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PCORI HEALTH CARE HORIZON SCANNING SYSTEM

SEPTEMBER 2020

Horizon Scanning COVID-19 Supplement High Impact Report Volume 1, Issue 1

Prepared for:

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

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Horizon Scanning COVID-19

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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 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.

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None of the individuals compiling this information have 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 to have high impact on 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 3 months) briefly list and describe all COVID-19-related topics identified, monitored, and recently archived. High Impact Reports (every 4 months) highlight 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 Gowri Raman, MBBS, 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

Background

Horizon scanning identifies technology and systems innovations that could disrupt or cause significant shifts in health care. Horizon scanning can identify new (and new uses of existing) diagnostic tests and procedures, health care delivery innovations, medical devices, mental and behavioral health interventions, pharmaceuticals, public health and health promotion activities, rehabilitation interventions, and therapeutic interventions.

Health care horizon scanning has typically informed strategic planning activities. Public and private entities around the world have long used formal or informal health care horizon scanning programs for purposes including commercial planning, health services research prioritization, financial or operational planning, controlled diffusion of technologies, and provision of information to policymakers, purchasers, and health care providers.

Horizon Scanning Process Overview

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.

The [*PCORI Health Care Horizon Scanning System: Horizon Scanning Protocol and Operations Manual COVID-19 Supplement*](#) (hereafter referred to as the Protocol) details the methodology and criteria we use to select and report on potential high-impact 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 inform 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 section, 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 Topic Selection and Reporting Methods

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.

Topics selected for inclusion are assigned to analysts for report drafting. An analyst may request topic-specific searches, if needed. The analyst then writes a summary of the topic, including highlights, a description of the topic, areas of potential impact, potential outcomes, and key stakeholder comments. An impact score based on stakeholder ratings is calculated and added to the summary. Topic summaries are compiled into the report chapter corresponding to the topic's content area (ie, devices, identifiable risk factors and prognostic indicators, screening and diagnostics, systems and management, treatments, and vaccines and prophylaxis). The project manager reviews each topic summary and writes a chapter introduction. Each chapter is then reviewed by a senior horizon scanning reviewer and medical copyeditor. All chapters are then compiled into the High Impact Report. The project manager reviews the report and writes a report introduction that includes background, an overview of the horizon scanning process specific to the COVID-19 Supplement, a description of the report methodology, and a reporting period summary.

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.

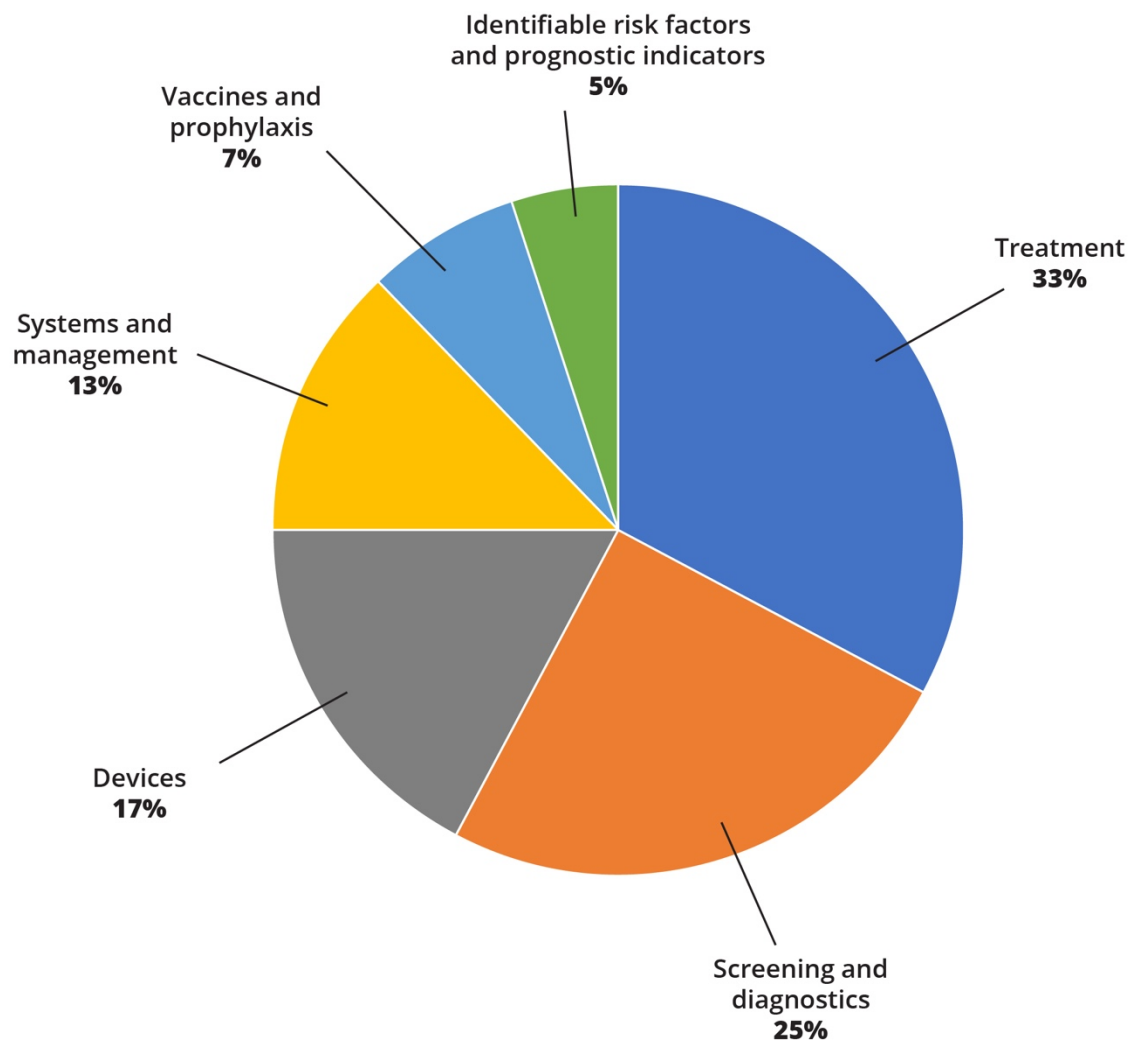
An archived topic may reenter the system at a later date if new information comes to light suggesting that the topic has high impact potential.

