

Title: AGA Rapid Review and Guideline for SARS-CoV2 Testing and Endoscopy Post-Vaccination: 2021 Update

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This document represents the official recommendations of the American Gastroenterological Association (AGA) Institute and was developed by select members of the Clinical Guideline Committee and Clinical Practice Update Committee and approved by members of the AGA Governing Board.

## Abstract:

This guideline provides updated recommendations on the role of pre-procedure testing for SARS-CoV2 in individuals undergoing endoscopy in the post-vaccination period and replaces the prior guideline from the American Gastroenterological Association (released July 29, 2020). Since the start of the pandemic, our increased understanding of transmission has facilitated the implementation of practices to promote patient and healthcare worker (HCW) safety. Simultaneously, there has been increasing recognition of the potential harm associated with delays in patient care as well as inefficiency of endoscopy units. With widespread vaccination of HCWs and the general population, a re-evaluation of AGA's prior recommendations was warranted. In order to update the role of pre-procedure testing for SARS-CoV2, the AGA guideline panel reviewed the evidence on (1) prevalence of asymptomatic SARS-CoV2 infections in individuals undergoing endoscopy, (2) patient and HCW risk of infections that may be acquired immediately before, during, or after endoscopy, (3) effectiveness of COVID-19 vaccine in reducing risk of infections and transmission, (4) patient and HCW anxiety, (5) patient delays in care and potential impact on cancer burden, and (6) endoscopy volumes. The panel considered the certainty of the evidence, weighed the benefits and harms of routine pre-procedure testing, and considered burden, equity, and cost using the GRADE framework. Based on very low certainty evidence, the panel made a conditional recommendation *against* routine pre-procedure testing for SARS-CoV2 in patients scheduled to undergo endoscopy. The panel placed a high value on minimizing additional delays in patient care, acknowledging the reduced endoscopy volumes, downstream impact on delayed cancer diagnoses and burden of testing on patients.

## Introduction

On December 11, 2020, the first vaccine to prevent COVID-19 received emergency use authorization (EUA) in the United States thereby signifying the start of the road to recovery from this devastating pandemic.<sup>1</sup> As of March 2021, 52% of HCWs had been vaccinated with population-wide vaccination strategies well underway, and with expanding eligibility, vaccination rates are expected to rise over time.<sup>2</sup> In light of our increased understanding of the effectiveness and availability of vaccinations, there is a need for updated guidance on the role of testing for SARS-CoV2 in asymptomatic individuals prior to endoscopy. This guideline replaces the prior set of recommendations released on July 29, 2020 and provides updated recommendations on the role of pre-procedure testing in the post-vaccination period.<sup>3</sup> A summary of the recommendations is outlined in **Table 1**.

### Table 1: Executive Summary of Recommendations

Summarized below are the recommendations with comments related to the role of testing in endoscopy. The strength of a recommendation is expressed as strong or conditional, based on the **GRADE** methodology and has the following interpretation:

**Strong recommendation:** All centers should follow the recommended course of action, and only a small minority may not.

**Conditional recommendation:** The majority of centers in this situation should follow the suggested course of action but many would not; different choices may be appropriate.

**These recommendations assume that**

(1) all centers have access to personal protective equipment (PPE) including face shield, eye protection and surgical mask or N95 (or N99, PAPR)  
(2) all centers have implemented universal screening of patients for COVID-19 symptoms, using a screening checklist and have implemented universal precautions including physical distancing, masks, and hand hygiene in the endoscopy unit

**Recommendation 1: The AGA suggests against routine pre-procedure testing for SARS-CoV2 in patients undergoing upper endoscopy\* or lower endoscopy\* irrespective of the vaccination status of patients**

***Conditional recommendation, very low certainty evidence***

**Remarks:**

*Centers that prioritize the small potential benefit (staff and patient reassurance, detection of asymptomatic positive cases) over the harms (burden of testing on patients, downstream consequences of false positives, potential delays in care and decreased endoscopy efficiency) may choose to implement a pre-procedure testing strategy as outlined in Recommendation 2.*

**Recommendation 2: In endoscopy centers that implement a pre-procedure testing strategy, the AGA suggests using standard nucleic acid testing (laboratory-based NAAT or rapid RT-PCR) rather than a rapid isothermal test or antigen tests, in patients undergoing upper endoscopy\* or lower endoscopy\* irrespective of the vaccination status of patients**

***Conditional recommendation, very low certainty evidence***

**Remarks:**

Rapid RT-PCR tests that can be easily performed on the day of endoscopy (results within 1 hour) are preferable as they pose less burden to patients. In the pre-procedure setting, the utility of rapid isothermal tests or antigen tests is limited due to concerns of assay sensitivity. There is no role of antibody tests for pre-procedure testing.

**TEST DESCRIPTIONS:**

- **Standard Nucleic Acid Amplification Tests (NAAT)** include *laboratory-based NAAT and rapid RT-PCR tests that detect viral RNA and have the best diagnostic test accuracy. Rapid RT-PCR tests are defined as tests that provide results in 1 hour.*

- **Rapid isothermal tests** detect viral RNA.

- **Antigen tests** detect viral proteins with the vast majority of tests detecting nucleocapsid antigen. Most antigen tests are rapid, providing results within 15 minutes.

\* the terms upper and lower endoscopy include all related gastrointestinal procedures (e.g. EUS, ERCP, flexible sigmoidoscopy)

## Scope and Purpose

We summarize the available data on the diagnostic test characteristics of tests for SARS-CoV2 infection and provide evidence-based clinical guidance on the role of pre-testing prior to

endoscopic procedures in the setting of ongoing vaccinations of healthcare workers and patients. 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 public, HCWs and the AGA membership at large.

### **Target Audience**

The target audience of 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 in the US. Patients, as well as policy makers, may also benefit from these guidelines. These guidelines are not intended to impose a standard of care for individual institutions, healthcare systems or countries. They provide the basis for rational informed decisions for clinicians, patients and other health care professionals. However, decisions may be constrained by local health system-level or state-level policies as well as availability of resources.

### **How to use this guideline**

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 results section. The implementation considerations section in this guideline will help clinicians implement these recommendations.

### **Methods**

This guideline was developed using the GRADE approach. Given the need for guidance during a major public health crisis, the methodological approach was modified according to the Guidelines International Network/McMaster checklist for the development of rapid recommendations.<sup>4</sup> For one of the recommendations, we utilized a process called GRADE-ADOLOPMENT, which allows for adaptation or modification of existing guideline recommendation (see below).<sup>5</sup>

### **Panel Composition**

The guideline panel included gastroenterologists, an infectious disease expert, and guideline methodologists. A preliminary draft of the recommendations was shared with anesthesiologists at one panel member's institution and the final draft was reviewed by a patient for feedback.

### **Guideline Funding and Conflict of Interest Management**

Development of the guideline was funded by the AGA and no panel members received any payments. Panel members disclosed all financial, intellectual or other potential conflicts of interest according to the AGA Institute policy. These are available from the AGA Clinical Guideline Committee staff liaison.

## **Perspective**

These recommendations assume a patient or population perspective. While the majority of HCWs have been, or will be, vaccinated against SARS-CoV2, the panel acknowledged that a subgroup of HCWs have declined vaccinations. Furthermore, the panel assumed that all endoscopy centers follow universal precautions and that staff have access to personal protective equipment (PPE).

## **Clinical Questions**

Using a PICO format (Population, Intervention, Comparison, Outcomes), the panel created an analytical framework. See **Supplement Figure 1** for Analytic Framework for pre-procedural testing and outcomes. Panel members prioritized the following patient-important outcomes for decision-making: **Patient safety (COVID-19 infection), Patient reassurance or anxiety, Patient delays in care and impact on cancer burden, HCW safety (COVID-19 infection), HCW reassurance or anxiety, Test burden** (feasibility, acceptability), **Cost**, and **Health Equity**. Patient delays in care and impact on cancer burden was deemed a critical outcome for decision-making.

## **Search Strategy**

### **Information sources and literature search**

We conducted a systematic literature search to identify all published 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 1, 2021 using the MeSH term developed for COVID-19. A systematic review of the literature identified 1651 references of which 42 informed the evidence base for these recommendations. See **Supplement Figure 2** for PRISMA Flow Diagram.

## **Study selection**

Six reviewers (OA, PD, JF, SS, SS, SMS) 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 pre-procedure testing and SARS-CoV2 infection among patients and HCWs exposed to endoscopy, patient and HCW anxiety/reassurance, endoscopy volumes, patient delays in care and impact on cancer burden (colorectal, esophageal and gastric). We excluded studies that reported on pre-procedure tests in non-endoscopy settings and survey studies of infections. With rapidly evolving aspects of effectiveness of COVID-19 vaccines in decreasing risk of infection and SARS-CoV2 transmission, we relied on updated documents published by the U.S. Centers for Disease Prevention and Control and pre-print servers. For equity considerations, since no studies reported specifically on pre-procedure testing, we highlighted select articles that reported on equity issues more broadly. For information about diagnostic test performance, the Infectious Disease Society of America (IDSA) living rapid guideline was used to inform diagnostic test accuracy for laboratory-based RT-PCR NAAT, rapid RT-PCR, antigen tests, and antibody tests.<sup>6</sup>

## Data Collection and Analysis

Reviewers (OA, PD, JF, SS, SS, SMS) extracted relevant information into a standardized data extraction form, which included study characteristics (authors, publication year, study dates, country, study design), endoscopy volumes, pre-procedure screening and testing, type of masks, infection rates in HCW and patients, prevalence of positive and negative tests, anxiety/reassurance in HCWs and patients, and numbers of observed or expected colorectal (CRC), esophageal, or gastric cancers. For studies on vaccine effectiveness, we extracted data on population vaccinated, type and timing of vaccine, asymptomatic/symptomatic infection, vaccine effectiveness or risk reduction. Because of the heterogeneity of studies and indirect evidence, the evidence was summarized narratively, and no formal meta-analysis was performed.

## Certainty of Evidence

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.<sup>7</sup> The GRADE summary of findings table and evidence profile was generated using the GRADEpro Guideline Development Tool.<sup>8</sup>

## Evidence to Recommendations

The panel evaluated the certainty of evidence, balance between benefits and harms, and burden of testing on patients (acceptability, feasibility), cost, and equity. For all recommendations, the panel reached consensus. As per GRADE methodology, recommendations are labeled as “strong” or “conditional”. The words “we recommend” indicate strong recommendations and “we suggest” indicate conditional recommendations.

For one of the recommendations, we utilized a process called GRADE-ADOLPMENT, which allows for adaptation or modification of existing guideline recommendation.<sup>5</sup> Briefly, the process of adaptation involves identifying the pertinent health care questions, searching for existing guidelines that addressed those questions, critically appraising them, and deciding whether to accept or modify all or selected recommendations. The adapted recommendation may have a change in the specific population, intervention, comparator than the original recommendation and a different certainty in the evidence. This decision also requires considering whether recommendations are credible, up to date, acceptable, applicable, and feasible to implement to one’s organizational context. For this guideline, the panel adapted the recommendation for asymptomatic testing as it applied to the pre-endoscopy setting.

## RESULTS

A summary of all of the recommendations is provided in **Table 1**.

**Recommendation 1: The AGA suggests against routine pre-procedure testing for SARS-CoV2 in patients undergoing upper endoscopy or lower endoscopy, irrespective of the vaccination status of patients. *Conditional recommendation, very low certainty evidence***

**Remarks:**

*Centers that prioritize the small potential benefit (staff and patient reassurance, detection of asymptomatic positive cases) over the harms (burden of testing on patients, downstream consequences of false positives, delays in care and decreased endoscopy efficiency) may choose to implement a pre-procedure testing strategy as outlined in Recommendation 2.*

**Rationale**

The panel reviewed the evidence on (1) prevalence of asymptomatic infections in individuals undergoing endoscopy, (2) patient/HCW infections after endoscopy, (3) effectiveness of the vaccine on reducing infections (4) patient/HCW anxiety (5) patient delays in care (endoscopy volumes) and impact on cancer burden. The panel then evaluated the certainty of the evidence, weighed the benefits and harms of pre-procedure testing, and considered burden, equity, and cost. The panel acknowledged the small potential benefit of pre-procedure testing with respect to patient and staff reassurance but no benefit with regard to infections since the risk of infection was extremely low (with symptom screening, adequate PPE, and protection from infection [both asymptomatic and symptomatic] due to vaccination). The panel also evaluated the yield of testing (rates of positive tests among asymptomatic individuals ranged from 0-0.5%) and the significant delays in care (reduced numbers of procedures across endoscopy centers with incomplete recovery of volumes) and reduced numbers of diagnoses of CRC, esophageal, and gastric cancers (compared to expected numbers from historical data). Based on low certainty evidence, the panel made a conditional recommendation against pre-procedure testing for SARS-CoV2. The panel placed a high value on minimizing additional delays in patient care, acknowledging the reduced endoscopy volumes, downstream impact on delayed cancer diagnoses and additional burden of testing on patients. See **Supplement Figure 3 for Implementation of a Pre-Endoscopic Testing Strategy.**

**Summary of the Evidence:**

The evidence is summarized in **Table 4: Summary of Findings Table**. We found no studies that provided comparative evidence of pre-procedure testing in combination with symptom screening versus symptom screening alone on the outcomes of interest: patient/HCW infections; patient/HCW reassurance or anxiety and patient delays in care and impact on cancer burden. We found indirect evidence to inform these outcomes as outlined below:

Prevalence of Asymptomatic Infection

We found 13 studies that reported on asymptomatic SARS-CoV2 among patients referred for endoscopic procedures who underwent testing.<sup>9-20</sup> Across these 13 studies, asymptomatic prevalence ranged from 0.0% to 1.5% but most studies reported a range from 0-0.5% regardless of local surges of COVID-19 cases. A notable example of this is highlighted in two UK studies, conducted by the same authors at different time periods and surges; during the first time period from May-June 2020 when local prevalence was low, the asymptomatic prevalence was 0.11% (n=2611) and during a surge in December 2020, the asymptomatic prevalence remained low (0.37%: 9/2449).<sup>15, 16</sup> The authors emphasized the role of symptom screening in maintaining low rates of SARS-CoV2 positivity in the endoscopy setting. Similarly, a large dataset from the VA healthcare system in the USA showed a low prevalence of 0.1%; 46 PCR

positive out of 47,980 individuals that screened negative for symptoms screening prior to endoscopy (Jason Dornitz/Andrew Gawron, personal communication). Finally, it is noteworthy that the few studies that reported on symptom screening results showed that symptom screening was higher yield than a pre-endoscopic testing strategy. Further information on reported rates of prevalence compared to local prevalence across studies is shown in **Supplement Table 1**.

