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PCORI HEALTH CARE HORIZON SCANNING SYSTEM

JULY 2020

Horizon Scanning COVID-19 Supplement Status Report Volume 1, Issue 1

Prepared for:

Patient-Centered Outcomes Research Institute
1828 L St., NW, Suite 900, Washington, DC 20036

Contract No. MSA-HORIZSCAN-ECRI-ENG-2018.7.12

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Statement of Funding and Purpose

This report incorporates data collected during implementation of the Patient-Centered Outcomes Research Institute (PCORI) Health Care Horizon Scanning System COVID-19 Supplement, operated by ECRI Institute under contract to PCORI, Washington, DC (Contract No. MSA-HORIZSCAN-ECRI-ENG-2018.7.12). The findings and conclusions in this document are those of the authors, who are responsible for its content. No statement in this report should be construed as an official position of PCORI.

An innovation that potentially meets inclusion criteria might not appear in this report simply because the Horizon Scanning System has not yet detected it or it does not yet meet inclusion criteria outlined in the *PCORI Health Care Horizon Scanning System: Horizon Scanning Protocol and Operations Manual COVID-19 Supplement*. Inclusion or absence of innovations in the horizon scanning reports will change over time as new information is collected; therefore, inclusion or absence should not be construed as either an endorsement or rejection of specific interventions.

A representative from PCORI served as a contracting officer's technical representative and provided input during the implementation of the Horizon Scanning System. PCORI does not directly participate in horizon scanning or assessing leads or topics and did not provide opinions regarding the potential impact of interventions.

Financial Disclosure Statement

None of the individuals compiling this information has any affiliations or financial involvement that conflict with the material presented in this report.

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Preface

Horizon scanning is a systematic process that serves as an early warning system to inform decision makers about possible future opportunities and threats. Health care horizon scanning identifies technologies, innovations, and trends with potential to cause future shifts or disruptions—positive or negative—in areas such as access to care, care delivery processes, care settings, costs of care, current treatment models or paradigms, health disparities, health care infrastructure, public health, and patient health outcomes.

The PCORI Health Care Horizon Scanning System (HCHSS) conducts horizon scanning to better inform its patient-centered outcomes research investments. Initially, PCORI defined the HCHSS project scope to focus on interventions with high potential for disruption in the United States in 5 priority areas: Alzheimer's disease and other dementias, cancer, cardiovascular diseases, mental and behavioral health conditions, and rare diseases. In addition, the system captures high-level disruptive trends across all clinical areas, which may lead PCORI to expand the project scope to include other priority areas in the future.

In early 2020, the COVID-19 pandemic created a fast-moving, widespread public health crisis. In May 2020, PCORI expanded its HCHSS to elucidate the landscape of potentially impactful applications for COVID-19. The HCHSS COVID-19 Supplement scans for, identifies, monitors, and reports on emerging and available COVID-19-related treatments, diagnostics, preventive measures, management strategies, and systems changes with potential for high impact to patient outcomes—for individuals and populations—in the United States in the next 12 months.

The HCHSS COVID-19 Supplement produces 3 main outputs. Status Reports (every 4 months) briefly list and describe all COVID-19-related topics identified, monitored, and recently archived. High-Impact Reports (every 4 months) highlight those topics that ECRI internal stakeholders (eg, physicians, nurses, allied health professionals, public health professionals, first responders, health systems experts, clinical engineers, researchers, business and finance professionals, information technology professionals) have identified as having potential for high impact relative to COVID-19 in the United States. Biweekly COVID-19 Scans provide ECRI Horizon Scanning with a vehicle to inform PCORI in a timely manner of important topics of interest identified during ongoing scanning and topic identification or through the ECRI stakeholder survey process.

For more information about the HCHSS COVID-19 Supplement outputs or the COVID-19-specific horizon scanning process, see the *PCORI Health Care Horizon Scanning System: Horizon Scanning Protocol and Operations Manual COVID-19 Supplement*.

We welcome comments on this document. Send comments by mail to William Lawrence, MD, MS, Patient-Centered Outcomes Research Institute, 1828 L St., NW, Suite 900, Washington, DC 20036, or by email to horizonscan@pcori.org.

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Introduction

The PCORI Health Care Horizon Scanning System (HCHSS) COVID-19 Supplement scans for, identifies, monitors, and reports on emerging and available COVID-19-related treatments, diagnostics, preventive measures, management strategies, and systems changes with high potential to impact patient outcomes—for individuals and populations—in the United States within the next 12 months.

COVID-19 Supplement Status Reports

The PCORI HCHSS COVID-19 Supplement produces Status Reports every 4 months. The reports summarize key data elements for all COVID-19 topics monitored in the system and, if applicable, recently archived topics (typically those archived since the last Status Report).

This Status Report is organized into 6 sections titled as follows: (1) Devices, (2) Identifiable Risk Factors and Prognostic Indicators, (3) Screening and Diagnostics, (4) Systems and Management, (5) Treatments, and (6) Vaccines and Prophylaxis. An appendix lists the abbreviations and acronyms used in the report.

Each of the 6 sections can contain 1 to 3 tables, depending on the topics included in that section: (1) topics added since the last Status Report, (2) currently monitored topics, and (3) recently archived topics. If no topics fall into a given category (ie, added, monitored, archived), no table will be included for that category in that section. Because this report is the first in its series, topics have been reported as currently monitored or recently archived topics. Therefore, each section contains only 2 tables.

Tables for newly added and currently monitored topics summarize information in each row, as shown in the following columns: Title; Description; Possible areas of impact; and Possible future impacts. Tables of archived topics summarize information in each row as shown in the following columns: Title, Description, and Archive reason. Within each table, topics are sorted alphabetically by Title.

ECRI Horizon Scanning has selected the topics included in this report as those with potential for impact relative to COVID-19 in the United States within the next 12 months. All views presented are preliminary and based on readily available information at the time of writing. Because these topics are rapidly developing, the accuracy of this information cannot be guaranteed after the date listed on this publication.

Information presented in the Possible areas of impact and Possible future impacts columns solely represent prospective views of ECRI Horizon Scanning and have typically not been vetted by other stakeholders. These statements represent an ECRI horizon scanning analyst's initial perspectives on a topic's possible impacts. Analysts have been instructed, in the absence of hard data, to consider a topic's possible areas of impact and possible future impacts in light of the developer's claims (ie, if the product does what the developer purports, where might it have impact and what might be its possible future impacts?). Therefore, information presented in the Possible areas of impact and Possible future impacts columns should be considered prospective and may be updated, amended, or deleted when new information becomes available or after stakeholder review.

No information in this report should be construed as an endorsement or rejection of any product listed in this report.

Topics initially added to the system for monitoring may be archived after review of new data or after stakeholder review (see COVID-19 Supplement Horizon Scanning Process Overview: Monitoring, Updating, and Archiving Topics), when it appears that the topic does not have high impact potential relative to COVID-19 in the United States in the next 12 months. An archived topic may reenter the system at a later date if new information comes to light suggesting that the topic has high impact potential.

COVID-19 Supplement Horizon Scanning Process Overview

The *PCORI Health Care Horizon Scanning System: Horizon Scanning Protocol and Operations Manual COVID-19 Supplement* (hereafter referred to as the Protocol) details the criteria we use to select topics. We briefly describe our process below.

Scanning, Lead Selection, and Topic Identification

Scanners (ie, medical librarians and research assistants) collect COVID-19-related information leads from broad scanning and enter them into a leads database, categorize them according to content area (ie, devices, identifiable risk factors and prognostic indicators, screening and diagnostics, systems and management, treatments, and vaccines and prophylaxis) and subcategory, and link them, if applicable, to existing topics in the COVID-19 topics database. A research assistant assigns each lead to a horizon scanning analyst for review.

Analysts review leads to discover potential topics. If a topic meets inclusion criteria, the analyst creates a new record in the COVID-19 topics database and enters a title and a description of the topic, possible areas of impact, and possible future impacts, which comprise the analyst's rationale for proposing the topic. This information represents the analyst's initial impressions of the topic prior to vetting with other stakeholders and should be considered prospective.

When populating the Possible areas of impact column, the analyst selects from the following terms (criteria for selection are listed after each term), based on her or his understanding of the currently available evidence, or, in the absence of hard evidence, his or her theoretical extrapolation based on the developer's claims:

- Patient outcomes: This topic might impact health outcomes for an individual patient.
- Population health: This topic might impact health outcomes across a group of individuals (eg, ethnicity, socioeconomic status, geographic area of residence, age). This is distinct from individual patient outcomes in that a particular intervention might impact individuals differently than it might impact populations (eg, a vaccine might carry certain risks to certain individuals but provide overall benefit to a population or populations).
- Clinician and/or caregiver safety: This topic might impact, positively or negatively, the safety of a clinician or caregiver.
- Health care delivery and process: This topic might impact the way health care is delivered to patients.
- Health care disparities: This topic might increase or decrease health care disparities (ie, differences in the burden of disease or access to health care between different groups or populations).
- Health care costs: This topic might substantially increase or decrease costs of care for patients, payers (ie, insurers), or health care providers.

Each proposed topic is rapidly reviewed and voted on for inclusion by a preselected 3-member panel of PCORI HCHSS senior team members. A majority vote includes or excludes a topic accordingly. All included topics are reported in the Status Report. Each included topic undergoes content review and is then activated as a summary for the stakeholder survey process.

Stakeholder Review Process

Topics are posted to an online bulletin board visible to a preselected panel of about 50 internal ECRI expert stakeholders (eg, physicians, nurses, allied health professionals, public health professionals, first responders, health systems experts, clinical engineers, researchers, business and finance professionals, information technology professionals). As topics are posted, stakeholders review them and complete an accompanying survey, which elucidates the stakeholder's perspective on the topic's potential for impact relative to the COVID-19 pandemic in the United States. The survey first prompts the stakeholder to indicate areas of potential impact, rating each area on a scale of 1 (no impact) to 4 (high impact). It then asks the stakeholder to rate the topic's overall impact potential, timing of the impact, and likelihood of the impact on the same 1 to 4 scale. Finally, the stakeholder is asked to provide a brief written rationale explaining her or his selections and ratings.

When a topic has received at least 5 completed surveys, it is eligible to be considered for inclusion in a High-Impact Report (see below); however, the questionnaire function remains active for all topics until the High-Impact Report selection process begins, allowing each member of the expert panel to comment on each topic as time permits.

High-Impact Report Topic Selection

Every 4 months, all currently monitored topics that have received at least 5 completed stakeholder surveys are considered for inclusion in the High-Impact Report. The purpose of the selection process is to identify topics that stakeholders have deemed to have potential for high impact relative to COVID-19 in the United States. Generally, topics that stakeholders agree have a moderately high to high overall impact potential and are likely to cause impact within the next 12 months in the United States are selected for inclusion. However, stakeholder comments must generally support conclusions suggested by ratings. For topics with borderline ratings, high variance, or questionable comments, a brief review and vote by a preselected 3-member panel of senior horizon scanning team members determines inclusion or exclusion. A majority affirmative vote selects the topic for inclusion. See the Protocol for a detailed explanation of how we select topics for inclusion in the High-Impact Report.

Monitoring, Updating, and Archiving Topics

Scanners use keywords and controlled vocabulary terms to monitor and search resources. When possible, scanners create automated alerts to capture new topic-specific information on an ongoing basis. These monitoring activities can trigger a change in topic status, depending on what has occurred.

Analysts update topics as new information arises to ensure that the content is current. When a topic is updated, stakeholders who have commented on the topic are alerted to review the new information and revise or update their survey ratings and rationales, if desired.

An included topic may be archived when new information overwhelmingly suggests that the topic is unlikely to cause significant impact relative to the COVID-19 pandemic in the United States in the next 12 months. Reasons may include one or more of the following:

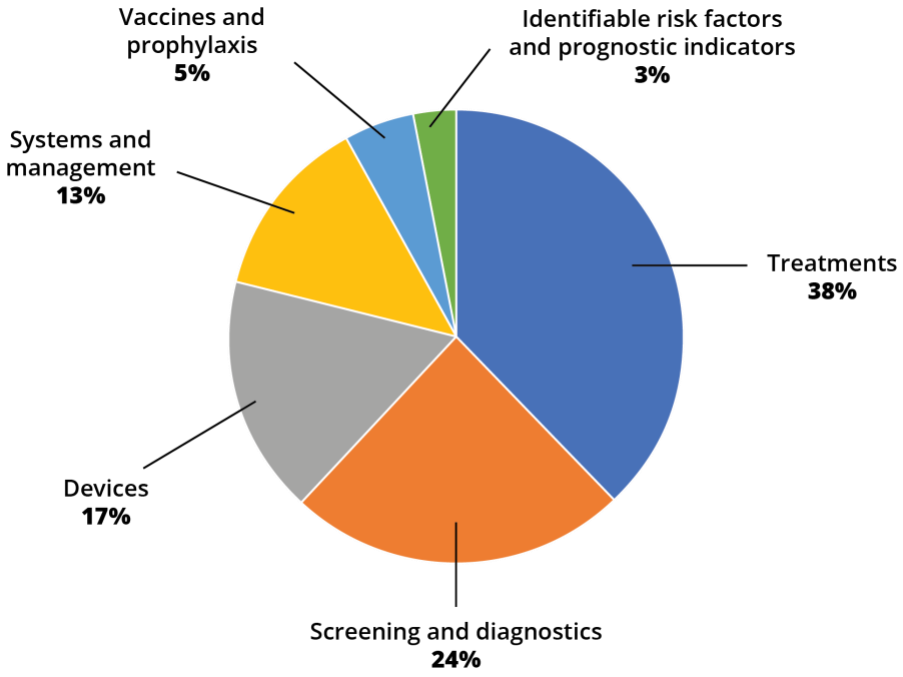
- Stakeholder ratings and comments strongly suggest that the topic does not have high impact potential.
- New data do not support the developer's claims relative to COVID-19.
- Development has ceased or stalled.
- The development timeline has shifted and the product is no longer likely to be available within the next 12 months.