Reporting Period Summary

The PCORI HCHSS COVID-19 Supplement began operating in May 2020. Since then, review of about 1500 information leads has led to the identification of 126 COVID-19-related topics across 6 content areas. As of July 30, 2020, after subjecting potential topics to our inclusion criteria and selection process, 108 topics have been selected as having potential for impact. Of these, 71 are being actively monitored in the system; 37 topics have been archived. These 108 topics span the 6 COVID-19-related content areas as follows (see also Figure 1):

- Devices: 18 topics (17%)
- Identifiable risk factors and prognostic indicators: 5 topics (5%)
- Screening and diagnostics: 27 topics (25%)
- Systems and management: 14 topics (13%)
- Treatments: 36 topics (33%)
- Vaccines and prophylaxis: 8 topics (7%)

Figure 1. Percentage of Actively Monitored Topics by Content Area

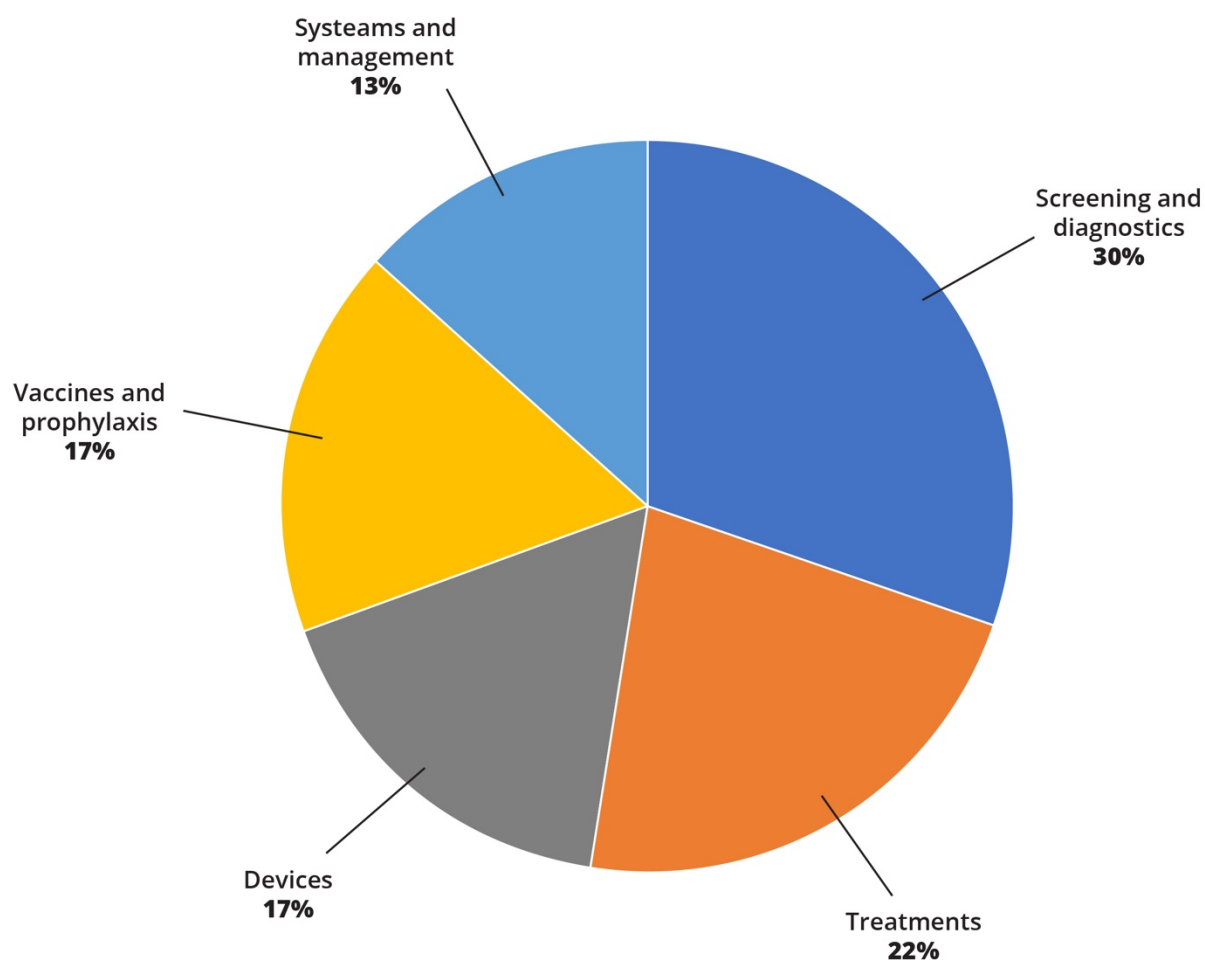


Of the 71 actively monitored topics, we have selected—based on the procedures described in High-Impact Topic Selection and Reporting Methods—23 topics for inclusion in this report, distributed across 5 COVID-19-related content areas as follows (see also Figure 2):

- Devices: 4 topics (17%)
- Screening and diagnostics: 7 topics (30%)
- Systems and management: 3 topics (13%)
- Treatments: 5 topics (22%)
- Vaccines and prophylaxis: 4 topics (17%)

Note: Total does not equal 100% because of rounding.

Figure 2. Percentage of Topics Selected for Report by Content Area



Chapter 1. Devices

Chapter Summary

As of July 30, 2020, we were monitoring 18 COVID-19-related device topics. Eleven of these topics are listed in the July 2020 *PCORI Health Care Horizon Scanning System: Horizon Scanning COVID-19 Supplement Status Report, Volume 1, Issue 1*. The remaining 7 topics will be listed in the October 2020 edition of the *COVID-19 Supplement Status Report*. All 18 topics were sent for comment to internal ECRI stakeholders, and each received at least 5 sets of ratings and comments from stakeholders between May 18, 2020, and July 29, 2020.

Topics Considered for Inclusion in This Report

Table 1.1 lists 4 topics selected for inclusion in this High Impact Report. Included topics received, on average, moderately high to high impact ratings and demonstrated high consensus among stakeholders, as evident in the ratings and comments. Topics are ordered first in descending order by potential impact score; topics with the same score are listed alphabetically by topic title.

Table 1.1. Included Device Topics

Topic title	Potential impact score
Reusable silicone respirators to protect against COVID-19	3.5
Isolation bags for safe computed tomography (CT) imaging in suspected COVID-19 cases	3.4
Decontamination systems for reprocessing of single-use N95 respirators	3.3
Negative-pressure tents to limit airborne transmission of coronavirus	3.2

Table 1.2 lists 14 topics considered, but not selected, for inclusion in this High Impact Report. Excluded topics received, on average, low to moderate impact ratings and were not considered by most stakeholder reviewers to have high impact potential. Topics are ordered first in descending order by potential impact score; topics with the same score are listed alphabetically by topic title.

Table 1.2. Device Topics Considered but Not Included

Topic title	Potential impact score
Extracorporeal blood filtration to treat COVID-19 ^a	3.0
Transvenous phrenic nerve stimulation to improve ventilator weaning	3.0
Noninvasive muscle stimulation to shorten mechanical ventilation duration ^a	2.9
Drone-based disinfection in public spaces ^a	2.8
Extracorporeal membrane oxygenation (ECMO) to treat COVID-19	2.8
Inhaled nitric oxide for treating COVID-19 ^a	2.8
Negative-pressure helmets to limit airborne transmission of coronavirus	2.8
Implantable diaphragm pacing (TransAeris) to improve ventilator weaning	2.7
Continuous positive airway pressure (CPAP) for noninvasive ventilatory support ^a	2.6
Extracorporeal carbon dioxide removal (Hemolung) to treat COVID-19 lung failure	2.6
Wearable physiologic monitors to remotely observe patients with COVID-19	2.6
Noninvasive vagus nerve stimulation to treat COVID-19	2.4
Ventilator splitting to treat 2 patients requiring different ventilator settings ^a	2.4
Proximity alarms to maintain social distance ^a	2.0

^a Topic has been archived. A description of the topic and the archive reason can be found in the July 2020 *PCORI Health Care Horizon Scanning System: Horizon Scanning COVID-19 Supplement Status Report, Volume 1, Issue 1*.

