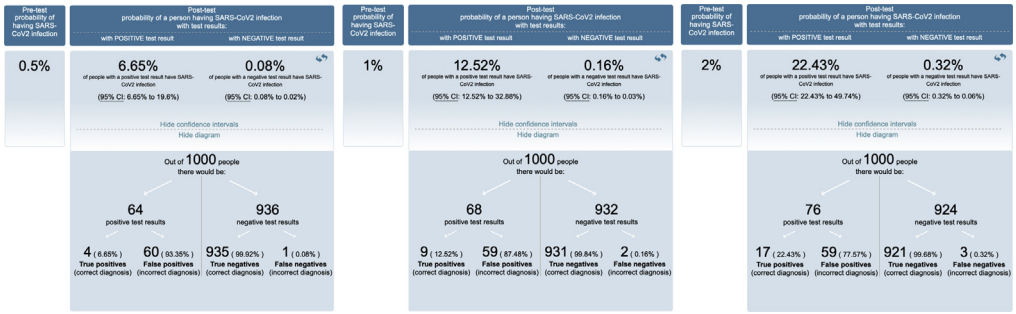

Figure 4. Interactive tool output showing variation in test performance with varying prevalence.

these data to calculate prevalence would be most directly applicable.

2. Use of locally available data from local public health departments regarding the prevalence of the asymptomatic individuals or, if not available, the disease overall. This approach may overestimate or underestimate the prevalence of asymptomatic individuals, depending on the availability and indications for testing in the area.

3. Use of publicly available data about the state or county through the CDC website, The COVID Tracking Project (https://covidtracking.com/), and the COVID-19 Dashboard by the Center for Systems Science and Engineering at Johns Hopkins University (https://coronavirus.jhu.edu/map.html). The websites provide the proportion of positive tests in the area. Unpublished data and the available models suggest that for each diagnosed symptomatic patient there can be 10 asymptomatic or undiagnosed individuals in the area.[29,30] This can be used to estimate the prevalence in the area by using the number of diagnosed cases during the past 2 weeks and the publicly available data about population count in each area. The use of the proportion of positive tests alone is likely an overestimation of the prevalence and should not be used alone to assess the prevalence.

The following steps for calculating state prevalence in the asymptomatic population for input in interactive Summary of Findings (iSOF) (Table 4). For more granular data that may be more relevant to your local setting, see Supplementary Video 1 https://gastro.org/news/use-this-tool-to-determine-your-pre-testing-strategy-prior-to-endoscopy/.

1. Visit the COVID Tracking Project website at https://covidtracking.com
2. Look up your state. In the example illustrated below, Missouri was selected.
3. Look up the cumulative number of cases as of June 30 (insert most recent date).
4. Look up the cumulative number of cases as of June 16 (14 days ago).
5. Subtract "4" – "3" (ie, cases from June 30 to June 16) = number of new cases in the past 14 days.
6. Adjust for asymptomatic population by multiplying by 10.[29,30]
7. Go to US Census Bureau website at https://www.census.gov/quickfacts/ and look up estimated state population.
8. Divide numbers above: "6" / "7" (cases assuming asymptomatic population / state population) = estimated prevalence in asymptomatic population.

Second, enter the test characteristics for your locally available test. The diagnostic test characteristics are defaulted to the pooled sensitivity and specificity derived from our meta-analysis described above, which encompasses commercially available US tests. This can, however, be customized to reflect performance of locally available tests in an individual setting. Of note, the lower end of the CI is used, given that these data are taken from symptomatic populations and testing accuracy is likely to be lower for asymptomatic patients. If your local test is an institutional laboratory-derived test, the sensitivity and specificity may differ. This can be modified in the online tool as well.

Third, based on assumptions of prevalence and test accuracy, the online tool will provide information on the false-negative rate and false-positive rate in your local setting (Figure 4). In intermediate prevalence areas, tradeoffs of testing should be considered (Figure 3) to help decide whether a pretesting strategy is implemented. The matrix shown in Figure 5 takes into account testing availability and PPE availability. This highlights that if testing capacity is severely limited, a no-testing approach is reasonable, regardless of prevalence. In this scenario, PPE use is determined by availability and risk-aversion threshold of endoscopists. In a high-prevalence area, the highest level of PPE should be worn. In a low-prevalence area, risk-aversion thresholds will be the determining factor for PPE decision-making.