Reporting Period Summary

The PCORI HCHSS COVID-19 Supplement began operating in May 2020. Since then, review of about 1100 information leads has led to the identification and selection of 63 COVID-19-related topics across the 6 content areas included in this Status Report, distributed as follows (also see Figure 1):

- Devices: 11 topics (17%)
- Identifiable risk factors and prognostic indicators: 2 topics (3%)
- Screening and diagnostics: 15 topics (24%)
- Systems and management: 8 topics (13%)
- Treatments: 24 topics (38%)
- Vaccines and prophylaxis: 3 topics (5%)

Figure 1. Percentage of Topics by Content Area



Section 1. Devices: 11 Topics

Table 1.1. Currently Monitored Device Topics: 4 Topics

Title	Description	Possible areas of impact	Possible future impacts
Decontamination systems for reprocessing single-use N95 respirators	Rapidly depleted supplies of N95 respirators for health care personnel have prompted several manufacturers to seek Emergency Use Authorization (EUA) from FDA for systems that purportedly decontaminate N95 respirators designed for single use, allowing them to be reused safely. As of June 18, 2020, FDA had granted 9 EUAs for use of N95 respirator decontamination systems during the COVID-19 outbreak. These systems typically use vapor hydrogen peroxide or steam for decontamination of compatible N95 respirators that may be contaminated with SARS-CoV-2, the virus that causes COVID-19, or other pathogenic microorganisms. Most systems with EUAs are authorized for decontaminating N95 respirators for single-user use for 2 to 20 (clearly marked) decontamination cycles. In most cases, health care facilities ship used respirators to a manufacturer site for decontamination using special handling and shipping procedures. N95 respirators that contain cellulose material are incompatible with decontamination systems with EUAs thus far.	Clinician and/or caregiver safety Health care delivery and process Health care costs	Might reduce shortages of N95 respirators for health care personnel Might be more economical than disposal of single-use respirators and purchase of new respirators at inflated costs due to supply shortages Might raise safety concerns among health care personnel if subsequent issues with respirator reprocessing arise
Extracorporeal blood filtration to treat COVID-19	Early available data suggest that a major contributor to poor outcomes in patients with COVID-19 infection is a cytokine storm, an overly aggressive immune response to the pathogen, that can damage healthy tissue. Removing inflammatory mediators from patients through an external blood filtering circuit has been proposed to lessen or prevent the cytokine storm. As of June 19, 2020, FDA had granted Emergency Use Authorizations to 4 manufacturers of extracorporeal blood filtration devices for use during the COVID-19 pandemic. When used with appropriate systems (eg, apheresis systems, continuous renal replacement therapy systems), these devices purportedly remove from patients' blood inflammatory cytokines and, depending on the specific filter, pathogens. Extracorporeal blood filtration increases the risk of several complications, including bleeding, blood clots (thrombosis), air embolism, destruction of red blood cells (hemolysis), infection, low blood pressure (hypotension), and unintentional removal of other blood substances (eg, vitamins, minerals, proteins, medications).	Patient outcomes Health care delivery and process	Might improve patient outcomes by avoiding or lessening severity of cytokine storms Might require additional staff experienced with extracorporeal blood filtration procedures Might increase treatment complexity and necessitate additional patient monitoring to quickly identify hematologic complications

Title	Description	Possible areas of impact	Possible future impacts
Implantable diaphragm pacing (TransAeris) to improve ventilator weaning	Prolonged mechanical ventilation can cause diaphragm muscle atrophy, making ventilator weaning difficult. The TransAeris Diaphragm Pacing System is intended to maintain diaphragm muscle strength by electrically stimulating the diaphragm with the intention of promoting more rapid weaning from mechanical ventilation. To deploy the system, a surgeon uses a needle to temporarily implant 4 electrode leads into the diaphragm, 2 on each side of the abdomen. The electrodes are tunneled through the skin and connected to an external pacing system that physicians program to deliver the electrical stimulation. The surgeon withdraws the implanted electrodes once the patient is successfully extubated after cessation of mechanical ventilation. On April 13, 2020, FDA granted Synapse Biomedical, Inc (Oberlin, Ohio), Emergency Use Authorization for the device to help wean patients deemed at high risk of weaning failure during the COVID-19 pandemic, to be used for no longer than 30 days.	Patient outcomes Health care delivery and process Health care costs	Might improve patient outcomes by increasing successful weaning attempts Might increase procedural costs for disposable electrodes and system control unit/pulse generator Might moderately reduce overall treatment costs by preventing incidence of ventilator weaning failures Might increase need for surgical staff to implant temporary electrodes, which might also increase exposure risk and the need for personal protective equipment (PPE) Might increase patient monitoring requirements during temporary electrode catheter placement
Transvenous phrenic nerve stimulation to improve ventilator weaning	Prolonged mechanical ventilation can cause diaphragm muscle atrophy, making ventilator weaning difficult. The Lungpacer Diaphragm Pacing Therapy System is intended to reduce diaphragm atrophy by stimulating the phrenic nerves, which control breathing through the diaphragm. Physicians temporarily insert a single-use, multielectrode catheter into the left subclavian vein at the left shoulder and advance it adjacent to the left and right phrenic nerves within the upper chest. Clinicians modulate electrical stimulation though the system's portable pulse generator and control unit. In May 2016, FDA granted Lungpacer Medical, Inc (Vancouver, British Columbia, Canada), Expedited Access Pathway (now Breakthrough Therapy) designation for the Lungpacer to treat patients unable to wean from ventilators. On April 14, 2020, FDA granted the developer Emergency Use Authorization to assist in weaning patients deemed at high risk of weaning failure during the COVID-19 pandemic, to be used for no longer than 30 days. In a clinical trial of patients on mechanical ventilation for general indications for more than 4 days with 2 failed weaning attempts, patients receive 120 total daily stimulation repetitions, delivered in 2 daily sessions, for an unspecified duration.	Patient outcomes Health care delivery and process Health care costs	Might improve patient outcomes by increasing successful weaning attempts Might increase procedural costs for disposable catheters and system control unit/pulse generator Might moderately reduce overall treatment costs by preventing incidence of ventilator weaning failures Might increase need for specialist staff experienced in placing indwelling intravenous catheters, which might also increase exposure risk and the need for personal protective equipment (PPE) Might increase patient monitoring requirements during temporary electrode catheter placement

Table 2.2. Recently Archived Device Topics: 7 Topics

Title	Description	Archive reason(s) based on data review and/or stakeholder ratings and comments
Continuous positive airway pressure (CPAP) for noninvasive ventilatory support	To mitigate shortages of mechanical ventilators, some researchers have proposed using CPAP machines to provide noninvasive breathing support in less severe cases of COVID-19 or in patients being weaned from invasive ventilation. CPAP units are typically used by patients at home to treat obstructive sleep apnea. When used on patients hospitalized for COVID-19, CPAP units must be retrofitted with an environmental filter to prevent pathogen release into ambient air. Some of the simplest design modifications purportedly can be assembled in several minutes using FDA-approved off-the-shelf components already in stock at most hospitals. For example, a New York University team developed the NYU Tandon AirMOD system using viral filters, oxygen-enrichment adaptors, T-connectors, and positive end-expiratory pressure (PEEP) valves to create a negative pressure tent around the patient.	CPAP for noninvasive ventilatory support is unlikely to cause large disruption to the care of patients with less-severe COVID-19. The technology is widely available and has been used regularly as noninvasive breathing support for other types of respiratory distress.
Drone-based disinfection in public spaces	The COVID-19 pandemic has created a need for surface decontamination in public spaces. Advances in drone technology have recently expanded the use of commercial drones into decontamination services. Firms specializing in decontamination may offer drone-based dispersal of disinfectants approved by the US Environmental Protection Agency (EPA) in large indoor spaces (eg, gymnasiums, warehouses, theaters). Another approach that might be more appropriate for smaller indoor areas (eg, patient rooms, waiting areas, breakrooms, restrooms) is the use of drones that deliver germicidal irradiation for surface cleaning using ultraviolet light in the 200 to 280 nm range (ie, ultraviolet C band), commonly used in health care applications and water disinfection. Drones might allow widespread decontamination of public spaces with a smaller maintenance workforce.	The cost and uncertain efficacy of drone-based disinfection would likely limit its uptake. Aerial spraying is unlikely to reach all potentially infected surfaces compared with manual cleaning procedures. Further, airborne disinfectants might cause allergic reactions, skin irritation, or simple panic if people are present during drone-based disinfection.

Title	Description	Archive reason(s) based on data review and/or stakeholder ratings and comments
Extracorporeal membrane oxygenation (ECMO) to treat COVID-19	ECMO is a highly invasive form of cardiopulmonary bypass that can be used to replace respiratory function in patients with severely compromised lungs (eg, due to infection). Physicians may use ECMO when lungs cannot adequately oxygenate blood even with supplemental oxygen or when lungs cannot remove carbon dioxide even when assisted by a mechanical ventilator. However, ECMO is used sparingly because it can increase risk of bleeding, blood clots, stroke, kidney failure, and infection. With little established guidance for ECMO use for COVID-19, research teams in China and the United States recently reported their respective initial experiences using ECMO to treat patients with severe COVID-19 infection. Researchers found that ECMO might help improve outcomes for severe COVID-19 cases under certain conditions. However, ECMO appeared to provide greater benefit in patients who had only impaired lung function compared with those patients who had both compromised lung and heart function, likely because the latter patients were much sicker to begin with.	ECMO is highly invasive, is costly, has limited availability, and requires highly specialized personnel. It is used sparingly for other respiratory distress indications because of the stress it places on patients, who are already often in fragile conditions.
Inhaled nitric oxide (NO) to treat COVID-19	Inhaled NO purportedly acts as a potent vasodilator to improve arterial oxygenation and might contribute to preventing viral replication. At least 2 manufacturers (Beyond Air, Inc [Garden City, New York]; Bellerophon Therapeutics, Inc [Warren, New Jersey]) are conducting FDA-authorized clinical trials of their respective inhaled NO systems (LungFit, INOpulse) to treat patients with COVID-19. The portable devices extract and concentrate NO from ambient air and deliver it to patients through a face mask or nasal cannula. Previous research has suggested that inhaled NO to treat severe acute respiratory syndrome (SARS), another coronavirus-caused disease, improved arterial oxygenation and allowed reduced levels of supplemental oxygen therapy and airway pressure support. Additionally, NO-treated patients in this study exhibited increased oxygen saturation and decreased spread or density of lung infiltrates that persisted after discontinuation of NO, which the authors hypothesized could be evidence of an antiviral response induced by NO.	NO might provide a small benefit for some patients. However, it will not likely have a large impact on care because it will be one of many less-than-optimal options for treating patients who have COVID-19.

Title	Description	Archive reason(s) based on data review and/or stakeholder ratings and comments
Noninvasive muscle stimulation to shorten mechanical ventilation duration	Prolonged use of mechanical ventilation can cause breathing muscles to atrophy, complicating efforts to wean patients off ventilators. The VentFree Respiratory Muscle Stimulator is intended to reduce respiratory muscle atrophy, potentially shortening the duration of mechanical ventilation. Clinicians place noninvasive, adhesive electrode patches on the middle of the chest and modulate neuromuscular electrical stimulation with a control unit to contract the abdominal wall muscles in synchrony with exhalation during mechanical ventilation. A pilot study suggested that the device might reduce ventilation duration and length of intensive-care unit stay. On May 4, 2020, FDA granted Liberate Medical, LLC (Crestwood, Kentucky), Emergency Use Authorization for the VentFree system. It is authorized for use by providers in health care settings during the COVID-19 pandemic to reduce disuse atrophy of the abdominal wall muscles, which might reduce the days of ventilator support in adults who require mechanical ventilation. FDA in January 2019 granted the developer Breakthrough Device Designation for preventing breathing muscle atrophy and reducing the number of days of ventilator support in adults who require mechanical ventilation.	More long-term data in a larger population are needed to determine the true effect of noninvasive muscle stimulation to shorten mechanical ventilation times, discounting the placebo effect. Similar technologies have not shown definitive efficacy in improving other respiratory distress conditions. Therefore, the intervention might provide an incremental improvement in care but will not likely have a major impact.
Proximity alarms to maintain social distance	The need for individuals to maintain social distancing while communities begin reopening has prompted several companies (eg, Engineering USA [Chicago, Illinois], Proxxi [Vancouver, British Columbia, Canada], Teltonika [Vilnius, Lithuania], Triax Technologies [Norwalk, Connecticut]) to develop small devices worn on a belt, lanyard, or wristband to promote effective social distancing. These wearable devices alert individuals with audible, visible, or tactile alarms when proper distance from other people in their vicinity who are also wearing the same manufacturer's devices is not maintained. The systems are often promoted as allowing staff to safely return to work in indoor or outdoor environments where employees are likely to mingle to perform their duties. The wearable devices are effective for achieving social distancing only with identical devices used by all tracked individuals. Some devices allow automated collection of device data to allow contact tracing among users at a facility.	Several barriers to the adoption of proximity alarms exist, including privacy concerns, only partial acceptance, alarm fatigue, and the proprietary nature of some closed systems. In addition, overreliance on proximity alarms might lead to a false sense of security for some users, possibly resulting in a lower level of adherence to other recommended safety measures.

