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# Journal Pre-proof

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# AGA Institute Rapid Recommendations for Gastrointestinal Procedures During the COVID-19 Pandemic

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## Introduction

In early December 2019, a series of pneumonia cases was reported in Wuhan, China resulting from a novel coronavirus infection designated as SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) by the International Committee on Taxonomy of Viruses (ICTV) as of January 7, 2020, and named coronavirus-19 disease (COVID-19) by the World Health Organization (WHO) as of February 11, 2020.[1] SARS-CoV-2 is a novel enveloped RNA betacoronavirus, that represents the seventh member of the coronavirus family, which includes four common human coronaviruses (229E, NL63, OC43, HKU1) and two other strains including SARS-CoV and MERS-CoV.[2,3] SARS-CoV-2 has approximately 79% and 50% phylogenetic similarity to SARS-Co-V and MERS-CoV, respectively.[2]

This virus is suspected to have a zoonotic origin and is estimated to have resulted in 591,802 cases in 176 countries with 26,996 deaths as of March 27, 2020.[4] COVID-19 was first reported in the United States (U.S.) on January 20, 2020 and accounted for a total number of 100,717 cases and 1544 deaths as of March 27, 2020.[4] The morbidity and mortality associated with COVID-19 exceeds previous coronavirus infection outbreaks including SARS (8,098 infections, 774 deaths) and MERS (2,458 infections, 848 deaths).[5,6] An initial analysis of 72,314 cases from China revealed that an estimated 81% of infections are characterized as mild, 14% are severe, and 5% are critical (defined as respiratory failure, septic shock, and/or multiple organ dysfunction or failure), with an overall fatality rate of 2.3%.[7] In the U.S., an analysis of 4,226 cases from the Center for Disease Control and Prevention (CDC) as of March 16, 2020 reported estimated rates of hospitalization (20.7-31.4%), Intensive Care Unit (ICU) admission (4.9-11.5%), and case fatality (1.8-3.4%).[8] The WHO declared a global health emergency on January 30, 2020[9] and pandemic status on March 11, 2020, respectively.[10]

The most common presenting symptoms for COVID-19 include fever, cough, and shortness of breath, although other frequently observed symptoms include fatigue, headache, and muscle soreness. Extrapulmonary symptoms may occur early in the disease course. Gastrointestinal (GI) symptoms, including anorexia, nausea, vomiting, abdominal pain, and/or diarrhea may occur early, but are rarely the sole presenting feature[11]; GI symptoms may be associated with poor clinical outcomes including higher risk of mortality.[11] Of note, the first reported case of COVID-19 in the U.S. presented with a 2-day history of dry cough, fatigue, nausea and vomiting, followed by diarrhea on hospital day #2, with subsequent confirmation of SARS-CoV-2 in a stool specimen.[12] Subsequent studies have confirmed positive SARS-CoV-2 cases using real-time reverse transcriptase polymerase chain reaction (rRT-PCR) in stool specimens of

patients with COVID-19 infection [13-14], with immunofluorescence data demonstrating that ACE2 (angiotensin converting enzyme II) is abundantly expressed in gastric, duodenal, and rectal epithelia, thereby implicating ACE2 as a potential viral receptor for entry to uninfected host cells, and raising the possibility for fecal-oral transmission although it is unclear if the viral concentration in the stool is sufficient for transmission.[14] Furthermore, ACE2 receptors may additionally be expressed in hepatic cholangiocytes, potentially permitting direct infection of hepatic cells, and early cohort studies of COVID-19 have revealed that abnormal liver enzymes are commonly observed.[15]

**Scope and Purpose**

Multiple questions have been raised regarding the gastrointestinal and liver manifestations of COVID-19 infection, and implications of SARS-CoV-2 infection on gastrointestinal endoscopy. A joint society statement of the American Gastroenterological Association (AGA), the American Association for the Study of Liver Diseases (AASLD), the American College of Gastroenterology (ACG), and the American Society for Gastrointestinal Endoscopy (ASGE) on March 15, 2020 highlighted the potential for SARS-CoV-2 transmission through droplets, an established mode of transmission, and possibly fecal shedding, and the associated risk for transmission to endoscopy personnel during gastrointestinal endoscopy procedures.[16]

In this document, we seek to summarize the data and provide evidence-based recommendation and clinical guidance. This rapid recommendation document was commissioned and approved by the AGA Institute Clinical Guidelines Committee (CGC), AGA Institute Clinical Practice Updates Committee (CPUC), and the AGA Governing Board to provide timely, methodologically rigorous guidance on a topic of high clinical importance to the AGA membership and the public.

**Panel Composition and Conflict of Interest Management**

This rapid guideline was developed by gastroenterologists and guideline methodologists from the AGA CGC and CPUC, who were assembled on March 15, 2020 in collaboration with the AGA Governing Board to define time-urgent clinical questions, perform systematic reviews, develop summary evidence profiles, and formulate rapid recommendations. Additionally, to ensure representation of the public/consumer, this guideline was reviewed by two COVID-19 positive patients. Panel members disclosed all potential conflicts of interest according to the AGA Institute policy.

**Target Audience**

The target audience of these guidelines includes gastroenterologists, hepatologists, advanced practice providers, nurses, and other healthcare professionals involved in GI endoscopy. Patients, the public, 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 patients, parents, clinicians, and other health care professionals in the setting of a pandemic.

**Methods**

This rapid review and guideline was developed using a process described elsewhere.[17] Briefly, the AGA process for developing clinical practice guidelines uses the GRADE framework and best practices as outlined by the National Academy of Medicine (formerly known as the Institute of Medicine) and Guidelines International Network (GIN).[18]

**Information Sources and Literature Search**

With the help of an information specialist, we electronically searched OVID Medline to identify all relevant English studies from inception to March 23, 2020 (including randomized controlled trials, observational studies, and cases series) related to COVID-19 using the newly developed MeSH term. Additionally, we looked for indirect evidence related to Severe Acute Respiratory Syndrome, Middle East Respiratory Syndrome, Ebola, and influenza using the systematic review filter. The reference lists of relevant articles were scanned for additional studies. See **Supplementary Materials** for Search Strategy (Supplemental Figure1) and PRISMA flow diagram (Supplemental Figure2).

**Study Selection and Data Extraction**

One reviewer (SS) screened titles and abstracts and retrieved relevant articles for each question. A second reviewer (OA, PD, JF, SMS) confirmed the selected studies and, in certain circumstances, conducted additional Google scholar searches to identify relevant articles. The following websites were also reviewed for relevant articles: WHO and CDC. Pairs of reviewers extracted the data from the primary studies identified from existing systematic review documents, reviewed the judgments for risk of bias and conducted specific subgroup analyses using Review Manager.[19]

Certainty in the Evidence

Evidence profiles were used to display the summary estimates as well as the judgments about the overall certainty of the body of evidence for each clinical question across outcomes. Within the GRADE framework, evidence from randomized controlled trials (RCTs) start as high-certainty evidence and observational studies start out as low-certainty evidence but can be rated down for several reasons: risk of bias, inconsistency, indirectness, imprecision, and publication bias. Additionally, evidence from well conducted observational studies start as low certainty evidence but can be rated up for large effects or dose-response. Judgments about the certainty were determined via video conference discussion to achieve consensus. The certainty of evidence was categorized into 4 levels ranging from very low to high (see Table 1). For each question, an overall judgment of certainty of evidence was made based on critical outcomes.

Evidence to Decision Considerations:
During online communications and conference calls, the guideline panel developed several recommendations based on the following elements of the GRADE evidence to decision framework: the certainty of the evidence, the balance of benefits and harms, assumptions about values and preferences, and resource implications. For each guideline statement, the strength of the recommendation and the certainty of evidence to support the recommendation is provided. The words "the AGA recommends" are used for strong recommendations, and "the AGA suggests" for conditional recommendations (see Table 2). The panel deliberated over the impact of resource limitations on the feasibility and implementation of these recommendations.  Therefore, the panel's main recommendations assume an ideal scenario where there are no resource constraints. However, in settings in which resources require rationing, additional guidance is also provided.

Low confidence in effect estimates may rarely be tied to strong recommendations. Within the GRADE framework, there are 5 paradigmatic situations in which strong recommendations may be warranted despite low or very low certainty of evidence[20] These situations can be conceptualized as ones in which there are clear benefits in the setting of a life-threatening situation, clear catastrophic harms, or equivalence between two interventions with clear harms for one of the alternatives. The panel invoked these paradigmatic situations in developing these recommendations.

Update
Recommendations in this document may not be valid in the near or immediate future. We will conduct periodic reviews of the literature and monitor the evidence to determine if recommendations require modification. Based on the rapidly evolving nature of this pandemic, this guideline will likely need to be updated within the next few months.