Fourth, if a decision is made to implement a pretesting strategy, there are several logistical considerations. Many health care facilities may already have mechanisms in place for pre-procedure testing and specimen collection. If not, setting up testing at your endoscopy center can be considered. It is important to maximize test performance using high-quality specimen collection and sampling technique, as

Table 3. Checklist for Endoscopy Center Reopening

1. Pre-arrival symptom screening for patients using the CDC checklist.[42]
2. Limit entry of individuals of nonessential individuals (patients, visitors, and staff).
3. All individuals (patients, visitors, and staff) should wear masks at all times, unless access to the nose or mouth are necessary for patient care.
4. Set up waiting rooms to allow patients to be at least 6 feet apart. If your facility does not have a waiting area, then use partitions or signs to create designated areas or waiting lines.
5. Maintain physical distancing (at least 6 feet) in waiting areas between visitors. When space is limited, consider providing alternate areas for visitor waiting and/or requesting visitors wait outside of the facility.
6. Per institutional and local governmental protocols, additional consent regarding the risks of contracting COVID-19 may be required.
7. Frequent and scrupulous hand hygiene for all individuals in the health care facility.
8. Ensure best practices in donning, doffing, and disposal of PPE.
9. Appropriate disposal of all single-use equipment after use and decontamination of reusable equipment strictly in line with the manufacturer's instructions.

outlined in Supplementary Table 5. Test result follow-up should occur in a timely fashion. In the event of a positive result, patients should be notified according to local institutional policies, with instructions to self-isolate accordingly. In some cases, repeat testing may be required to clear the patient for endoscopy, although this policy is controversial and not universal. Another consideration is that local prevalence may change over time and require reassessment of the implemented strategy, and periodic re-evaluaton of prevalence to inform local endoscopy center practices will be necessary.

Conclusions

The COVID-19 pandemic is a global economic, societal, and health crisis. Procedural volumes have drastically declined to 60%–80% of baseline volumes, indicating the impact on gastroenterology practices.[32,44,45] The provision of health care services, including the reintroduction of endoscopy across health care systems and ambulatory care centers is critical to reducing the long-term consequences of this crisis. Ensuring safety for patients, staff, and endoscopists is an important consideration in the resumption of endoscopy, however, endoscopy centers across the United States face many unique challenges with respect to availability and access to testing, understanding geographic variability in SARS-CoV-2 prevalence rates, and availability of PPE.

In areas where testing is more widely available, the 2 main considerations that should drive the decision to implement a pretesting strategy are local prevalence of SARS-CoV-2 (in asymptomatic individuals) and diagnostic test performance (ie, sensitivity and specificity). These test characteristics combined with prevalence drive the likelihood of obtaining false-positive and false-negative results. If a pretesting strategy is implemented, it is important to consider the logistics of testing (for patients and endoscopy centers), the informative value of the test, and downstream consequences with respect to triaging of patients, ensuring safety with endoscopy, and PPE use. In areas where testing

Table 4. How to Calculate Prevalence of Asymptomatic SARS-CoV-2: Case Example

Variable	Data
Cumulative no. of cases diagnosed as of June 30, 2020 in Missouri	21,551
Cumulative no. of cases diagnosed as of June 16, 2020 in Missouri	16,416
No. of cases diagnosed between June 16 and June 30, 2020 in Missouri	5137
Estimated no. of cases after correcting for asymptomatic individuals	51,370
Estimated state population	6,137,428
Estimated prevalence after correcting for asymptomatic individuals, %	0.8