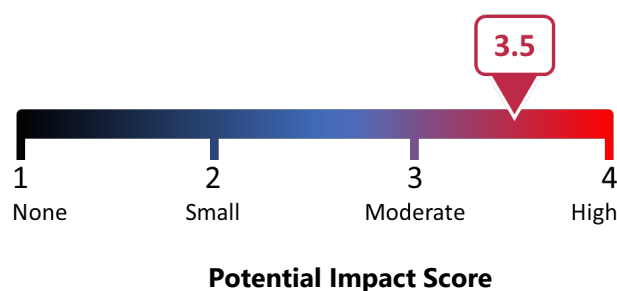
Topic Summaries

We present below 4 summaries on topics deemed to have moderately high to high impact potential. Topics are ordered first in descending order by potential impact score; topics with the same score are listed alphabetically by topic title.

Reusable Silicone Respirators to Protect Against COVID-19 Infection

Potential Impact Score

Stakeholders reviewing this topic thought that reusable silicone respirators to protect against COVID-19 infection could have a moderately high to high impact on patient-oriented health care relative to COVID-19 in the United States within the next 12 months.



Highlights

- Researchers at the Massachusetts Institute of Technology (MIT) have developed a reusable silicone respirator that purportedly can be sterilized and safely reused multiple times while retaining its elasticity and personal protective properties.

- Developers assert the reusable silicone respirator could be inexpensive to mass produce using conventional injection molding manufacturing methods.
- Researchers have made the design specifications of their reusable respirator publicly available to facilitate its widespread access.
- Stakeholders reviewing this topic thought a reusable silicone respirator might help alleviate shortages of single-use N95 respirators and offer an environmental benefit by reducing the volume of medical waste.

Description

Shortages of N95 respirators can increase risk of coronavirus infection for frontline personnel. A team at MIT has designed a modular, reusable filtering facepiece respirator as an alternative to single-use N95 respirators.¹ The new silicone-based design, called the Injection Molded Autoclavable, Scalable, Comfortable (iMASC) system, can purportedly be mass produced at a relatively low cost with standard injection molding manufacturing techniques.² The reusable mask is a tight-fitting, elastomeric (ie, stretchable) respirator with a bidirectional filter. It can be sterilized and reused multiple times without sacrificing its effectiveness. The single-use filter insert is replaced during decontamination reprocessing and purportedly uses less filter material than disposable masks.

The developers have made the iMASC Open Standard Respirator, Model 1, design publicly available and are reportedly awaiting FDA Emergency Use Authorization for the mask, which entered production in the United States, Portugal, and other countries in June 2020.¹

In a feasibility study of the iMASC system, researchers performed mask fit testing on 24 health care workers from an emergency department and outpatient oncology clinic who previously underwent N95 respirator fit testing.³ They found that the iMASC system successfully fit different face sizes and shapes using an approved testing method, and results warranted additional certification testing to allow use in health care settings. On a 5-point Likert scale of user experience (1 = excellent, 5 = very poor), iMASC had an average fit score of 1.75, a breathability score of 1.6, and an ease of filter replacement score of 2.05.³

Possible Areas of Impact

- Clinician or caregiver safety
- Health care costs

Possible Future Impacts

The availability of a reusable respirator could enhance safety for health care providers and first responders by helping alleviate shortages of single-use N95 respirators. Sterilization of reusable silicone respirators might be simpler than decontamination of single-use N95 respirators, which typically requires specialized equipment or shipment to an outside vendor for reprocessing. A reusable respirator that can be mass produced using standard manufacturing techniques might lower supply costs for personal protective equipment compared with single-use N95 respirators. The visual esthetics of reusable silicone respirator systems might also be less intimidating to patients than the gas masks that health care providers wear during N95 respirator shortages.

Key Stakeholder Perspectives

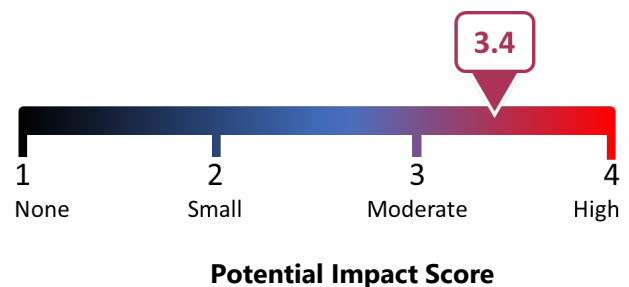
Between July 15, 2020, and July 24, 2020, six ECRI stakeholders, reflecting nursing, research, allied health, health systems, and clinical engineering perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- A reusable respirator could help alleviate shortages of single-use N95 respirators, provided that sufficient supplies of the disposable filter component are available to meet demand.
- Reusable silicone filters could reduce the volume of medical waste for hospitals since only the filters are replaced after each use, thus providing potential cost and environmental benefits.
- The labor and material costs of reprocessing used silicone respirators need to be considered; decontamination of single-use N95 respirators has been demonstrated to be costly and can degrade respirator materials in fewer than 5 decontamination cycles.
- Widespread acceptance of reusable silicone respirators will require reprocessing procedures that do not create substantial change or additional work for users.

Isolation Bags for Safe Computed Tomography (CT) Imaging in Suspected COVID-19 Cases

Potential Impact Score

Stakeholders reviewing this topic thought that isolation bags for safe CT imaging in suspected COVID-19 cases could have a moderately high impact on patient-oriented health care relative to COVID-19 in the United States within the next 12 months.



Highlights

- To reduce the number of labor-intensive cleaning procedures between cases, researchers have proposed disposable isolation bags worn over the head and chest for patients with suspected COVID-19 who require chest CT scans.
- Researchers claim that if isolation bags reduce the need for some intensive cleaning procedures between cases, they might allow hospitals to scan up to nearly 14 times more patients per day on a single CT machine.
- Isolation bags might provide an additional layer of personal protection for health care providers performing CT scans on patients with suspected or confirmed COVID-19.
- Stakeholders commenting on this topic thought isolation bags might improve staff and patient safety during imaging scans while increasing emergency department patient throughput on CT machines.