**Results**

**What are the GI Manifestations of COVID-19?**
Guan et al published the largest cohort study to date which included 1,099 hospitalized patients with confirmed COVID-19 infection from China. They reported that 5.0% of COVID-19 infected patients had nausea or vomiting and 3.8% had diarrhea.[21] Across the different published cohort studies, 2.0-13.8% of patients had diarrhea, 1.0-10.1% had nausea or vomiting, and one study reported the presence of abdominal pain in 2.2% of patients. The cohorts ranged in size from 13 up to 191 patients, primarily from Hubei Province, China.[22,23,24,25,26,27,28,29] Most recently, Pan et al reported in a cross-sectional study of 204 COVID-19 positive patients from 3 hospitals in Hubei Province, that 29 patients (14.3%) developed diarrhea, 8 patients (3.9%) experienced vomiting,

and 4 patients (2.0%) had abdominal pain.[30] A recent meta-analysis of 4243 patients from China suggested that approximately 17.6% of patients had any gastrointestinal symptom, including 9.2% with pain, 12.5% with diarrhea, 10.2% with nausea/vomiting.[31] One of the concerns with many of the published studies is the possible duplicate inclusion of the patients across reports, thereby limiting valid performance of pooled estimates in a meta-analysis.[32]

There is evidence for the presence of SARS-CoV-2 RNA in stool specimens independent of the presence of diarrhea. Some studies showed that stool continued to be positive for SARS-CoV-2 RNA even after respiratory samples became negative. Chen et al reported a case of COVID-19 based on compatible symptoms and lung imaging in a patient with positive stool real-time RT-PCR for SARS-CoV-2 RNA but negative pharyngeal swabs and sputum samples.  Furthermore, Wang et al reported confirmation of SARS-CoV-2 positive fecal samples in 2 patients without diarrhea.[12, 35, 36, 37,38,39,40]

**What are the liver manifestations of COVID-19?**
Liver injury is estimated to occur in up to 20-30% of patients at the time of diagnosis with SARS-CoV-2 infection.[14] Severe hepatitis has been reported but liver failure appears to be rare.[39] The pattern of liver injury appears to be predominantly hepatocellular, and the etiology remains uncertain but may represent a secondary effect of the systemic inflammatory response observed with COVID-19 disease, although direct viral infection and drug-induced liver injury cannot be excluded. One study of liver biopsy specimens obtained from a patient with COVID-19 disease revealed microvesicular steatosis and mild lobular and portal activity, suggestive of either SARS-CoV-2 infection or drug-induced liver injury.[41] Abnormal liver enzymes may be observed in both adults and children with COVID-19,[42] and do not appear to be a major predictor of clinical outcomes.[15]  Early studies have multiple methodologic limitations, with variable laboratory thresholds, limited longitudinal assessment of liver enzymes, heterogeneous evaluation for alternative etiologies, and limited information regarding baseline liver diseases and confounding variables.  Additional studies are needed to further characterize the unique clinical considerations for SARS-CoV-2 infection in patients with chronic liver disease and/or cirrhosis,[43] although preliminary guidance has been provided by the AASLD on March 23, 2020.[44]

**What are the potential risks to health care workers performing endoscopy?**
SARS-CoV-2 is presumed to spread primarily via respiratory droplets from talking, coughing, sneezing, and close contact with symptomatic individuals. However human-to-human transmission can occur from unknown infected persons (e.g. asymptomatic

carriers or individuals with mild symptoms) as well as individuals with virus shedding during the pre-incubation period before symptoms develop.[45]

Data related to the spread of SARS-CoV-2 in the early phase of the pandemic have confirmed that health care professionals are at higher risk of infection than the general population. The WHO and Chinese Center for Disease Control and Prevention (China CDC) reported infection of 2055 health care workers as of February 20, 2020 during the index outbreak in Hubei Province, with health care workers facing a rate of infection approximately three times the general population.[46] This prompted the Chinese Department of Health Reform to deploy more than 40,000 additional health-care workers to the region, preserve personal protective equipment (PPE), and implement surveillance measures and quarantine protocols.[46] Such measures appear to have slowed the spread to health care workers, with recent cases primarily attributable to household contacts rather than occupational exposure. Similar trends have been observed in Europe, with an estimated 20% of COVID-19 infections in Italy occurring in health care workers.[47] Preliminary reports in the US also suggest that health care workers are at risk of nosocomial infections, including infection of 20 health care workers among the first 67 COVID-19 positive individuals in Philadelphia, and additional health care workers cases in WA, NY, and MA.[48,49,50]

The spread of disease via health care workers is concerning for several reasons: a) appropriate PPE may not be utilized effectively, especially when COVID-19 patients cannot be identified quickly, b) shortage of health care workers due to infection and/or quarantine, and c) the concern of the role of infected health care workers to act as a vector for transmission to patients.

While COVID-19 is spread primarily through droplet transmission, endoscopic procedures can lead to aerosolization and subsequent airborne transmission. Currently there is significant debate about the type of PPE that should be worn by health care workers involved with endoscopy.

**What kinds of PPE are needed during endoscopy?**
This section outlines a series of recommendations addressing PPE recommendations for GI endoscopy personnel in the context of the COVID-19 pandemic. We review the evidence on masks (surgical masks, N95s, or respirator masks), gloves (single versus double), and type of rooms (e.g. negative pressure) that should be utilized when performing endoscopy. All recommendations are included in **Table 3**.

*Aerosol-generating procedures*
Aerosol-generating procedures, procedures that generate small droplet nuclei in high concentrations and permit airborne transmission, include upper GI endoscopic

procedures such as esophagogastroduodenoscopy, small bowel enteroscopy, endoscopic ultrasound, endoscopic retrograde cholangiopancreatography (ERCP), breath tests, and esophageal manometry. Aerosolization of viral particles may occur during insertion of the scope into the pharynx during intubation as well as during insertion and removal of instruments through the endoscope channel.[51,52,53,54] The risk of aerosolization of viral particles during lower GI procedures, such as colonoscopy, sigmoidoscopy and anorectal manometry, has been less well studied.

*COVID-19 status of patients during community spread*
As outlined by the WHO, phases 5 and 6 of a pandemic refer to sustained community outbreaks at a global level with human-to-human transmission.[55] Once community spread has been established in these pandemic phases and there is documentation of spread via asymptomatic individuals, pre-screening checklists have limited utility. Additionally, given the currently limited COVID-19 testing in the US, individuals at-risk of spreading disease cannot be easily identified.[45] Our panel acknowledges that recommendations may change if rapid testing is available, and GI patients can be tested prior to undergoing procedures. However, all patients undergoing endoscopy should be considered potentially infected or capable of infecting others.

*Description of masks*
<u>Surgical masks</u> (also known as medical masks) are used often for droplet precautions, as they are designed to block large particles, but are less effective in blocking smaller particle aerosols (<5 μm). Unlike surgical masks, <u>respirator masks</u> are designed to block aerosols. Respiratory protection in health care for airborne precautions commonly follows two filtering device paths, N95 mask respirators and powered air-purifying respirators (PAPRs). The N95 masks filter at least 95% of aerosols (<5 μm) and droplet-size (5 μm to 50 μm) particles and are not resistant to oil. Light-weight, no-hose, powered air-purifying respirators (PAPR) are a highly effective alternative to face masks. Air is forced through a large, multi-layer filter housed in the helmet and provide positive pressure within the face-shield compartment. These devices are approved by US National Institute for Occupational Safety and Hazard (NIOSH) and can provide high level protection from common airborne viruses that exceed N95 face masks without the need for "fit-testing" and have been used in a variety of settings.[56] PAPR also has the advantage of providing head and neck protection. See **Figures 1 and 2**.