Patient/HCW Infections after Endoscopy:

We found 8 studies (2 prospective and 6 retrospective cohort studies) that reported rates of infection among HCWs and individuals undergoing endoscopy.<sup>11, 15, 16, 21-25</sup> Of these studies, 5 were in the context of a pre-procedure testing strategy<sup>11, 15, 16, 22, 24</sup>, and 3 did not have an explicit pre-procedure testing strategy.<sup>21, 23, 25</sup> Among **patients** who underwent endoscopy, the rates of infection ranged from 0% to 0.4%. Among **HCWs**, the rates of infection ranged from 0% to 4.0%. The study reporting 4% (42/968) was from Italy during the first wave of the pandemic (January-March 2020).<sup>23</sup> A notable limitation is the lack of robust contact tracing in included studies; the cases of COVID-19 were attributed to endoscopy exposure if there was no other known exposure. However, this would bias in favor of over-estimating infection and transmission, and despite this, cases of reported transmission are rare (see **Table 2**).

**Table 2: Included studies reporting on infections after endoscopy**

Study Author, Design, Dates	Pre-procedure testing	PPE / Masks	Patient infections (Data source)	HCW Infections (Data source)	Total endoscopic cases
Hayee (prospective cohort) <sup>15</sup> 12/14/2020 to 12/31/2020 after emergence of UK variant	Universal Symptom screening* and pre-procedure testing	BSG guidance**	3  (Post-endoscopy symptom screening day 7 and day 14 and testing as indicated)	0  (Reporting by local endoscopy centers)	2440
Hayee (prospective cohort) <sup>16</sup> 4/30/2020 to 6/30/2020	Universal Symptom screening *  Some endo units with PCR testing (n=2611)	BSG guidance**	0  (Post-endoscopy symptom screening day 7 and day 14)	0  (Reporting by local endoscopy centers)	6208
Huang (retrospective cohort) <sup>22</sup> 2/1/2020 to 3/31/2020	Universal Symptom screening*  PCR testing if symptom screening positive	N95s or medical surgical masks	0  (Post-endoscopy follow-up)	0/33  (Symptom screening, temperature monitoring, PCR testing)	1808

D'Ovidio <sup>25</sup> (retrospective cohort)  3/9/2020 to 5/4/2020	Universal Symptom Screening*	NR	0  (Post- endoscopy follow-up)	0  (PCR and serologic testing)	60
Pena Ray (retrospective cohort) <sup>21</sup>  3/13/2020 to 5/11/2020	Universal Symptom Screening*	NR	0  NR	0 "No cases associated with endoscopy" unclear if this included HCWs  NR	3310
Repici (retrospective cohort) <sup>23</sup>  1/27/2020 to 3/13/2020	Screening/triage protocols evolved during this time	Active rationing of N95s; mix of N95s and surgical masks	1  (Post- endoscopy follow-up at 2 weeks)	42/968***  (HCW survey)	802
Jagannath (retrospective cohort) <sup>24</sup> 4/2/2020 to 5/31/2020	Universal Symptom screening*  PCR testing if symptom screening positive	N95s	6***	4/74 (0.26%/100 endoscopies)	1549
Casper (retrospective cohort) <sup>11</sup>  3/23/2020 to 5/10/2020	Universal Symptom Screening*  PCR testing	BSG Guidance**	0  (NR)	0  (weekly testing of HCWs)	313

\*Universal Symptom Screening includes both patient's symptoms as well as screening for high-risk exposures (travel/sick contacts).

\*\*BSG guidance recommends the following: if COVID negative: surgical masks for all cases; if COVID status unknown but symptom screening negative: N95 for upper endoscopy and surgical masks for lower endoscopy

\*\*\*Of note, all 6 cases by Jagannath occurred within 48 hours after endoscopy (unlikely that endoscopy was the source). Also, it is unclear if the 42 HCW cases in this study were related to endoscopy or other exposures (contact tracing was not done) and the majority of the cases, 85.7%, were recorded prior to implementation of stringent preventive measures including PPE.

Vaccination Effectiveness against Infection: There were no studies reporting on rates of infection in the context of endoscopy after vaccination of patients or HCWs. However, we utilized data from an existing Centers for Disease Control and Prevention (CDC) review and found an additional six prospective cohort studies that reported vaccine effectiveness against symptomatic or asymptomatic infection.<sup>26-29</sup> See **Table 3**. Based on these studies, vaccine effectiveness for Pfizer/Moderna against asymptomatic SARS-CoV-2 infection and transmission at 7-14 days after the second dose ranges from 80-94%. Additionally, studies reported that the absolute risk of testing positive for SARS-CoV-2 after vaccination among HCWs ranged from

0.5-1.19%. It is worthwhile to note that the CDC no longer requires quarantine after known COVID-19 exposure for vaccinated individuals, which include the majority of HCWs<sup>30</sup>.

**Table 3: Included studies on vaccine effectiveness against SARS-CoV-2 infection**

Study (Author/Year, Country)	Population (HCWs vs general, n)	Vaccine(s)	Timing	Outcome	Vaccine effectiveness or risk reduction
Tande 2021 <sup>28*</sup> US	General adult population	Pfizer-BioNTech or Moderna	0 days after second dose	Asymptomatic infection	80%
Levine-Tiefenbrun 2021* Israel <sup>31</sup>	General adult population	Pfizer-BioNTech	14 days after second dose	Asymptomatic infection	94%
Hall 2021 <sup>26</sup> SIREN study UK	HCWs; n=25,661	Pfizer-BioNTech	7 days after second dose	Asymptomatic infection	86%
Thompson 2021 <sup>27</sup> CDC MMWR US	HCWs and other frontline workers; n=3,950	Pfizer-BioNTech or Moderna	=>14 days after second dose	Asymptomatic infection	90%
Keehner 2021 <sup>32</sup> US	HCWs; n=36,659	Pfizer-BioNTech or Moderna	=>14 days after second dose	Asymptomatic infection	SARS-CoV-2 positivity rate: 0.05%
Jacobson 2021 <sup>33</sup> US	HCWs; n=22,729	Pfizer-BioNTech or Moderna	=>14 days after second dose	SARS-CoV-2 infection	COVID-19 positivity rate: 0.11%
Zaqout 2021, Qatar <sup>34</sup>	General adult population; n=199,219	Pfizer-BioNTech (35% with 2 doses)	=> 28 days after second dose (or first in patients who had received only 1 dose)	SARS-CoV-2 infection	Incidence rate ratio (vs. test positivity within 7days of vaccination): 0.15 (95% CI, 0.13-0.18)
Bjork 2021 <sup>35</sup> Sweden	General adult population; n=26,587	Pfizer-BioNTech	=> 7 days after second dose	SARS-CoV-2 infection	86%

\*These data were extracted from the CDC.<sup>29</sup> Studies reported in this table are limited to cohorts that received US EUA-approved vaccines (Pfizer BioNTech and Moderna; no reported data on Johnson and Johnson). If a study reported multiple rates at different timepoints, only the last timepoint after complete vaccination was reported here. Studies reporting on effectiveness for non-EUA approved vaccines were excluded

### Patients'/HCWs' Attitudes and Anxiety prior to Endoscopy

We identified 2 studies that reported on patients' attitude and anxiety regarding endoscopy during the early phases of the pandemic.<sup>36, 37</sup> In one survey study, individuals felt that on-site

testing was important but despite testing they did not feel reassured. In another study of hospitalized and ambulatory individuals, 83% reported feeling safer because of the testing strategy. Three cross-sectional survey studies reported on pre-procedural testing and HCW anxiety during the pandemic and reported a reduction in anxiety about acquiring infection and infecting family members after implementation of a pre-testing strategy.<sup>38-40</sup> There were no studies on anxiety in the post-vaccination setting.

#### Patient Delays in Care and Endoscopy Volumes

Fourteen studies (1 survey study and 13 cohort studies mostly based on administrative datasets) reported on endoscopy volumes from the US, UK, Netherlands, Canada, China, Spain, Japan and Taiwan during the initial three-four months of the pandemic.<sup>21, 22, 38, 41-51</sup> Four studies report on the later period in the pandemic. Across studies, in the early phases of the pandemic, the total number of upper endoscopies and colonoscopies decreased by 51%-72% and 59%-85% respectively. This was compared to the same time period from prior years. During the most "COVID-19 impacted" phase (April 2020), the decrease in upper endoscopy and colonoscopy was 78%-87% and 92%-95%. Four studies, one from the UK, one from Spain and 2 from the US (Veterans Affairs Healthcare System and TriNetX database) reported on endoscopy volumes in the late stages of the pandemic.<sup>21, 42, 48, 51</sup> The reported endoscopy utilization was between 40-70% in the US, 40-100% in Europe and around 70% of expected volumes in the VA study. A modeling study from Canada estimated that it will take 41 months to complete all the backlog of colonoscopies. They also suggest that changing low yield colonoscopies to FIT would reduce recovery time.<sup>50</sup> No studies were identified reporting on endoscopy volumes in the post-vaccination period.

#### Patient Delays in Care and Impact on Cancer Burden

We identified 9 studies (US, UK, Netherlands, Japan, Hong Kong) that reported on the impact of COVID-19 on cancer diagnoses.<sup>42, 43, 45-49, 52, 53</sup> We included studies that focused on the following GI cancers: esophageal, gastric and CRC (GI cancers that we perform screening/surveillance for or that are diagnosed endoscopically) and excluded studies reporting on pancreatic and liver cancers. Most studies estimated the reduction in cancer diagnoses based on 2019 expected numbers using administrative datasets. The authors estimated that endoscopic cancer detection was reduced by 31%-71% for CRC, by 27%-37% for esophageal cancer, and 27% to 52% for gastric cancer during the early phases of the pandemic. During the late phase of the pandemic, the decline in new diagnoses of malignant CRC was 12% and for esophageal and gastric cancer was 20%. In one Japanese single center retrospective study of 123 CRC patients who underwent surgery during COVID-19, patients were more likely to present with advanced CRC and more patients needed emergency admission for obstructive CRC (39% vs 15%).<sup>47</sup> See details of studies in **Supplement Table 2**. It is important to note that none of these studies specifically reported on whether implementation of pre-procedure testing additionally contributed to delays in endoscopy. However, it is possible that pre-procedure testing would impose additional burden on patients and may promote procedure cancellation. This is particularly problematic when the testing windows are short and turnaround times for results are prolonged.

## Benefits and Harms:

In making a recommendation, the panel weighed the potential benefits of a pre-testing strategy in the post-vaccination setting against the downsides of testing. The panel acknowledged the small potential benefit of pre-procedure testing with respect to patient and staff reassurance but no benefit with regard to infections. Based on the evidence, there were few to no cases of infections reported among HCWs (performing endoscopy) and patients. Among the few reported cases, the authors could not clearly distinguish between community-acquired infections or healthcare acquired infections. Furthermore, with symptom screening, adequate PPE, and the significant protection from infection (both asymptomatic and symptomatic) due to vaccination, the risk of infection was felt to be negligible. The panel also evaluated the yield of testing (rates of positive tests among asymptomatic individuals ranged from 0-0.5%) and the significant delays in care (reduced numbers of procedures across endoscopy centers with incomplete recovery of volumes) and reduced numbers of diagnoses of CRC, esophageal, and gastric cancers (compared to expected numbers from historical data). The panel placed a high value on minimizing additional delays in care in light of the downstream impact on cancer diagnoses. See **Supplement Table 3 for Evidence to Decision Table.**

## Certainty of Evidence

The overall certainty of evidence was very low across outcomes as detailed in **Table 4: Summary of Findings Table.** We rated down for risk of bias (observational studies with many limitations), indirectness (no studies in the post-vaccination period), and inconsistency across the various outcomes. We acknowledged limitations of this body of evidence including the lack of evidence comparing the impact of a pre-testing strategy (combined with screening) versus screening alone on relevant clinical outcomes. Studies reporting on HCW and patient infections did not perform adequate contact tracing and we could not determine if infections were community acquired or healthcare acquired. No studies directly informed us about the role of pre-procedure testing in providing reassurance or reducing anxiety (for patients or HCWs) in the post-vaccination setting. No studies reported on endoscopy volumes in the post-vaccination period, and it is unclear how much pre-procedural testing led to reduced endoscopy volumes and if endoscopy centers are now at 100% capacity and efficiency.