Title	Description	Archive reason(s) based on data review and/or stakeholder ratings and comments
Ventilator splitting to treat 2 patients requiring different ventilator settings	The rapid surge of patients who require mechanical ventilation to treat COVID-19 has prompted frontline health care providers to devise workarounds to increase ventilator capacity. Ventilator splitting using a shared breathing circuit has been proposed as an option to ventilate multiple patients with a single ventilator; however, this method exposes both patients to the same breathing circuit dynamics and, therefore, is unable to compensate for differing target tidal volumes or lung compliance between patients. One approach to address this issue has been to modify configurations of ventilator breathing circuits and accessories to allow a single ventilator to support 2 patients who may need different levels of respiratory support. In response, some companies have developed modified ventilator circuits and related accessories to provide hospitals with an off-the-shelf option for splitting ventilators between patients. These more readily available alternatives can be produced via 3-D printing, and at least one such device already has FDA Emergency Use Authorization for use during the COVID-19 pandemic.	Because the anticipated ventilator shortage did not develop in the United States as many had predicted, the need to split ventilators might not be as urgent as previously thought. In addition, limitations of this approach would offer suboptimal care for both patients on a shared ventilator, making physicians more hesitant to use it widely. Ventilator splitting also increases risks of cross-contamination.

Section 2. Identifiable Risk Factors and Prognostic Indicators: 2 Topics

Table 2.1. Currently Monitored Risk Factor and Prognostic Indicator Topics: 1 Topic

Title	Description	Possible areas of impact	Possible future impacts
Interleukin-6 (IL-6) levels as a prognostic factor in patients with COVID-19	Some COVID-19 patients have relatively mild symptoms, whereas others develop severe disease. Additionally, the clinical course of patients hospitalized for COVID-19 is variable, and patients may deteriorate rapidly to respiratory failure, requiring ventilation and intensive-care unit admission. Research suggests that IL-6 levels might be a potential biomarker of predicting severe COVID-19. Elevated IL-6 levels have been associated with cytokine-mediated lung damage that can result in severe respiratory distress in COVID-19 patients. Results from a clinical study conducted in hospitalized patients suggested that IL-6 levels above 80 pg/mL are indicative of a high risk of respiratory failure. To that end, FDA has granted the Roche Diagnostics (Basel, Switzerland) Elecsys IL-6 test an Emergency Use Authorization to help identify patients with confirmed COVID-19 who are at risk of intubation and mechanical ventilation. IL-6 testing is also available through multiple clinical laboratories (eg, ARUP Laboratories, LabCorp, Quest Diagnostics).	Patient outcomes Population health Clinician and/or caregiver safety Health care delivery and process Health care disparities Health care costs	Might streamline the triage of patients based on the potential need for mechanical ventilation Might reduce overall costs by improving utilization of hospital resources Might improve understanding of the pathogenesis of COVID-19 disease

Table 2.2. Recently Archived Risk Factor and Prognostic Indicator Topics: 1 Topic

Title	Description	Archive reason(s) based on data review and/or stakeholder ratings and comments
Atopic diseases that might reduce risk of infection with SARS-CoV-2, the virus that causes COVID-19	Researchers are trying to identify risk factors that could predispose individuals to SARS-CoV-2 infection or development of severe COVID-19 disease. The Centers for Disease Control and Prevention (CDC) indicates that people with moderate to severe asthma are at high risk of severe COVID-19. However, emerging data have suggested that people with allergic asthma and other atopic conditions might actually be at a lower risk of SARS-CoV-2 infection or severe COVID-19 disease. One hypothesis to explain this observation is supported by data indicating that people with atopic conditions express lower levels of angiotensin-converting enzyme 2 (ACE2), which is the cellular receptor that mediates viral entry into cells. As part of the HEROS study, sponsored by the National Institutes of Health (NIH), investigators will evaluate whether patients with allergic diseases have a reduced risk of being severely infected with SARS-CoV-2. By means of active surveillance, this clinical study can help identify effective disease management strategies for people with these comorbidities.	This hypothesis does not portend a large population health impact, given the low percentage of individuals with atopic illnesses. Additionally, the ongoing HEROS study is recruiting children who are not at high risk for COVID-19, calling any resulting data from this study into question.

Section 3. Screening and Diagnostics: 15 Topics

Table 3.1. Currently Monitored Screening and Diagnostic Topics: 8 Topics

Title	Description	Possible areas of impact	Possible future impacts
Accula SARS-CoV-2 point-of-care (POC) test to diagnose COVID-19	The Accula SARS-CoV-2 test is a polymerase chain reaction (PCR) assay developed by Mesa Biotech, Inc (San Diego, California), as a POC COVID-19 test. SARS-CoV-2 is the virus that causes COVID-19. The test is intended for use in temporary screening facilities, physician office laboratories, urgent care, and long-term nursing facilities. The Accula system consists of a single-use cassette that contains the reagents needed to amplify viral nucleic acids. Using nasal and throat swabs, the sample is added into the cassette and then is placed in the Accula Dock. The dock is a palm-sized device that controls reaction temperatures, timing, and fluid movement within the cassette. At the end of the reaction, results indicating whether viral nucleic acids have been detected in the patient sample are visually read on the side of the cassette. The Accula system purportedly yields laboratory-quality results in about 30 minutes and is intended to complement central laboratories, where most current testing is performed. In March 2020, FDA granted the Accula SARS-CoV-2 test Emergency Use Authorization (EUA). A published study evaluated the performance of the Accula SARS-CoV-2 test in 100 nasopharyngeal samples previously tested by the SARS-CoV-2 PCR assay, an EUA test developed by Stanford Health Care Clinical Virology Laboratory (Palo Alto, California). The Accula SARS-CoV-2 test had a sensitivity of 68%, a specificity of 100%, and an overall percentage agreement of 84%.	Patient outcomes Population health Health care delivery and process Health care costs	Might allow health centers to diagnose COVID-19 soon after a symptomatic patient arrives at a health center Might help triage infected and uninfected patients on the same day they are tested Might be more affordable than tests performed in central laboratories Might increase the rate of false-negative test results if the assay does not detect very low levels of viral nucleic acids Might not be broadly available in all health centers

Title	Description	Possible areas of impact	Possible future impacts
Artificial intelligence (AI)–assisted echocardiography guidance for nonexpert users	The American College of Cardiology recommends diagnostic cardiac ultrasound (ie, echocardiography) for patients with a COVID-19 diagnosis and symptoms of heart failure, enlarged heart, arrhythmia, or changes in electrocardiogram readings. The American Society of Echocardiography has issued advice for protecting patients and ultrasound operators when performing echocardiograms on patients with COVID-19, because some echocardiography techniques might risk spreading the virus due to the patient coughing or gagging during the exam. On May 12, 2020, FDA granted Caption Health expedited De Novo pathway clearance of an updated version of its Caption Guidance software, which purportedly allows nonexpert medical professionals to perform diagnostic-quality echocardiograms. The software uses AI to emulate expert sonographer guidance on image optimization and transducer placement and give automated feedback on image quality. According to Caption Health, the updated software features 88% more types of guidance than the original version, improved algorithm performance, and optimized workflow. The developer stated FDA's expedited review was prompted by requests from clinicians at several US hospitals detailing how the software could enable frontline providers to quickly assess cardiac function, reduce coronavirus exposure risk for health care personnel, and improve resource utilization in emergency departments and intensive-care units.	Clinician and/or caregiver safety Health care delivery and process	Might reduce overall staff exposure to COVID-19 by enabling appropriate patients to receive cardiac ultrasound scans without departmental transfers Might reduce personal protective equipment (PPE) consumption if fewer personnel are needed to perform diagnostic-quality echocardiograms
COVID-19 at-home self-collection kits	The at-home COVID-19 self-collection test kit consists of a nasal cotton swab or saliva collection tube, a biohazard specimen bag, and an overnight shipping envelope. The kit permits at-home collection of a sample appropriate to perform a nucleic acid–based molecular diagnostic test for SARS-CoV-2, the virus that causes COVID-19. The kit is meant for individuals with COVID-19 symptoms or for those who have had possible exposure to the virus. The self-collection kit purportedly reduces the risk of infected individuals transmitting the virus to others. Because the test kit does not require a clinician to collect a nasal or saliva specimen, it might also reduce the demand for personal protective equipment (PPE). On average, self-collection kits cost about $115 per test. Out-of-pocket costs may be waived for individuals deemed eligible by a survey or reimbursed at the discretion of the patient's health insurance. FDA has granted Emergency Use Authorization to the COVID-19 self-collection test kit (Laboratory Corporation of America Holdings, Burlington, North Carolina), COVID-19 test home collection kit (EverlyWell, Inc, Austin, Texas), and Oragene Dx OGD-510 kit (DNA Genotek, Inc, Ottawa, Ontario, Canada).	Patient outcomes Population health Clinician and/or caregiver safety Health care delivery and process	Might reduce risk of patients transmitting SARS-CoV-2 to medical staff and other patients Might reduce the need for PPE in testing departments Might increase the rate of false-negative test results if the patient does not acquire a specimen with sufficient amount of the virus to be detected Might pose limits, depending on whether the sample is safely shipped to a testing facility

Title	Description	Possible areas of impact	Possible future impacts
CoviTact point-of-care (POC) protease assay to diagnose COVID-19	CoviTact is a protease assay developed by ViroTact BV (Groningen, the Netherlands), a subsidiary of Detact Diagnostics BV (Groningen, the Netherlands), intended as a POC COVID-19 test. It is intended to be used in temporary screening facilities, physician office laboratories, urgent care, and long-term nursing facilities. CoviTact consists of a short peptide that is bound to a near infrared light (NIRL)–emitting molecule and a quencher molecule that absorbs NIRL. The peptide has been designed to contain a specific amino acid sequence that can be recognized and cleaved only by the main protease (M_{pro}) of SARS-CoV-2, the virus that causes COVID-19. Once M_{pro} cleaves the peptide, the NIRL-emitting molecule is no longer in close proximity to the quencher molecule and NIRL can be detected using a fluorometer. CoviTact can purportedly detect SARS-CoV-2 in saliva samples, nasal swabs, or other possibly infectious bodily fluids. If M_{pro} is present in a patient sample, CoviTact purportedly confirms COVID-19 cases within minutes in a highly specific way.	Patient outcomes Population health Health care delivery and process Health care costs	Might allow the detection of very low levels of SARS-CoV-2 particles Might detect COVID-19 infection more quickly than nucleic acid–based tests Might be more affordable than nucleic acid–based tests Might increase the rate of false-negative test results if the assay does not emit detectable NIRL in the presence of very low levels of M_{pro}
FebriDx point-of-care (POC) test to predict viral or bacterial infection	The FebriDx test is a rapid, POC diagnostic test that uses a fingerstick blood sample to predict whether an acute respiratory infection is caused by a virus or bacteria. The test assesses the pathogen-induced host immune response through the in vitro detection of both myxovirus resistance protein A (MxA) and C-reactive protein (CRP) directly from the whole blood sample. Elevated CRP is a highly sensitive marker for infection, but cannot reliably differentiate between viral and bacterial infections. Conversely, MxA is highly specific for viral infections. By combining these biomarkers, the FebriDx purportedly optimizes the sensitivity and specificity of both MxA and CRP, thereby reliably differentiating between viral and bacterial respiratory infections	Patient outcomes Population health Health care delivery and process Health care costs	Might improve population health outcomes by identifying the cause of the infection sooner Might assist hospital staff to triage patients more effectively and curb the spread of COVID-19 Might reduce health care utilization Might reduce overprescribing of antibiotic treatments Might increase medical burden, health care costs, and poor patient outcomes due to device errors

Title	Description	Possible areas of impact	Possible future impacts
QIAstat-Dx Respiratory SARS-CoV-2 Panel test to diagnose COVID-19	The QIAstat-Dx Respiratory SARS-CoV-2 Panel, a real-time polymerase chain reaction (PCR) assay (Qiagen, NV, Hilden, Germany), is intended to diagnose COVID-19 and differentiate it from 20 other causes of respiratory infection. The test is authorized to be used in laboratories certified under the Clinical Laboratory Improvement Amendments of 1988. The panel consists of a single-use cartridge that includes all reagents needed for nucleic acid extraction, nucleic acid amplification, and detection of 3 bacteria and 18 viruses (or their subtypes) that cause respiratory symptoms—including SARS-CoV-2, the virus that causes COVID-19. Using nasopharyngeal swabs, the sample is added into the cassette and then is placed in the QIAstat-Dx Analyzer 1.0. The real-time PCR assay should be performed only by laboratory professionals trained in the use of QIAstat-Dx Analyzer 1.0. At the end of the reaction, results indicating whether pathogen nucleic acids have been detected in the patient sample are displayed on the analyzer's screen. The panel purportedly requires a small sample volume and minimal hands-on time, and the results are available in about 1 hour. In March 2020, FDA granted the QIAstat-Dx Respiratory SARS-CoV-2 Panel Emergency Use Authorization. A published study evaluated the performance of the panel for detecting SARS-CoV-2 in 69 samples previously tested by a reverse transcriptase PCR test recommended by the World Health Organization (Geneva, Switzerland). QIAstat-Dx had a sensitivity of 100%, a specificity of 93%, and an overall percentage agreement of 97%.	Patient outcomes Population health Health care delivery and process Health care disparities Health care costs	Might allow health centers to diagnose COVID-19 soon after a patient arrives at a health center and determine whether symptoms are caused by SARS-CoV-2 or a different infectious agent Might help triage infected and uninfected patients on the same day they are tested Might be more affordable than tests performed in central laboratories Might increase the rate of false-negative test results if the assay does not detect very low levels of viral nucleic acids Might create disparities for patients who live far from health centers with capabilities and certifications to offer the test