*Description of Negative Pressure Rooms:*
Airborne isolation rooms utilize negative pressure ventilation to create inward directional airflow to prevent generated aerosols from diffusing outside the room. The door of the room should remain closed except when entering and leaving. An anteroom that contains another sink separates the isolation room and the hallways. The anteroom is utilized to transition patients and health care workers in and out of the room, storage of

PPE, and donning and doffing of PPE. The negative pressure rooms are designed to maintain a pressure differential and air flow differential between the isolation room and the anteroom in addition to a minimum number of air changes per hour.[57]

**I. Masks for health care workers during endoscopy**

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**Recommendation 1**: In health care workers performing *upper GI procedures*, **regardless of COVID-19 status***, the AGA recommends use of N95 (or N99, or PAPR) masks instead of surgical masks, as part of appropriate personal protective equipment (Strong recommendation, moderate certainty of evidence)

**Recommendation 2**: In health care workers performing *lower GI procedures*, **regardless of COVID-19 status***, the AGA recommends the use of N95 (or N99 or PAPR) masks instead of surgical masks as part of appropriate personal protective equipment. (Strong recommendation, low certainty of evidence)

**Recommendation 3**: In health care workers performing *any GI procedure*, **in known or presumptive COVID-19 patients**, the AGA recommends **against** the use of **surgical masks only,** as part of adequate personal protective equipment (Strong recommendation, low certainty of evidence)

*These recommendations assume the absence of widespread reliable and accurate rapid testing for the diagnosis of COVID-19 infection or immunity

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Summary of the Evidence

Our systematic literature search did not identify any studies that provided direct evidence to inform our clinical questions for PPE in COVID-19. However, several studies from the SARS outbreak were identified that provide indirect evidence. The SARS outbreak reinforced the vital role of PPE in protecting health care workers from occupationally acquired infection. We used data from two existing systematic reviews by Offeddu 2017 and Tran 2012 to inform our recommendations.[58,59] First, the systematic reviews by Offeddu et al included a meta-analysis of 3 observational studies that showed a benefit in using N95 respirators over standard masks in protecting health care workers from SARS (OR = 0.86; 95% CI: 0.22–3.33), with corresponding RRs of 0.88 (95% CI: 0.26–2.27) and 0.94 (95% CI: 0.41–1.34) under baseline risks of 20% and 60%, respectively (though the results were imprecise).

Data from 3 RCTs demonstrated a reduction in laboratory-confirmed viral infections from coronavirus species, though the results were imprecise. (RR = 0.78; 95% CI: 0.54–1.14). See Evidence Profile **Table 4A**. In addition, there was a strong association between use of N95 respirators (compared to no masks) and protection from SARS

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infection in health care workers (OR=0.12; 95% CI: 0.06-0.26). See **Evidence Profile Table 4B**). Second, a systematic review from Tran et al revealed an increased risk of viral transmission in health care workers performing aerosol-generating procedures (mostly bronchoscopy or tracheal intubation).[59] (**Supplemental Figure 3**). Zamora and colleagues investigated the amount of contamination on the neck and face from individuals using a PAPR mask (in combination with N95) compared with a N95 mask alone[60]; Individuals who used the PAPR-based strategy experienced a lower risk of face and neck contamination compared to N95 mask alone (RR = 0.08; 95% CI: 0.03–0.19). See **Evidence Profile Table 5**, **Supplemental Figure 4**. Limitations of these studies include small numbers of health care workers, and data on tracheal intubation or bronchoscopy, not GI endoscopy.

Discussion and Rationale:

To estimate the risk of viral transmission in endoscopic procedures, we examined data evaluating non-GI aerosolizing-generating procedures such as bronchoscopy and tracheal intubation. Our search strategy did not yield comparative studies on the degree of aerosolization with upper or lower GI endoscopy compared with bronchoscopy or tracheal intubation. However, we assume that insertion of the endoscope into the pharynx and esophagus is likely to be associated with a similar risk of aerosolization of respiratory droplets to that of bronchoscopy.

To inform our estimate of the risk of infection for individuals performing endoscopy, we used evidence from the review by Tran et al which examined the risk of respiratory infections among health care workers from aerosol generating procedures.[59] We conducted an original meta-analysis of retrospective cohort studies identified in this review. The data revealed a higher risk of viral transmission to health care workers exposed to aerosol generating procedures compared to unexposed health care workers (RR = 4.66; 95% CI: 3.13–6.94). Therefore, we recommend utilizing N95s (or masks that are equivalent or better), for all patients regardless of COVID-19 status, given higher risk of transmission during aerosol-generating procedures.

Finally, the panel's decision to extend this recommendation to all patients, regardless of COVID-19 status, is specifically in the context of documented community spread during a pandemic. It also assumes a small proportion of persons who are negative or have recovered from COVID-19; this may change with the availability of wider testing and the ability to test for past infection or immunity. Recent data from China, by Chang et al, revealed the greatest risk of COVID-19 exposure to health care workers during early stages of the pandemic when testing was not yet widely available.[61] In a JAMA report published from Zhongnan Hospital in Wuhan, 29.3% (40 of 138) of COVID-19 infected patients were health care workers who presumably had hospital-acquired infections.[27] Among 493 health care workers caring for hospitalized patients, 10/493 health care

workers became infected with COVID-19; all 10 were unprotected health care workers (no mask) caring for patients on medical wards with a low risk of exposure (no known or suspected COVID-19 patients). In contrast, none of the 278 protected health care workers (N95 mask) caring for high risk patients (known or suspected COVID-19) became infected (aOR 464.82; 95% CI: 97.73 to infinite).[62] One study, evaluating health care worker exposure in the care of one COVID-19 positive patient, revealed that none of 41 health care workers (surgical masks only) developed infection despite absence of N95 mask, although studies evaluating health care workers in context of larger cohorts of COVID-19 positive patients are not yet available.[63]

The decision to extend the recommendation to lower GI procedures is based on evidence of possible aerosolization during colonoscopy especially during the insertion and removal of instruments through the biopsy channel.[53] and the uncertain risks associated with evidence of the presence of SARS-CoV-2 RNA in fecal samples. These data provided indirect evidence to extend the recommendation to lower GI procedures pending more definitive evidence.[33]

<u>Limited resource settings</u>

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**Recommendation 4:** In extreme resource-constrained settings involving health care workers performing ***any GI procedures*, regardless of COVID-19 status,** the AGA suggests extended use/re-use of N95 masks over surgical masks, as part of appropriate personal protective equipment. (Conditional recommendation, very low certainty evidence).

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<u>Summary of the Evidence</u>
No direct evidence on the prolonged use or reuse of N95, N99, or PAPR masks in a COVID-19 pandemic was identified. We also did not find indirect comparative evidence on any mask reuse strategies that would impact infection rates and subsequent morbidity and mortality of health care workers. Furthermore, there were no studies on aerosol-generating procedures in context of SARS or MERS. The available evidence was limited to low quality reports evaluating N95 protection in combination with face shield or surgical mask, mathematical models, experimental studies examining decontamination strategies for PPE preservation during pandemics, and laboratory tests evaluating durability and fit endurance of respirator masks.

CDC recommendations during H1N1 pandemic included guidance to use a cleanable face shield or surgical mask over the N95 respirator to reduce contamination and extend respirator use.[64] These strategies were utilized during the SARS outbreak, but the effects of prolonged use of a combination of a face shield or surgical mask over an N95 mask have not been reported.[65] During the H1N1 pandemic, an estimated 40% or

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more of health care workers reported reuse of their N95 respirator but no data are available to estimate the impact on influenza infections.[66,67] A mathematical model to calculate the potential influenza contamination of facemasks from aerosol sources in various exposure scenarios revealed that the amount of exposure in a single cough (≈19 viruses) is much lower than that transmitted from aerosols (4,473 viruses on N95 masks, 3,476 viruses on surgical masks).[68] Finally, in laboratory testing, an estimated 5 consecutive donnings of PPE can be performed before fit factors consistently drop to unsafe levels.[46] In addition, in experiments examining decontamination of N95 with hydrogen peroxide and mechanical testing, up to 50 cycles of exposure to hydrogen peroxide did not lead to any degradation of the filtration media but the elastic straps were stiffer after exposure to up to 20 cycles and this could impair proper fit.[69] See **Evidence Profile Table 6A and Table 6B**). The data on PAPR re-use after cleaning and disinfection were also limited with select institutions reporting on their experience with established PAPR programs and instructions for cleaning.[70]

Discussion and Rationale

There is insufficient evidence to comment on the safety of re-use (up to 5 consecutive donnings) and extended use (over 8 hours) of masks and other PPE. Limited indirect evidence suggests loss of durability and fit of N95 masks under these conditions. With regards to PAPRs with disposable protective shields, the protective shields may be disinfected with standard biocidal containing wipes and reused. However, no evidence of safety of such an approach was identified.

## II. Gloves during COVID-19

> **Recommendation 5**: In health care workers performing *any GI procedure*, regardless of **COVID-19 status**, the AGA recommends the use of double gloves compared with single gloves as part of appropriate personal protective equipment (Strong recommendation, moderate quality evidence)

Summary of the Evidence

The evidence to support this recommendation is largely derived from observations of health care workers during the SARS epidemic in 2003. Transfer of organisms from contaminated PPE to hands or clothing may contribute to infection of health care workers and associated contacts. Casanova and colleagues performed a human challenge study using the bacteriophage MS2 for simulated droplet contamination.[71] One group of participants donned a full set of PPE with one pair of gloves. The second group donned identical PPE with 2 pairs of latex gloves. The first (inner) pair of gloves was applied so that the wrist of the glove was under the elastic cuff at the wrist of the gown sleeve. The second (outer) pair, one size larger, was worn over the first pair so

that the wrist of the glove was positioned over the gown sleeve. During the doffing phase, the inner pair of gloves was removed last. The double-glove strategy was associated with less contamination than the single-glove strategy (RR 0.36; 95% CI 0.16 to 0.78) See **Evidence Profile Table 7, Supplemental Figure 4.**

Discussion and Rationale
The Casanova et al study highlights the importance of double gloving as part of the doffing process for PPE with either N95 mask or PAPR to minimize contamination and reduce the risk of viral transmission.