Description

CT scans can be used in alternative diagnostics or to guide management of COVID-19 complications. However, protecting patients and staff requires lengthy cleaning procedures

between patients to adequately decontaminate imaging equipment and examination rooms. An international team led by US National Institutes of Health (NIH) researchers has developed a simple, inexpensive bag intended to safely isolate patients during CT scans.⁴

The disposable isolation bag is made from readily available translucent (ie, almost clear) plastic material commonly used to protect patients and imaging and surgical equipment in other health care settings. The bag covers the patient's head and chest. The bag has an integrated N95 filter patch and is secured at the waist with a disposable elastic or Velcro belt. The patient wears an N95 respirator or surgical mask to block respiratory droplets and a hat with visor to keep the polymer bag off the face. A supply line connected through the bag's oxygen input nozzle delivers oxygen to the patient.⁴

Researchers estimate that using this inexpensive and easily implementable isolation bag could allow about 14 times more patients per day to undergo chest imaging on a single CT scanner in a hospital emergency department.⁴

Possible Areas of Impact

- Clinician or caregiver safety
- Health care costs
- Health care delivery and process
- Population health

Possible Future Impacts

Isolation bags might reduce patient or health care staff exposure to coronavirus by better isolating patients during imaging procedures. This intervention might also increase emergency department patient throughput on CT machines. Use of isolation bags during chest CT scans might lower procedural and maintenance costs if this procedure can safely eliminate the need for some more intensive disinfection procedures currently used between patients undergoing CT imaging.

Some patients—especially those experiencing breathing difficulty or those who experience discomfort in enclosed spaces—may be reluctant to allow health care providers to place an isolation bag over their head. Therefore, use of the bags might require additional time for patient assurance and education by health care staff.

Key Stakeholder Perspectives

Between June 23, 2020, and June 30, 2020, five ECRI stakeholders, reflecting nursing, health systems, and clinical engineering perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

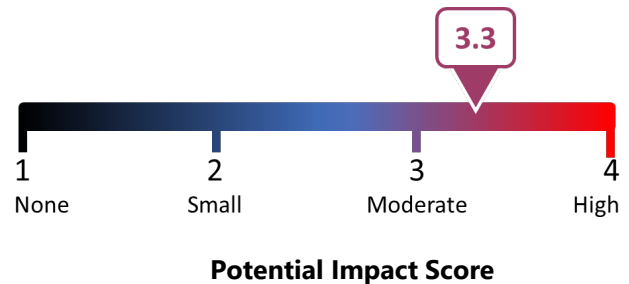
- Use of isolation bags might significantly increase patient throughput by alleviating some deep-cleaning steps between imaging patients.
- Isolation bags might improve patient and staff safety by adding another layer of personal protection and reducing air and surface contamination in the imaging suite.
- Isolation bags might decrease the need to designate a “dirty” CT scanner for use only with patients with confirmed COVID-19, an option that does not solve the problem of cross-contamination or help protect patients with suspected COVID-19 who require a CT scan for confirmation.

- If material costs are low, isolation bags could have long-lasting impacts if imaging departments continue to use them in nonpandemic environments when the potential for the spread of infectious agents exists.

Decontamination Systems for Reprocessing of Single-Use N95 Respirators

Potential Impact Score

Stakeholders reviewing this topic thought that decontamination systems for reprocessing of single-use N95 respirators could have a moderately high impact on patient-oriented health care relative to COVID-19 in the United States within the next 12 months.



Highlights

- Rapidly increasing COVID-19 case volumes, combined with shortages of personal protective equipment (PPE), prompted FDA to allow emergency use of systems for decontaminating single-use N95 respirators for repeated use by health care providers.
- Data assessing N95 respirator reprocessing are lacking. Existing data come primarily from laboratory analyses and real-world evidence about respirator decontamination.
- Laboratory data suggest that single-use N95 respirators might be safely reprocessed for far fewer cycles than some manufacturers have claimed.
- Stakeholders commenting on this topic thought that reprocessing of single-use N95 respirators might increase the immediate availability of PPE, but that this benefit would likely be nullified when respirator manufacturing capacity rebounds to meet current demand.

Description

The rapid depletion of N95 respirator supplies prompted several manufacturers to seek FDA Emergency Use Authorization (EUA) for systems that purportedly decontaminate single-use N95 respirators and allow them to be reused. As of early August 2020, FDA had granted 10 EUAs for use of N95 respirator decontamination systems during the COVID-19 pandemic.⁵ Most systems with EUAs are authorized for decontaminating N95 respirators for single-user use for up to 20 decontamination cycles. Some health care facilities ship used respirators to a facility for decontamination using special handling and shipping procedures. So far, N95 respirators that contain cellulose material are incompatible with decontamination systems with EUAs.⁵

A US National Institutes of Health (NIH) laboratory study found that N95 respirators can be decontaminated effectively and maintain functional integrity for up to 3 decontamination cycles, depending on the decontamination process used.⁶ A recent systematic review of the safety and effectiveness of N95 respirator decontamination concluded that a single decontamination cycle successfully removes pathogens with little or no change in mask function, fit, or appearance.⁷ Investigators noted that most of the studies in their systematic review tested new respirators in

laboratory settings, making it uncertain whether extended use in clinical practice would alter their findings. Investigators suggested that additional decontamination cycles might be possible; however, more research is needed about how multiple decontamination cycles would affect mask fit and function in a real-world setting before a safe upper limit for respirator reprocessing can be established.⁷ (Note: Neither the NIH study nor the review article has yet undergone peer review.)

Possible Areas of Impact

- Clinician or caregiver safety
- Health care costs
- Health care delivery and process

Possible Future Impacts

Reusing decontaminated N95 respirators intended for single use might alleviate acute shortages of this protective equipment for health care providers treating patients. Reprocessing used N95 respirators might be less costly than purchasing all new single-use N95 respirators if supply shortages continue to drive up the prices. Hospitals implementing respirator decontamination programs would likely need to develop new procedures to determine which respirators in use would be eligible for decontamination and then to safely identify, collect, store, transport, and redistribute reprocessed N95 respirators to appropriate users. Instructions for several respirator decontamination systems state that reprocessed respirators should be returned to the same user and are not authorized for distribution to multiple users.

Health care providers might raise safety concerns about the decontamination and reuse of single-use N95 respirators since little published evidence is available to assess this procedure in actual clinical practice.

Key Stakeholder Perspectives

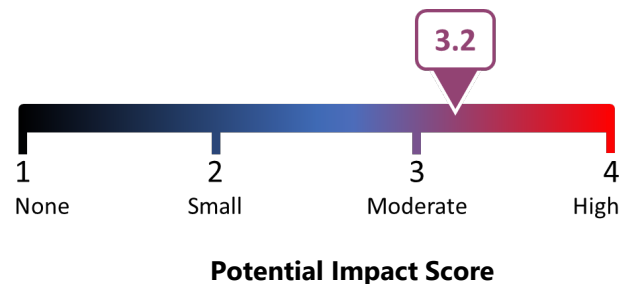
Between June 4, 2020, and June 5, 2020, six ECRI stakeholders, reflecting physician, nursing, and health systems perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- Use of N95 respirator decontamination could continue at many US hospitals while COVID-19 surges and until N95 manufacturing and distribution capacity rebounds enough to make respirator decontamination economically and logistically unattractive.
- Adoption of decontamination and reuse of single-use N95 respirators could be abandoned after the COVID-19 pandemic subsides as hospitals explore other alternatives for addressing potential future shortages.
- Recent anecdotal evidence suggests manufacturer claims may overstate how many decontamination cycles single-use N95 respirators can safely undergo to adequately maintain protection for users.
- Real-world evidence about the safety, utility, and economic effects of N95 respirator decontamination during pandemics is lacking but needed to assess the proper role of this practice.