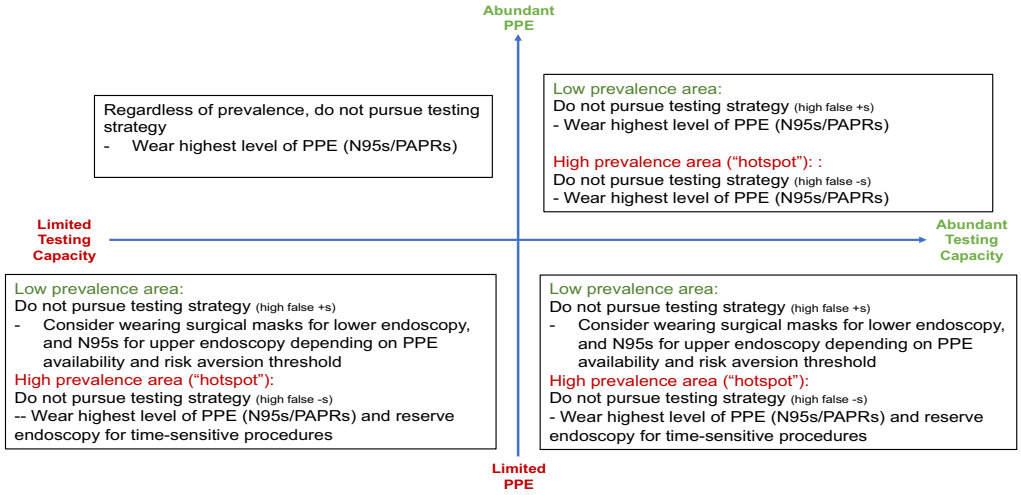

Figure 5. Testing strategy considerations in low- and high-prevalence areas accounting for testing and PPE availability. Highest level of PPE includes N95/N99 respirators and PAPRs, along with a face shield. A *hotspot* is defined by a surge in COVID-19 cases with an acute burden on hospital capacity. In limited PPE settings, extended use and reuse of N95/N99 respirators can be considered.[7]

capacity is limited, diverting limited resources for procedural testing of outpatient asymptomatic individuals before endoscopy may further compound the problem. Increasing the number of tests is essential, but many areas struggle with rationing of tests and being able to provide test results in a timely manner.

The online interactive tool created as a result of this guideline aims to help endoscopy centers determine the downstream effects of implementing a pretesting strategy (https://gastro.org/news/use-this-tool-to-determine-your-pre-testing-strategy-prior-to-endoscopy/). We provide guidance for gastroenterologists to calculate the prevalence of SARS-CoV-2 infection in asymptomatic individuals, input sensitivity and specificity of their local test, and determine the rates of positive and negative tests to help guide decision making. Periodic re-evaluaton of prevalence to inform local endoscopy center practices is recommended in light of geographic variability and predictions of more surges during the next 12–18 months.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at http://dxdoi.org/10.1053/j.gastro.2020.07.043.

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Correspondence
Address correspondence to: American Gastroenterological Association, National Office, 4930 Del Ray Avenue, Bethesda, Maryland 20814. e-mail: ewilson@gastro.org.