**III. Negative Pressure Room during COVID-19**

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**Recommendation 6**: In health care workers performing *any GI procedure*, with **known or presumptive COVID-19**, the AGA suggests the use of negative pressure rooms over regular endoscopy rooms, when available (Conditional recommendation, very low certainty of evidence).

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Summary of the Evidence
We did not find any direct evidence to inform this recommendation but indirect evidence was identified to confirm the viability of coronaviruses as an aerosol. In an experimental model, Van Doremalen et al demonstrated that SARS-CoV-2 could remain viable in aerosol form for up to 3 hours, similar to what has been previously reported for the SARS-CoV-1 virus.[72] Epidemiologic and airflow dynamics modeling studies from the SARS 2003 and MERS-CoV outbreaks additionally support airborne spread.[73,74,75] As GI procedures may generate aerosols, indirect evidence to support the viability of the SARS-CoV-2 virus in aerosols and airborne transmission support a recommendation in favor of preferential use of negative pressure rooms pending further evidence.

Discussion and Rationale
The experimental study by van Doremalen et al further demonstrated that SARS-CoV-2 may stay viable on copper surfaces up to 4 hours, on cardboard surfaces up to 24 hours, and on plastic and stainless steel surfaces up to 72 hours.[72] These data combined with the available epidemiologic and airflow dynamics studies of related coronavirus infections, suggest that GI procedures may contribute to nosocomial transmission of COVID-19. Thus, the use of negative pressure rooms with anterooms may mitigate the spread of the infection within health care facilities. The panel acknowledges that the use of a negative pressure room may impact efficiency and procedural workflow but anticipate that GI procedures performed during the initial pandemic phase will be predominantly limited to time-sensitive procedures performed in hospitalized settings.

In **limited-resource settings** where negative pressure rooms are unavailable, portable industrial-grade high-efficiency particulate air (HEPA) filters may be a reasonable alternative. Industrial-grade HEPA filters are alternatives suggested by the CDC to enhance filtration when air supply systems are not optimal, when anterooms are not available for patients in airborne isolation rooms, and during intubation and extubation of patients with active tuberculosis patients.[76,77]

## IV. Endoscopic decontamination during COVID-19

> <u>Recommendation 7</u>: For endoscopes utilized on patients **regardless of COVID-status**, the AGA recommends continuing standard cleaning endoscopic disinfection and reprocessing protocols (Good practice statement).

<u>Summary of the Evidence:</u>
Current guidelines for infection control during GI endoscopy include mechanical and detergent cleaning, followed by high-level disinfection (HLD), rinsing and drying through sterilization, using FDA-approved liquid chemical germicide solutions.[78] Cleaning must precede HLD to remove any organic debris (e.g., blood, feces, and respiratory secretions) from the external surface, lumens, and channels of flexible endoscopes. Studies examining the natural bioburden levels detected on flexible GI endoscopes show ranges from $10^5$ CFU/ml to $10^{10}$ CFU/ml after clinical use; appropriate cleaning followed by HLD (a process that eliminates or kills all vegetative bacteria, mycobacteria, fungi, and viruses, except for small numbers of bacterial spores) reduces the number of microorganisms and organic debris by 4 logs, or 99.99%.[79] Studies examining the risk of viral transmission of hepatitis B, C or HIV among patients have demonstrated a very low risk of transmission.[80] Several cases of patient-to-patient HCV transmission have been reported but these were related to inadequate cleaning and disinfection of GI endoscopes and accessories and/or the use of contaminated anesthetic vials or syringes. A recent review by Kampf et al shows effective inactivation of coronaviruses, including SARS-CoV, by standard biocidal agents, which are active ingredients in current endoscopic disinfecting solutions (**Table 8**).[81]

<u>Discussion and Rationale</u>
Decontamination of coronavirus species has been confirmed with commonly used biocidal agents for decontamination, such as hydrogen peroxide, alcohols, sodium hypochlorite or benzalkonium chloride.[81,82] There are ample data to support continuation of current endoscope decontamination practices in the context of known COVID-19.[79] Similar biocidal agents are additionally present in hospital-grade disinfecting wipes commonly used to decontaminate surfaces for endoscopy room cleaning.[81]

**PPE Implementation Considerations**

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1. *Review and be observed practicing PPE don and doff. Make sure that you have been fitted for an N95.* ***See Figure 4 for Donning and Doffing of PPE***

2. *Do not take personal belongings (such as phones, stethoscopes), into any procedural area as these may become contaminated.*

3. *Minimize the number of personnel in the room during any endotracheal intubation. Only the anesthesia team should remain during intubation if possible.*

4. *Review and determine the appropriateness of trainee involvement in procedures with consideration of procedural time and PPE supply.*

5. *Avoid personnel switches during procedures.*

6. *Consider nursing teams that follow the patient from the pre-procedure area to the procedure room and to the recovery area, to minimize personnel exposure.*

7. *Consider teams (MD, RN, tech, anesthesia) that remain together for the entire day so as to compartmentalize and minimize personnel exposure.*

8. *Non-procedural personnel should avoid entering any procedure room once a patient has entered.*

## v. **How should gastroenterologists triage GI procedures?**

Since the WHO declared COVID-19 a global pandemic on March 11, 2020, U.S. health systems started implementing infection control measures, planning for surge capacity in health-care facilities, and proposing triage of health-care services. The Surgeon General and the American College of Surgeons recommended suspension of all elective surgeries,[84, 85] and on March 15, 2020, a joint society statement by four GI organizations recommended that elective non-urgent procedures be rescheduled to mitigate COVID-19 spread and preserve PPE.  However, this raises difficult questions about which procedures can be safely postponed.

<u>Guidance on how to implement a triage system</u> See accompanying **Flowchart Figure 5**

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*All procedures should be reviewed by trained medical personnel and categorized as time-sensitive or not time-sensitive using the framework outlined below in Table 9 (Good practice statement)*

*In an open access endoscopy system where the listed indication alone may provide insufficient information to make a determination about the time-sensitive nature of the procedure, consideration should be given for the following options (i) a telephone consultation with the referring provider or (ii) a telehealth visit with the patient or (iii) a multidisciplinary team approach or (virtual) disease/tumor board to facilitate decision-making for complicated patients. (Good practice statement)*

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Summary of the Evidence:

Data on the urgency of when to perform GI procedures and complications related to delays on patient important outcomes are sparse. Studies in lower GI bleeding suggest little difference in outcomes such as blood transfusions or surgery when comparing urgent colonoscopy (< 24 hours) vs delayed colonoscopy (up to 72 hours after presentation)[86,87] In a pandemic setting, one might consider opting to delay the procedure (especially while awaiting COVID-19 testing). In contrast, a patient presenting with an upper GI bleed likely should have an EGD performed within 24 hours.[88,89]

The impact of delays in diagnosis may also have significant ramifications on immediate management (e.g. in question of inflammatory bowel disease diagnosis or treatment) and on cancer treatment decisions (e.g. colon cancer, pancreatic cancer etc). Additionally, tests related to treatment of precancerous lesions may also lead to anxiety among patients and providers (e.g. treatment of high-grade dysplasia in Barrett's or an endoscopic mucosal resection for a larger colon polyp). Indirect evidence supports that delays of weeks to a few months in some cancer diagnoses may not lead to progression of stage or worse clinical outcomes even when symptoms are present in some GI cancers.[90,91,92]

Non-time sensitive procedures are most routine screening and surveillance colonoscopy. There is evidence to suggest that following a positive FIT test, a colonoscopy can be delayed up to six months without negatively impacting patient outcomes. Corley et al. reported on 70,124 patients with a positive FIT test and found no difference in outcome of colorectal cancer diagnosis and advanced stage disease when the colonoscopy was performed in 8-30 days following the test vs waiting up to six months. However, when delaying 7-9 months there was a non-significant increase in risk and a more profound increase risk when delayed > 12 months. Using data from this study, one could suggest that in patients undergoing colorectal cancer screening, even when a test suggests a possible polyp or cancer, delaying the procedure for some period of time may not be harmful on the population level.[93]

Discussion/Rationale:

In the setting of a pandemic, the limited availability of resources (such as critical shortages of PPE) combined with the risk of potential exposure and spread of infection to patients and the availability of appropriate health care workers, often become the main drivers for provision of health care services. The proposed framework of separating procedures into time-sensitive and non-time sensitive cases may be useful in determining which procedures if delayed may negatively impact on patient-important outcomes. The panel intentionally chose to focus on patient-important outcomes as a

driver for decision-making acknowledging the difficulties with using specific indications to categorize procedures as elective versus non-elective. The panel also acknowledged the limitations of the body of evidence in assessing the time-sensitive nature of endoscopic procedures. While there were data to support a delay of up to 3-6 months for patients undergoing colonoscopy for +FIT and this was likely generalizable to patients undergoing colonoscopy for polyp surveillance, the data to support delays for procedures such EMR for large polyps, are lacking. Moreover, there may be added issues around patient anxiety or worry and concerns about medico-legal risks that may influence decisions about deferring procedures; therefore, the panel suggests the use of a multidisciplinary team approach to facilitate decision-making for complicated patients.