Title	Description	Possible areas of impact	Possible future impacts
Sofia 2 SARS Antigen FIA point-of-care (POC) test to diagnose COVID-19	The Sofia 2 SARS Antigen Fluorescent Immunoassay (FIA) was developed by Quidel Corp (San Diego, California) as a SARS-CoV-2 antigen detection assay. It is intended for use in POC, including temporary screening facilities, ambulatory care centers, and long-term nursing facilities. The Sofia 2 SARS FIA is a cassette-based lateral flow immunoassay that detects the nucleocapsid protein from SARS-CoV (which causes severe acute respiratory syndrome), and SARS-CoV-2 (which causes COVID-19) using antibodies. After a nasal or nasopharyngeal swab is treated with a solution that exposes the viral nucleocapsid, the sample is added to the cassette and placed in the Sophia Analyzer. The analyzer reads the cassette and reports whether viral antigen was detected in the patient sample. The SOFIA 2 SARS FIA purportedly requires a small sample volume and minimal hands-on time, and the results are available in about 10 minutes. In May 2020, FDA granted the Sofia 2 SARS Antigen FIA Emergency Use Authorization, the first SARS-CoV-2 antigen test to receive such approval. Similar to nucleic acid–based tests widely used to diagnose SARS-CoV-2 infection, antigen tests are used to detect active infections, and they may present advantages and disadvantages relative to nucleic acid–based diagnostics.	Patient outcomes Population health Health care delivery and process Health care costs	Might allow health centers to diagnose COVID-19 soon after a patient arrives at a health center and determine whether symptoms are caused by SARS-CoV-2 or a different infectious agent Might help triage infected and uninfected patients on the same day they are tested Might be more affordable than tests performed in central laboratories Might not be broadly available in all health centers Might increase the rate of false-negative test results if the assay does not detect very low levels of viral nucleocapsid proteins
Wastewater testing to assess scale of COVID-19 outbreak	The spread of COVID-19 infection, especially by asymptomatic individuals, coupled with a limited clinical testing capacity, has spurred research into alternative testing methods to detect the scope and dispersal patterns of COVID-19 infection. Several researchers have proposed testing wastewater from sewage systems for an early warning, especially using localized testing of high-risk communities such as nursing homes. Wastewater testing might indicate COVID-19 community infection before cases are identified at health care facilities through diagnostic testing. Further, increased viral particle levels of SARS-CoV-2, the virus that causes COVID-19, detected in wastewater could predict increasing numbers of infected individuals requiring treatment. Applying nucleic acid−based polymerase chain reaction (PCR) assays to wastewater testing has high specificity and sensitivity, but this approach can be costly and requires more time and specialized personnel to perform the tests. Simpler and cheaper DNA detection methods, such as paper-based microfluidic indicators, enzyme-linked immunosorbent assay (ELISA), or biosensors, might allow for high-quality precision diagnosis of COVID-19 in localized regions. Biobot Analytics, Inc (Somerville, Massachusetts), is one US-based firm offering sewage testing to local governments.	Population health	Might improve public health preparedness for future outbreaks by analyzing disease patterns Might allow better preemptive resource allocation by identifying potential disease clusters before health care facilities begin receiving high case volumes

Table 3.2. Recently Archived Screening and Diagnostic Topics: 7 Topics

Title	Description	Archive reason(s) based on data review and/or stakeholder ratings and comments
Artificial intelligence (AI)–assisted cough/temperature detector (FluSense) for infectious disease forecasting	The FluSense device was developed to detect coughing and crowd size in real time, then analyze collected data to directly monitor flu-like illnesses in public spaces. Researchers at the University of Massachusetts, Amherst, created and tested their FluSense device to monitor influenza trends, but they note the technology could apply to other viral respiratory outbreaks, such as COVID-19 or severe acute respiratory syndrome (SARS). The box, which, according to the developer, is "about the size of a large dictionary," contains a small neural computing engine, microphone array, and thermal imaging camera that stores no personally identifiable information. Researchers placed the FluSense devices in 4 health clinic waiting rooms from December 2018 to July 2019. The devices collected and analyzed more than 350 000 thermal images and 21 million nonspeech audio samples from the public waiting areas. Researchers concluded that FluSense monitoring strongly correlated with laboratory-based testing for influenza and other flu-like illnesses, and accurately predicted daily illness rates at the university clinic.	FluSense might not effectively identify asymptomatic COVID-19 carriers, thus limiting its usefulness. In addition, the high cost and logistics needed for widespread implementation of these monitors as a public health tool will limit their adoption.
BioFire Respiratory 2.1 Panel test to diagnose COVID-19	The BioFire Respiratory 2.1 (RP2.1) Panel is a multiplex, reverse transcriptase polymerase chain reaction (RT-PCR) assay (BioFire Diagnostics, LLC, Salt Lake City, Utah, a subsidiary of bioMérieux SA, Marcy l'Étoile, France). It is intended to diagnose COVID-19 and differentiate it from 18 other causes of respiratory infection. The test is authorized to be used in laboratories certified under the Clinical Laboratory Improvement Amendments of 1988. The panel consists of a single-use pouch that includes all reagents needed for nucleic acid extraction, nucleic acid amplification, and detection of 4 bacteria and 15 viruses (or their subtypes), including SARS-CoV-2, the virus that causes COVID-19. After using nasopharyngeal swabs, the sample is added into the pouch and then placed in a FilmArray system. The RT-PCR assay should be performed only by laboratory professionals trained in the use of FilmArray systems. At the end of the reaction, results indicating whether pathogen nucleic acids have been detected in the patient sample are displayed on the system's screen. The panel purportedly requires a small sample volume and minimal hands-on time, and the results are available in about 45 minutes. In May 2020, FDA granted the BioFire RP2.1 Panel Emergency Use Authorization.	Although a test that could tell COVID-19 apart from other respiratory diseases would be useful, BioFire has not been validated and might yield higher-than-average false-positive or false-negative results compared with other available tools.

Title	Description	Archive reason(s) based on data review and/or stakeholder ratings and comments
Cue COVID-19 point-of-care (POC) test to diagnose COVID-19	The Cue COVID-19 test is an isothermal amplification assay developed by Cue Health, Inc (San Diego, California), as a COVID-19 test for use in POC settings. It is intended for use in temporary screening facilities, physician office laboratories, urgent care, and long-term nursing facilities. Cue Health is seeking additional FDA authorization for use of its COVID-19 test in settings such as the workplace, schools, and at home. The Cue COVID-19 test consists of a Cue Sample Wand, a Cue COVID-19 Test Cartridge, a Cue Cartridge Reader, and a Cue Health App. After a nasal sample is taken with the sample wand, the sample is transferred to the test cartridge and placed in the cartridge reader to automatically begin the test. The cartridge reader controls reaction temperatures, timing, and fluid movement within the cartridge. At the end of the reaction, results indicating whether viral nucleic acids have been detected in the patient sample are sent to the Cue Health App loaded on a mobile device. The Cue COVID-19 test purportedly requires a small sample volume and minimal hands-on time to yield laboratory-quality results in about 15 minutes. It is intended to complement central laboratories, where most current testing is performed. In June 2020, FDA granted the Cue COVID-19 test Emergency Use Authorization.	Point-of-care testing with a rapid turnaround time will be valuable in treating COVID-19; however, Cue is only one of a number of available tests. In addition, its accuracy has not been demonstrated.
ID NOW COVID-19 point-of-care (POC) test to diagnose COVID-19	ID NOW COVID-19 (Abbott Diagnostics Scarborough, Inc, Scarborough, Maine) is an isothermal amplification assay. It is intended for use in POC settings, including temporary screening facilities, physician office laboratories, urgent care, and long-term nursing facilities. ID NOW COVID-19 is a cartridge-based test that performs a nicking endonuclease amplification reaction to detect nucleic acids from SARS-CoV-2, the virus that causes COVID-19. After a nasal, nasopharyngeal, or throat swab is treated with a solution that exposes the viral nucleic acids, the sample is transferred to the cartridge and placed in the ID NOW Instrument. The instrument controls reaction temperatures, timing, and fluid movement within the cartridge and reports whether viral nucleic acids were detected in the patient sample. The ID NOW COVID-19 test purportedly requires a small sample volume and minimal hands-on time to yield laboratory-quality results in about 15 minutes. It is intended to complement central laboratories, where most current testing is performed. In March 2020, FDA granted the ID NOW COVID-19 test Emergency Use Authorization (EUA). A published study evaluated the performance of the ID NOW COVID-19 test in 61 samples previously tested with either of 2 EUA tests. ID NOW COVID-19 had a sensitivity of 72%, a specificity of 100%, and an overall percentage agreement of 79%. ECRI has published a position paper that discusses this topic, which cites a warning issued by FDA regarding potential accuracy issues with the ID NOW COVID-19 test.	ID NOW will be one of several other available point-of-care tests, and only robust accuracy data will make it stand out from the rest. ID NOW is unlikely to replace testing in central laboratories (standard of care) and it is not expected to decrease testing demand because it can test only one sample at a time.

Title	Description	Archive reason(s) based on data review and/or stakeholder ratings and comments
Online symptom checkers to identify COVID-19	Many individuals consult online symptom checkers (ie, chatbots) to evaluate a wide range of health conditions, and multiple organizations have developed COVID-19 symptom checkers. For example, online tools offered by the Centers for Disease Control and Prevention (CDC) might advise consulting a physician and considering isolation based on reported symptoms. These tools might provide a low-cost, widely disseminated symptom screening method that could inform patients while reducing the burden of initial symptom screening on health care workers. However, a recent analysis of 10 online symptom checkers concluded that results diverged widely, from some being fairly accurate to others that approximate random guesses. Additionally, as more is learned about COVID-19, online symptom checkers might not be updated to include the latest knowledge, thereby making some chatbots less accurate. Such divergent results potentially endanger patients and others around them.	Online symptom checkers will have low impact on public health and outcomes of patients with COVID-19. The variety of symptoms affecting different age groups and the widely variable accuracy of these online tools greatly limit their potential. In addition, most patients with concerning symptoms will likely contact a health care professional for advice.
Wearable activity monitors to identify COVID-19 cases	The widespread use of wearable fitness or activity monitors has prompted some researchers to assess whether the devices can help identify emerging cases of COVID-19. The TemPredict study at the University of California, San Francisco, will test whether temperature, heart rate, and related metrics collected from an Oura Ring can help researchers create an algorithm to predict the onset of COVID-19 symptoms including fever, cough, and fatigue. Also, the Scripps Research Translational Institute has launched the Digital Engagement & Tracking for Early Control & Treatment (DETECT) study to test whether wearables (eg, Apple Watch, Fitbit) that measure heart rate, which can increase with viral infections, can help scientists spot viral outbreaks earlier. In addition to using data collected by the wearable devices themselves, both studies allow participants to submit additional data, such as patient-logged symptoms, disease diagnosis, and disease treatments.	Although wearable devices might provide public health officials with useful research data, they have limited potential to improve individual patient outcomes or prevent disease spread compared with standard care. In addition, data privacy concerns and prohibitive cost could limit use of this intervention among the most vulnerable populations that might benefit.

Title	Description	Archive reason(s) based on data review and/or stakeholder ratings and comments
Xpert Xpress SARS-CoV-2 point-of-care (POC) test to diagnose COVID-19	Xpert Xpress SARS-CoV-2 is a polymerase chain reaction (PCR) assay developed by Cepheid, Inc (Sunnyvale, California), as a COVID-19 test. SARS-CoV-2 is the virus that causes COVID-19. The test is intended for use in POC settings, including temporary screening facilities, ambulatory care centers, and long-term nursing facilities. The Xpert Xpress system consists of a single-use cartridge that contains the reagents needed to amplify viral nucleic acids. A nasal, nasopharyngeal, oropharyngeal, or throat swab sample is added to the cartridge and placed in a GeneXpert (Dx, Infinity, or Xpress) system. The analyzer system controls reaction temperatures, timing, and fluid movement within the cartridge. At the end of the reaction, it reports whether viral nucleic acids were detected in the patient sample. The Xpert Xpress system purportedly requires a small sample volume and minimal hands-on time to yield laboratory-quality results in about 45 minutes. It is intended to complement central laboratories, where most current testing is performed. In March 2020, FDA granted the Xpert Xpress SARS-CoV-2 test Emergency Use Authorization. A published study evaluated the performance of Xpert Xpress in 483 nasopharyngeal samples previously tested at a central laboratory with a standard-of-care test. Xpert Xpress had a sensitivity of 100%, a specificity of 96%, and an overall percentage agreement of 98%.	The accuracy of Xpert Xpress and other point-of-care tests has not been demonstrated. Therefore, while there is a need for additional testing, false-positive or false-negative results might cause harm from a public health perspective.