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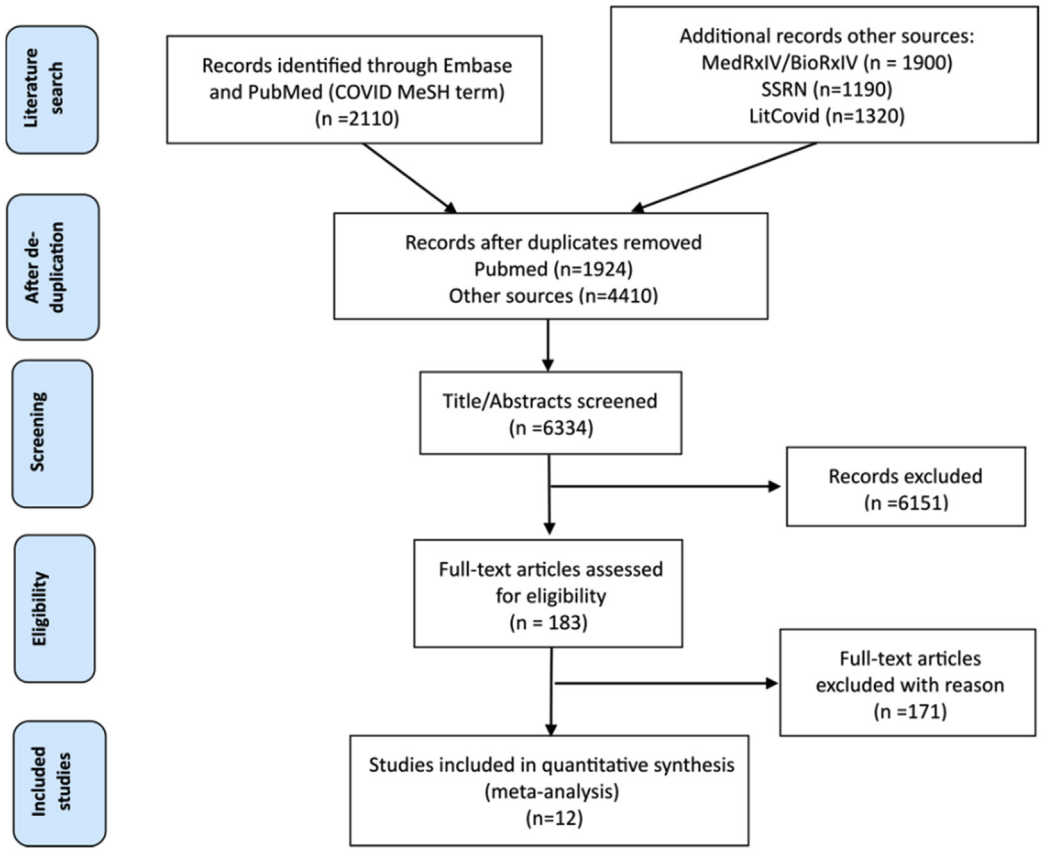
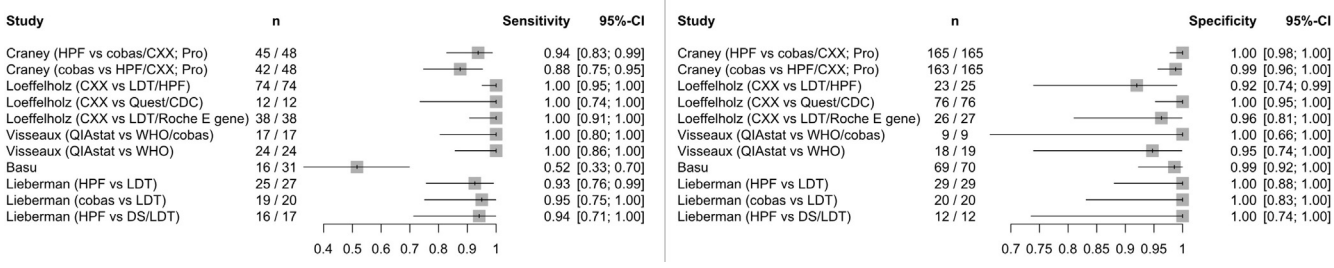
Conflicts of interest
All members were required to complete the disclosure statement. These statements are maintained at the American Gastroenterological Association headquarters in Bethesda, Maryland. The authors disclose no conflicts.

This document represents the official recommendations of the American Gastroenterological Association Institute and was developed by select members of the Clinical Guideline Committee and Clinical Practice Update Committee and approved by members of the American Gastroenterological Association Governing Board. **Expiration Date:** 6 months.



Supplementary Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses Flow Diagram of Studies. MeSH, Medical Subject Heading.



Supplementary Figure 2. Test accuracy (pooled sensitivity and specificity) of studies with low risk of bias.

Supplementary Table 2. Interpretation of the Certainty in Evidence of Effects Using the GRADE Framework

GRADE	Description
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.
Very low	We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect

Supplementary Table 3. Interpretation of Strong[a] and Conditional[b] Recommendations Using the GRADE Framework

Implications	Strong recommendation	Conditional recommendation
For patients	Most individuals in this situation would want the recommended course of action and only a small proportion would not.	The majority of individuals in this situation would want the suggested course of action, but many would not.
For clinicians	Most individuals should receive the intervention. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	Different choices will be appropriate for individual patients consistent with his or her values and preferences. Use shared-decision making. Decision aids may be useful in helping patients make decisions consistent with their individual risks, values and preferences.
For policy-makers	The recommendation may be adapted as policy or performance measure in most situations	Policy-making will require substantial debate and involvement of various stakeholders. Performance measures should assess whether decision-making is appropriate.