**Table 4 Summary of Findings Table**

Outcomes	No of participants (studies) Follow up	Certainty of the evidence (GRADE)	Impact
Patient safety (infections)	Infection rates (2 prospective and 5 retrospective studies)	⊕○○○ VERY LOW a,e,b,g,h,i	Based on very low certainty evidence, there were little to no infections in the healthcare settings and high effectiveness of protection from infection after vaccination. Rates of asymptomatic infection and potential transmission were also low. There is no direct evidence from RCT and comparative cohort studies on infection rates in patients and HCWs with and without pre-procedure testing strategy. We evaluated direct evidence from single arm cohort studies that reported on rates

<p>HCW safety (infections)</p>	<p>Asymptomatic prevalence (13 cohort studies)</p> <p>Vaccination (9 cohort studies)</p>	<p>⊕○○○</p> <p>VERY LOW</p> <p>a,e,b,g,h,i</p>	<p>of infection and also reviewed indirect evidence from asymptomatic prevalence and protection from vaccination.</p> <p><b>Infection rates:</b> Based on two prospective and six retrospective cohort studies [refs] the rates of infection in <b>patients</b> ranged from 0% to 0.4% and in <b>HCWs</b> ranged from 0% to 4.0%. Five studies reported use of a pre-testing strategy while three did not.</p> <p><b>Asymptomatic prevalence:</b> Based on 13 cohort studies, asymptomatic prevalence ranged from 0.0% to 1.5% but most studies reported a range from 0-0.5% regardless of local surges of COVID-19 case counts.</p> <p><b>Protection from vaccination:</b> Based on an existing CDC review and six additional prospective cohort studies (US, UK, Israel, Sweden, Qatar) among HCWs and the general population, large risk reductions in SARS-CoV2 infection were reported ranging from 80% to 94% (7-14 days after the 2<sup>nd</sup> shot of Pfizer-BioNTech or Moderna).</p>
<p>Patient reassurance or anxiety</p>	<p>(2 observational studies)</p>	<p>⊕○○○</p> <p>VERY LOW</p> <p>a,b,c</p>	<p>Based on very low certainty evidence from two studies, reporting on patients' attitude and anxiety regarding having GI procedures during the COVID pandemic showed mixed results. There is no direct evidence from RCT and comparative cohort studies reporting on patient anxiety with pre-procedural SARS-CoV2 testing versus no testing in the post-vaccination setting.</p> <p>Study 1: In one survey study (early in the pandemic) 81% of patients valued testing staff for COVID-19 while 66% felt that on-site patient testing was important but despite testing, they did not feel reassured.<sup>37</sup></p> <p>Study 2: In hospitalized and ambulatory individuals, 83% reported feeling safer because of the testing strategy.<sup>36</sup></p>
<p>HCW reassurance or anxiety</p>	<p>(3 observational studies)</p>	<p>⊕○○○</p> <p>VERY LOW</p> <p>a,d</p>	<p>Based on very low certainty evidence from three cross-sectional studies, implementation of a pre-testing strategy was associated with moderate reduction in anxiety. There is no direct evidence from RCT and comparative cohort studies reporting on patient anxiety with pre-procedural SARS-CoV2 testing versus no testing in the post-vaccination setting.</p> <p>Study 1: Survey study of 47 endoscopy unit personnel regarding pre-procedural testing implementation.<sup>40</sup> Anxiety regarding contracting infection decreased from 58.1% pre- to 44.7% post-implementation. Anxiety regarding infecting family members decreased from 88.4% pre- to 68.4% post-implementation of testing and self-isolation (living in a separate room from the family) decreased from 21.3% pre- to 10.8% post-implementation of testing).</p> <p>Study 2: Survey of 407 gastroenterologists evaluated psychological symptoms impacting the HCW, but there was no pre-procedural testing data.<sup>38</sup> Eighty one percent (330/407) reported some sort of psychological symptoms, 74 /407 (18%) had a concern of being</p>

			<p>infected with COVID 19 at work, and 145/470 (35%) reported a high level of concern about infecting family members.</p> <p>Study 3: In a survey study of 106 providers, four measures were ranked as important or critical by 90% of respondents: patients wear surgical masks at all times, patients are screened for fever, COVID-19 symptoms, and COVID-19 exposure.<sup>39</sup> Universal pre-procedure testing was ranked among the three most important measures. With the proposed institution of these measures, the proportion of providers who were very or somewhat concerned decreased from 66% to 35%.</p>
Delays in patient care and cancer burden	(16 observational studies)	⊕○○○ VERY LOW <sup>a, j, k</sup>	<p>There was very low certainty evidence demonstrating reduced rates of endoscopy volumes in the early phase of the pandemic (decreased by 50-80%) and variable rates of recovery (40% to 100% utilization) in the late phase of the pandemic. No increased colonoscopy utilization noted. It is unclear how much pre-procedural testing directly impacted endoscopy volumes. There was very low certainty evidence of moderate reductions in cancer diagnoses (based on 2019 expected numbers) for colorectal cancer, esophageal cancer, and gastric cancer.</p> <p>No comparative evidence from RCT or observational studies reporting on pre-procedure testing and its impact on endoscopy volumes and cancer burden was found. We identified indirect evidence from reports on endoscopy volumes throughout different periods of the pandemic and database modeling studies on reduction in cancer diagnoses based on 2019 expected numbers.</p> <p><b>Endoscopy volumes:</b> Fourteen studies (1 survey study and 13 cohort studies mostly based on administrative datasets) reported on endoscopy volumes from the US, UK, Netherlands, Canada, China, Spain, Japan and Taiwan. Initial phase of pandemic: across studies, on average, the <b>total number of upper endoscopies decreased by 51-72% and colonoscopies decreased by 59-85% compared to the same time in the prior years.</b> with the majority of endoscopy centers not reaching pre-COVID endoscopy volumes over the ensuing three to four months. Late phase of the pandemic: based on four studies from the UK, Spain, and US (VAHCS and TriNetX), the reported <b>endoscopy utilization was 40-70% in the US, 100% in the UK, and 70% of expected volumes in the VA.</b> No studies were identified reporting on endoscopy volumes in the post-vaccination period.</p> <p><b>Cancer burden</b> Nine studies (US, UK, Netherlands, Asia) reported on the impact of COVID-19 on the following GI cancers: esophageal, gastric and colorectal cancer.<sup>42, 43, 45-49, 52, 53</sup> Most studies estimated the reduction in cancer diagnoses based on 2019 expected numbers using administrative datasets. In the early phase of the pandemic: <b>Endoscopic cancer detection of CRC reduced by 31% to 71.1%</b></p>

			<p><b>Endoscopic cancer detection of esophageal cancer was reduced by 27%- 37.1%</b>  <b>Endoscopic cancer detection of gastric cancer was reduced by 27% to 52.3%</b></p> <p>In the late phase of the pandemic,  <b>Diagnoses of new malignant colorectal cancer was reduced by 11.74%, Esophageal and gastric cancer by 19.78%.</b></p> <p>One Japanese study (in the late pandemic period) of 123 CRC patients who underwent surgery, during COVID-19, more patients needed emergency admission, more had obstructive CRC (39% vs 15%), more had partial/complete obstructions (67% vs 19-42%) and patients were more likely to present with advanced CRC.<sup>47</sup></p>
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**Explanations**

- a. Serious risk of bias: No comparison group, Selection bias (some studies did not include all patients undergoing procedures, just the ones that had PCR test) and recall bias
- b. Serious indirectness on the level of population and no data on the post-vaccination period.
- c. The mixed results most likely to be explained by serious inconsistency due to different study periods
- d. Serious indirectness on the level of intervention, as one of the studies did not include data on pre-procedure testing
- e. Residual confounding: could not clearly distinguish between community-acquired infections or healthcare acquired infections
- f. While most studies reported on testing for patient cohorts undergoing gastrointestinal (GI) procedures only, a few studies that reported on larger cohorts included both GI and non-GI cases.
- g. Asymptomatic prevalence was used as an indirect marker for infection rates
- h. Serious inconsistency across study results possibly attributable to differences across study time period. Two studies reported time points with asymptomatic prevalence over 1% with the highest being 1.27% during the month of May in New York City. One study reporting 4% (42/968) HCWs was from Italy during the first wave of the pandemic (January-March 2020).
- i. Although there were not many events, there were few large studies with several thousands of patients, thus we did not rate down for imprecision
- j. Serious indirectness: on the level of (1) intervention (no studies reporting on pre- procedural testing), (2) outcome no studies are reporting on patient important outcomes such as increase in cancer related mortality and presentation at more advanced stages
- k. Serious inconsistency across study results possibly attributable to differences across study time period and study populations (different countries and healthcare systems), different baseline risk.

**Recommendation 2: In endoscopy centers that implement a pre-procedure testing strategy, the AGA suggests using standard nucleic acid testing (rapid RT-PCR or laboratory-based NAAT) rather than a rapid isothermal test, antigen tests, in patients undergoing upper endoscopy\* or lower endoscopy\* irrespective of the vaccination status of patients. *Conditional recommendation, very low certainty evidence***

**Remarks:**

Rapid RT-PCR tests that can be easily performed on the day of endoscopy (results within 1 hour), are preferable as they pose less burden to patients. In the pre-procedure setting, the utility of rapid isothermal tests or antigen tests is limited due to concerns of assay sensitivity. There is no role of antibody tests for pre-procedure testing.

**Rationale**

Diagnostic test accuracy has important downstream implications on clinical practice. Utilizing tests with the best sensitivity and specificity allows providers to reduce the numbers of false positives (i.e., individuals who test positive for SARS-CoV-2 but do not have the infection) and false negatives (i.e., 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-isolation for 14 days, apprehension, and loss of work.<sup>3</sup>

### Summary of the Evidence

Evidence on the diagnostic test accuracy of available tests in the US was obtained from the recent IDSA guidelines on SARS-CoV2 infection.<sup>6</sup> Six studies evaluated the diagnostic test performance of **lab-based RT-PCR tests**, **rapid RT-PCR tests**, and **rapid isothermal NAATs** compared to a composite reference standard of multiple lab-based NAATs. The studies included 672 patients. Lab-based and rapid RT-PCR tests had comparable sensitivity (0.99 with 95% CI 0.96-0.99 versus 0.98 with 95% CI 0.95-1.00, respectively) and specificity (0.98 with 95% CI 0.94-0.99 versus 0.97 with 95% CI 0.89-0.99). Rapid isothermal NAATs had a lower sensitivity (0.81, 95% CI 0.75-0.86) but comparable specificity (0.99, 95% CI 0.96-1.00).<sup>54</sup> The IDSA also identified 5 studies comprised of 6946 patients that evaluated the diagnostic test performance of **rapid antigen tests** in adult asymptomatic patients. The pooled sensitivity of rapid antigen tests was 0.52 (95% CI 0.42-0.62) and pooled specificity was 1.00 (95% CI 0.99-1.00).<sup>6</sup> The IDSA guideline and review on **SARS-CoV 2 antibodies tests** included 12 studies that evaluated the sensitivity of IgM antibodies in week 1 after symptoms onset, 13 studies of IgG antibodies in week 1 after symptom onset, and 16 studies of IgM and IgG antibodies in weeks 2 after symptom onset. They also identified 21 studies that evaluated the specificity of IgM antibodies and 25 studies of IgG antibodies. The pooled sensitivity in week 1 after symptom onset ranged from 0.23 to 0.33 and in week 2 was 0.68 to 0.73, while the specificity was 0.98 to 0.99, see **Table 5**.<sup>55</sup>

**Table 5: Summary of Findings Table of Lab-Based RT-PCR, Rapid RT-PCR, Rapid Isothermal NAAT, Rapid Antigen Tests, and Antibody Tests**