Negative-Pressure Tents to Limit Airborne Transmission of Coronavirus

Potential Impact Score

Stakeholders reviewing this topic thought that negative-pressure tents to limit airborne transmission of coronavirus could have a moderately high impact on patient-oriented health care relative to COVID-19 in the United States within the next 12 months.



Highlights

- Negative-pressure tents can remove the air—including droplets exhaled by the patient—using an attached vacuum motor and high-efficiency particulate air filter before releasing the air into the room.
- These portable units might reduce the risk of airborne coronavirus transmission to health care providers during care, transport, or aerosol-generating procedures.
- They might also reduce the need for expensive negative-pressure rooms in health care facilities and could improve patient throughput.
- Stakeholders commenting on this topic thought negative-pressure tents might help reduce transmission of coronavirus while providing health care workers with a safer work environment. Although implementing negative-pressure tents would be less costly than building full-sized rooms, the resources needed to set up these tents might still limit their widespread use in health care facilities.

Description

Full-sized negative-pressure rooms can effectively contain the spread of airborne pathogens, but the number of COVID-19 cases can overload this resource. Compact negative-pressure patient tents might reduce the need for full-sized negative-pressure rooms, decrease the risk of airborne transmission to frontline health care providers, and increase patient throughput.⁸

The tent is a portable unit placed at the top of the bed over the patient's head. Tents are constructed of either clear rigid plastic (resembling a box) with hand-access ports or clear soft plastic over a reusable frame (resembling a clamshell-like camping tent) with slits in the walls to allow provider access. A vacuum hose connected to the hospital air-evacuation system creates the negative-pressure environment.⁸

On June 13, 2020, FDA granted Oceanetics, Inc (Annapolis, Maryland), Emergency Use Authorization (EUA) for its NRSVR-100 negative-pressure portable tent system to enhance personal barrier protection for providers during airway management, medical procedures, or transport of patients with COVID-19.⁹ University of Michigan researchers have developed a similar negative-pressure tent (Aerosolve) that the developers think might soon receive EUA for use during the COVID-19 pandemic.¹⁰

Possible Areas of Impact

- Clinician and/or caregiver safety

-
- Health care costs
 - Health care delivery and process
 - Patient health outcomes

Possible Future Impacts

Portable negative-pressure patient tents might increase the availability of negative-pressure environments for patients with COVID-19 to enhance protection for frontline health care providers. The compact units might reduce costs associated with increasing the number of negative-pressure care environments available and provide benefits in high-volume care delivery centers, which would be of particular importance in economically disadvantaged areas.

Key Stakeholder Perspectives

Between July 1, 2020, and July 24, 2020, five ECRI stakeholders, reflecting allied health, health systems, physician, and research perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- Negative-pressure tents might provide an alternative safe environment for health care professionals to care for COVID-19 patients and reduce the strain on hospital resources (eg, by eliminating the need for full-sized negative-pressure rooms).
- The tent technology might provide more immediate access to negative-pressure environments during emergency situations (eg, COVID-19 pandemic) since it allows easy deployment and dismantling of the tent.
- Conventional negative-pressure rooms require significant financial expenditures and are difficult to construct on short notice. Negative-pressure tents might provide a faster, less expensive way to implement negative-pressure environments for individual patients. However, the setup for negative-pressure tents would still increase costs and resources needed per patient compared with standard rooms, which might prevent hospitals from using these tents.

Chapter 2. Identifiable Risk Factors and Prognostic Indicators

Chapter Summary

As of July 30, 2020, we were monitoring 3 COVID-19-related identifiable risk factor and prognostic indicator topics. Two of these topics are listed in the July 2020 *PCORI Health Care Horizon Scanning System: Horizon Scanning COVID-19 Supplement Status Report, Volume 1, Issue 1*. The remaining topic will be listed in the October 2020 edition of the *COVID-19 Supplement Status Report*. All 3 topics were sent for comment to internal ECRI stakeholders, and each received at least 5 sets of ratings and comments from stakeholders between May 18, 2020, and July 29, 2020. Internal ECRI stakeholders did not think that any of these 3 topics have moderately high to high impact potential relative to COVID-19-related patient-oriented health care in the United States within the next 12 months; therefore, none of the 3 topics were selected for inclusion in this report.

Topics Considered for Inclusion in This Report

Table 2.1 lists 3 topics considered, but not selected, for inclusion in this High Impact Report. Excluded topics received, on average, low to moderate impact ratings and were not considered by most stakeholder reviewers to have high impact potential. Topics are ordered first in descending order by potential impact score; topics with the same score are listed alphabetically by topic title.

Table 2.1. Identifiable Risk Factor and Prognostic Indicator Topics Considered but Not Included

Topic title	Potential impact score
Interleukin 6 (IL-6) levels as a prognostic factor in COVID-19 patients	3.0
Artificial intelligence (AI)-based assessment of clinical data to determine COVID-19 prognosis	2.9
Atopic diseases might reduce risk of coronavirus infection ^a	2.4

^a Topic was archived. A description of the topic and the archive reason can be found in the July 2020 *PCORI Health Care Horizon Scanning System: Horizon Scanning COVID-19 Supplement Status Report, Volume 1, Issue 1*.

Chapter 3. Screening and Diagnostics

Chapter Summary

As of July 30, 2020, we were monitoring 27 COVID-19-related screening and diagnostics topics. Fifteen of these topics are listed in the July 2020 *PCORI Health Care Horizon Scanning System: Horizon Scanning COVID-19 Supplement Status Report, Volume 1, Issue 1*. The remaining 12 topics will be listed in the October 2020 edition of the *COVID-19 Supplement Status Report*. All 27 topics were sent for comment to internal ECRI stakeholders; 26 received at least 5 sets of ratings and comments from stakeholders between May 18, 2020, and July 29, 2020. One topic, Isothermal amplification assays to test for COVID-19 in community or field settings, had received fewer than 5 sets of ratings and comments by July 29, 2020, and was not considered for inclusion in this report.

Another topic of note, BinaxNOW COVID-19 Ag Card point-of-care antigen test to diagnose COVID-19,¹¹ was added to the system after the deadline for consideration for inclusion in this report. Scanning for the PCORI HCHSS COVID-19 Supplement began on May 11, 2020, and no signal was detected for this topic through scanning until BinaxNOW received FDA Emergency Use Authorization on August 26, 2020.¹² This topic has been added to the system and is currently undergoing stakeholder review. It will be included in the October 2020 edition of the *PCORI Health Care Horizon Scanning System: Horizon Scanning COVID-19 Supplement Status Report*, and it will be considered for inclusion in the January 2020 edition of the *PCORI Health Care Horizon Scanning System: Horizon Scanning COVID-19 Supplement High Impact Report*.