[a]Strong recommendations are indicated by statements that lead with "we recommend."
[b]Conditional recommendations are indicated by statements that lead with "we suggest."

Supplementary Table 4. Quality Assessment of Diagnostic Accuracy Studies-2 Assessment of Risk of Bias for Diagnostic Test Accuracy Studies

Study first author[a] (test comparison subcohort)	Patient selection	Index test	Reference standard	Flow and timing
Craney[17] (HPF vs cobas/CXX)	High	High	Low	Low
Craney[17] (cobas vs HPF/CXX)	High	High	Low	Low
Craney[17] (HPF vs cobas/CXX)	Low	Low	Low	Low
Craney[17] (cobas vs HPF/CXX)	Low	Low	Low	Low
Loeffelholz[18] (CXX vs LDT/HPF)	Low	Low	Low	Low
Loeffelholz[18] (CXX vs Quest/CDC)	Low	Low	Low	Low
Loeffelholz[18] (CXX vs RealStar)	Low	Low	Unclear	Low
Loeffelholz[18] (CXX vs GFRA/Allplex)	Low	Low	Unclear	High
Loeffelholz[18] (CXX vs LDT/Roche E gene)	Low	Low	Unclear	Low
Loeffelholz[18] (CXX vs Abbott RT)	Low	Low	Unclear	Low
Loeffelholz[18] (CXX vs DS)	Low	Low	Unclear	Low
Visseaux[20] (QIAstat vs WHO/cobas)	Low	Low	Low	Low
Visseaux[20] (QIAstat vs WHO)	Low	Low	Low	Low
Mitchell[19] (AIDN vs CDC or LDT)	High	Low	Low	High
Basu[21] (AIDN vs CXX)	Low	Unclear	Low	Low
Lieberman[22] (HPF vs LDT)	Low	High	Low	Unclear
Lieberman[22] (DS vs LDT)	Low	High	Low	Unclear
Lieberman[22] (cobas vs LDT)	Low	High	Low	Unclear
Lieberman[22] (HPF vs DS/LDT)	Low	High	Low	Unclear
Lieberman[22] (CXX vs LDT; parallel)	High	High	Unclear	Unclear
Lieberman[22] (HPF vs LDT; parallel)	High	High	Unclear	Unclear
Lieberman[22] (DS vs LDT, parallel)	High	High	Unclear	Unclear
Lieberman[22] (cobas vs LDT; parallel)	High	High	Unclear	Unclear
Smith[28] (HPF vs BioFire/Aptima)	High	Unclear	Unclear	Unclear
Smith[28] (Biofire vs HPF/Aptima)	High	Unclear	Unclear	Unclear
Smith[28] (Aptima vs HPF/BioFire)	High	Unclear	Unclear	Unclear
Bordi (SD vs LDT WHO)	Low	Low	High	Low
Broder[24] (CXX vs cobas)	High	High	Low	Low
Smithgall[25] (AIDN vs cobas)	High	Low	High	Low
Smithgall[25] (CXX vs cobas)	High	Low	High	Low
Uhteg[26] (ePlex vs RealStar)	High	Low	High	Low
Zhen[27] (CXX vs HPF)	High	Low	High	Low
Zhen[27] (AIDN vs HPF)	High	Low	High	Low
Zhen[27] (ePlex vs HPF)	High	Low	High	Low

AIDN, Abbott ID Now; CXX, Cepheid Xpert Xpress; DS, Diasorin Simplexa; LDT, laboratory-developed test; HPF, Hologic Panther Fusion; WHO, World Health Organization.
[a]All articles were published in 2020.