Test	Lab-based RT-PCR <sup>a</sup>	Rapid RT-PCR <sup>a</sup>	Rapid Isothermal NAAT <sup>a</sup>	Rapid Antigen Tests <sup>b</sup>	IgM Antibodies <sup>c,d</sup>	IgG Antibodies <sup>c,d</sup>
	Assuming 1% prevalence: Effect per 1,000 patients tested					
<b>Sensitivity</b>	0.99 (0.96 to 0.99)	0.98 (0.95-1.00)	0.81 (0.75-0.86)	0.52 (0.42-0.62)	0.33 (0.25-0.41) <sup>c</sup> 0.73 (0.66-0.78) <sup>d</sup>	0.23 (0.16-0.32) <sup>c</sup> 0.68 (0.62-0.73) <sup>d</sup>
<b>No of studies (No of patients)</b>	6 studies (376 patients)	4 studies (230 patients)	4 studies (288 patients)	5 studies (271 patients)	12 studies (919 specimens) <sup>c</sup> 16 studies (2,309 specimens) <sup>d</sup>	13 studies (1,343 specimens) <sup>c</sup> 16 studies (2,708 specimens) <sup>d</sup>
<b>True positives (patients with SARS-CoV2)</b>	10 (10 to 10)	10 (10 to 10)	8 (8 to 8)	5 (4 to 6)	3 (3 to 4) <sup>c</sup> 7 (7 to 8) <sup>d</sup>	2 (2 to 3) <sup>c</sup> 7 (6 to 7) <sup>d</sup>

<b>False negatives</b> (patients incorrectly classified as not having SARS-CoV2)	0 (0 to 0)	0 (0 to 0)	2 (1 to 2)	5 (4 to 6)	7 (6 to 7) <sup>c</sup> 3 (2 to 3) <sup>d</sup>	8 (7 to 8) <sup>c</sup> 3 (3 to 4) <sup>d</sup>
<b>Test accuracy</b> Certainty of Evidence	⊕⊕⊕○ <sup>e</sup>	⊕⊕⊕○ <sup>e</sup>	⊕⊕⊕○ <sup>e</sup>	⊕⊕○○ <sup>f,g</sup>	⊕○○○ <sup>e,g,h</sup>	⊕○○○ <sup>e,g,h</sup>
<b>Specificity</b>	0.98 (0.94 to 0.99)	0.97 (0.89-0.99)	0.99 (0.96-1.00)	1.00 (0.99-1.00)	0.98 (0.97-0.99)	0.99 (0.99-0.99)
<b>№ of studies (№ of patients)</b>	6 studies (296 patients)	4 studies (164 patients)	4 studies (209 patients)	5 studies (6,675 patients)	21 studies (7,165 specimens)	25 studies (11,887 specimens)
<b>True negatives</b> (patients without SARS-CoV2)	970 (931 to 980)	960 (881 to 980)	980 (950 to 990)	990 (980 to 990)	970 (960 to 980)	980 (980 to 980)
<b>False positives</b> (patients incorrectly classified as having SARS-CoV2)	20 (10 to 59)	30 (10 to 109)	10 (0 to 40)	0 (0 to 10)	20 (10 to 30)	10 (10 to 10)
<b>Test accuracy</b> Certainty of Evidence	⊕⊕⊕○ <sup>e</sup>	⊕⊕⊕○ <sup>e</sup>	⊕⊕⊕○ <sup>e</sup>	⊕⊕⊕○ <sup>f</sup>	⊕○○○ <sup>i,j,k</sup>	⊕○○○ <sup>i,j,k</sup>
<b>Considerations</b>	Most patients were symptomatic	Most patients were symptomatic	Most patients were symptomatic	Most patients were asymptomatic; suboptimal reference standard	Case-control studies; suboptimal reference standard	Case-control studies; suboptimal reference standard

a, compared to a composite reference of multiple lab-based RT-PCR tests in symptomatic individuals  
b, compared to rapid or lab-based RT-PCR reference standard in asymptomatic adults  
c, compared to rapid or lab-based PCR reference in week 1 after symptom onset  
d, compared to rapid or lab-based PCR reference in week 2 after symptom onset  
e, rated down for serious indirectness, as the studies included mainly symptomatic individuals  
f, rated down for serious risk of bias as the reference was single RT-PCR tests (rapid or lab-based)  
g, rated down for observed serious unexplained inconsistency with considerably variable sensitivity  
h, rated down for very serious risk of bias as most of the studies had case-control design, reported results per specimens rather than individual patients, and the reference was single RT-PCR tests (rapid or lab-based).  
i, rated down for very serious risk of bias as most of the studies had case-control design and reported results per specimens rather than individual patients.  
j, rated down for observed serious unexplained inconsistency with considerably variable specificity  
k, rated down for serious indirectness as the many of the studies included stored specimens from time periods prior to the COVID-19 pandemic  
⊕⊕⊕⊕ = high certainty, ⊕⊕⊕○ = moderate certainty, ⊕⊕○○ = low certainty, ○○○○ = very low certainty

\* These data do not represent comparative differences between tests.

### Benefits and Harms:

In making this recommendation, the panel weighed the potential benefits of the tests (true positives and true negatives) against the downsides of the test (false positives and false negatives) in addition to the logistics of testing (delays from test collection to test results). The panel acknowledged that a small minority of endoscopy centers may still choose to implement a pre-testing strategy. In this setting, the SARS-CoV2 test should be a NAAT based test (which have the best sensitivity and specificity based on moderate certainty evidence) or ideally a rapid RT-PCR that can be performed at the endoscopy center on the day of procedure (to reduce the

patient burden of needing to get tested prior to the procedure). Availability and access to tests is an important consideration. The panel deliberated over the utility of the rapid antigen tests in the pre-procedure setting but had concerns about the false negative rates which may provide false reassurance. Additionally, the lower sensitivity of the rapid isothermal test, would lead to an increase in false negative results compared to rapid RT-PCR tests; the rapid isothermal test referred to in this document is *IDNOW™*. Finally, antibody tests have no role in detection of asymptomatic infection. See **Supplement Table 3**.

### **Certainty of Evidence**

The overall certainty of evidence was moderate to very low across the various tests. For the RT-PCR/isothermal tests, the studies included mainly symptomatic patients, thus, the certainty of evidence was rated down to moderate for serious indirectness. For the antigen tests, the studies used single lab-based or rapid RT-PCR tests as reference standards and there was considerable variability in the sensitivity in the included studies, thus the certainty of evidence was rated down for serious risk of bias and serious inconsistency. Finally for the antibody tests, the certainty of evidence was very low due to very serious risk of bias, and serious inconsistency and indirectness.

### **Other Evidence to Decision Considerations:**

The panel additionally evaluated the burden of testing, if access to testing may magnify any health inequities, and if there were any cost-effectiveness studies. The panel identified one study where authors reported that 3,228 patients out of 5,881 did not get pre-procedural/pre-surgical testing: 30.5% were not tested due to inability to reach the patient while the remaining patients (69.5%) declined.<sup>14</sup> The most common reasons for declining were: lack of interest in testing (19.2%), distance from testing facility (19.0%), and perception of not being at risk due to self-isolation (9.8%). About 4.1% reported that they did not get tested due to lack of transportation and 1.1% reported fear of going to a testing center. See **Supplement Table 3**.

### Cost-effectiveness of a pre-procedure testing strategy

We identified 2 modelling studies reporting on cost-effectiveness of a pre-endoscopic testing strategy. One single-center retrospective study utilized baseline data from the first week of re-opening during the pandemic in March 2020 to simulate costs and concluded that implementing PCR testing is a cost-effective strategy to resume endoscopy.<sup>56</sup> However, the assumptions used in this modelling study were not relevant for our guideline and they did not account for vaccinations: 1. PPE rationing is no longer widespread, 2. Asymptomatic prevalence is very low, 3. Utilization of pre-procedure symptom screening is not discussed, 4. Assumptions about HCW infections were higher than reported and did not take into account vaccination status or the need to no longer quarantine, per new CDC guidance.<sup>30</sup>

A second modelling study concluded that testing is most cost effective when there is a high prevalence of COVID-19, and high-risk PPE is used.<sup>57</sup> However, this study did not take into account diagnostic accuracy of testing; as the prevalence rises, false positives also increase, which have additional economic downstream consequences, such as quarantining individuals away from work or school unnecessarily. Similarly, this study did not take into account symptom

screening as pre-procedure protocol. Despite these studies' limitations, they highlight the importance of accounting for potential costs of utilizing high-risk PPE for patients with unknown COVID status.

### Equity

Our search did not yield any direct evidence on equity issues in the context of pre-procedure testing. However, our guideline panel acknowledges the widespread indirect data supporting health disparities in access to testing, clinical care, and vaccines during the COVID-19 pandemic.<sup>58-62</sup> Given this, our guideline panel discussed and acknowledged the potential for testing to serve as an additional barrier to care for underserved populations who may already have disparities in care.

### **Implementation Considerations:**

Additional considerations are outlined below:

1. These recommendations are based on high efficacy and real-world effectiveness of COVID-19 vaccine against prevalent variants of SARS-CoV2. If new variants of the virus, which are resistant to the vaccine, dominate in the coming months, then safety of HCWs and patients, and risk of asymptomatic transmission may be prioritized by endoscopy centers.
2. The guideline was developed with the intent to be implemented across all different practice settings including academic and private practices, and hospital-based and ambulatory surgical centers performing elective endoscopy.
3. The guidelines apply to all upper endoscopic and lower endoscopic procedures. While the majority of the procedures in the included studies were EGDs and colonoscopies, a few studies included EUS and ERCP procedures. Data on implementation of these recommendations for motility procedures (e.g. esophageal manometry) is unknown as studies did not include data on esophageal manometry. However, indirect evidence from endoscopic procedures would provide a similar recommendation suggesting against pre-procedure testing for motility procedures. We were unable to specifically address whether pre-procedure testing may be appropriate for patients undergoing endotracheal intubation as part of their endoscopic procedure; endotracheal intubation generates a larger volume of aerosols (than endoscopy) and may pose a higher risk of asymptomatic transmission if patients were infected with SARS-CoV2, however assuming that HCWs have appropriate PPE and are vaccinated, the risk of infection in this setting is likely low.
4. All patients should undergo pre-procedure screening for symptoms suggestive of COVID-19 prior to endoscopy. The CDC provides an updated symptom-based screening questionnaire that can be utilized by centers.<sup>63</sup> Unfortunately, the majority of symptoms have poor diagnostic accuracy to rule in or rule out COVID-19. In a recent Cochrane review, presence of fever and cough have sensitivity of 64-67%; isolated diarrhea had a sensitivity of 11%. Patients who are positive on symptom screen should be referred for pre-procedure testing with standard NAAT tests.<sup>64</sup>
5. The recommendations are contingent upon access to, and proper use of, PPE including face shield, eye protection and surgical mask or N95 (N99, PAPR) by HCW during endoscopic procedures. Endoscopy centers would continue to take steps to minimize

risk of transmission through adequate physical distancing measures and use of facemasks by all patients.

6. In centers that choose to perform pre-procedure testing, a rapid RT-PCR (with test result within 1 hour) on the day of the endoscopy is preferred to reduce patient burden. Furthermore, if this strategy is adopted, patient scheduling, patient arrival time, and testing related logistics must be considered.
7. The evidence base does not support limiting testing to certain subgroups of individuals, such as those who are unvaccinated or elderly. There were no reported subgroups of populations at higher risk for obtaining infection in the context of endoscopy. Theoretically, immunocompromised individuals may remain at higher risk despite vaccination. Our review outlines very low rates of asymptomatic prevalence and even lower rates of potential transmission during endoscopy to patients or staff; infections associated with endoscopy were a rare event.
8. In (non-immunocompromised) symptomatic individuals who test positive for SARS-CoV2, it is estimated that 88% to 95% of their specimens no longer yield replication-competent virus after 10-15 days following symptom onset (as per CDC).<sup>65</sup> Also, recovered individuals may continue to have SARS-CoV2 detected for up to 12 weeks after symptom onset. Based on this information, asymptomatic SARS-CoV2 individuals are also unlikely to have replication-competent virus that is associated with increased risk of infection and these individuals can probably undergo elective endoscopy after 15 days without the need for repeat testing.

### **Plans for Updating**

In order for guidelines to remain useful, they must be updated as new conclusive information accumulates. This document will be updated or will expire in 12 months.

### **Research Gaps**

In reviewing the existing evidence and developing these guidelines, we identified several important research gaps.

1. While delays in patient care have been universally observed in the course of the pandemic, the exact contribution of pre-procedure testing, typically performed with standard laboratory-based NAAT tests, to delay in endoscopy was unclear; however, it was assumed to be a barrier to endoscopy.
2. There is paucity of data on patient and HCW values and preferences for pre-procedure testing in the post-vaccination period.
3. The aerosol generation potential of different endoscopic procedures and the risk of asymptomatic SARS-CoV2 transmission is uncertain and warrants further study. There is also very limited data on the impact of room turnover time or number of air exchanges and risk of transmission of SARS-CoV2.
4. Better evidence is needed to understand the downstream impact on cancer diagnoses among different ethnic and racial groups.

## Discussion

Since the original release of the AGA guidelines on pre-procedure testing (July 29, 2020), our knowledge and understanding of disease transmission, infection risk from endoscopy, and most recently protection from vaccinations, has drastically increased. This accumulation of evidence underscored the need to provide an updated guideline focused on SARS-CoV2 testing and endoscopy in a post-vaccination setting. Unlike the previous guideline, when our limited understanding of transmission risks associated with endoscopy and resources constraints (related to PPE and tests) prompted the panel to place a high value on HCW and patient safety, in this updated guideline, the panel prioritized patient outcomes, specifically patient delays in care from a population perspective.