Topics Considered for Inclusion in This Report

Table 3.1 lists 7 topics selected for inclusion in this High Impact Report. Included topics received, on average, moderately high to high impact ratings and demonstrated high consensus among stakeholders, as evident in the ratings and comments. Topics are ordered first in descending order by potential impact score and second in ascending order alphabetically by topic title.

Table 3.1. Included Screening and Diagnostics Topics

Topic title	Potential impact score
Accula SARS-CoV-2 point-of-care test to diagnose COVID-19	3.7
CoviTact point-of-care protease assay to diagnose COVID-19	3.6
Next-generation sequencing assays to diagnose COVID-19	3.4
Population-wide antibody testing to quantify coronavirus infection rates	3.4
Rapid point-of-care breath test to detect COVID-19	3.4
Employee coronavirus testing programs to reopen businesses	3.3
QIAstat-Dx Respiratory SARS-CoV-2 Panel test to diagnose COVID-19	3.2

Table 3.2 lists 19 topics considered, but not selected, for inclusion in this High Impact Report. Excluded topics received, on average, low to moderate impact ratings and were not considered by most stakeholder reviewers to have high impact potential. Topics are ordered first in descending order by potential impact score; topics with the same score are listed alphabetically by topic title.

Table 3.2. Screening and Diagnostics Topics Considered but Not Included

Topic title	Potential impact score
COVID-19 at-home self-collection kits	3.1
CRISPR-based coronavirus assays to diagnose COVID-19	3.1
3D-printed nasopharyngeal swabs for COVID-19 testing	3.0
College and university coronavirus testing programs to prevent COVID-19 spread among returning students	3.0
Sofia 2 SARS antigen FIA point-of-care test to diagnose COVID-19	3.0
Pooled sample testing for screening or diagnosis of COVID-19	2.9
Xpert Xpress SARS-CoV-2 point-of-care test to diagnose COVID-19 ^a	2.9
Artificial intelligence (AI)-assisted echocardiography guidance for nonexpert users	2.8
BioFire Respiratory 2.1 Panel test to diagnose COVID-19 ^a	2.8
Cue COVID-19 point-of-care test to diagnose COVID-19 ^a	2.8
ID NOW COVID-19 point-of-care test to diagnose COVID-19 ^a	2.8
Artificial intelligence (AI)-assisted radiographic image assessment for COVID-19 screening or diagnosis	2.7
Febrile Dx POC Test to predict viral or bacterial infection	2.7
IMMUNO-COV test to detect neutralizing antibodies against coronavirus	2.6
Wearable activity monitors to identify COVID-19 cases ^a	2.5
Wastewater testing to assess scale of COVID-19 outbreak	2.3
Artificial intelligence (AI)-assisted screening for low LVEF in suspected COVID-19 infection	2.0
Online symptom checkers for identifying COVID-19 ^a	2.0
Artificial intelligence (AI)-assisted cough/temperature detector (FluSense) for infectious disease forecasting ^a	1.7

^a Topic has been archived. A description of the topic and the archive reason can be found in the July 2020 *PCORI Health Care Horizon Scanning System: Horizon Scanning COVID-19 Supplement Status Report, Volume 1, Issue 1*.

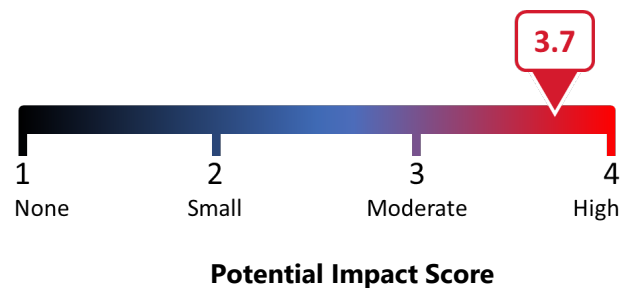
Topic Summaries

We present below 7 summaries on topics deemed to have moderately high to high impact potential. Topics are ordered first in descending order by potential impact score; topics with the same score are listed alphabetically by topic title.

Accula SARS-CoV-2 Point-of-Care Test to Diagnose COVID-19

Potential Impact Score

Stakeholders reviewing this topic thought that the Accula SARS-CoV-2 point-of-care test to diagnose COVID-19 could have a high impact on patient-oriented health care relative to COVID-19 in the United States within the next 12 months.



Highlights

- The Accula SARS-CoV-2 test uses a process called polymerase chain reaction (PCR) to detect coronavirus nucleic acids (ie, building blocks of RNA and DNA) in a patient sample to diagnose COVID-19.
- The test is intended for point-of-care testing, with results in about 30 minutes from nasal and throat swabs (compared with standard nasopharyngeal swabs), and might be used in temporary screening facilities, ambulatory care facilities, and long-term care facilities.
- FDA granted the Accula SARS-CoV-2 test Emergency Use Authorization (EUA) in March 2020, with amendments added in August 2020.
- Stakeholders commenting on this topic thought that, if Accula SARS-CoV-2 is accurate for detecting the coronavirus, it could help reduce the spread of coronavirus by informing infected patients of their need to self-isolate.

Description

The Accula SARS-CoV-2 test is a PCR assay (ie, test) developed by Mesa Biotech, Inc (San Diego, California), as a point-of-care COVID-19 test.¹³ The test is intended to be used at temporary screening facilities, ambulatory care facilities, and long-term care facilities.

The Accula system consists of a single-use cassette that contains chemicals needed to detect viral nucleic acids. A nasal or throat swab sample is added into the cassette, which is then placed in the Accula Dock. The dock is a palm-sized device that controls chemical reaction temperatures, timing, and fluid movement within the cassette. When the chemical reaction is complete, the device displays the test result indicating whether viral nucleic acids have been detected.^{13,14}

The manufacturer claims that the Accula system yields laboratory-quality results in about 30 minutes.¹³ It is intended to complement central laboratories, where most current testing is performed. In March 2020, FDA granted the Accula SARS-CoV-2 test EUA.¹⁵ In August 2020, FDA amended the test's EUA to include nasal swabs as an authorized sample, updated swab types acceptable for use, and added new data on the test's performance.¹⁶

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 the Stanford Health Care Clinical Virology Laboratory (Palo Alto, California). The Accula SARS-CoV-2 test had a sensitivity of 68% and a specificity of 100%.¹⁴ The test's performance was also evaluated using 30 negative samples and 30 positive samples (negative samples spiked with different concentrations of coronavirus nucleic acids). The test showed a 100% agreement with expected results.¹⁷

Possible Areas of Impact

- Health care costs
- Health care delivery
- Patient outcomes
- Population health