Section 4. Systems and Management: 8 Topics

Table 4.1. Currently Monitored Systems and Management Topics: 6 Topics

Title	Description	Possible areas of impact	Possible future impacts
Contact tracing software systems to mitigate epidemic scenarios	Software developers from across the world are collaborating to combat COVID-19 by creating contact tracing tools that can inform governments and public health agencies about the spread of the virus that causes COVID-19, SARS-CoV-2. Apple and Google have launched exposure notification systems using Bluetooth-enabled devices such as smartphones to track physical proximity between people. Users of the system can opt to report a COVID-19 diagnosis, allowing for efficient contact tracing by alerting users whose devices have been in close proximity with their own. Additionally, access to the data will be granted to public health systems, which may allow them to provide advice on next steps to potentially exposed users. Another developer in this space is EnGenius Technologies (Costa Mesa, California), a wireless networking company that has developed a new feature on its cloud platform to identify surrounding user devices using Wi-Fi. The state governments of North Dakota, South Dakota, and Utah are already using mobile applications for contact tracing, namely Care19 and Healthy Together, that rely on a combination of Bluetooth and GPS data to track person-to-person transmissions, as well as transmission zones, in their states.	Patient outcomes Population health Health care delivery and process Health care disparities	Might help governments and health agencies develop policies to reduce the spread of COVID-19 Might increase privacy concerns, especially for COVID-19-positive users Might lead to poor population health outcomes due to targeted advertising and mistaken self-diagnoses

Title	Description	Possible areas of impact	Possible future impacts
Drive-through prenatal care model	The COVID-19 pandemic has shifted a substantial amount of health care to the telehealth setting. However, some assessments that are part of routine prenatal care still require direct interaction between patients and health care providers. To provide access to prenatal care while limiting COVID-19 exposure risk for obstetric providers and patients, investigators at Baylor College of Medicine (Houston, Texas) developed a drive-through prenatal care model in which pregnant women would remain in their cars while being assessed by health care providers. Services such as blood pressure measurement, fetal heart rate assessment, and select ultrasound assessments are provided during drive-through appointments. Additionally, the developers purport that the availability of these professional interactions might reduce patient anxiety related to having fewer prenatal clinic visits and could ease pandemic-related fears related to potential exposure within the clinic. The program uses equipment and disposables common to obstetric clinics in the United States. The investigators estimate that a drive-through prenatal care model might reduce the number of in-person clinic visits by 33% per patient compared with standard prenatal care modalities.	Patient outcomes Population health Clinician and/or caregiver safety Health care delivery and process Health care disparities Health care costs	Might reduce potential exposure to COVID-19 infection for both the patient and health care staff Might reduce patient anxiety by continuing planned prenatal visits that cannot be completed using telehealth visits Might yield cost savings for the patient due to reduced health care utilization Might offer convenient, timely prenatal care for patients who have inadequate internet access or limited computer literacy for telehealth visits Might lead to long wait times if the drive-through test center is overwhelmed
Immunity certification to set public health directives for individuals previously infected with SARS-CoV-2, the virus that causes COVID-19	Some countries are considering setting reduced restrictions (eg, social distancing directives, travel restrictions) on individuals who have recovered from SARS-CoV-2 infection. The reductions are based on the assumption that these individuals are likely immune to subsequent infection. So-called immunity passports or risk-free certificates might facilitate opening up the economies of these countries. A brief by the World Health Organization highlights results from studies showing that people with SARS-CoV-2 infection typically develop an antibody response that should prevent previously infected individuals from getting severe COVID-19 disease. However, the brief also notes that "no study has evaluated whether the presence of antibodies to SARS-CoV-2 confers immunity to subsequent infection by this virus in humans." Nonetheless, interest exists in using serological tests to determine eligibility for immunity certification and, as of June 19, 2020, FDA had granted Emergency Use Authorization to 21 serum COVID-19 antibody tests that could be used in this manner. While an immunity certificate could allow loosening of restrictions on some individuals, a recent article in *JAMA* sheds light on how such a program could increase health disparities in the population along with adding possible ethical and legal concerns related to inaccurate antibody tests. ECRI has also published a position paper that discusses this topic.	Patient outcomes Population health Clinician and/or caregiver safety Health care delivery and process Health care disparities	Might streamline public health policy and reopening procedures Might misinform policymakers by relying solely on antibody tests Might increase burden on laboratories due to repeated testing needed for the population to ensure ongoing immunity Might increase socioeconomic disparities by permitting only people with an immunity advantage to return to work

Title	Description	Possible areas of impact	Possible future impacts
Machine learning to predict the spread of COVID-19	COVID-19 has had significant social, political, economic, and public health impacts globally. The Centers for Disease Control and Prevention (CDC) has partnered with several universities to forecast national and state-level changes in infection rates and deaths due to COVID-19. Typically, projections for the spread of infectious diseases are performed by curve-fitting, using reported cases. Machine learning models are now being used to predict the spread of this rapidly evolving disease. One such prediction model that feeds into the CDC's online forecast is the UCLA-SuEIR, developed at the University of California, Los Angeles, by the UCLA Statistical Machine Learning Laboratory. This machine learning model purportedly infers the spread of infection while accounting for the underlying epidemic dynamics, making it a more comprehensive prediction model.	Patient outcomes Population health Clinician and/or caregiver safety Health care delivery and process Health care disparities Health care costs	Might improve population health outcomes by predicting changes in national and state-level spread of SARS-CoV-2, the virus that causes COVID-19 Might inform public health agencies to establish appropriate reopening procedures Might reduce overall health care costs by predicting possible resurgence in cases earlier than other models, thereby helping with emergency preparedness
Rapid expansion of telemedicine driven by widespread COVID-19 response	Response to the COVID-19 pandemic (ie, stay-at-home orders, strict social distancing guidelines) has prompted health care providers across all clinical specialties to rapidly adopt methods of care for non-COVID-19 patients. Whether for patients with acute or chronic conditions, the new methods are meant to maintain the safety of patients and clinical staff. Telemedicine technologies offer providers and patients multiple ways to connect with virtual visits that attempt to compensate for the lack of in-person physician-patient contact and to help maintain care plans. The pandemic has prompted regulators and insurers to loosen regulations and reimbursement restrictions that traditionally limited telemedicine to rural areas with limited access to providers. Thus, adoption has increased broadly. The wide spectrum of telemedicine vendors suggests that providers can select a platform that best suits the needs of their practices. However, the need to rapidly adopt telemedicine systems can present obstacles to a smooth transition in patient care for providers who lack telemedicine experience. Some experienced centers have offered guidance for quickly implementing a telemedicine system into clinical practice. Other experts have noted that the broad expansion of health care information technology (IT) use prompted by COVID-19 provides an opportunity to improve public health surveillance during infectious disease outbreaks that would be optimized by an as yet unrealized robust national health IT infrastructure.	Patient outcomes Clinician and/or caregiver safety Health care delivery and process Health care disparities	Might facilitate remote or home monitoring of suspected COVID-19 cases without increasing burden on health care facilities Might reduce disruptions in care continuity for individual patients with acute or chronic conditions unrelated to COVID-19 Might present technical and operational challenges to provider practices without telemedicine experience Might lead to long-term changes in how care is delivered after the pandemic subsides, depending on patient and provider experiences

Title	Description	Possible areas of impact	Possible future impacts
Statewide surge line for patient load management	The Arizona Department of Health Services (ADHS) has launched a statewide patient load–balancing system to help with transferring patients between facilities during the COVID-19 public health emergency. The Arizona Surge Line is a 24/7 toll-free call line for health care providers, wherein a surge line transfer agent reviews critical care availability for each hospital in the state and transfers the call to the appropriate destination. This helps with between-facility transfer of patients with presumed or confirmed COVID-19 or transfer of patients to postacute care facilities. The surge line might also provide clinical consultation if a transfer is declined or delayed. This surge line might trigger other states to create similar statewide hubs with real-time visibility into bed capacity and availability of ventilators across all facilities and health care systems.	Patient outcomes Population health Clinician and/or caregiver safety Health care delivery and process Health care disparities Health care costs	Might optimize between-facility transfer of patients during the COVID-19 outbreak or similar emergency situations Might assist health care staff with effective time management by reducing their call time to find the right level of care for their patients Might improve patient survival outcomes by enabling appropriate care in a timely manner; however might worsen survival outcomes if patients are too critical for transfer Might enhance government policies and public health emergency guidance Might increase economic burden on tertiary care centers if uninsured or underinsured patients are disproportionately transferred

Table 4.2. Recently Archived Systems and Management Topics: 2 Topics

Title	Description	Archive reason(s) based on data review and/or stakeholder ratings and comments
Disinfecting spray (Clyraguard) to prevent personal protective equipment (PPE) contamination	Frontline workers are at elevated infection risk due to their frequent exposure to infected individuals. With the surge in COVID-19 cases and shortage of PPE products (eg, respirators, surgical masks) across the country, health care professionals are at an even higher risk than before. Disinfectant sprays with antiviral and antimicrobial properties might help prevent contamination of PPE, but could pose health risks due to inhalation of these chemicals. A recent study at Galveston National Laboratory at the University of Texas Medical Branch showed that a proprietary copper iodine product, Clyraguard, purportedly inactivated (99.999% kill rate) the SARS-CoV-2 virus, the cause of COVID-19 disease. This product is a spray that can be applied directly on PPE worn by frontline health care workers to prevent contamination. Clyraguard is currently registered with FDA as a Class I general purpose disinfectant.	Although disinfectant sprays such as Clyraguard might allow some reuse of PPE and so might reduce costs for health care facilities, they carry significant safety risks that will likely limit their use.

Title	Description	Archive reason(s) based on data review and/or stakeholder ratings and comments
Expanded availability of digital health therapeutic devices for psychiatric conditions during COVID-19 public health emergency	FDA issued guidance in April 2020 to increase the availability of certain unapproved digital health devices and products for treating psychiatric disorders to consumers during the COVID-19 public health emergency. The scope of the guidance included computerized behavioral therapy devices and other digital health therapeutic devices and low-risk general wellness and digital health products for mental health or psychiatric conditions. The guidance is intended to facilitate social distancing by reducing patient contact with health care providers and to ease the burden on health care professionals and facilities experiencing increased demand due to COVID-19. Products released in response to the guidance include Endeavor, a smart device application that intends to treat attention-deficit/hyperactivity disorder (ADHD) through interactive, task-oriented game play; and Pear-004, a smart device application that intends to alleviate symptoms of schizophrenia through social skills training, cognitive behavioral therapy for psychosis, and illness self-management training. FDA's policy is intended to remain in effect only for the duration of the COVID-19 public health emergency.	These devices will not likely have a large impact on standard care during the COVID-19 public health emergency. They will not replace care by a clinician, there are barriers to access (eg, data privacy), and they provide no clear impact on COVID-19 outcomes.

Section 5. Treatments: 24 Topics

Table 5.1. Currently Monitored Treatment Topics: 17 Topics

Title	Description	Possible areas of impact	Possible future impacts
Anakinra (Kineret) to treat COVID-19 with acute respiratory distress syndrome and hyperinflammation	Anakinra (Kineret) is an interleukin-1 receptor antagonist FDA has approved to treat rheumatoid arthritis and cryopyrin-associated periodic syndromes. It also is under study as a treatment for patients with COVID-19. Some patients with COVID-19 develop a maladaptive inflammatory response that can lead to acute lung injury and respiratory insufficiency; investigators are studying existing anti-inflammatory drugs as COVID-19 treatments. Anakinra acts as a competitive antagonist of the cytokine receptor IL-1R1, which acts as a driver of proinflammatory signaling. A small, retrospective study of patients with moderate to severe COVID-19-related acute respiratory distress syndrome (ARDS) reported 21-day survival of 90% for patients (n = 29) who received high-dose anakinra (5 mg/kg, twice daily) plus standard of care (SoC) compared with survival of 56% in a cohort of patients (n = 16) who received SoC alone. A second study of patients with severe COVID-19-related bilateral pneumonia reported that 25% of patients (n = 52) who received anakinra (200 mg/day on days 1-3, 100 mg/day on days 4-10) required mechanical ventilation or died, compared with 73% of patients (n = 44) in a historical control group. Additionally, multiple studies involving anakinra treatment for patients with COVID-19 are registered at the National Library of Medicine trial registry, including a large multicenter randomized trial in France (ANACONDA, NCT04364009) with a primary completion date in September 2020.	Patient outcomes	Might improve health outcomes by reducing mechanical ventilation time and increasing survival in patients with ARDS Might improve overall health and quality of life by reducing related health complications and risk for long-term sequelae Might improve population health outcomes if mechanical ventilator shortages are minimized Might reduce health care costs if length of hospitalization is reduced and fewer intensive-care resources are needed

Title	Description	Possible areas of impact	Possible future impacts
Anti-GM-CSF monoclonal antibodies to treat COVID-19	Some patients with COVID-19 experience an inflammatory condition leading to pulmonary dysfunction and cardiovascular events thought to contribute to COVID-19-related death. Patients with COVID-19 exhibit elevated levels of various proinflammatory cytokines, including granulocyte-macrophage colony-stimulating factor (GM-CSF). Therefore, investigators are studying several investigational anti-GM-CSF monoclonal antibodies as potential treatments for COVID-19, including gimsilumab, lenzilumab, mavrilimumab, namilumab, and TJM2 (TJ003234). Limited clinical data are available for use of these antibodies in treating COVID-19. Kiniksa, the developer of mavrilimumab, reported data from a nonrandomized, pilot trial of 13 non–mechanically ventilated patients with COVID-19 pneumonia treated at a single center in Italy. Compared with results from a 26-patient matched control group, patients who received mavrilimumab exhibited increased rates of clinical improvement (85% vs 42%; $p = .017$), reduced incidence of death (0% vs 27%; $p = .046$), and reduced rates of mechanical ventilation (8% vs 35%; $p = .077$). Additionally, data are available on the initial clinical use of lenzilumab. However, further study in larger, randomized trials is needed. Multiple anti-GM-CSF monoclonal antibody trials are registered at the National Library of Medicine trial registry, including placebo-controlled randomized controlled trials of gimsilumab (NCT04351243), lenzilumab (NCT04351152), mavrilimumab (NCT04399980, NCT04397497), and TJM2 (NCT04341116).	Patient outcomes Population health Health care costs	Might improve health outcomes by reducing mechanical ventilation time and increasing survival in patients with acute respiratory distress Might improve overall health and quality of life by reducing related health complications and risk for long-term sequelae Might improve population health outcomes if mechanical ventilator shortages are minimized Might reduce health care costs if length of hospitalization is reduced and fewer intensive resources are needed