Early in the pandemic, many centers and patients were forced to reduce endoscopy volumes resulting in delays in care and implemented pre-procedure testing in efforts to safely resume endoscopy. Based on published studies of pre-procedure testing, asymptomatic infections in patients undergoing endoscopy throughout the pandemic including times of COVID surges remained low (nearly 0.5%) after a negative screening questionnaire. In light of the very low prevalence of SARS-CoV2 in asymptomatic patients, the extremely low risk of infection among vaccinated individuals, and the significant delays in endoscopy, the panel advises that the majority of centers should not routinely perform pre-procedure testing (conditional recommendation against). Multiple modeling studies have assessed the impact of delays in colonoscopy (for CRC screening/surveillance) related to the pandemic and these delays are projected to lead to a substantial increase in cancer-related mortality through 2050.

Forgoing pre-procedure testing allows patients to undergo endoscopic procedures with fewer obstacles, allows for improved access to care, reduces inequalities related to the ability to obtain pre-procedure testing, and allows for endoscopy centers to optimize their procedure volumes. The recommendations were developed with a number of assumptions including that centers having adequate PPE, follow universal precautions and use a screening checklist prior to endoscopy.

Nonetheless, the panel acknowledges that a small minority of centers may still choose to continue pre-procedure testing despite the increased burden of testing on patients, downstream consequences of false positives, delays in care, and decreased endoscopy efficiency. If testing is performed, it is important that centers utilize a nucleic acid test rather than a rapid isothermal test or antigen test. The performance of these tests has downstream implications on clinical practice related to false positives resulting in inappropriate cancellations of patient procedures, and inappropriate patient anxiety and harms from requiring them to self-quarantine and conduct contact tracing. Finally, the panel also acknowledges that local, state, and health system policies may dictate decisions about PPE use and requirements for pre-procedural testing of asymptomatic patients.

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**TABLES IN TEXT**

**Table 1: Executive Summary of Recommendations**

**Table 2: Included studies Reporting on Infections After Endoscopy**

**Table 3: Included studies on Vaccine Effectiveness Against SARS-CoV-2 infection**

**Table 4: Summary of Findings Table**

**Table 5: Summary of Findings Table of Lab-Based RT-PCR, Rapid RT-PCR, Rapid Isothermal NAAT, Rapid Antigen Tests, and Antibody Tests**

**Supplement  
FIGURES**

**Figure 1:** Analytic Framework for pre-procedural testing and outcomes.

**Figure 2:** PRISMA Flow Diagram

**Figure 3:** Implementation of a Pre-Endoscopic Testing Strategy

**Figure 1:** Analytic Framework for pre-procedural testing and outcomes.

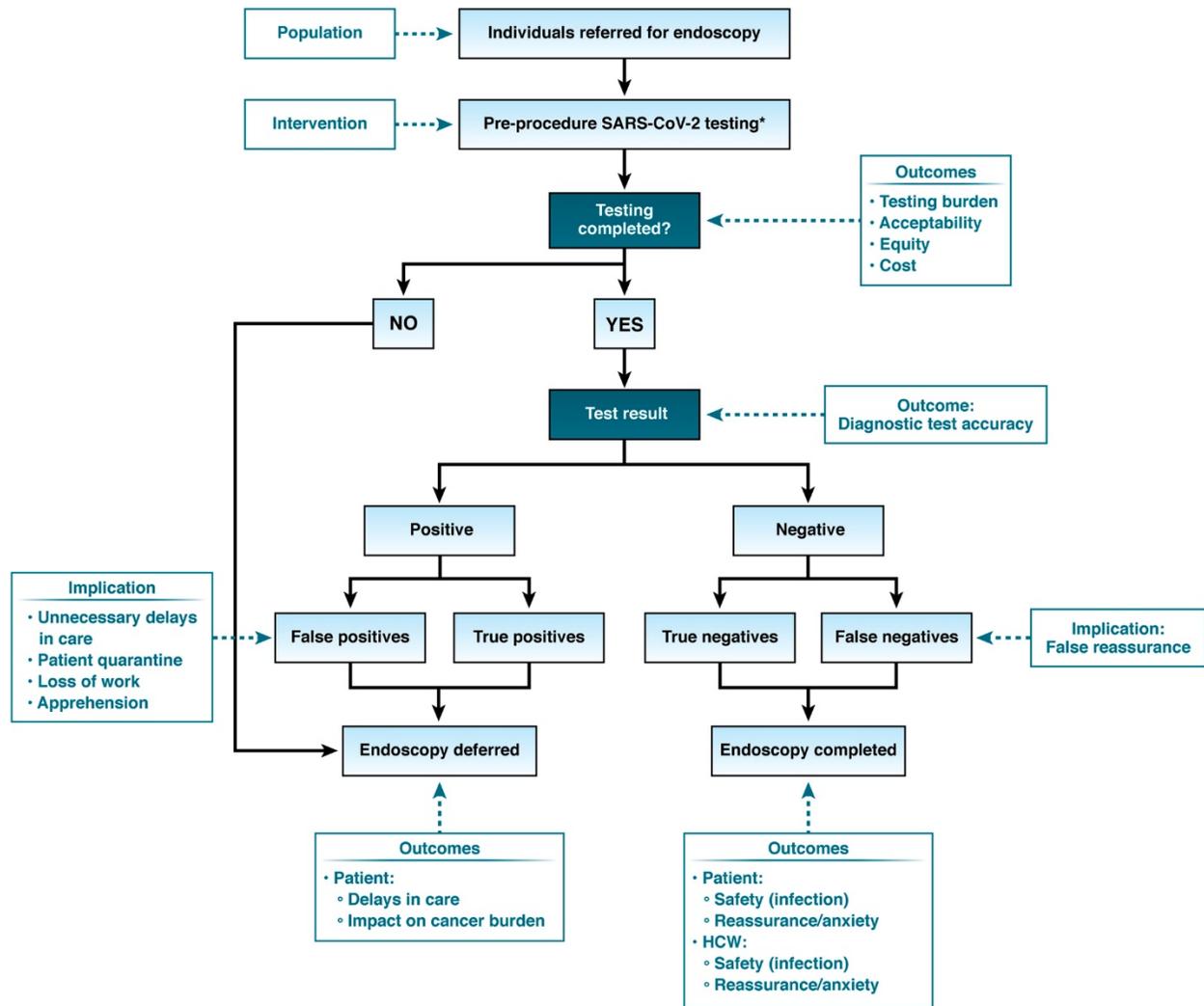


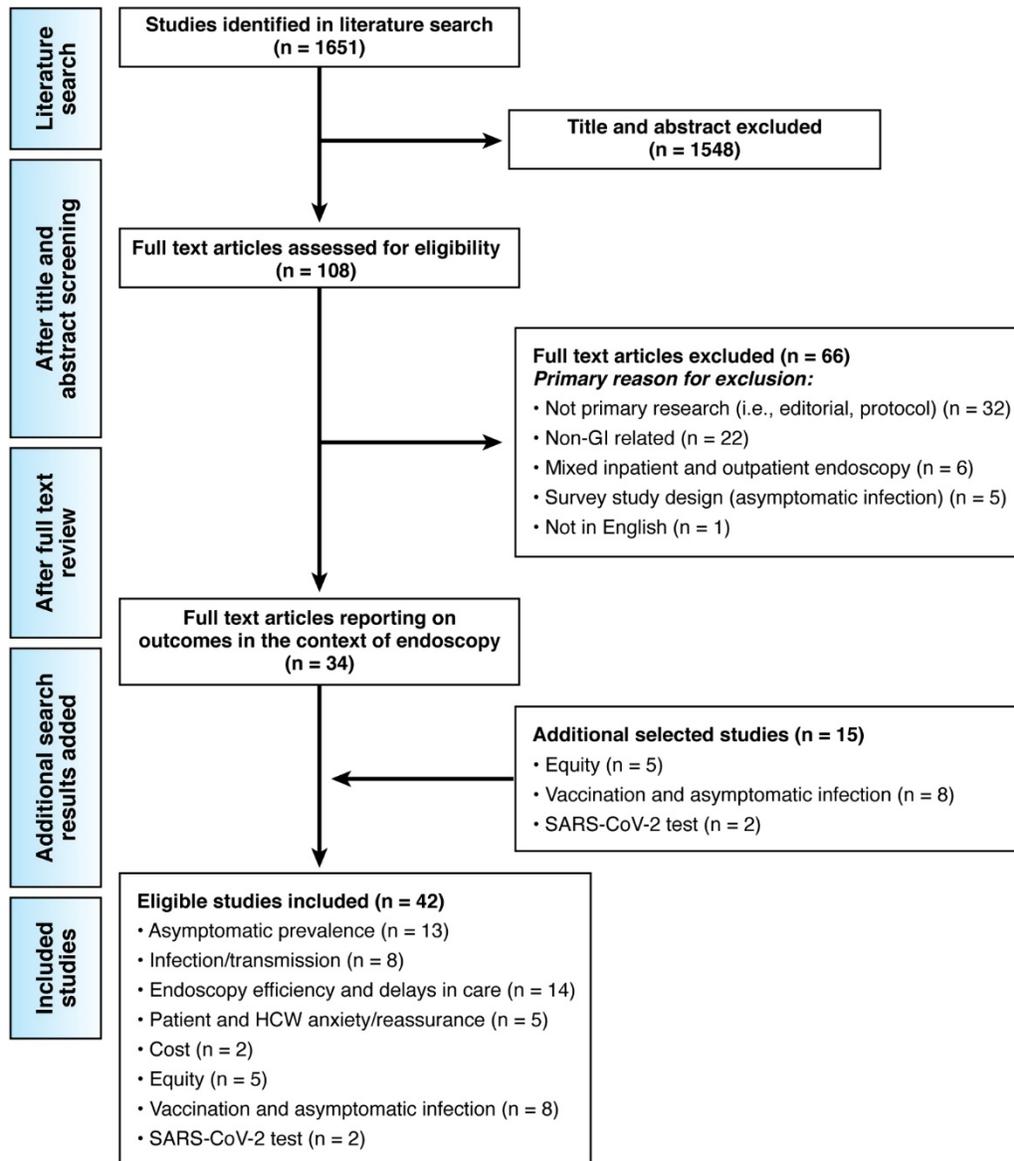
Figure legend: Analytic framework of downstream consequences of pre-procedure testing. This framework is based on the assumption that the majority of endoscopy centers are conducting pre-procedure testing during the pandemic.

\*Pre-procedure SARS-CoV2 testing in conjunction with universal symptom screening per CDC guidelines.

False positives = individuals who test positive for SARS-CoV-2 but do not have the infection

False negatives = individuals who test negative for SARS-CoV-2 but do have the infection.

**Figure 2: PRISMA Flow Diagram**



Legend: PRISMA Diagram of Included studies and reasons for exclusion. Note that the number of total studies is lower than the sum of each category, as some studies reported on more than one outcome. There were no studies reporting directly on cost or vaccine effectiveness in the context of endoscopy. We therefore utilized existing reviews from the Centers for Disease Control and Prevention (CDC) in non-endoscopy settings with an updated search to indirectly inform our guidance as outlined in this document.