Telemedicine also provides an opportunity to communicate with patients and provide continued patient care while reducing risk of exposure to COVID-19 to patients and health care workers. The AGA and a number of other professional medical organizations have been working to lift restrictions on reimbursement for telehealth visits.[94]

The panel chose the time period of 8 weeks based on consensus from the group that some procedures require endoscopy within 24 hours, but others are not as time-sensitive and can be delayed in the short-term for a few weeks without affecting important patient outcomes related to the disease state. As there is uncertainty about the duration of the pandemic, a pre-defined time period should be used for re-assessment of all deferred procedures especially if resources become available and the time-sensitive nature of the procedure changes.

Moreover, as innovations in testing (rapid tests, serologic tests of immunity) and treatment or vaccines allow for better risk stratification, one may be able to consider restarting non-time sensitive procedures.

Public Perspective

The panel also sought feedback from two patients affected by COVID-19 to ensure that we captured the consumer/patient perspective. They understood and agreed with the importance and process of triaging procedures. One patient additionally expressed concerns about the focus on limiting PPE for health care workers when "they are the ones who need the protection the most" and the lack of clear evidence on the variability of GI symptoms.

**Conclusions**

Clinical guidelines should be informed by a systematic review of evidence and an assessment of the desirable and undesirable consequences of alternative care options.

Rapid guidelines, typically completed within 1-3 months, are needed to provide guidance in response to a time-sensitive need such as during a public health emergency.[95,96] Using a rapid guideline process, the AGA aims to provide timely guidance on appropriate PPE and triage of GI endoscopy in context of the COVID-19 pandemic in the U.S. Due to the paucity of evidence specific to SARS-CoV-2 infection, many questions regarding clinical management remain unanswered, including implications and clinical considerations for vulnerable populations, such as individuals with IBD or other autoimmune GI or liver conditions on immunosuppression, patients with cirrhosis or end-stage liver disease, and individuals with GI malignancies requiring systemic chemotherapy. International registries such as the Surveillance Epidemiology of Coronavirus (COVID-19) Under Research and Exclusion, or SECURE-IBD, (https://covidibd.org), may serve as a valuable data source in the future as clinicians engage in information sharing to inform stronger evidence-based guidance. Ongoing clinical trials for COVID-19 treatment may be associated with GI adverse effects and increase the demands for GI consultative care. Furthermore, the severity and duration of resource limitations for SARS-CoV-2 testing and PPE may further challenge clinical management decisions. Importantly, due to the rapidly evolving nature of the COVID-19 pandemic, these recommendations will likely need to be updated within a short timeframe.

**Table 1**: Interpretation of the Certainty in Evidence of Effects using the GRADE framework

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

**Table 2**: Interpretation of strong and conditional recommendations using the GRADE framework

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

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**Table 3**: Executive Summary of Recommendations

| RECOMMENDATION STATEMENTS | | Strength of Recommendation and Certainty of Evidence |
|---|---|---|
| I MASKS | | |
| | In healthcare workers performing *upper GI procedures***, regardless of COVID-19 status\***, the AGA recommends use of N95 (or N99, or PAPR) instead of surgical masks, as part of appropriate personal protective equipment. | Strong recommendation, moderate certainty of evidence |
| | In healthcare workers performing *lower GI procedures* **regardless of COVID-19 status\***, the AGA recommends the use of N95 (or N99 or PAPR) masks instead of surgical masks as part of appropriate personal protective equipment. | Strong recommendation, low certainty of evidence |
| | In healthcare workers performing *upper GI procedures*, **in known or presumptive COVID-19 patients**, the AGA recommends **against** the use of surgical masks **only**, as part of adequate personal protective equipment | Strong recommendation, low certainty of evidence |
| II. GLOVES | | |
| | In healthcare workers performing *any GI procedure*, regardless of **COVID-19 status**, the AGA recommends the use of double gloves compared with single gloves as part of appropriate personal protective equipment. | Strong recommendation, moderate certainty of evidence |
| III. NEGATIVE PRESSURE ROOMS | | |
| | In healthcare workers performing *any GI procedures* **with known or presumptive COVID-19**, the AGA suggests the use of negative pressure rooms over regular endoscopy rooms when available. | Conditional recommendation, very low certainty of evidence |
| IV ENDOSCOPIC DISINFECTION | | |
| | For endoscopes utilized on patients **regardless of COVID-status**, the AGA recommends continuing standard cleaning endoscopic disinfection and reprocessing protocols. | Good practice statement |
| IV TRIAGE | | |
| | All procedures should be reviewed by trained medical personnel and categorized as time-sensitive or not time-sensitive as a framework for triaging procedures. | Good practice statement |

| | | |
|---|---|---|
| | In an open access endoscopy system where the listed indication alone may provide insufficient information to make a determination about the time-sensitive nature of the procedure, consideration should be given for the following options (i) a telephone consultation with the referring provider or (ii) a telehealth visit with the patient or (iii) a multidisciplinary team approach to facilitate decision-making for complicated patients. | Good practice statement |

*These recommendations assume the absence of widespread reliable rapid testing for the diagnosis of COVID-19 infection or immunity

**Table 4A. Evidence Profile: N95 compared to surgical masks for COVID19 prevention for GI upper endoscopic procedures**

| № of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | N95 | surgical masks | Relative (95% CI) | Absolute (95% CI) | Certainty |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | |
| **SARS Infection** | | | | | | | | | | | |
| 3 | observational studies | serious [a] | not serious | not serious [b] | serious [c] | none | 4/141 (2.8%) | 24/452 (5.3%) | **OR 0.86** (0.22 to 3.33) | **7 fewer per 1,000** (from 41 fewer to 104 more) | ⊕○○○ VERY LOW |
| **Viral Respiratory Infection** | | | | | | | | | | | |
| 3 | randomised trials | not serious [d] | not serious | serious [e] | serious [c] | none | 48/1740 (2.8%) | 52/1274 (4.1%) | **OR 0.78** (0.54 to 1.14) | **9 fewer per 1,000** (from 18 fewer to 5 more) | ⊕⊕○○ LOW |

**Explanations**

a. Concern for recall bias

b. Although studies are on SARS population given the similarities in the virus we did not rate down for indirectness

c. Low event rate and crosses the clinical threshold

d. Although the compliance to the assigned mask type was self reported and is not clear if there is a performance, bias study staff was doing regular checks on the study participants to control for performance bias, thus, we did not rate down for risk of bias

e. Not only coronaviruses but other URI viruses

**Table 4B. Evidence Profile: N95 compared to no PPE for COVID19 prevention for GI upper endoscopic procedures**

| № of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | N95 | no PPE | Relative (95% CI) | Absolute (95% CI) | Certainty |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **SARS infection** | | | | | | | | | | | |
| 5 | observational studies | not serious | not serious | not serious [a] | not serious | strong association | 9/163 (5.5%) | 86/234 (36.8%) | **OR 0.12** (0.06 to 0.26) | **302 fewer per 1,000** (from 334 fewer to 236 fewer) | ⊕⊕⊕○ MODERATE |

**Explanations**

a. Although studies are on SARS population given the similarities in the virus we did not rate down for indirectness

**Table 5. Evidence Profile: PAPR (+N95) vs N95 in health care workers during GI procedures**

| № of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | PARP | N95 | Relative (95% CI) | Absolute (95% CI) | Certainty |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | **Certainty assessment** | | | | **№ of patients** | **Effect** | | **Certainty** |

*Efficiency in particulate air*

| № of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | PARP | N95 | Relative (95% CI) | Absolute (95% CI) | Certainty |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | observational studies | not serious | not serious | not serious | serious [a] | none | | | High-efficiency particulate air (HEPA) filters filter at least 99.97% of particles 0.3 μm in diameter, compared to N95 masks that filter at least 95% of aerosol (<5 μm) | | ⊕⊕⊕◯ MODERATE |

*Contaminated areas on face and neck*

| № of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | PARP | N95 | Relative (95% CI) | Absolute (95% CI) | Certainty |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | observational studies | not serious | not serious | not serious | very serious [b] | none | 4/150 (2.7%) | 59/150 (39.3%) | **RR 0.08** (0.03 to 0.19) | **362 fewer per 1,000** (from 382 fewer to 319 fewer) | ⊕⊕◯◯ LOW |