Title	Description	Possible areas of impact	Possible future impacts
Anti-interleukin-6 (IL-6) monoclonal antibodies to treat hospitalized patients in respiratory distress	Some patients with COVID-19 experience an inflammatory condition leading to pulmonary dysfunction and cardiovascular events thought to contribute to COVID-19-related death. Investigators are studying whether anti-IL-6 monoclonal antibodies can treat COVID-19 by inhibiting the IL-1/IL-6 pathway thought to be a key driver of this inflammation. Multiple trials of commercially available (eg, sarilumab, siltuximab, tocilizumab) and investigational (eg, clazakizumab, levilimab, sirukumab) IL-6 antibodies are ongoing. These include company-sponsored randomized controlled trials of sarilumab (NCT04315298) and tocilizumab (COVACTA). In the phase 2 portion of the company-sponsored sarilumab trial, hospitalized patients who required oxygen supplementation but not ventilation (ie, severe; n = 126) or patients who required ventilation (ie, critical; n = 358) received a subcutaneous injection of sarilumab (at one of 2 doses) or placebo. Among critical patients, 28% in the high-dose group, 46% in the low-dose group, and 55% in the placebo group reportedly died or required ventilation. Conversely, most clinical outcomes among patients in the severe cohort reportedly exhibited negative trends. The phase 3 portion of the trial is restricting enrollment to critical patients using high-dose sarilumab. A randomized trial of tocilizumab in 129 hospitalized patients with COVID-19 and moderate to severe pneumonia treated with standard of care (SoC) plus IV tocilizumab or SoC alone revealed that significantly fewer patients treated with tocilizumab died or required ventilation. At the doses used in clinical trials, tocilizumab and sarilumab would cost about $4800 and $3600, respectively, per patient.	Patient outcomes	Might improve health outcomes by reducing mechanical ventilation time and increasing survival in patients with acute respiratory distress syndrome Might improve overall health and quality of life by reducing related health complications and risk for long-term sequelae Might improve population health outcomes if mechanical ventilator shortages are minimized Might reduce health care costs if length of hospitalization is reduced and fewer intensive-care resources are needed

Title	Description	Possible areas of impact	Possible future impacts
Canakinumab (Ilaris) to treat COVID-19	Some patients with COVID-19 experience an inflammatory condition leading to pulmonary dysfunction and cardiovascular events thought to contribute to COVID-19-related death. An interleukin (IL) pathway called IL-1/IL-6 is thought to be a key driver of this inflammation, and patients with COVID-19 have exhibited elevated levels of various proinflammatory cytokines, including IL-1ß. Therefore, investigators are studying whether the anti-IL-1ß monoclonal antibody canakinumab (Ilaris), intended to block IL-1 signaling, can treat COVID-19. Canakinumab is commercially available, having been FDA approved to treat periodic fever syndromes and systemic juvenile idiopathic arthritis. Data from a small retrospective study of 10 canakinumab-treated patients indicated that the drug led to reductions in inflammatory markers and improvement in oxygenation. Multiple canakinumab trials are registered at the National Library of Medicine trial registry, including 2 randomized control trials. Novartis is sponsoring a randomized, placebo-controlled trial of a single intravenous infusion of canakinumab in 450 patients hospitalized for COVID-19 pneumonia who are not currently on mechanical ventilation (NCT04362813). The trial is scheduled for primary completion in July 2020. The Cleveland Clinic is sponsoring a randomized, placebo-controlled trial of a single intravenous infusion of canakinumab in 45 patients hospitalized for COVID-19 with evidence of acute myocardial injury (NCT04365153). The trial is scheduled for primary completion in December 2020.	Patient outcomes Population health Health care costs	Might improve health outcomes by reducing mechanical ventilation time and increasing survival in patients with acute respiratory distress Might improve overall health and quality of life by reducing related health complications and risk for long-term sequelae Might improve population health outcomes if mechanical ventilator shortages are minimized Might reduce health care costs if length of hospitalization is reduced and fewer intensive-care resources are needed; however, costs might increase if these expensive drugs are used inappropriately. Therefore, a need exists for clear physician and pharmacy oversight of use in only the appropriate patient populations.

Title	Description	Possible areas of impact	Possible future impacts
Convalescent plasma (CP) to treat COVID-19	CP obtained from patients who have recovered from SARS-CoV-2 infection (which causes COVID-19) is under study to treat the disease. CP transfusion has been used to treat viral infections including severe acute respiratory infections caused by the coronaviruses MERS and SARS-CoV-1. Plasma is the cell-free liquid component of blood, which contains high levels of blood proteins that may have both antiviral and immunomodulatory effects. In particular, neutralizing antibodies against SARS-CoV-2 present in CP might confer passive immunity against the virus. CP is separated from the blood obtained from patients who recovered from COVID-19. Each donation might provide sufficient plasma to treat up to 4 patients of matching blood type. Many COVID-19 CP studies are registered at the National Library of Medicine trial registry, including several actively recruiting, phase 3, multicenter, randomized controlled trials (NCT04348656, NCT04342182, NCT04385043) and a number of US-based randomized controlled trials. Additionally, FDA has opened an expanded access protocol to facilitate access to CP. A randomized controlled trial of convalescent plasma in 103 patients with severe or life-threatening COVID-19 failed to demonstrate a statistically significant improvement in the number of patients who exhibited clinical improvement within 28 days (51.9% in CP treated vs 43.1% in control group, hazard ratio [HR] 1.40; $p = .26$). Authors note that the study was terminated early because too few eligible patients were available and, therefore, the study was statistically underpowered.	Patient outcomes Population health Health care costs	Might improve health outcomes by reducing mechanical ventilation time and increasing survival in patients with acute respiratory distress Might improve overall health and quality of life by reducing related health complications and risk for long-term sequelae Might improve population health outcomes if mechanical ventilator shortages are minimized Might reduce health care costs if length of hospitalization is reduced and fewer intensive-care resources are needed

Title	Description	Possible areas of impact	Possible future impacts
Dexamethasone to treat severe COVID-19	Dexamethasone is a corticosteroid being investigated as an intravenous or oral treatment for severe COVID-19. Hyperinflammation is thought to underlie acute respiratory distress syndrome (ARDS) in COVID-19 and the need for mechanical ventilation. Therefore, use of corticosteroids to reduce inflammation might be beneficial. However, concerns have been raised regarding the use of corticosteroids to treat COVID-19, because the risks of immunosuppression and increased replication of SARS-CoV-2 (the virus that causes COVID-19) could potentially outweigh benefits. Data reported in a news release from a randomized, phase 3 clinical trial (NCT04381936) in the United Kingdom showed that hospitalized participants who had COVID-19 and were treated with dexamethasone (n = 2104) compared with participants who received standard of care (n = 4321) had a one-third decrease in deaths in the subset of participants who were ventilated, a one-fifth decrease in deaths in the subset that received oxygen only, and no benefit in the subset that did not require respiratory support. A phase 2 trial (NCT04360876) in the United States investigating dexamethasone versus placebo to treat moderate to severe ARDS is ongoing, with a primary completion date in September 2020. Based on available clinical trial dosing and pricing information, we estimate a course of COVID-19 treatment with dexamethasone to cost between $9 and $135.	Patient outcomes Population health Health care costs	Might improve patient health outcomes and increase survival Might improve population health outcomes by reducing the burden on the health care system and reducing the risk of mechanical ventilator shortages Might decrease health care costs associated with hospitalization and intensive-care resources, especially because dexamethasone is a widely available, inexpensive drug Might improve understanding of hyperinflammation in COVID-19 disease and the role of anti-inflammatory drugs for treatment
Dociparstat to treat COVID-19	Dociparstat (DSTAT) is a glycosaminoglycan derivative of heparin being investigated by Chimerix (Durham, North Carolina) as an intravenous treatment for COVID-19 in hospitalized adult patients. Hypercoagulability in patients who have COVID-19 is commonly observed and associated with worse outcomes. It might occur in part due to damage to endothelial cells from infection with SARS-CoV-2, the virus that causes COVID-19. Treatment with anticoagulants such as heparin has been linked to increased survival in patients with severe COVID-19. Dociparstat, a derivative of heparin, purportedly reduces excessive inflammation, immune cell infiltration, and hypercoagulability associated with poor outcomes in severe COVID-19. It can be given at larger doses without the same risk for bleeding as heparin. Dociparstat is in a developer-sponsored phase 2/3 clinical trial (NCT04389840) that intends to enroll more than 500 hospitalized adults who have COVID-19 and acute lung injury requiring supplemental oxygen or noninvasive ventilation. The trial has a primary completion date in February 2021.	Patient outcomes Population health Health care costs	Might improve patient health outcomes and increase survival Might improve population health outcomes by reducing the burden on the health care system and reducing mechanical ventilator shortages Might decrease health care costs associated with hospitalization and intensive-care resources Might improve understanding of anticoagulation and anti-inflammatory drugs in treating COVID-19

Title	Description	Possible areas of impact	Possible future impacts
EIDD-2801 to treat COVID-19	EIDD-2801 (Ridgeback Biotherapeutics, Miami, Florida; and Merck, Kenilworth, New Jersey) is an antiviral drug being investigated to treat COVID-19. It is an orally bioavailable prodrug of EIDD-1931, a ribonucleoside analogue developed to treat respiratory viruses. EIDD-2801 has demonstrated broad-spectrum antiviral activity in animal models against SARS-CoV-2 (the virus that causes COVID-19), SARS-CoV (the virus that causes severe acute respiratory syndrome), and MERS-CoV (the virus that causes Middle East respiratory syndrome). Like remdesivir, another antiviral in development to treat COVID-19, EIDD-2801 targets viral RNA polymerase to block successful viral RNA replication. Preclinical studies suggest that EIDD-2801 might have activity against viral RNA polymerase harboring remdesivir resistance mutations. EIDD-2801 is taken by mouth, which might be more convenient than the intravenous route of remdesivir. Ongoing clinical trials of EIDD-2801 to treat COVID-19 include developer-sponsored phase 2 studies NCT04405570 in the outpatient setting and NCT04405739 in the inpatient setting, both with primary completion dates in August 2020.	Patient outcomes Population health Health care delivery and process Health care costs	Might improve patient health outcomes and increase survival Might improve population health outcomes if burden on the health care system is reduced Might decrease health care costs associated with hospitalization and intensive-care resources Might offer more convenient dosing compared with intravenous antivirals, which might help shift the treatment of COVID-19 to the home setting sooner
Leronlimab to treat COVID-19	Some patients with COVID-19 experience an inflammatory condition leading to pulmonary dysfunction and cardiovascular events thought to contribute to COVID-19-related death. The CCL5 (RANTES)-CCR5 signaling axis might contribute to this hyperinflammatory response by promoting the chemotaxis (homing and accumulation) of immune cells, thereby amplifying inflammatory responses. Leronlimab is an investigational monoclonal antibody that purportedly acts as a CCR5 antagonist, inhibiting CCR5-mediated trafficking of proinflammatory immune cells. A study of patients (n = 10) treated with compassionate-care leronlimab found reductions in proinflammatory cytokines (eg, interleukin-6) and decreased coronavirus in the blood. Randomized placebo-controlled trials of subcutaneous leronlimab are ongoing in patients with mild to moderate COVID-19 (phase 2, NCT04343651) and patients with severe or critical COVID-19 (phase 2/3, NCT04347239). The developer (CytoDyn, Inc, Vancouver, Washington) also intends to submit a protocol to FDA for a trial that will combine leronlimab with the antiviral drug remdesivir. Although leronlimab is not commercially available, it is also being developed as a potential treatment for patients with HIV, and a New Drug Application for that indication was submitted to FDA in April 2020.	Patient outcomes Population health Health care costs	Might improve health outcomes by reducing mechanical ventilation time and increasing survival in patients with acute respiratory distress Might improve overall health and quality of life by reducing related health complications and risk for long-term sequelae Might improve population health outcomes if mechanical ventilator shortages are minimized Might reduce health care costs if length of hospitalization is reduced and fewer intensive-care resources are needed

Title	Description	Possible areas of impact	Possible future impacts
Losartan to treat COVID-19	Losartan, an angiotensin II receptor blocker (ARB), is an FDA-approved blood pressure medication being investigated to prevent lung injury and disease progression in patients who have COVID-19 with or without underlying high blood pressure. By binding to angiotensin-converting enzyme 2 (ACE2) receptors for cellular entry, the SARS-CoV-2 virus that causes COVID-19 is thought to downregulate the expression of ACE2 and cause an excess of the peptide angiotensin II, which might contribute to various renal, cardiovascular, and immune symptoms in COVID-19. Losartan blocks the action of angiotensin II at the angiotensin II type 1 (AT1) receptor. It has been shown preclinically to reduce lung inflammation in SARS-CoV infection (which causes severe acute respiratory syndrome) and improve survival in avian influenza H5N1 infection. A retrospective, multicenter study of hospitalized patients with hypertension and COVID-19 in China, published April 17, 2020, found a lower risk of all-cause death in angiotensin-converting enzyme inhibitor (ACEI) or ARB users compared with patients who do not use an ACEI or ARB. Ongoing US clinical trials of losartan to treat COVID-19 include the phase 4 NCT04340557, phase 2/3 NCT04328012, phase 2/3 NCT04349410, phase 2 NCT04311177, and phase 2 NCT04312009 trials. An unphased trial, NCT04338009, is investigating differences between continuing or discontinuing ACEIs or ARBs in hospitalized patients already taking them and who have COVID-19.	Patient outcomes Health care disparities Health care costs	Might improve patient health outcomes by reducing illness severity and increasing survival Might improve population health outcomes if burden on the health care system is reduced Might reduce health care costs if hospitalization can be avoided, hospitalization length is reduced, or fewer intensive-care resources are needed Might improve understanding of the role of the renin-angiotensin system (RAS) in COVID-19 disease pathology and ACEIs or ARBs as potential treatments Might complicate care delivery and adherence for patients with hypertension
Lowering testosterone levels to treat COVID-19 infection	Researchers at Columbia University Irving Medical Center report that lowering testosterone may reduce the severity or duration of COVID-19. This research shows that the SARS-CoV-2 virus, which causes COVID-19, can be prevented from entering human lung cells by interfering with lung cell expression of transmembrane serine protease 2 (TMPRSS2), which is required for viral entry. Further, the research shows that androgenic and estrogenic compounds function as modulators of TMPRSS2 expression. Consequently, the US Department of Veterans Affairs has launched a clinical trial to evaluate the use of a prostate cancer drug, degarelix (sold as Firmagon), to treat hospitalized male patients with COVID-19 who are not in intensive care. This drug might increase the production of TMPRSS2 in females and, therefore, is unsuitable for this patient population.	Patient outcomes Population health Health care delivery and process Health care costs	Might improve survival and other patient health outcomes by reducing the severity of the illness Might reduce health care costs if length of hospitalization is reduced and fewer intensive resources are needed Might raise quality-of-life concerns due to adverse effects of hormone therapy Might increase treatment costs, depending on patients' insurance coverage