**Figure 3: Implementation of a Pre-Endoscopic Testing Strategy**

Benefits		Harms
<p><b>Patient anxiety and reassurance</b></p>	<p><b>Transmission of infection:</b> Very low rates (0%–0.5%) of infection regardless of testing</p>	<p><b>Delays in care and impact on cancer burden:</b> Endoscopy volumes decreased by 50%–80% with variable rates of recovery (40%–100% utilization) with diagnoses of new malignant colorectal cancer reduced by 11.74% and esophageal and gastric cancer by 19.78%</p>
<p><b>HCW anxiety and reassurance</b></p>	<p><b>Informed rationing of N95s:</b> PPE shortages are no longer widespread in the US</p>	
		<p><b>Cost and patient burden of testing</b></p>
		<p><b>Potential to exacerbate health disparities (i.e., access to testing and care)</b></p>
		<p><b>Downstream consequences of false negatives (false reassurance) and false positives (unnecessary quarantine, delays in care, apprehension)</b></p>
<p><b>The AGA suggests against routine pre-procedure testing for SARS-CoV-2 in patients undergoing upper or lower endoscopy, irrespective of vaccination status of patients</b></p>		
<p><b>Assumptions:</b></p> <ol style="list-style-type: none"> <li>1. All centers have access to personal protective equipment (PPE) including face shield, eye protection, and surgical mask or N95 (or N99 or PAPR)</li> <li>2. All centers have implemented universal screening of patients for COVID-19 symptoms, using screening checklist and have implemented universal precautions including physical distancing, masks, and hand hygiene in the endoscopy unit</li> </ol> <p><b>Remarks:</b> (Conditional recommendation, very low certainty of evidence): Centers that prioritize the small potential benefit (staff and patient reassurance) over the downsides (burden of testing on patients, downstream consequences of false positives, potential delays in care, and decreased endoscopy efficiency) may choose to implement pre-procedure testing strategy as outlined in Recommendation 2.</p>		

## **TABLES**

**Supplement Text:** Narrative Summary of Included Studies on Infections

**Supplement Table 1:** Included Studies on Prevalence of Asymptomatic Infection

**Supplement Table 2:** Included Studies on Patient Delays in Care

**Supplement Table 3:** Evidence to Decision Framework

**Supplement Text:** Narrative Summary of Included Studies on Infections

### **Patient and HCW infections after endoscopy**

We found 8 studies that provided insight on the risk of transmission during endoscopy, with reported rates of infections in HCW or Patient following the endoscopy.<sup>1-8</sup>

There were no randomized control trials informing transmission of COVID19 during endoscopy. There were 2 prospective cohort studies<sup>2,3</sup> and 6 retrospective cohort studies.<sup>1,4-8</sup> Of these studies, 5 were in the context of a pre-procedure testing strategy<sup>1-3,5,7</sup>, and 3 did not have an explicit pre-procedure testing strategy.<sup>4,6,8</sup>

There were two multicenter prospective studies conducted by Hayee et al in the UK.<sup>2,3</sup> The first was conducted in the UK from April 30-June 30, 2020 and reported 0 transmissions to patients or staff across 18 centers in the UK (n=6208 procedures). These transmission data were based on follow-up telephone screening of patients at 7 and 14 days. All patients (n=6208) underwent pre-procedure screening using the SCOTS criteria (Symptoms, infectious Contacts, Occupational risk, Travel risk, Shielding status) and some patients (n=2611) additionally performed pre-procedure nasopharyngeal PCR testing which was dependent on the endoscopy unit practices. Of note, the asymptomatic prevalence in this subpopulation was 0.11% (3/2611). PPE was not detailed in this study, but there was acknowledgement of British Society of Gastroenterology guidance which supports the use of surgical masks for COVID-negative patients, or N95 for upper endoscopy and surgical masks for lower endoscopy.<sup>3</sup> The second study was conducted in December 2020, after the emergence of the UK variant, with rising local prevalence of COVID19.<sup>2</sup> In this study, the asymptomatic prevalence was overall still low 0.37% (9/2449). Similar to the other study, telephone screening of patient was performed at 7 and 14 days. Patients who screened positive underwent PCR testing, and contact tracing which entailed the following: patient had to have developed symptoms of COVID-19 within 10 days of endoscopy with no other more likely source identified on direct questioning by the local care team. There were 3 patient cases of PCR confirmed COVID-19 were presumed to be attributed to endoscopy after thorough questioning and no other exposures were identified. Of note, there were 15 patients (0.61%) who were COVID+ on post-procedure follow-up calls however, they were attributed to other known exposures. It is important to note that 0 HCWs were infected despite these potential exposures.

Retrospective study data reported infections in patients after endoscopy ranged from 0%-0.4%, and 0-4% in HCWs, with the caveat that this includes data during early stages of the pandemic, prior to implementation of COVID19 precautions and PPE. The study reporting 4% rates of infection was from Italy during the first wave of the pandemic during January to March 2020.<sup>6</sup> This data was collected based on a healthcare worker's web based survey and it is unclear how many of the 42 reported cases were actually transmitted during endoscopy. The average infection rate among HCW during that time in Italy was still higher at around 10%. It is notable however that despite this, the rate of transmission to patients was quite low in this study (0.12%). This study was limited by a lack of robust contact tracing, unclear attribution of COVID19 cases to the hospital or community settings.

However, the majority of the data show low rates of infection to both patients and staff. Four retrospective studies reported 0 cases of transmission to patients and staff (total number of cases =310, 60, 1808, 3310, respectively).<sup>1,4,5,8</sup> PPE was not explicitly reported, and pre-procedure testing was not performed routinely in these three studies. Finally, a retrospective cross-sectional questionnaire of 5 endoscopy centers in India during April-May 2020 also found a low rate of infections in HCWs and patients across 1549 endoscopies.<sup>7</sup> In this study, N95s were worn by HCWs, and 1 out of 5 centers conducted pre-procedure testing (total endoscopies with testing NR). This study reported that 0.4% (6/1549) patients tested positive for COVID19 within 72 hours of the procedure, but 0/1549 tested positive between 72 hours and 14 days of the procedure, indicating that the early positive cases may not be procedure related. Of note, the community prevalence of COVID-19 during this time was 4.5-5.1% and was considered a surge phase. For HCWs, survey data reported 3/74 (4%) endoscopy personnel who were COVID-19 positive and concluded that the risk of HCWs getting COVID-19 positive was 0.26% per 100 endoscopies. Limitations to this study include unclear description of whether symptom screening, lack of contact tracing for both patients and HCWs.

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**Supplement Table 1: Included Studies on Prevalence of Asymptomatic Infection**

Study Author/Year Design, Setting Dates	Local prevalence	Symptom screening		Testing strategy			
		Type of screening	Positive screening	Type of test Timing of test	Positive asymptomatic cases (n)	Total cases (n)	Asymptomatic Prevalence (%)
Bowyer 2020 <sup>10</sup> Retrospective  US (IL)  5/22/20 - 6/28/20	8.4% local positivity rate for Winnebago County, IL between 9/1-9/2020	ASGE pre-procedure Risk Screening questionnaire	122/1000 = 12.2% positive  Of those, 3/122 (2.46%) were SARS-CoV-2 positive	NP swab Roche COBAS 6800/8800 RT-PCR  72 hours prior	5	878	0.57%
Casper 2021 <sup>11</sup> Retrospective  Germany  3/23-5/10/2020	Cumulative incidence in Saarland: 279 per 100,000.  During study period, 2514 tested positive in Saarland	Symptom screening*	NR	NP swab RT-PCR  Testing for all outpatients starting April 2020  < 5 days prior	0	313	0%
Haider 2020 <sup>14</sup> Prospective  US (PA, NY)  <u>Period 1:</u> April 21- June 11, 2020 <u>Period 2:</u> June 12- Sept 10, 2020 <u>Period 3:</u> Sept 11- Dec 15, 2020 (universal testing de-implemented)	Total new cases in Allegheny County:  Period 1: 1056  Period 2: 10014  Period 3: 30524	Symptom screening: fever, cough, and shortness of breath, and asked to self-report other symptoms  <7 days of procedure, 1-4 days prior, and day of procedure	16/817 (1.9%)	NP swab Cepheid Xpert Xpress RT-PCR  1-4 days pre-procedure with results in <24 hours with a subset of negative patients randomly selected for repeat testing on the same day of the procedure (with results <1 hour)	Period 1: 10  Period 2: 54  Period 3: 101	Period 1: 10539  Period 2: 34948 ("Summer surge")  Period 3: 24741 ("Fall surge")	Period 1: 0.10%  Period 2: 0.15%  Period 3: 0.41%

Hernandez Camba 2020 <sup>17</sup> Retrospective  Spain  4/27/20-6/15/20	NR	Screening questionnaire (fever, cough, sore throat, or breathing problems, known exposure, and loss of smell or taste)  3 days prior and 14 days after	0/211: 0%	SARS-CoV-2 <u>antibody</u> test followed by RT-PCR if positive only  within 48 hours	0**	211	0%
Lewis 2020 <sup>18***</sup> Retrospective  US (NC)  3/31/2020- 4/20/2020	NR	Symptom Screening*	NR	5 in house tests: CDC's 2019-nCoV RT-PCR diagnostic panel, Diasorin Simplexa COVID-19 direct assay, Cepheid Xpert Xpress, Abbott real-time SARS-CoV02 assay, Abbott ID NOW  72 hours prior	6	1580	0.4%
Tworek 2020 <sup>20</sup> Retrospective  US (MI)  April 15-May 15, 2020	NR	Symptom Screening*  2 days prior	NR	ID Now  RT-PCR (Gold standard)	ID Now: 0  RT-PCR: 3	386	ID Now: 0%  RT-PCR 0.77%
Hayee 2020 <sup>16</sup> Multicenter prospective study  UK  4/30/2020 - 6/30/2020	NR	Telephone screening (SCOTS: questions on symptoms, infectious contacts, occupational risk, travel, shielding status)	NR	NP swab Type of test NR	3	2611	0.11%
Hayee 2021 <sup>15</sup> Multicenter prospective study  UK	Rising incidence after emergence of new UK variant: at least 800 cases per 100,000 population per week	Telephone screening (SCOTS: questions on symptoms, infectious contacts, occupational risk, travel, shielding status)	NR	NP swab Type of test NR	9	2449	0.37%

Mays 2020 <sup>19</sup> Cross-sectional  US (University of Washington)  13 April 2020	2-5% region prevalence	Symptom screening*	137/133 6 (10.3%)	PCR testing (DiaSorin Simplexa SARS-COV-2, Hologic Panther Fusion, or Roche cobas) prior admission or surgical procedure	5	787	0.6%
Albedin-Iglesias <sup>9</sup> Prospective observational cross-sectional  Spain  April 15 - May 15 2020	3.34/100,0 00 between May 1 and May 15th 2020	NR	NR	NP or OP with Allplex 2019-nCoV Assay (Seegene Soul South Korea)	21	363	0.27%
Dollinger 2020 <sup>12</sup> Retrospective single center study US (NYC)  May 1, 2020 to June 30 2020	May NY State prevalence 5.34% and NYC 6.27% June NY State prevalence 1.20% and NYC 1.43%	NR	NR	PCR testing 48-72 hours before procedures	6	623	0.96%
Gawron 2021 (personal communication) Retrospective multicenter VAHCS US  March 18-Dec 31, 2020	NR	Symptom screening (flu, cough, fever), travel history, known exposure  7 days prior to endoscopy	2497/57, 892 869 PCR positive (1.5%)	RT-PCR within 7 days of procedure	106	129,41 0 92,030	0.1%
Forde 2020 <sup>13</sup>  Retrospective single center study US (Florida)	Miami- Dade County: 12.7%. In system's catchment area: 5.4%- 9.5%	Symptom Screening (fever, conjunctivitis, cough, sore throat, difficulty breathing, diarrhea, body aches, or lack of smell or taste in the last 3 days), travel history, known exposure  7-9 days prior, and on day of procedure	NR	CE-IVD kit Gene-Finder COVID-19 Plus RealAmp Kit, QIAstat-Dx Respiratory 2019-nCoV- 2, and Cepheid Xpert Xpress SARS-CoV-2	1	396	0.25%

\*Symptom screening indicates that authors reported using symptom screening but provided no details as to the type of screening tool or questions

\*\*In this study, antibody testing was utilized instead of RT-PCR. If IgM positive, SARS-CoV-2 PCR testing was conducted. If positive, endoscopy was postponed. If negative, PCR was repeated and if negative again, endoscopy was performed. In this study, 1.9% (4/211) patients (95% CI: 0.07-4.8%) were positive for SARS-CoV-2 antibodies which does not indicate active infection; asymptomatic prevalence was 0% (RT-PCR was negative in the 4 patients with positive antibody testing)

\*\*\*In the study, pre-procedure testing included all ambulatory procedures, encompassing endoscopy. If cases were urgent, providers wore N95s/PAPRs if COVID status was unknown

**Supplement Table 2: Included Studies on Patient Delays in Care**

Study Author/Year, Design, Dates	Country/Setting  Pre-procedure testing	Endoscopy volume	Impact on cancer burden
Moraveji 2020 <sup>38</sup>  Cross-sectional survey study  May 2020	US  407 respondents 276 centers (51% academic or university)  Pre-procedure testing: NR	Procedure volumes 81% of centers reported a > 60% reduction for <b>upper endoscopy</b> 82% of centers reported a > 60% reduction for <b>colonoscopy</b> 71% of centers reported a > 60% reduction for <b>deep enteroscopy</b>	NR
Lui 2020 <sup>45</sup>  Multi-center, retrospective cohort, and modeling data  Oct 1, 2019 to March 31, 2020	Hong Kong  All public hospitals  Comparing procedure burden and cancer detection within similar time periods from 2017-2019  Pre-procedure testing: NR	Mean number of <b>upper endoscopies</b> performed per week dropped by 51.0% (from 1813 to 887)  Mean number of <b>lower endoscopies</b> performed per week dropped 58.8% (from 1190 to 491)	Mean gastric cancer and colorectal cancer diagnosed per week fell by 46.2% (from 22.9 to 12.3) and 37.0% (from 92.1 to 58), respectively.  Based on the Markov model prediction: 4.6% of patients with gastric cancer and 6.4% of patients with colorectal cancer would have higher stage shifting at 6 months. The proportion of stage IV cancers increased (gastric: 30.5% to 32.4%; and colorectal: 23.5% to 26.8%).
Markar 2020 <sup>46</sup>  Multi-center retrospective cohort  January 1-April 30, 2020	UK  All hospital trusts (n=122)  Comparing procedures and cancer diagnoses for similar time period from 2019  Pre-procedure testing: NR	Number of <b>diagnostic endoscopies</b> was around 28% lower than in the same period in 2019 (149,043 vs 208,212)	Estimated number of undiagnosed oesophageal and gastric cancers was 750 across England, with a median of 47.3 (IQR 35.7–57.5) across cancer vanguards, or regions Estimated number of undiagnosed oesophageal and gastric cancers that would have been treated curatively was 213 across England, with a median of 11.0 (IQR 6.3–14.4) across cancer vanguards, or regions
Morris 2021 <sup>48</sup>  Administrative population-based datasets  January-October 2020	UK  NHS dataset  Comparing colonoscopies, CRC diagnoses, and operations for 2 time periods from 2019  Pre-procedure testing: NR	<b>Number of colonoscopies:</b> <b>April 2020:</b> 92% reduction (95% CI 89-95) from a mean of 46,441 colonoscopies to 3,484 colonoscopies.  <b>October 2020:</b> 46,295 colonoscopies; similar to 2019 monthly average	Number of confirmed CRC diagnoses: April 2020: 22% reduction (95% CI 8-24) from 2781 individuals to 2158 individuals October 2020 similar to 2019  Number of monthly CRC operations: April 2020: 31% reduction (95% CII 19-42) from mean of 2003 to 1378 October 2020: remained below 2019 monthly average  Estimated that from April to October 2020, >3500 fewer people diagnosed and treated for CRC in England than would have been expected