Possible Future Impacts

Compared with nucleic acid–based tests performed in central laboratories, which are considered the standard of care to diagnose COVID-19, using Accula SARS-CoV-2 as a point-of-care test might allow health centers to diagnose COVID-19 soon after a symptomatic patient arrives at a health center.¹⁸ With results being available in about 30 minutes, the test might help reduce the spread of the disease because it could significantly improve triage times for infected and uninfected patients.¹⁹

The daily volume of COVID-19 cases in the United States has left many central laboratories with a backlog of samples that need to be tested.²⁰ The use of Accula SARS-CoV-2 in the point-of-care setting has potential to decrease the testing burden at central laboratories and reduce testing costs. Until effective treatments and vaccines against COVID-19 are available, the primary methods to reduce the spread of the disease are face masks, social distancing, testing, and contact tracing. Diagnostic tests are extremely important for containing the disease because they enable the implementation of control measures that limit COVID-19 spread: case identification, isolation, and contact tracing. Accula SARS-CoV-2 might also have affect COVID-19 screening of the general population.²¹

Key Stakeholder Perspectives

Between May 28, 2020, and May 29, 2020, six ECRI stakeholders, reflecting allied health, clinical engineering, health systems, nursing, and research perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

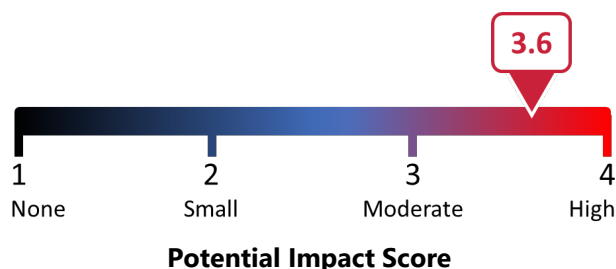
- The Accula SARS-CoV-2 test might address an unmet need for testing in settings other than central laboratories.
- Because the test provides results within 30 minutes, if accurate, it might reduce the prevalence of COVID-19 in the population by quickly identifying infected individuals, allowing isolation and contact tracing to begin.
- The test might also be ideal for screening asymptomatic service personnel who work with the elderly. These personnel pose a high risk for spreading COVID-19 among vulnerable populations.

- Concerns exist regarding the test's accuracy; they are based on a study reporting a sensitivity of 68%, which can lead to false-negative results and decrease the test's usefulness for screening asymptomatic people before they return to work or school.

CoviTact Point-of-Care Protease Assay to Diagnose COVID-19

Potential Impact Score

Stakeholders reviewing this topic thought that the CoviTact point-of-care assay for diagnosing COVID-19 could have a moderately high to high impact on patient-oriented health care relative to COVID-19 in the United States within the next 12 months.



Highlights

- CoviTact is a test that measures the enzymatic activity of the coronavirus main protease (ie, an enzyme the coronavirus uses to break down proteins) to diagnose COVID-19.
- CoviTact is designed to detect low levels of coronavirus from a patient saliva sample or nasal swab, purportedly 30 seconds after testing the sample.
- CoviTact is a point-of-care test intended to help providers diagnose COVID-19 soon after a patient arrives at a health center.
- Stakeholders commenting on this topic thought that, if CoviTact works well as a point-of-care test, it could help reduce the spread of COVID-19 by encouraging patients who test positive to self-isolate to prevent spreading the virus to other people; more accuracy data are needed to assess CoviTact's reliability for diagnosing COVID-19.

Description

CoviTact is a protease assay developed by ViroTact BV (Groningen, the Netherlands), a subsidiary of Detact Diagnostics BV (Groningen, the Netherlands).²² It is intended for point-of-care COVID-19 testing at temporary screening facilities, ambulatory care facilities, and long-term care facilities. CoviTact consists of a short peptide (ie, a string of amino acids, which are protein building blocks) bound to a near-infrared light (NIRL)-emitting molecule and a quencher molecule that absorbs NIRL.^{22,23} The peptide contains a specific amino acid sequence that is recognized and cleaved only by the coronavirus main protease.^{22,24}

Once the protease cleaves the peptide and the NIRL-emitting molecule is no longer close to the quencher molecule, the NIRL can be detected using a fluorimeter, a device designed to measure various wavelengths of light.²² The manufacturer claims that CoviTact can detect low levels of coronavirus in saliva samples, nasal swab samples, and possibly other infectious body fluids and can confirm COVID-19 cases, within 30 seconds of performing the test, in a highly specific way.²³

Possible Areas of Impact

- Health care costs
- Health care delivery
- Population health
- Patient outcomes

Possible Future Impacts

Nucleic acid–based tests performed in central laboratories are considered the current standard of care to diagnose COVID-19. However, it takes several days for laboratories to return test results to health care providers and their patients.^{18,19} CoviTact might enable health care providers to detect very low levels of coronavirus in test samples within minutes.

CoviTact has potential to improve patient outcomes because it might decrease triage time for infected and uninfected patients. CoviTact might also contribute to population health by providing real-time patient management and infection control decisions. Compared with standard of care tests performed in central laboratories, CoviTact is expected to cost less and provide test results sooner.

Until effective therapies become available, increased testing will be crucial for safely reopening businesses and schools.²¹ If CoviTact is implemented to screen for COVID-19 in the general population, it has potential to help identify uninfected individuals who can safely return to work or school and infected individuals who should self-isolate before having contact with other people.

Key Stakeholder Perspectives

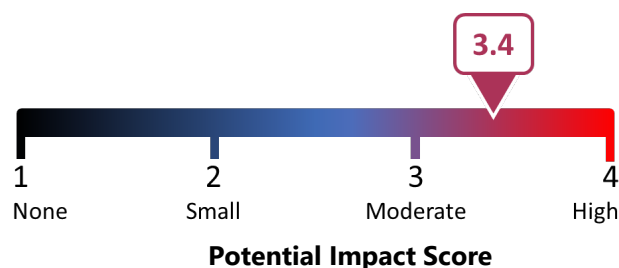
Between May 27, 2020, and June 2, 2020, five ECRI stakeholders, reflecting clinical engineering, health systems, nursing, and research perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- Point-of-care tests, such as CoviTact, are critical to helping reduce the spread of COVID-19.
- Implementing CoviTact for clinical use might impact population health by enabling increased testing, contact tracing, and isolation of positive cases.
- Without accuracy data (ie, sensitivity and specificity), it is challenging to assess CoviTact's reliability for diagnosing COVID-19.
- Besides testing in a clinical setting, CoviTact might also enable widespread screening for COVID-19 in the general population as towns and cities open up activities and businesses.

Next-Generation Sequencing Assays to Diagnose COVID-19

Potential Impact Score

Stakeholders reviewing this topic thought that next-generation sequencing assays to diagnose COVID-19 could have a moderately high impact on patient-oriented health care relative to COVID-19 in the United States within the next 12 months.