Title	Description	Possible areas of impact	Possible future impacts
Monoclonal antibodies targeting SARS-CoV-2 Spike protein receptor binding domain to treat COVID-19	The entry into cells of SARS-CoV-2, the virus that causes COVID-19, depends on an interaction between the viral-surface protein Spike (S) and the cell-surface protein angiotensin-converting enzyme 2 (ACE2). Therefore, monoclonal antibodies targeting the S protein receptor binding domain (RBD) that have the potential to interfere with this interaction are being developed as treatments for COVID-19. These virus neutralizing antibodies have the potential to provide short-term, passive immunity to SARS-CoV-2, potentially reducing viral load and improving patient outcomes. Compared with other sources of SARS-CoV-2 neutralizing antibodies requiring donations from recovered patients (eg, convalescent plasma, hyperimmune intravenous immunoglobulin [IVIG]), monoclonal neutralizing antibodies would represent a more scalable and consistent product. However, monoclonal neutralizing antibodies would target a smaller repertoire of SARS-CoV-2 epitopes than these polyclonal alternatives. Neutralizing antibodies in development include single monoclonal antibodies and cocktails containing 2 or more monoclonal antibodies that bind nonoverlapping RBD epitopes. As of June 17, 2020, clinical trials of 3 neutralizing antibody products have been initiated: LY-CoV555 developed by Lilly/AbCellera (NCT04427501, NCT04411628); JS016 developed by Lilly/Junshi Biosciences (no registered trials); and REGN-COV2 developed by Regeneron (NCT04425629 and NCT04426695).	Patient outcomes Population health Health care costs	Might improve health outcomes by reducing mechanical ventilation time and increasing survival in patients with acute respiratory distress syndrome Might improve overall health and quality of life by reducing related health complications and risk for long-term sequelae Might improve population health outcomes if mechanical ventilator shortages are minimized Might reduce health care costs if length of hospitalization is reduced and fewer intensive-care resources are needed; however, costs might increase if these expensive drugs are used inappropriately. Therefore, a need exists for clear physician and pharmacy oversight of use in only the appropriate patient populations.
Proteomics to identify human protein targets to treat COVID-19	Researchers at the University of California, San Francisco, have developed a protein interaction map for SARS-CoV-2, the virus that causes COVID-19. The map might facilitate repurposing of drugs approved or in development for other indications to treat COVID-19. The team identified 66 druggable human proteins or host factors targeted by 69 compounds, made up of 29 FDA-approved drugs, 12 drugs in clinical trials, and 28 preclinical compounds. Researchers identified 2 drug classes with antiviral activity: mRNA (messenger RNA) translation inhibitors and predicted regulators of the Sigma1 and Sigma2 receptors. Researchers suggest these agents could result in new therapeutic approaches to treat COVID-19.	Patient outcomes	Might speed development of new COVID-19 therapeutics from approved drugs Might uncover potential treatment targets for new therapeutic agents

Title	Description	Possible areas of impact	Possible future impacts
Remdesivir to treat severe COVID-19	Remdesivir is an intravenously administered antiviral adenosine analogue prodrug that purportedly inhibits the replication of multiple RNA viruses and has demonstrated in vitro activity against SARS-CoV-2, the virus that causes COVID-19. FDA issued Emergency Use Authorization on May 1, 2020, for the use of remdesivir to treat severe COVID-19 based on data from 2 global clinical trials. Data published May 22, 2020, from the phase 3 trial NCT04280705 (n = 1063) found that a 10-day course of remdesivir improved recovery time to 11 days compared with 15 days in the placebo group and improved mortality estimates at 14 days from 7.1% with remdesivir compared with 11.9% with placebo. Data published May 27, 2020, from the developer-sponsored phase 3 trial NCT04292899 (n = 6000) suggested similar outcomes between 5-day and 10-day dosing. Recently completed (June 2020), manufacturer-sponsored clinical trials investigating remdesivir include the phase 3 NCT04292899 (n = 6000) and phase 3 NCT04292730 (n = 1600) trials. Topline data released June 1, 2020, from the latter trial demonstrated that patients in the 5-day remdesivir treatment group were 65% more likely to have clinical improvement at day 11 than patients in the control group. Institute for Clinical and Economic Review (ICER) released pricing models of cost-effectiveness of remdesivir on May 1, 2020.	Patient outcomes Health care delivery and process Health care costs	Might improve patient health outcomes by reducing COVID-19 disease course length and severity and improving survival Might improve population health if the burden on the health care system is reduced Might reduce health care costs related to hospitalization and intensive-care resources Might improve understanding of antiviral treatments for COVID-19
RLF-100 (Aviptadil) to treat COVID-19-induced nonacute lung injury and acute respiratory distress syndrome (ARDS)	RLF-100 (Aviptadil) is a synthetic human vasoactive intestinal polypeptide (VIP) being investigated to treat both nonacute lung injury and ARDS in patients who have COVID-19. The virus that causes COVID-19, SARS-CoV-2, is thought to invade and damage type 2 cells in the air sacs of the lungs, releasing inflammatory cytokines and causing impaired production of surfactant, a lipoprotein important for oxygen exchange. This injury to the lungs can progress to ARDS, difficulty breathing due to fluid accumulation in the lungs, which can result in respiratory failure and the need for mechanical ventilation. RLF-100 might bind to type 2 cells to inhibit cytokine-mediated inflammation and upregulate surfactant production to reduce inflammation in the lungs and promote oxygen exchange. It might reduce the risk of life-threatening ARDS in patients who have nonacute lung injury and decrease mechanical ventilation and increase survival in patients who develop ARDS. In a phase 2/3 trial (NCT04360096), hospitalized adult patients with nonacute lung injury receive RLF-100 by inhalation. In a phase 2 trial (NCT04311697), hospitalized adult patients who have COVID-19-induced ARDS and medical necessity for mechanical ventilation receive RLF-100 intravenously. Both trials have primary completion dates in August 2020.	Patient outcomes Population health Health care costs	Might improve patient health outcomes by reducing risk of progression to ARDS in patients who have nonacute lung injury and reducing mechanical ventilation time and increasing survival in patients who have ARDS Might improve overall health and quality of life by reducing health complications and risk for long-term sequelae Might improve population health outcomes if mechanical ventilator shortages are minimized and burden on the health care system is decreased Might reduce health care costs if length of hospitalization is reduced and fewer intensive-care resources are needed

Title	Description	Possible areas of impact	Possible future impacts
TD-0903 to treat acute lung injury in COVID-19	TD-0903 (Theravance Biopharma, Dublin, Ireland) is an investigational inhaled Janus kinase (JAK) inhibitor intended to prevent, in patients with COVID-19, the progression of acute lung injury to life-threatening acute respiratory distress syndrome (ARDS). ARDS in COVID-19 is thought to be caused, in part, by a rapid influx of inflammatory proteins called cytokines into the lungs (ie, cytokine storm). This causes severe inflammation and leads to fluid accumulation and impaired oxygen exchange that often results in the need for mechanical ventilation. Intervening early to block cytokine storm in COVID-19 pneumonia might be critical for survival. TD-0903 purportedly broadly inhibits the activity of JAKs that play a central role in cytokine signaling. It is taken in a nebulized form to target hyperinflammation in the lungs specifically and limit suppression of the immune system systemically. A developer-sponsored phase 2 study (NCT04402866) has begun in the United Kingdom and is planned to expand to include US clinical sites. The trial has a primary completion date in October 2020.	Patient outcomes Population health Health care costs	Might improve patient health outcomes and increase survival Might improve population health outcomes if it reduces the burden on the health care system and reduces the risk of mechanical ventilator shortages Might decrease health care costs associated with hospitalization and intensive resources Might improve understanding of JAK inhibitors and/or inhibiting cytokine storm in acute respiratory illnesses such as COVID-19
Tranexamic acid to treat COVID-19	Tranexamic acid is a commercially available antifibrinolytic protease inhibitor that is being investigated to treat adults with COVID-19. Tranexamic acid, a synthetic analogue of the amino acid lysine, inhibits the conversion of plasminogen to the protease plasmin and also inhibits the activity of plasmin itself. Elevated plasmin is a risk factor for COVID-19 susceptibility. Elevated plasmin may induce a hyperfibrinolytic state, which may contribute to COVID-19 organ damage caused by misregulation of coagulation. Additionally, plasmin could cleave the viral Spike (S) protein (a step required for viral entry) and, therefore, elevated plasmin might increase the infectivity and virulence of SARS-CoV-2, the virus that causes COVID-19. Tranexamic acid is in 2 phase 2 trials at one research institute to assess its efficacy for treating adults who have COVID-19 (NCT04338074 in the outpatient setting, NCT04338126 in the non–intensive care inpatient setting). Additionally, a novel formulation of tranexamic acid, LB1148, is being evaluated in a phase 2 trial (NCT04390217) as a potential therapy for hospitalized patients who have COVID-19 and acute respiratory distress syndrome (ARDS) and multiorgan dysfunction syndrome (MODS). The cost of generic tranexamic acid is as low as $26 for a 30-day supply (650-mg tablets), and the drug is covered by Medicare.	Patient outcomes Health care delivery and process Health care costs	Might improve patient health outcomes and survival Might improve population health outcomes by reducing burden on the health care system Might decrease health care costs if hospitalizations are reduced, hospitalization lengths are shortened, and/or fewer intensive-care resources are needed per patient Might improve understanding of antifibrinolytics used to treat COVID-19

Table 5.2. Recently Archived Treatment Topics: 7 Topics

Title	Description	Archive reason(s) based on data review and/or stakeholder ratings and comments
Anti-C5 monoclonal antibodies to treat COVID-19	Some patients with COVID-19 experience an inflammatory condition leading to pulmonary dysfunction and cardiovascular events thought to contribute to COVID-19-related death. The complement system is a component of the innate immune response whose activation might contribute to this maladaptive immune response. Therefore, investigators are studying whether inhibition of the complement system protein C5 by anti-C5 monoclonal antibodies can moderate the immune response and improve outcomes in patients with COVID-19. Clinical data on the safety and efficacy of C5 inhibitors in treating COVID-19 are limited. In April 2020, a Chinese group posted a preprint article to *MedRxiv* that reported improved clinical condition and decreased levels of markers of inflammation in 2 patients treated with an experimental C5 inhibitor (BDB-001). Multiple trials of 2 commercially available, intravenously administered anti-C5 antibodies (eculizumab [Soliris], ravulizumab-cwvz [Ultomiris]) are ongoing, including several randomized controlled trials (NCT04346797, primary completion September 2020; NCT04369469, primary completion November 2020; and NCT04390464, primary completion May 2021). The number of treatments and dosage of eculizumab and ravulizumab-cwvz vary among trials and, therefore, costs are difficult to estimate. Both drugs have annual treatment costs approaching $500 000.	Limited available data on patient outcomes for anti-C5 monoclonal antibodies and the high cost of this intervention currently limit its potential impact.
Bruton tyrosine kinase (BTK) inhibitors to treat COVID-19	BTK inhibitors are a class of small-molecule drugs that inhibit the kinase BTK, which plays a critical role in the development of the B cells of the immune system. BTK inhibitors are being investigated to reduce the likelihood of respiratory failure in hospitalized patients with COVID-19. Some patients with COVID-19 experience an inflammatory condition leading to pulmonary dysfunction and cardiovascular events thought to contribute to COVID-19-related death. Patients with COVID-19 exhibit elevated levels of various proinflammatory cytokines that contribute to this inflammatory condition. BTK inhibitors might help reduce pulmonary cytokines, lung injury, and death by disrupting proinflammatory signaling in various immune cells. Data published June 5, 2020, from a prospective clinical study of off-label use of acalabrutinib in 19 hospitalized patients with severe COVID-19 demonstrated improvements in oxygenation and measures of inflammation. The results support using BTK inhibitors as a therapeutic strategy to treat severe COVID-19. Ongoing US clinical trials investigating BTK inhibitors to treat COVID-19 include the following phase 2 trials: NCT04380688 (acalabrutinib), NCT04375397 (ibrutinib), and NCT04382586 (zanubrutinib). All 3 trials have primary completion dates in the third quarter of 2020.	If proved effective, BTK inhibitors will likely benefit only a small number of patients with severe disease. More data are needed; therefore, impact in the next 12 months is not certain.