<p>London 2020<sup>52</sup></p> <p>Administrative population-based datasets</p> <p>January 1, 2020 through April 30, 2020</p> <p>Monthly data reported</p>	<p>TriNetX Research Network UK and US institutions</p> <p>Comparing number of patients with CRC for similar time period from 2019</p> <p>Pre-procedure testing: NR</p>	<p>NR</p>	<p><b>Number of patients with CRC-related encounters:</b></p> <p>January 2020 – 2.5%</p> <p>February 2020 – 7.1%</p> <p>March 2020 – 18.4%</p> <p>April 2020 – 39.9%</p> <p><b>Number of patients with new CRC diagnoses:</b></p> <p>January 2020 7.8%</p> <p>February 2020 -6.7%</p> <p>March 2020 – 16.3%</p> <p>April 2020 – 54.2%</p>
<p>Lantinga 2020<sup>43</sup></p> <p>Retrospective cohort study</p> <p>March 15-May 15, 2020 (n=9776) compared to March 15-May 15, 2019 (n=19296)</p>	<p>Netherlands</p> <p>20 Dutch hospitals (3 academic, 17 non-academic)</p> <p>Comparing number of endoscopies and cancers for a similar time period from 2019</p> <p>Pre-procedure testing: NR</p>	<p>Endoscopic volume: EGD decreased by 57% (7846 to 4467), Colonoscopy decreased by 45% (12219 to 5609)</p> <p>Stable endoscopic volume: ERCP (578 to 522)</p>	<p>Endoscopy results identifying cancer decreased (524 to 340). Likelihood of detecting cancer during endoscopy increased from 2.7% in 2019 (95% CI: 2.5-3.0) vs. 3.5% in 2020 (95% CI: 3.1-3.9, p&lt;0.001).</p>
<p>Pena Ray 2020<sup>21</sup></p> <p>Retrospective observational study</p> <p>May 5-October 31, 2020 (n=3310 colonoscopies)</p>	<p>Spain</p> <p>Galician Programme for the Early Detection of Colon Cancer: Primary Care programme affiliated with 7 hospitals performing endoscopy</p> <p>No pre-procedure testing; only symptom screening</p>	<p>Decrease in colonoscopy volume: 3310 in 2020 as compared to 7491 in 2019</p>	<p>NR</p>

<p>Rutter 2020<sup>49</sup></p> <p>Administrative population-based datasets</p> <p>(1) Pre-COVID period: January 6 - March 15, 2020, n= 35 478</p> <p>(2) Transition period: March 16–22, n=4315</p> <p>(3) COVID-impacted period: March 23 – May 31 n=6974</p>	<p>UK</p> <p>NHS dataset</p> <p>Comparing referrals of colonoscopies, CRC diagnosis, and operations for two time periods with pre-COVID period</p> <p>Pre-procedure testing: NR</p>	<p>(1) Pre-COVID 35 478 endoscopies performed per week (by 3007 endoscopists; mean 12 procedures per endosco-pist)</p> <p>(2) Transition week: fell by one-third, to 23 827.</p> <p>(3) COVID-impacted period: 12% of the pre-COVID volume of procedures were conducted (average 4315 per week, performed by 922 endoscopists; mean 4 procedures per endoscopist. At its low point, by the end of March, fewer than 1800 procedures per week were being conducted: 5% of pre-COVID activity.</p> <p>In the end of the period 2 weeks of May, start recovering on average 6974 but still only 20% of pre-COVID activity.</p>	<p>CRC detected per week Pre- COVID 394 (1.97 per 100 procedures) COVID impacted 112 (5.77 per 100 procedures) Missing CRC in COVID impacted period 2828 (71.7%)</p> <p>Esophageal cancers detected per week Pre- COVID 205 (1.37 per 100 procedures) COVID impacted 129 (6.16 per 100 procedures) Missing Esophageal cancers in COVID impacted period 759 (37.1%)</p> <p>Gastric cancers detected per week Pre- COVID 61 (0.41 per 100 procedures) COVID impacted 29 (1.40 per 100 procedures) Missing Gastric cancers in COVID impacted period 320 (52.3%)</p>
<p>Maringe 2020<sup>53</sup></p> <p>Modelling study</p> <p>March 16, 2020 modeled to March 15, 2021</p> <p>Compared to 1-year period Jan 1, 2010- Dec 31, 2010, with follow-up data until Dec 31, 2014 n=24,975 colorectal cancer, n= 6,744 esophageal cancer</p>	<p>UK</p> <p>Modeling study that estimate the impact of delays in diagnostic pathways due to pandemic lockdown on cancer survival</p> <p>Pre-procedure testing: NR</p>	<p>NR</p>	<p>Estimate a for colorectal cancer, 1445 additional deaths (15.3–16.6% increase); Estimate for esophageal cancer, 330 additional deaths, (5.8–6.0% increase) up to 5 years after diagnosis.</p>
<p>Cheng 2020<sup>41</sup></p> <p>Single center observational cohort study</p> <p>December 2019 - April 2020, n=6392</p>	<p>Taiwan</p> <p>Comparing trends in compliance to diagnostic colonoscopy in FIT positive patients with corresponding periods in the last 3 years</p> <p>Pre-procedure testing: NR</p>	<p>Screening uptake during COVID-19 was 88.8% compared to 91.2-92.7% in the prior 3 years</p> <p>Colonoscopy rate during COVID-19 was 66.1% compared to 70.2-77.5% in the prior 3 years</p> <p>Rescheduling/cancellation was increased to 10.9% during COVID-19</p> <p>50% of FIT positive patients declined diagnostic colonoscopy or rescheduled due to fears of being infected from COVID-19</p>	<p>NR</p>

<p>Tinmouth 2021<sup>50</sup></p> <p>Retrospective population-based modelling study</p> <p>March 2020 to August 2020</p>	<p>Canadian</p> <p>Comparing colonoscopy procedures performed pre COVID and in COVID period and estimated hospital-based outpatient colonoscopy volume and time to recovery</p> <p>Pre-procedure testing: NR</p>	<p>Predicted backlog colonoscopies for screening estimated to take 41 months to complete all the backlog of colonoscopies</p> <p>Changing low yield colonoscopies to FIT would reduce recovery time:  25% reduction to FIT reduces backlog to 28 months  50% reduction to FIT reduces backlog to 22 months  75% reduction to FIT reduces backlog to 19 months</p>	<p>NR</p>
<p>Mizuno 2020<sup>47</sup></p> <p>Single center retrospective cohort study</p> <p>(1) Period 1: Dec 18, 2018 -April 16, 2019  (2) Period 2: April 17 - August 14, 2019,  (3) Period 3: Dec19, 2019-April 16, 2020  (4) Period 4: April 17 - August 14, 2020</p>	<p>Japan</p> <p>Analyses of 123 of CRC patients who underwent CRC surgery in 4 different periods</p> <p>Pre-procedure testing: NR</p>	<p>Colonoscopies decreased starting in March 2020 until May 21, 2020 with assumption that this led to fewer diagnoses of CRC</p>	<p>No significant change in number of CRC patients who underwent surgeries</p> <p>During COVID-19 period more patients needed emergency admission and more had obstructive CRC (39% vs 15%)  Partial/complete obstructions were also increased (67% vs 19-42%). Increased patients with advanced CRC in period 4</p>
<p>Leeds 2020<sup>44</sup></p> <p>Retrospective cohort study</p> <p>(1) Period 1, pre-lockdown: March 9- March 22, 2020  (2) Period 2, the national lockdown: March 2 -April 19, 2020  (3) Period 3, early recovery phase: April 20– May 29, 2020</p>	<p>UK</p> <p>Chart review via endoscopy reporting system</p> <p>Comparing number of procedures, and key performance indicators for 3 time periods with 2019</p> <p>Pre-procedure testing performed</p>	<p>Period 2 ('lockdown'): 13.3% of expected activity (187 procedures compared to 1402 expected)</p> <p>Period 3 recovery: 28.9% of the expected activity (644 procedures compared to 2154)</p> <p>During period 3: only 84.2% of colonoscopy slots were filled. 25.8% not filled due to patient cancellation or reluctance to attend</p>	<p>NR</p>

<p>Gawron 2020<sup>51</sup></p> <p>Retrospective population-based study</p> <p>(1) March 2020 and April 2020 (2) September 2020</p>	<p>US</p> <p>VA National Database</p> <p>Comparing number of procedures, in COVID impacted period and recovery period</p> <p>Describes the outcomes from the pre-endoscopy PCR testing and reports around 25% procedure cancelation rate, but can't distinguish how many were from testing strategy</p>	<p>Decrease in EGD volume compared with a historical average: March 2020 33% April 2020 78%</p> <p>Decrease in colonoscopy volume compared with a historical average: March 2020 42% April 2020 93%</p> <p>Recovery phase September 2020: Overall recover to 70 % from the historical average EGD recover to 86% Colonoscopy recover to 61%</p>	<p>NR</p>
<p>Huang 2021<sup>22</sup></p> <p>Single center retrospective cohort</p> <p>February 1 to May 31, 2020</p>	<p>China</p> <p>Comparing number of procedures, and endoscopic diagnosis in the COVID period with same period in 2019</p> <p>Pre-procedure testing: NR</p>	<p>Study period: a total of 1,808 endoscopic operations compared with 5,903 in the same period in 2019 - 30.63% of the expected activity</p>	<p>NR</p>
<p>Khan 2021<sup>42</sup></p> <p>Retrospective population-based study</p> <p>(1) Early pandemic: March 15, 2020 and July 15, 2020 (2) Later in the pandemic: July to November 2020</p>	<p>US</p> <p>TriNetX database</p> <p>Comparing number of procedures, and diagnosis of new GI cancer in the early COVID-19 pandemic period with same period in 2019</p> <p>Pre-procedure testing: NR</p>	<p>(1) Early pandemic: Estimated decline in patients who underwent endoscopy (71.84%), colonoscopy (84.66%).</p> <p>(2) Later in the pandemic: Estimated decline in patients who underwent endoscopy (64.74%), colonoscopy (61.64%).</p>	<p>(1) Early pandemic: Decline in new diagnoses of malignant colorectal (30.91%), esophageal and gastric (26.96%) cancers per 100,000 patients</p> <p>(2) Later in the pandemic: Decline in new diagnoses of malignant colorectal (11.74%), esophageal and gastric (19.78%)</p>

\*NR=not reported

### Supplement Table 3: Evidence to Decision Framework

#### QUESTION

Should pre-procedure testing be performed prior to upper and lower endoscopy?	
POPULATION:	Asymptomatic individuals (adults) referred for outpatient endoscopy
INTERVENTION:	Symptom screening in combination with pre-procedure testing using standard nucleic acid testing (laboratory-based NAAT or rapid RT-PCR), rapid isothermal test, or antigen tests
COMPARISON:	Symptom screening alone
OUTCOMES:	Panel members prioritized the following patient-important outcomes for decision-making: Patient safety (COVID-19 infection), Patient reassurance or anxiety, Patient delays in care and impact on cancer burden, HCW safety (COVID-19 infection), HCW reassurance or anxiety, Testing burden (feasibility, acceptability), Cost, and Health equity. <i>Patient delays in care and impact of cancer burden was deemed a critical outcome for decision-making.</i>
SETTING:	Outpatient
PERSPECTIVE:	Population (Patients)
BACKGROUND:	With increasing vaccination of healthcare workers (HCWs) and the general population, there is greater understanding of transmission and implementation of practices to promote patient and HCW safety, and increasing recognition of potential downsides associated with delays in patient care and inefficiency of endoscopy units, this guideline provides updated recommendations on the role of pre-procedure testing for SARS-CoV2 in individuals undergoing endoscopy in the post-vaccination period and replaces the prior guideline from the AGA (released on July 29, 2020).
CONFLICTS OF INTEREST:	No panel members had any conflicts of interest