**Explanations**
a. Only one study
b. Very small number of events

**Table 6A. Evidence Profile: Reuse of N95 compared to surgical masks for health care workers during GI procedures**

| Certainty assessment | | | Impact |
|---|---|---|---|
| № of studies | Study design | Certainty | |

**Infection with COVID 19**

| | | | |
|---|---|---|---|
| 8 | Anecdotal reports<br><br>Experiments under laboratory conditions | ⊕◯◯◯<br>VERY LOW[a,b,c] | No direct evidence was found in regards to the safety of reuse of masks (surgical masks (SM) and N95) during a COVID-19 pandemic. Furthermore, indirect evidence from other pandemic outbreaks did not reveal empiric data on infection rates, but rather reports of anecdotal experience or experiments under laboratory conditions or mathematical models. Anecdotal reports on using SMs over N95 as a barrier to pathogens and extend the useful life of the N95 respirator has been published[65]. This was sparingly utilized during the SARS outbreak, but the effects of prolonged use of this combination on HCWs and the infection rate have not been reported. Similarly, reports exists that more than 40% of HCWs reused their N95 during the H1N1 pandemic[66, 67]. Furthermore, a mathematical model to calculate the potential influenza contamination of facemasks from aerosol sources in various exposure scenarios, showed that single cough (≈19 viruses) were much less than likely levels from aerosols (4,473 viruses on FFRs and 3,476 viruses on SMs)[68]. In laboratory testing has been reported that 5 consecutive donning's can be performed before fit factors consistently drop to unsafe levels[69]. In addition, decontamination of N95 with hydrogen peroxide has showed that exposure up to 50 cycles does not degrade the filtration media and mechanical testing but has demonstrated that the elastic straps were stiffer after exposure to up to 20 HPV cycles. Thus, more than 20 cycles may impair proper fit[70]. There have been narrative reports, news conference reports and the **CDC recommendation**[98] during H1N1 pandemic suggesting use of a cleanable face shield or surgical mask to reduce N95 respirator contamination[64]. |

**Explanations**
a. Risk of bias: There is no comparator with optimal PPE to understand the risk of the acceptable protection from COVID 19
b. There are multiple layers of indirectness. The population is different - studies were done on Influenza virus or simulation studies on healthy volunteers, and there are no studies on AGP. Outcome is indirect as well; most of these studies have tolerability of the mask or laboratory testing as outcomes.
c. Unable to assess for imprecision since outcome cannot be measured.

**Table 6B. Evidence Profile: Prolonged use of N95 compared to surgical masks for health care workers during GI procedures as a last resort in resource-limited settings**

| Certainty assessment | | | Impact |
|---|---|---|---|
| № of studies | Study design | Certainty | |

**Infection with COVID 19**

| | | | |
|---|---|---|---|
| 4 | Anecdotal reports<br><br>Experiments under laboratory conditions | ⊕◯◯◯<br>VERY LOW[a,b,c] | No direct evidence was found in regards to the safety of extended use of masks (surgical masks (SM) and N95) during a COVID-19 pandemic. Furthermore, indirect evidence from other pandemic outbreaks did not reveal empiric data on infection rates, but rather reports of anecdotal experience or experiments under laboratory conditions or mathematical models. Experiment on tolerability of the N95 with prolonged use on HCW showed that HCWs were able to tolerate the N95 for 89 of 215 (41%) total shifts of 8 hr. Other 59% mask was discarded before 8 hr because it became contaminated or intolerance[99]. Furthermore, a mathematical model to calculate the potential influenza contamination of facemasks from aerosol sources in various exposure scenarios, showed that single cough (≈19 viruses) were much less than likely levels from aerosols (4,473 viruses on FFRs and 3,476 viruses on SMs)[68]. Additionally, there was a survey on HCWs during H1N1 pandemic and more than 40 % of the HCWs were reusing or had a prolong use on their N95[66, 67]. |

**Explanations**
a. Risk of bias: There is no comparator with optimal PPE to understand the risk of the acceptable protection from COVID 19
b. There are multiple layers of indirectness. The population is different - studies were done on Influenza virus or simulation studies on healthy volunteers, and there are no studies on AGP. Outcome is indirect as well; most of these studies have tolerability of the mask or laboratory testing as outcomes.
c. Unable to assess for imprecision since outcome cannot be measured.

**Table 7. Evidence Profile: Double gloves compared to single gloves for health care workers during GI procedures**

| № of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Double gloves | Single gloves | Relative (95% CI) | Absolute (95% CI) | Certainty |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | |

*Certainty assessment* spans the first seven columns; *№ of patients* spans Double gloves / Single gloves; *Effect* spans Relative / Absolute.

**Contamination**

| 1 | observational studies | not serious | not serious | not serious [a] | serious [b] | none | 5/18 (27.8%) | 14/18 (77.8%) | **RR 0.36** (0.16 to 0.78) | **498 fewer per 1,000** (from 653 fewer to 171 fewer) | ⊕⊕⊕◯ MODERATE |

**Explanations:**
a. Study was done with the bacteriophage MS2, but the drops size was similar to SARS and COVID 19 to simulate droplet contamination, so we decided not to rate down. We recognize that there is some indirectness but we also took into account the large effect size.
b. Low event rate

**Table 8: Biocidal agents against SARS-CoV**

| Study | Biocidal agent | Exposure time | Efficacy (reduction of viral infectivity by log10) |
|---|---|---|---|
| Rabenau Kampf 2005[100] | 95% Ethanol<br>85% Ethanol<br>80% Ethanol | 30s<br>30s<br>30s | ≥ 5.5<br>≥ 5.5<br>4.3 |
| Rabenau Cinatl 2005[101] | 78% Ethanol<br>100% 2-Propanol<br>70% 2-Propanol<br>45% and 30% 2-Propanol<br>1% Formaldehyde<br>0.7% Formaldehyde<br>0.5% Glutardialdehyde | 30s<br>30s<br>30s<br>30s<br>2 min<br>2 min<br>2 min | ≥ 5.0<br>≥ 3.3<br>≥ 3.3<br>≥ 4.3<br>> 3.0<br>> 3.0<br>> 4.0 |
| Siddharta A 2017[102] | 75% 2-Propanol | 30s | > 4.0 |

*Subgroup analysis taken from Kampf 2020[82]

**Table 9.** Framework for Triage. Time-sensitive procedures are defined as procedures that if deferred may negatively impact patient-important outcomes. The decision to defer a procedure should be made on a case-by-case basis.

| Time-Sensitive* (within 24 hours-8 weeks) | | | Non-Time Sensitive |
|---|---|---|---|
| Threat to the patient's life or permanent dysfunction of an organ | Risk of metastasis or progression of stage of disease | Risk of rapidly worsening progression of disease or severity of symptoms | No short-term impact on patient-important outcomes |
| e.g. diagnosis and treatment of GI bleeding or cholangitis | e.g. work up of symptoms suggestive of cancer | e.g. management decisions, such as treatment for IBD | e.g. screening or surveillance colonoscopy, follow up colonoscopy for +FIT |

**Figure 1: Surgical Masks and N95 Masks**

**Figure 2:  PAPR Mask**

**Figure 3: WHO Phases of a Pandemic**

Figure 4: Donning and Doffing of PPE



**SEQUENCE FOR PUTTING ON PERSONAL PROTECTIVE EQUIPMENT (PPE)**

The type of PPE used will vary based on the level of precautions required, such as standard and contact, droplet or airborne infection isolation precautions. The procedure for putting on and removing PPE should be tailored to the specific type of PPE.