Supplementary Table 5. Frequently Asked Questions About Diagnostic Tests for SARS-CoV-2

Question	Answer
What kinds of SARS-CoV-2 diagnostic tests are currently available in the United States?	On February 4, 2020, the Secretary of the US Department of Health and Human Services determined there was a public health emergency that justified the authorization of emergency use of in vitro diagnostics for COVID-19. Commercial manufacturers and clinical laboratories were required to submit details about SARS-CoV-2 assays to the US Food and Drug Administration (FDA) for review and Emergency Use Authorization (EUA). EUA was established as part of the Project BioShield Act of 2004 and allows the FDA to issue emergency approval of drugs, devices, and diagnostic tests to help combat a crisis.[46] The regulations to obtain approval differ substantially from the standard FDA approval process. Although the FDA does not typically regulate laboratory tests, in the setting of an EUA, the FDA is issued the authority to establish which laboratory tests can be used and what testing standards are needed before obtaining FDA approval.[47] In the setting of a public health emergency, the FDA only requires a standard of "may be effective" to approve a diagnostic test. To achieve this, test developers are expected to test their assay against a minimum 30 positive samples and 30 negative samples.[48] Ideally, positive clinical samples are recommended, but contrived reactive specimens can be used as well. Although these standards are significantly lower than what is typically needed to obtain approval for a new diagnostic test, the EUA allows the FDA to review this limited data and issue approval. Importantly, once the public health emergency is discontinued, EUAs are no longer in effect and manufacturers must submit standard data requirements supporting their test's diagnostic accuracy. Multiple commercial test manufacturers and clinical laboratories, including academic medical centers, have received EUA for a SARS-CoV-2–specific molecular diagnostic test. As of July 8, 2020, 104 tests have received EUA.[49]
What additional factors can impact test performance?	Source of specimen: Specimen sources for SARS-CoV-2 testing include nasopharyngeal (NP), mid-turbinate (MT), nasal, throat, or saliva. In symptomatic patients, a recent meta-analysis and guideline from the Infectious Disease Society of America (IDSA) suggests collecting NP or MT or nasal swabs rather than oropharyngeal swabs or saliva alone for diagnostic testing.[4] However, no recommendation was made for asymptomatic patients, which comprise our outpatient endoscopy population, as available data are limited. Collection method: Collection technique also impacts diagnostic test accuracy. Particularly for NP sample collection, training is beneficial to ensure adequate specimen collection. A useful resource for NP sample technique is available from the *New England Journal of Medicine*, which includes both a description and video for training purposes.[50] Other technique instructions for diagnostic testing are available on the FDA's website.[51] In addition, collection of specimens is most commonly performed by health care workers, but some tests allow for patient self-collection as well. Published guidance from the IDSA indicates that there is no role for self-collection of samples in asymptomatic individuals and therefore this practice is not recommended in the context of endoscopy operations.[4]
How can the RT-PCR test be a false negative or a false positive?	False negatives can result when there is inadequate specimen collection as described above, or the viral load is low and the test is unable to detect SARS-CoV-2 at that threshold. Conversely, false positives can result because of cross-reactivity of other coronaviruses, or more commonly, specimen contamination.

Supplementary Table 5. Continued

Question	Answer
Do we need negative pressure rooms or air exchanges for aerosol-generating procedures?	Aerosol generation occurs when air accelerates across a fluid surface and creates aerosols that contain virus. However, whether aerosol has infective potential is impacted by many factors, including where the fluid originates (eg, upper airway, lower respiratory tract, upper or lower gastrointestinal tract) the amount of virus present in the aerosols, and how much aerosolization occurs (which may differ according to the procedure). Depending on the type of aerosol-generating procedure and the risk of airborne transmission, PPE at the level of airborne protection may be indicated. In some locations, engineering modification can change a positive pressure room or entire ward to a negative pressure. Having a room with good ventilation, that is, a high rate of air exchanges, is likely to be more important than whether it is at positive or negative pressure. In hospitals, room ventilation will clear viral aerosols fairly quickly. Each "air exchange" removes approximately 63% of the virus, after *n* room exchanges, the remaining viral load is 0.37^n. After 2 exchanges, there is 14% and after 5 air exchanges $<1\%$ (0.37^5) of the original viral load in the room, respectively. If there are 12 air exchanges per hour, 5 exchanges will take 25 min. This may be the case in the intensive care unit. If there are 25 air exchanges per hour, 5 air exchanges will take 12 min. Until the room is clear of aerosol (the viral clearance period), the level of PPE worn should be at the level of airborne protection.