#### ASSESSMENT

Problem: Is the problem a priority?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input checked="" type="radio"/> <b>Yes</b> <input type="radio"/> Varies <input type="radio"/> Don't know	<p>Yes. Early in the pandemic, many centers and patients were forced to reduce endoscopy volumes resulting in delays in patient care. Pre-procedure testing was variably implemented by endoscopy centers in efforts to safely resume endoscopy. As vaccinations are underway, updated recommendations are needed regarding the role of pre-procedure testing.</p>	

Desirable Effects: How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li><input checked="" type="radio"/> Trivial</li> <li><input type="radio"/> Small</li> <li><input type="radio"/> Moderate</li> <li><input type="radio"/> Large</li> <li><input type="radio"/> Varies</li> <li><input type="radio"/> Don't know</li> </ul>	<p>Trivial benefit for patient and HCW infections. There were little to no infections in healthcare settings and high effectiveness of protection from infection after vaccination. Rates of asymptomatic infection and potential transmission were also low.</p> <p>No direct data on patient reassurance/anxiety or HCW reassurance/anxiety in the post-vaccination setting.</p>	<p>Based on survey studies in the early pandemic period, prior to vaccination, possibly small benefit with respect to patient reassurance or anxiety and moderate reduction in anxiety for HCWs from a pre-testing strategy.</p>
Undesirable Effects: How substantial are the undesirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li><input type="radio"/> Large</li> <li><input checked="" type="radio"/> Moderate</li> <li><input type="radio"/> Small</li> <li><input type="radio"/> Trivial</li> <li><input type="radio"/> Varies</li> <li><input type="radio"/> Don't know</li> </ul>	<p>Moderate delays in patient care (reduction in endoscopy volumes, reduced diagnoses of expected cancers leading to cancer burden). In the early phase of the pandemic, endoscopy volumes decreased by 50-80% with variable rates of recovery (40% to 100% utilization) in the late phase of the pandemic. No increased colonoscopy utilization noted.</p> <p>Studies estimating the reduction in cancer diagnoses based on 2019 expected numbers using administrative datasets demonstrated the following reductions in endoscopic cancer detection: in the early phase of the pandemic: <b>Detection of CRC reduced by 31% to 71.1%, detection of esophageal cancer reduced by 27%- 37.1%, detection of gastric cancer reduced by 27% to 52.3%</b></p> <p>In the late phase of the pandemic: <b>Diagnoses of new malignant CRC reduced by 11.74%, and esophageal and gastric cancer by 19.78%.</b></p> <p>Small to moderate burden of pre-procedure testing (with variable feasibility and acceptability)</p>	<p>It is unclear how much pre-procedural testing directly impacted endoscopy volumes.</p> <p>Cost and health equity considerations outlined below</p>

Certainty of evidence: What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input checked="" type="radio"/> <b>Very low</b> <input type="radio"/> Low <input type="radio"/> Moderate <input type="radio"/> High <input type="radio"/> No included studies	All outcomes were rated as very low certainty of evidence. The evidence supporting the recommendations were mostly observational studies with study limitations (selection bias), indirectness (at the population, intervention, and outcome level), and inconsistency.	

Values: Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Important uncertainty or variability <input checked="" type="radio"/> <b>Possibly important uncertainty or variability</b> <input type="radio"/> Probably no important uncertainty or variability <input type="radio"/> No important uncertainty or variability	Patient values and preferences may differ on the value of pre-testing; however, there is unlikely to be significant variability in how much patients value receiving timely care and avoiding cancer diagnoses.	

Balance of effects: Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Favors the comparison <input checked="" type="radio"/> <b>Probably favors the comparison</b> <input type="radio"/> Does not favor either the intervention or the comparison <input type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input type="radio"/> Don't know	Pre-procedure testing (in addition to symptom screening) = intervention No pre-procedure testing (symptom screening only) = comparison The net balance of effects favors no pre-procedure testing.	

Resources required: How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li><input type="radio"/> Large costs</li> <li><input type="radio"/> Moderate costs</li> <li><input checked="" type="radio"/> Negligible costs and savings</li> <li><input type="radio"/> Moderate savings</li> <li><input type="radio"/> Large savings</li> <li><input type="radio"/> Varies</li> <li><input type="radio"/> Don't know</li> </ul>	<p>No direct data on resources associated with pre-procedure testing in the post-vaccination period; however, the panel surmised that there may be resource implications and indirect costs to patients to complete testing. Additionally, resources related to testing platforms and materials is also important to acknowledge.</p>	

Certainty of evidence of required resources: What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li><input type="radio"/> Very low</li> <li><input type="radio"/> Low</li> <li><input type="radio"/> Moderate</li> <li><input type="radio"/> High</li> <li><input checked="" type="radio"/> No included studies</li> </ul>		

Cost effectiveness: Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li><input type="radio"/> Favors the comparison</li> <li><input checked="" type="radio"/> Probably favors the comparison</li> <li><input type="radio"/> Does not favor either the intervention or the comparison</li> <li><input type="radio"/> Probably favors the intervention</li> <li><input type="radio"/> Favors the intervention</li> <li><input type="radio"/> Varies</li> <li><input type="radio"/> No included studies</li> </ul>	<p>Studies have shown significant costs associated with testing; the cost savings modelled in the evidence base were in the context of PPE rationing and avoiding quarantine for potential exposure of HCWs – both of which are no longer relevant in the post-vaccination phase, indicating overall increased costs of testing without downstream cost savings</p>	<p>For vaccinated asymptomatic HCWs after exposure the CDC does not require quarantine and therefore missed work.</p>

Equity: What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li><input type="radio"/> Reduced</li> <li><input type="radio"/> Probably reduced</li> <li><input type="radio"/> Probably no impact</li> </ul>	<p>Our search did not yield any direct evidence on equity issues in the context of pre-procedure testing. There is widespread indirect data supporting health</p>	

<input checked="" type="radio"/> <b>Probably increased</b> <input type="radio"/> Increased <input type="radio"/> Varies <input type="radio"/> Don't know	disparities in access to testing, clinical care, and vaccines during the COVID-19 pandemic. Pre-procedure testing may serve as an additional barrier to care for underserved populations who already have disparities in care.	
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**Acceptability: Is the intervention acceptable to key stakeholders?**

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input checked="" type="radio"/> <b>Probably yes</b> <input type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know	The intervention (pre-procedure testing) is acceptable to patients, however the panel identified one study where authors reported that 3,228 patients out of 5,881 did not get tested; 30.5% were not tested due to inability to reach the patient while the remaining 69.5% patients declined. The most common reasons for declining were: lack of interest in testing (19.2%), distance from testing facility (19.0%), perception of not being at risk due to self-isolation (9.8%), lack of transportation (4.1%) and fear of going to a testing center (1.1%).	

**Feasibility: Is the intervention feasible to implement?**

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input checked="" type="radio"/> <b>Yes</b> <input type="radio"/> Varies <input type="radio"/> Don't know	Pre-procedure testing is feasible however the panel acknowledged barriers to testing for many patients as well as scheduling challenges in endoscopy centers	

**TYPE OF RECOMMENDATION**

Strong recommendation against the intervention <input type="radio"/>	<input checked="" type="radio"/> <b>Conditional recommendation against the intervention</b>	Conditional recommendation for either the intervention or the comparison <input type="radio"/>	Conditional recommendation for the intervention <input type="radio"/>	Strong recommendation for the intervention <input type="radio"/>
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## CONCLUSIONS

### Recommendation

**Recommendation 1: The AGA suggests against routine pre-procedure testing for SARS-CoV2 in patients undergoing upper endoscopy or lower endoscopy, irrespective of the vaccination status of patients. *Conditional recommendation, very low certainty evidence***

**Remarks:**

*Centers that prioritize the small potential benefit (staff and patient reassurance) over the harms (burden of testing on patients, downstream consequences of false positives, delays in care and decreased endoscopy efficiency) may choose to implement a pre-procedure testing strategy as outlined in Recommendation 2.*

### Justification

The panel reviewed the evidence on (1) prevalence of asymptomatic infections in individuals undergoing endoscopy, (2) patient/HCW infections after endoscopy, (3) effectiveness of the vaccine on reducing infections (4) patient/HCW anxiety (5) patient delays in care (endoscopy volumes) and impact on cancer burden. The panel then evaluated the certainty of the evidence, weighed the benefits and downsides of pre-procedure testing, and considered burden, equity, and cost. The panel acknowledged the small potential benefit of pre-procedure testing with respect to patient and staff reassurance but no benefit with regard to infections since the risk of infection was extremely low (with symptom screening, adequate PPE, and protection from infection [both asymptomatic and symptomatic] due to vaccination). The panel also evaluated the yield of testing (rates of positive tests among asymptomatic individuals ranged from 0-0.5%) and the significant delays in care (reduced numbers of procedures across endoscopy centers with incomplete recovery of volumes) and reduced numbers of diagnoses of colorectal (CRC), esophageal, and gastric cancers (compared to expected numbers from historical data). Based on low certainty evidence, the panel made a conditional recommendation against pre-procedure testing for SARS-CoV2. The panel placed a high value on minimizing additional delays in patient care, acknowledging the reduced endoscopy volumes, downstream impact on delayed cancer diagnoses and additional burden on patients.

### Implementation considerations

9. These recommendations are based on high efficacy and real-world effectiveness of COVID-19 vaccine against prevalent variants of SARS-CoV2. If new variants of the virus, which are resistant to the vaccine, dominate in the coming months, then safety of HCWs and patients, and risk of asymptomatic transmission may be prioritized by endoscopy centers.
10. The guideline was developed with the intent to be implemented across all different practice settings including academic and private practices, and hospital-based and ambulatory surgical centers performing elective endoscopy.
11. The guidelines apply to all upper endoscopic and lower endoscopic procedures. While the majority of the procedures in the included studies were EGDs and colonoscopies, a few studies included EUS and ERCP procedures. Data on implementation of these recommendations for motility procedures (e.g. esophageal manometry) is unknown as studies did not include data on esophageal

manometry. However, indirect evidence from endoscopic procedures would provide a similar recommendation suggesting against pre-procedure testing for motility procedures. We were unable to specifically address whether pre-procedure testing may be appropriate for patients undergoing endotracheal intubation as part of their endoscopic procedure; endotracheal intubation generates a larger volume of aerosols (than endoscopy) and may pose a higher risk of asymptomatic transmission if patients were infected with SARS-CoV2, however assuming that HCWs have appropriate PPE and are vaccinated, the risk of infection in this setting is likely low.

12. All patients should undergo pre-procedure screening for symptoms suggestive of COVID-19 prior to endoscopy. The CDC provides an updated symptom-based screening questionnaire that can be utilized by centers.<sup>63</sup> Unfortunately, the majority of symptoms have poor diagnostic accuracy to rule in or rule out COVID-19. In a recent Cochrane review, presence of fever and cough have sensitivity of 64-67%; isolated diarrhea had a sensitivity of 11%. Patients who are positive on symptom screen should be referred for pre-procedure testing with standard NAAT tests.<sup>64</sup>
13. The recommendations are contingent upon access to, and proper use of, PPE including face shield, eye protection and surgical mask or N95 (N99, PAPR) by HCW during endoscopic procedures. Endoscopy centers would continue to take steps to minimize risk of transmission through adequate physical distancing measures and use of facemasks by all patients.
14. In centers that choose to perform pre-procedure testing, a rapid RT-PCR (with test result within 1 hour) on the day of the endoscopy is preferred to reduce patient burden. Furthermore, if this strategy is adopted, patient scheduling, patient arrival time, and testing related logistics must be considered.
15. The evidence base does not support limiting testing to certain subgroups of individuals, such as those who are unvaccinated or elderly. There were no reported subgroups of populations at higher risk for obtaining infection in the context of endoscopy. Theoretically, immunocompromised individuals may remain at higher risk despite vaccination. Our review outlines very low rates of asymptomatic prevalence and even lower rates of potential transmission during endoscopy to patients or staff; infections associated with endoscopy were a rare event.
16. In (non-immunocompromised) symptomatic individuals who test positive for SARS-CoV2, it is estimated that 88% to 95% of their specimens no longer yield replication-competent virus after 10-15 days following symptom onset (as per CDC).<sup>65</sup> Also, recovered individuals may continue to have SARS-CoV2 detected for up to 12 weeks after symptom onset. Based on this information, asymptomatic SARS-CoV2 individuals are also unlikely to have replication-competent virus that is associated with increased risk of infection and these individuals can probably undergo elective endoscopy after 15 days without the need for repeat testing.

## Research priorities

In reviewing the existing evidence and developing these guidelines, we identified several important research gaps.

5. While delays in patient care have been universally observed in the course of the pandemic, the exact contribution of pre-procedure testing, typically performed with standard laboratory-based NAAT tests, to delay in endoscopy was unclear; however, it was assumed to be a barrier to endoscopy.
6. There is paucity of data on patient and HCW values and preferences for pre-procedure testing in the post-vaccination period.

7. The aerosol generation potential of different endoscopic procedures and the risk of asymptomatic SARS-CoV2 transmission is uncertain and warrants further study. There is also very limited data on the impact of room turnover time or number of air exchanges and risk of transmission of SARS-CoV2.
8. Better evidence is needed to understand the downstream impact on cancer diagnoses among different ethnic and racial groups.