**1. GOWN**
- Fully cover torso from neck to knees, arms to end of wrists, and wrap around the back
- Fasten in back of neck and waist

**2. MASK OR RESPIRATOR**
- Secure ties or elastic bands at middle of head and neck
- Fit flexible band to nose bridge
- Fit snug to face and below chin
- Fit-check respirator

**3. GOGGLES OR FACE SHIELD**
- Place over face and eyes and adjust to fit

**4. GLOVES**
- Extend to cover wrist of isolation gown

**USE SAFE WORK PRACTICES TO PROTECT YOURSELF AND LIMIT THE SPREAD OF CONTAMINATION**

- Keep hands away from face
- Limit surfaces touched
- Change gloves when torn or heavily contaminated
- Perform hand hygiene

CDC

## HOW TO SAFELY REMOVE PERSONAL PROTECTIVE EQUIPMENT (PPE) EXAMPLE 1

There are a variety of ways to safely remove PPE without contaminating your clothing, skin, or mucous membranes with potentially infectious materials. Here is one example. **Remove all PPE before exiting the patient room** except a respirator, if worn. Remove the respirator **after** leaving the patient room and closing the door. Remove PPE in the following sequence:

### 1. GLOVES

- Outside of gloves are contaminated!
- If your hands get contaminated during glove removal, immediately wash your hands or use an alcohol-based hand sanitizer
- Using a gloved hand, grasp the palm area of the other gloved hand and peel off first glove
- Hold removed glove in gloved hand
- Slide fingers of ungloved hand under remaining glove at wrist and peel off second glove over first glove
- Discard gloves in a waste container
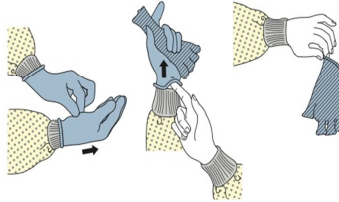
### 2. GOGGLES OR FACE SHIELD

- Outside of goggles or face shield are contaminated!
- If your hands get contaminated during goggle or face shield removal, immediately wash your hands or use an alcohol-based hand sanitizer
- Remove goggles or face shield from the back by lifting head band or ear pieces
- If the item is reusable, place in designated receptacle for reprocessing. Otherwise, discard in a waste container

### 3. GOWN

- Gown front and sleeves are contaminated!
- If your hands get contaminated during gown removal, immediately wash your hands or use an alcohol-based hand sanitizer
- Unfasten gown ties, taking care that sleeves don't contact your body when reaching for ties
- Pull gown away from neck and shoulders, touching inside of gown only
- Turn gown inside out
- Fold or roll into a bundle and discard in a waste container

### 4. MASK OR RESPIRATOR

- Front of mask/respirator is contaminated — DO NOT TOUCH!
- If your hands get contaminated during mask/respirator removal, immediately wash your hands or use an alcohol-based hand sanitizer
- Grasp bottom ties or elastics of the mask/respirator, then the ones at the top, and remove without touching the front
- Discard in a waste container
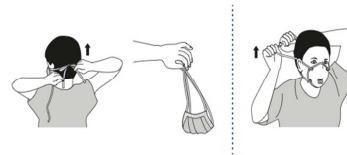
### 5. WASH HANDS OR USE AN ALCOHOL-BASED HAND SANITIZER IMMEDIATELY AFTER REMOVING ALL PPE

**OR**
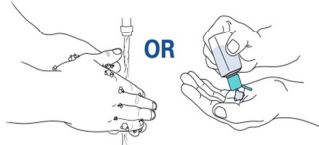
## PERFORM HAND HYGIENE BETWEEN STEPS IF HANDS BECOME CONTAMINATED AND IMMEDIATELY AFTER REMOVING ALL PPE

CDC

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**Figure 5 Flowchart**



Should I perform the endoscopic procedure?
(The decision tree may change once rapid serologic testing is available to check COVID-19 status)

Is the procedure time sensitive?
Are there adequate PPE to consider non-time sensitive procedures? (if no only consider doing time-sensitive procedures)

Question:

> Is there a threat to the patient's life or permanent dysfunction of an organ?
> Is there a risk of metastasis or progression of stage for a specific condition?
> Is there a risk of rapidly worsening progression of disease or symptoms?

Question:

> Is there short-term impact on patient-important outcomes?
> Is delaying the procedure 8 weeks going to cause harm to the patient?

Yes

Unsure

No

Time-sensitive

Not time sensitive

Determine time-sensitive nature of the procedure - within 24 hours or can it be delayed but performed sometime within 8 weeks

Consider:
(i) a telephone consultation with the referring provider or (ii) a telehealth visit with the patient or (iii) a multidisciplinary team approach or (virtual) tumor board to facilitate decision-making for complicated patients

Delay the procedure for 8 weeks If non-time sensitive procedures are delayed further reassess if it is still appropriate to delay the procedure

Examples:
Within 24 hour indication:
-Cholangitis
-Upper GI bleeding
-Food impaction
-Some hospitalized patients

Examples:
Within 8 weeks indication:
-Lower GIB
-Large colonic EMR
-Sigmoidoscopy for evaluation of ulcerative colitis

Examples:
Beyond 8 week delay indication:
-Screening colonoscopy
-Colonoscopy following FIT positive test
-EGD for dyspepsia
-EGD for intestinal metaplasia

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**Supplemental Figures:**

Supplemental Figure 1: PRISMA Flow Diagram of Included Studies
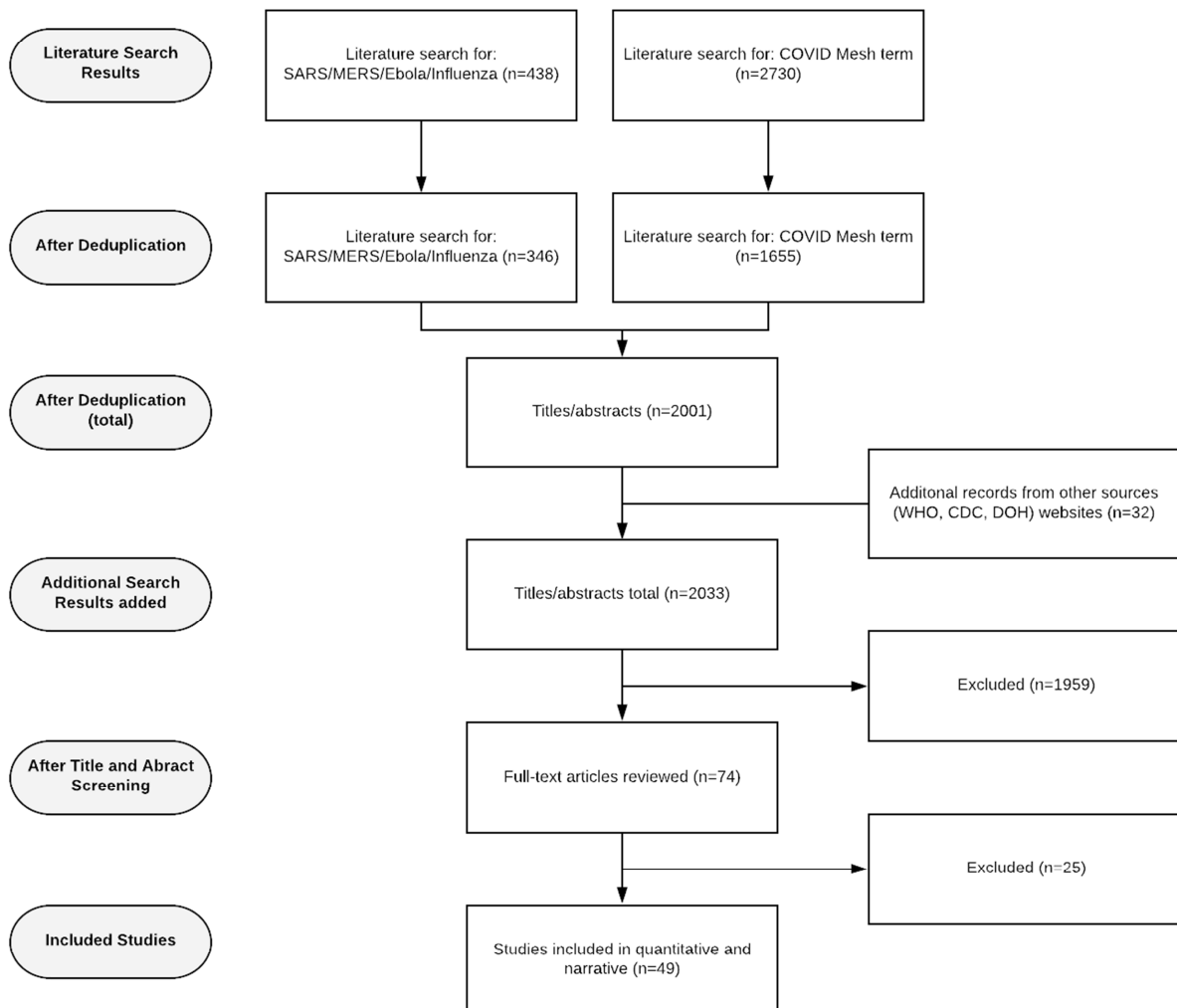
Supplemental Figure 2 Search Strategy

Search date: March 17, 2020
Databases searched: Ovid MEDLINE: Epub Ahead of Print, In-Process & Other Non-Indexed
Citations, Ovid MEDLINE® Daily and Ovid MEDLINE® 1946-Present, Embase Classic+Embase 1947
to 2020 March 16
Limits: None
Filters: Systematic Reviews/Meta-Analyses (except COV Only search on Line 49)