Title	Description	Archive reason(s) based on data review and/or stakeholder ratings and comments
Chloroquine and hydroxychloroquine to treat COVID-19	Chloroquine and hydroxychloroquine are closely related, anti-inflammatory, immunomodulating drugs most commonly known for their FDA approval to treat malaria and rheumatoid arthritis. They became off-label, standard-of-care treatment for hospitalized adolescents and adults who have COVID-19 after FDA issued both drugs an Emergency Use Authorization (EUA) on March 28, 2020. Since then, clinical data published May 7, 2020, May 11, 2020, and May 22, 2020 (later retracted after the data set could not be verified) and reported June 5, 2020 (United Kingdom) have failed to demonstrate an association between hydroxychloroquine use and prevention of intubation or death. Concerns about the safety of the drugs were supported by findings in an analysis published May 22, 2020, of adverse drug reaction case reports, which described potentially deadly cardiotoxicity findings of hydroxychloroquine use. FDA revoked the EUA for hydroxychloroquine and chloroquine to treat COVID-19 on June 15, 2020, stating the criteria for their authorized use were no longer met. FDA concluded, after reviewing clinical data and other information, that the drugs might not be effective to treat COVID-19 and that potential benefits of their use do not outweigh potential risks.	Data increasingly suggest chloroquine and hydroxychloroquine are ineffective in treating COVID-19 and might carry significant negative side effects.
Famotidine (Pepcid) to treat COVID-19	Famotidine (Pepcid) is an over-the-counter histamine H_2-receptor antagonist commonly used to treat acid indigestion, gastroesophageal reflux disease (GERD), heartburn, and stomach ulcers. A retrospective study of patient records from Wuhan, China, revealed a trend among elderly COVID-19 survivors with heartburn. In this cohort, patients who took the less expensive famotidine for their heartburn had a 14% mortality rate, compared with a 27% mortality rate in patients who took the more expensive omeprazole (Prilosec). Famotidine might act directly on a key enzyme of SARS-CoV-2, the virus that causes COVID-19, to resolve infections sooner and mitigate symptoms. In the phase 3 MATCH study, investigators at Northwell Health (New York, New York) are investigating the use of intravenous famotidine at a concentration up to 9 times higher (360 mg/day) than the dosage typically used for heartburn (40 mg daily). This study will treat up to 1170 patients with intravenous famotidine in combination with oral hydroxychloroquine or intravenous placebo and oral hydroxychloroquine for 14 days or until hospital discharge. Primary completion is expected September 7, 2020. A case series published June 4, 2020, of 10 nonhospitalized patients with COVID-19 taking high-dose (80 mg) famotidine suggests it is well tolerated and associated with improved patient-reported outcomes.	Studies with famotidine were confounded by the inclusion of hydroxychloroquine; therefore, no preliminary conclusions can be drawn regarding famotidine's effectiveness in treating COVID-19. More and better-designed studies are needed.

Title	Description	Archive reason(s) based on data review and/or stakeholder ratings and comments
Lopinavir/ritonavir to treat COVID-19	Lopinavir/ritonavir is a combination antiviral drug consisting of 2 HIV protease inhibitors being investigated to treat COVID-19 by preventing replication of SARS-CoV-2, the virus that causes the disease. The drug demonstrated activity in cell cultures against the closely related coronavirus SARS-CoV that causes severe acute respiratory syndrome (SARS) and positive initial clinical findings in patients with SARS. A randomized controlled trial of lopinavir/ritonavir in hospitalized adults with severe COVID-19 in China demonstrated no benefit of lopinavir/ritonavir over standard of care. National Institutes of Health (NIH) COVID-19 treatment guidelines last updated May 12, 2020, recommend against the use of lopinavir/ritonavir or other HIV protease inhibitors. NIH cited concerns about whether adequate drug levels can be achieved with oral dosing. US clinical trials investigating lopinavir/ritonavir to treat COVID-19 include NCT04372628 and NCT04328012. The drug is taken in tablet form as brand name Kaletra (AbbVie, North Chicago, Illinois). Based on available pricing and trial dosing information, we estimate one course of treatment costs about $100.	Available data suggest that lopinavir/ritonavir is ineffective at treating COVID-19 and so is unlikely to have a significant impact relative to COVID-19 in the United States.
Ruxolitinib (Jakafi) to treat COVID-19	Ruxolitinib (Jakafi), is a Janus kinase inhibitor FDA has approved to treat myelofibrosis, polycythemia vera, and acute graft-versus-host disease. It also is being investigated to treat COVID-19. Some patients with COVID-19 experience an inflammatory condition leading to pulmonary dysfunction and cardiovascular events thought to contribute to COVID-19-related death. Patients with COVID-19 exhibit elevated levels of various proinflammatory cytokines that contribute to this inflammatory condition. Ruxolitinib inhibits the Janus-associated kinases JAK1 and JAK2, key signaling molecules in the cytokine signaling pathway whose inhibition might moderate the overactive immune response. Ruxolitinib is in multiple US clinical trials, including phase 2/3 NCT04348071 and manufacturer-sponsored phase 3 NCT04362137 and phase 3 NCT04377620 trials, with primary completion dates ranging from August to October 2020. Based on available pricing and trial dosing information, we estimate one course of treatment costs about $14 000.	Any potential benefits from ruxolitinib will likely be realized by only a small number of patients. In addition, its high cost might limit its use even in this narrow patient population, thereby limiting its overall impact relative to COVID-19.

Title	Description	Archive reason(s) based on data review and/or stakeholder ratings and comments
Tissue plasminogen activator to treat COVID-19	Tissue plasminogen activator (tPA) is a thrombolytic drug FDA has approved to treat acute myocardial infarction, pulmonary embolism, acute ischemic stroke, and central venous catheter occlusion. It is being investigated as a treatment for acute respiratory distress syndrome (ARDS) in COVID-19. tPA breaks down blood clots by promoting the formation of plasmin, an enzyme that breaks down the structural support of blood clots, fibrin. Hypercoagulopathy with inflammation is commonly seen in severe COVID-19 and is correlated with worse outcomes. Early findings published in February 2020 from 183 hospitalized patients in Wuhan, China, revealed 71.4% of patients who died met criteria for disseminated intravascular coagulopathy (DIC) compared with only 0.6% of survivors. Coagulopathy in COVID-19 is thought to be predominantly prothrombotic (ie, clot-inducing), evidenced from abnormal blood test findings and higher rates of thrombotic events (eg, central line thrombosis, vascular occlusion events) observed in critically ill patients. Prophylactic anticoagulation has been suggested for preventing COVID-19-related thrombotic events, but its efficacy for that application is unknown. Case reports of off-label use of tPA in patients who have ARDS and respiratory failure suggest respiratory improvement with tPA treatment. An ongoing US phase 2 trial (NCT04357730) is administering tPA to hospitalized patients who have ARDS. The trial has a primary completion date in September 2020.	tPA is expensive and carries significant risks for bleeding. If used for treatment of COVID-19, it will likely provide benefits for only a small subset of patients.

Section 6. Vaccines and Prophylaxis: 3 Topics

Table 6.1. Currently Monitored Vaccine and Prophylaxis Topics: 2 Topics

Title	Description	Possible areas of impact	Possible future impacts
BNT162 mRNA (messenger RNA) vaccines to prevent infection from SARS-CoV-2, the virus that causes COVID-19	Pfizer and BioNTech have partnered to develop and manufacture 4 lipid nanoparticle encapsulated mRNA vaccine candidates (BNT162a, BNT162b1, BNT162b2, and BNT162c2) that encode the viral Spike (S) protein. S protein is expressed on the virus surface and is responsible for receptor binding and cellular entry. The mRNA vaccines purportedly enter the cytosol of antigen-presenting cells and induce the expression of viral proteins that can elicit host immune responses to prevent future infection. The vaccine candidates have different structural components that might impact immunogenicity, efficacy of protein expression, and stability. Two candidates incorporate nucleoside modified mRNAs, one candidate incorporates uridine-containing mRNA, and a fourth candidate incorporates self-amplifying mRNA technology. Two candidates encode a larger S sequence and 2 candidates encode a smaller optimized receptor-binding domain. The manufacturers were selected as finalists in Operation Warp Speed, a US government program intended to expedite vaccine development. If the vaccine is effective, the manufacturers expect to produce millions of doses by the end of 2020 and hundreds of millions of doses in 2021. The companies dosed the first US patients in May 2020, in a phase 1/2 trial (n = 200; NCT04380701) with primary completion in August 2020. A larger phase 1/2 trial (n = 600; NCT04368728) has primary completion in June 2021.	Patient outcomes Population health Clinician and/or caregiver safety Health care delivery and process Health care disparities Health care costs	Might reduce coronavirus infection risk and improve patient health outcomes Might reduce the cost of treating severe infections Might relax social distancing protocols Might not provide the level of protection hoped for, because of the accelerated approval process Might have undiscovered adverse events, because of the accelerated approval process Might have vaccine shortages, if effective, because of limited production capacity

Title	Description	Possible areas of impact	Possible future impacts
mRNA-1273 vaccine to prevent infection from SARS-CoV-2, the virus that causes COVID-19	mRNA-1273 (Moderna, Cambridge, Massachusetts) is a lipid nanoparticle encapsulated mRNA (messenger RNA) vaccine against coronavirus. It encodes a prefusion stabilized form of the viral Spike (S) protein expressed on the surface of the virus, which is responsible for viral fusion and entry into cells. The mRNA vaccine purportedly enters the cytosol of antigen-presenting cells and induces the expression of viral proteins that are capable of inducing host immune responses to prevent future infection. The mRNA-1273 vaccine is in phase 2 development (NCT04405076), with primary completion expected in March 2021. The company reported positive interim phase 1 results after healthy adults (n = 30) were given 2 doses of either 25 µg or 100 µg of vaccine. At day 43, all patients with available neutralizing antibody data (n = 8) purportedly seroconverted with antibody and neutralizing antibody levels "at or above levels generally seen in convalescent sera." The vaccine also provided full protection against pulmonary viral replication in a mouse challenge model. On May 12, 2020, FDA granted mRNA-1273 Fast Track designation. The manufacturer announced a phase 3 trial (n = 30 000), expected to begin in July 2020.	Patient outcomes Population health Clinician and/or caregiver safety Health care delivery and process Health care disparities Health care costs	Might reduce coronavirus infection risk and improve patient health outcomes Might reduce the cost of treating severe infections Might relax social distancing protocols Might have undiscovered adverse events, because of the accelerated approval process Might have vaccine shortages, if effective, because of limited production capacity

Table 6.2. Recently Archived Vaccine and Prophylaxis Topics: 1 Topic

Title	Description	Archive reason(s) based on data review and/or stakeholder ratings and comments
Hydroxychloroquine to prevent COVID-19	Off-label use of the antimalarial drug hydroxychloroquine became standard of care for treating adolescents and adults hospitalized with COVID-19 after FDA issued an Emergency Use Authorization (EUA) on March 28, 2020. However, FDA revoked the EUA on June 15, 2020, stating the criteria for the drug's authorized use were no longer met; specifically, hydroxychloroquine might not be effective to treat COVID-19 and the potential benefits for its use do not outweigh the potential risks. Investigators have been examining whether hydroxychloroquine might prevent SARS-CoV-2 infection (which causes COVID-19) in healthy individuals, particularly in those with a high risk of infection, such as health care workers. In vivo and in vitro data published May 6, 2020, did not find hydroxychloroquine to have antiviral activity against SARS-CoV-2. Multiple US phase 3 clinical trials are investigating the use of hydroxychloroquine as preexposure prophylaxis (eg, NCT04341441, NCT04352946, NCT04363450). Clinical data published June 3, 2020, from a phase 3 trial (NCT04308668) found no significant difference in new illness incidence between participants (n = 821) receiving hydroxychloroquine and those receiving placebo for postexposure prophylaxis.	Available data suggest that hydroxychloroquine carries significant safety risks that might outweigh potential benefits and could negatively impact patient outcomes.

Appendix. Abbreviations and Acronyms

ACEI	angiotensin-converting enzyme inhibitor
ACE2	angiotensin-converting enzyme 2
ADHD	attention-deficit/hyperactivity disorder
ADHS	Arizona Department of Health Services
AI	artificial intelligence
ARB	angiotensin II receptor blocker
ARDS	acute respiratory distress syndrome
AT1	angiotensin II type 1
BTK	Bruton tyrosine kinase
C5	complement component 5
CCL5 (RANTES)-CCR5	C-C chemokine ligand 5 (regulated upon activation, normal T-cell expressed, and secreted)-C-C chemokine receptor type 5
CDC	Centers for Disease Control and Prevention
COVID-19	coronavirus disease 2019
CP	convalescent plasma
CPAP	continuous positive airway pressure
CRP	C-reactive protein
DIC	disseminated intravascular coagulopathy
ECMO	extracorporeal membrane oxygenation
ELISA	enzyme-linked immunosorbent assay
EPA	US Environmental Protection Agency
EUA	Emergency Use Authorization

FDA	US Food and Drug Administration
FIA	fluorescent immunoassay
GERD	gastroesophageal reflux disease
GM-CSF	granulocyte-macrophage colony-stimulating factor
GPS	global positioning system
HCHSS	Health Care Horizon Scanning System
HR	hazard ratio
ICER	Institute for Clinical and Economic Review
IL-1β	interleukin-1 beta
IL-1/IL-6	interleukin-1/interleukin-6
IL-1R1	interleukin 1 receptor type I
IL-6	interleukin-6
IT	information technology
IVIG	intravenous immunoglobulin
JAK	Janus kinase
JAK1	Janus kinase type 1
JAK2	Janus kinase type 2
MERS	Middle East respiratory syndrome
MERS-CoV	Middle East respiratory syndrome caused by coronavirus
MODS	multiorgan dysfunction syndrome
M_{pro}	SARS-CoV-2 main protease
mRNA	messenger RNA
MxA	myxovirus resistance protein A
N95	not resistant to oil mists, filters at least 95% of 0.3 micrometer droplets

NIH	National Institutes of Health
NIRL	near infrared light
NO	nitric oxide
PCORI	Patient-Centered Outcomes Research Institute
PCR	polymerase chain reaction
PEEP	positive end-expiratory pressure
POC	point-of-care
PPE	personal protective equipment
RAS	renin-angiotensin system
RBD	receptor binding domain
RT-PCR	reverse transcriptase polymerase chain reaction
S	Spike
SARS	severe acute respiratory syndrome
SARS-CoV	severe acute respiratory syndrome–associated coronavirus
SARS-CoV-1	severe acute respiratory syndrome coronavirus 1
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SoC	standard of care
TMPRSS2	transmembrane serine protease 2
tPA	tissue plasminogen activator
VIP	vasoactive intestinal polypeptide