Ovid MEDLINE(R), Embase

| # | Searches | Results |
|---|----------|---------|
| 1 | exp Severe Acute Respiratory Syndrome/ | 12640 |
| 2 | exp SARS Virus/ use ppez | 2874 |
| 3 | exp SARS coronavirus/ use emczd | 4593 |
| 4 | (sars or severe acute respiratory syndrome).ti,ab,kw. | 19960 |
| 5 | exp Middle East Respiratory Syndrome Coronavirus/ use ppez | 956 |
| 6 | exp Middle East respiratory syndrome/ use emczd | 791 |
| 7 | (mers or Middle East Respiratory Syndrome).ti,ab,kw. | 9251 |
| 8 | exp Hemorrhagic Fever, Ebola/ use ppez | 5252 |
| 9 | exp Ebola hemorrhagic fever/ use emczd | 5610 |
| 10 | exp Ebolavirus/ | 6318 |
| 11 | ebola.ti,ab,kw. | 17536 |
| 12 | (SARS-CoV-2 or covid19 or covid-19 or covid 19 or (novel adj2 coronavirus) or (new adj2 coronoavirus) or (coronovirus adj2 "2019") or (coronavirus adj "19") or ("2019" adj2 nCoV)).ti,ab,kw. | 2730 |
| 13 | or/1-12 | 52167 |
| 14 | exp Influenza, Human/ use ppez | 48207 |
| 15 | exp influenza/ use emczd | 93499 |
| 16 | exp Orthomyxoviridae/ use ppez | 56270 |
| 17 | exp Influenza virus/ use emczd | 35082 |
| 18 | (influenza or flu or Orthomyxovirus*).ti,ab,kw. | 234001 |
| 19 | or/14-18 | 268302 |
| 20 | exp Personal Protective Equipment/ use ppez | 29061 |
| 21 | exp protective equipment/ use emczd or exp mask/ use emczd | 86125 |
| 22 | exp Infection Control/ or exp Disinfection/ | 192620 |
| 23 | exp Disinfectants/ use ppez | 67094 |

| 24 | exp disinfectant agent/ use emczd | 534485 |
| 25 | exp Sterilization/ use ppez | 30303 |
| 26 | exp instrument sterilization/ use emczd | 26486 |
| 27 | exp Equipment Contamination/ use ppez | 12733 |
| 28 | exp medical device contamination/ use emczd | 820 |
| 29 | exp Cross Infection/pc | 34428 |
| 30 | (Steriliz* or disinfect* or sanitize).ti,ab,kw. | 134088 |
| 31 | (personal protective equipment or respirator or respirators or mask*).ti,ab,kw. | 194658 |
| 32 | exp Triage/ use ppez | 11275 |
| 33 | triage.ti,ab,kw. | 43591 |
| 34 | or/20-33 | 1208374 |
| 35 | meta-analysis/ or systematic review/ or meta-analysis as topic/ or "meta analysis (topic)"/ or "systematic review (topic)"/ or exp technology assessment, biomedical/ | 601046 |
| 36 | Meta Analysis.pt. | 112124 |
| 37 | (meta analy* or metaanaly* or health technolog* assess*).ti,ab,kw. | 402723 |
| 38 | (meta-analy* or metaanaly* or systematic review* or biomedical technology assessment* or bio-medical technology assessment*).mp,hw. | 768936 |
| 39 | (((systematic* or methodologic*) adj3 (review* or overview*)) or pooled analysis or published studies or published literature or hand search* or handsearch* or medline or pub med or pubmed or embase or cochrane or cinahl or data synthes* or data extraction* or HTA or HTAs or (technolog* adj (assessment* or overview* or appraisal*))).ti,ab,kw. | 791823 |
| 40 | (cochrane or (health adj2 technology assessment) or evidence report).jw. | 45743 |
| 41 | or/35-40 | 1064015 |
| 42 | 13 and 34 and 41 | 165 |
| 43 | remove duplicates from 42 | 123 |
| 44 | 34 and 41 and (13 or 19) | 438 |
| 45 | remove duplicates from 44 | 346 |
| 46 | 12 and 41 | 45 |
| 47 | remove duplicates from 46 | 28 |
| 48 | 12 | 2730 |
| 49 | remove duplicates from 48 | 1655 |

Supplemental Figure 3. Forest Plot. Exposed vs. Unexposed HCWs to tracheal intubation as a Risk Factor for SARS Transmission
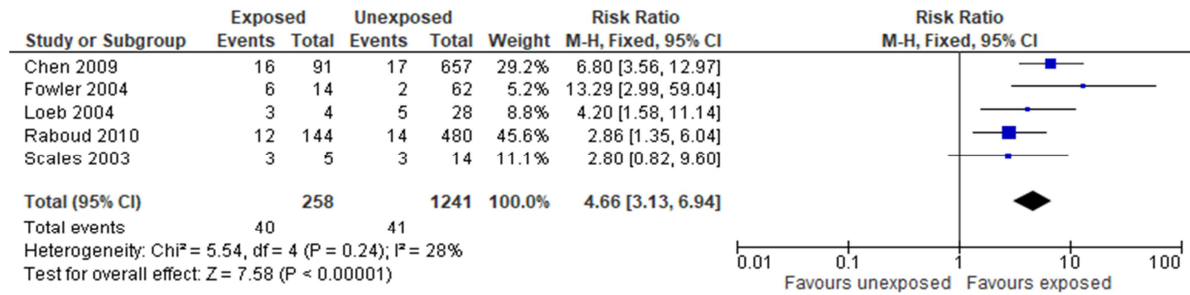
Supplemental Figure 4. Forest Plot PAPR +N95 vs. N95 in reducing contamination of HCWs

| | PAPR + N95 | | N95 | | | Risk Ratio | Risk Ratio |
|---|---|---|---|---|---|---|---|
| Study or Subgroup | Events | Total | Events | Total | Weight | M-H, Fixed, 95% CI | M-H, Fixed, 95% CI |
| **1.1.0 null** | | | | | | | |
| Zamora 2006 | 0 | 0 | 0 | 0 | | Not estimable | |
| **Subtotal (95% CI)** | | **0** | | **0** | | **Not estimable** | |
| Total events | 0 | | 0 | | | | |
| Heterogeneity: Not applicable | | | | | | | |
| Test for overall effect: Not applicable | | | | | | | |
| | | | | | | | |
| **1.1.1 Face** | | | | | | | |
| Zamora 2006 | 0 | 50 | 2 | 50 | 4.2% | 0.20 [0.01, 4.06] | |
| **Subtotal (95% CI)** | | **50** | | **50** | **4.2%** | **0.20 [0.01, 4.06]** | |
| Total events | 0 | | 2 | | | | |
| Heterogeneity: Not applicable | | | | | | | |
| Test for overall effect: Z = 1.05 (P = 0.29) | | | | | | | |
| | | | | | | | |
| **1.1.2 Neck** | | | | | | | |
| Zamora 2006 | 3 | 50 | 48 | 50 | 80.7% | 0.06 [0.02, 0.19] | |
| **Subtotal (95% CI)** | | **50** | | **50** | **80.7%** | **0.06 [0.02, 0.19]** | |
| Total events | 3 | | 48 | | | | |
| Heterogeneity: Not applicable | | | | | | | |
| Test for overall effect: Z = 4.95 (P < 0.00001) | | | | | | | |
| | | | | | | | |
| **1.1.3 Poserior Neck** | | | | | | | |
| Zamora 2006 | 1 | 50 | 9 | 50 | 15.1% | 0.11 [0.01, 0.84] | |
| **Subtotal (95% CI)** | | **50** | | **50** | **15.1%** | **0.11 [0.01, 0.84]** | |
| Total events | 1 | | 9 | | | | |
| Heterogeneity: Not applicable | | | | | | | |
| Test for overall effect: Z = 2.12 (P = 0.03) | | | | | | | |
| | | | | | | | |
| **Total (95% CI)** | | **150** | | **150** | **100.0%** | **0.08 [0.03, 0.19]** | |
| Total events | 4 | | 59 | | | | |

Heterogeneity: Chi² = 0.65, df = 2 (P = 0.72); I² = 0%
Test for overall effect: Z = 5.56 (P < 0.00001)
Test for subgroup differences: Chi² = 0.65, df = 2 (P = 0.72), I² = 0%

Favours PAPR + N95    Favours N95

Supplemental Figure 5. Forest Plot Double gloves compared to Single gloves for prevention of contamination

| Study or Subgroup | Double gloves Events | Total | Single gloves Events | Total | Weight | Risk Ratio M-H, Fixed, 95% CI | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|---|
| Casanova 2012 | 5 | 18 | 14 | 18 | 100.0% | 0.36 [0.16, 0.78] | |
| **Total (95% CI)** | | 18 | | 18 | 100.0% | **0.36 [0.16, 0.78]** | |
| Total events | 5 | | 14 | | | | |
| Heterogeneity: Not applicable | | | | | | | |
| Test for overall effect: Z = 2.57 (P = 0.01) | | | | | | | |

Favor Double gloves  Favor Single gloves