Highlights

- Next-generation sequencing (NGS) assays use deep sequencing and computational methods to diagnose COVID-19, distinguish between different infectious diseases, and enable tracking the spread of the coronavirus as well as screening of the general population for coronavirus exposure.
- NGS assays can purportedly test between 2000 and 3000 samples simultaneously. They may be performed only at laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA).
- FDA has granted Emergency Use Authorization (EUA) to 2 NGS assays. The agency is also evaluating additional assays.
- Stakeholders commenting on this topic thought that implementing NGS testing might help guide patient management and decrease the burden of central laboratories with a backlog of patient samples.

Description

Several NGS assays have been developed to diagnose COVID-19, including COVIDseq (Illumina, Inc, San Diego California),²⁵ CleanPlex SARS-CoV-2 (Paragon Genomics, Inc, Hayward, California),²⁶ COVID-19 NGS test (Fulgent Genetics, Inc, Temple City, California),²⁷ and Helix COVID-19 NGS test (Helix OpCo, LLC, San Mateo, California).²⁸ The potential impacts of these NGS assays were evaluated by stakeholders as a single topic because they use similar methods and are expected to yield relatively indistinguishable results. These tests may be performed only at CLIA-certified laboratories, including central laboratories and some laboratories at hospitals, research institutions, and academic institutions.

These assays employ deep sequencing (ie, a genetic sequencing technique that requires only a very small sample) and computational methods to detect nucleic acids of the coronavirus. Tests can amplify and detect sequences from the whole viral genome (ie, a string of about 30 000 nucleic acids) or several genomic regions. NGS assays purportedly offer high throughput, enabling 2000 to 3000 samples to be processed in about 12 hours, with accuracy comparable to that of standard PCR tests.²⁵⁻²⁸ These assays might also be used in epidemiology studies to track the spread of coronavirus or to screen individuals who are planning to return to work or school.²⁹

FDA has granted EUA to the COVIDseq and Helix COVID-19 NGS tests and is in the process of evaluating other NGS assays.^{30,31}

Possible Areas of Impact

- Health care delivery
- Health care disparities
- Health care costs
- Patient outcomes
- Population health

Possible Future Impacts

Nucleic acid–based tests performed in central laboratories are considered the standard of care to diagnose COVID-19. However, the daily increase in COVID-19 cases in the United States is causing many laboratories to have a backlog of samples and to run out of testing supplies.^{18,20} With some NGS platforms able to test between 2000 and 3000 samples within 12 hours, these tests have potential to decrease the testing burden at central laboratories. Implementing NGS testing also has potential to simultaneously identify multiple infectious agents in a single patient sample and exclude suspected infectious agents.³²

On average, the coronavirus accumulates about 2 variations in its nucleic acid sequence per month.²⁹ NGS has potential to help scientists investigate variation in the coronavirus during transmission and track the spread of the virus.³² Because NGS testing is available only at limited CLIA-certified laboratories, patient access to these tests might be restricted. NGS testing is also likely to increase health care costs because it requires expensive equipment and specialized personnel to operate the equipment and analyze data.³²

Key Stakeholder Perspectives

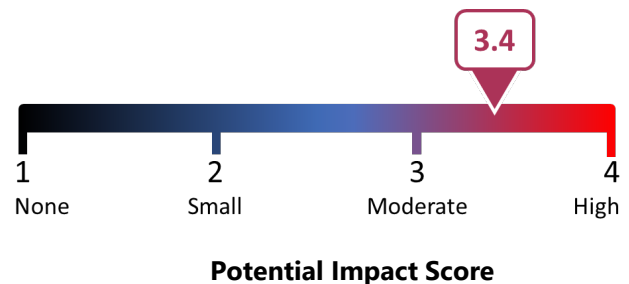
Between July 24, 2020, and July 29, 2020, five ECRI stakeholders, reflecting health care generalist, nursing, physician, and research perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- NGS testing might ease the burden on laboratories that are experiencing testing delays or shortages of testing supplies and have a backlog of untested patient samples.
- Implementing NGS testing might help guide patient management, because testing will enable clinicians to distinguish between infected and uninfected patients, isolate COVID-19 cases, and identify patients with noncoronavirus infections.
- NGS testing enables large-scale testing, which might improve public health efforts to contain COVID-19 spread by confirming COVID-19 cases, detecting variants in nucleic acid sequences, and identifying transmission patterns.
- Concerns exist regarding the possibility of a high rate of false-positive results and delaying factors, such as sample transportation and testing in large batches, which might hinder the reliability of NGS testing for diagnosing COVID-19.

Population-Wide Antibody Testing to Quantify Coronavirus Infection Rates

Potential Impact Score

Stakeholders reviewing this topic thought that population-wide antibody testing to quantify coronavirus infection rates could have a moderately high impact on patient-oriented health care relative to COVID-19 in the United States within the next 12 months.



Highlights

- Population-wide antibody testing could enable public health agencies to quantify the prevalence of coronavirus and inform public health policies.
- The US Centers for Disease Control and Prevention (CDC) and the US National Institutes of Health (NIH) are conducting population-wide antibody studies using samples from volunteer blood donors to better understand immune responses to the novel coronavirus at different points in time, locations, and populations in the United States.
- Stakeholders commenting on this topic thought that widespread serology testing might help public health professionals understand the spread of coronavirus; however, incorrect interpretation of negative test results could lead to further spread of COVID-19 if people stop following public health guidances (eg, wearing masks, social distancing).
- Stakeholders also raised legal, privacy, and security concerns if coronavirus antibody test results are used to influence policies such as employment, travel, and so on.

Description

The COVID-19 pandemic has caused substantial public health and economic crises that make testing for the prevalence of coronavirus infection, as well as potential immunity, critical to measure the spread of the disease. Medicare beneficiaries who may be at greater risk of serious COVID-19 can get an antibody test at no cost.³³ Testing for coronavirus-specific antibodies in the blood of individuals has potential to serve as a population health screening tool to identify persons who have been exposed to the virus regardless of whether they developed symptoms, and widespread serosurveys have potential to provide data on the extent of COVID-19 spread. However, ECRI recommends against using results from antibody testing for “immunity passports” or to provide assurance against future reinfection.^{34,35}

The CDC is conducting a country-wide COVID-19 study that plans to test blood samples of up to 325 000 donors in 25 selected cities over the course of 18 months.³⁶ Preliminary results reporting the rates of coronavirus antibody positivity (ie seroprevalence) from 10 states ranged from 1.0% in the San Francisco Bay Area to 6.9% in the New York City metro area.³⁷ A nonprofit blood service provider, Vitalant, has partnered with the CDC and the NIH to collect samples for this serologic study.³⁸ The NIH also launched a similar study of 15 000 participants with no known coronavirus infection or exposure. The NIH is collecting blood samples from employee volunteers at its Bethesda campus and using at-home blood collection kits developed by Neoteryx (Torrance, California) from other volunteers.³⁹

Possible Areas of Impact

- Clinician and/or caregiver safety
- Health care costs
- Health care delivery and process
- Health care disparities
- Population health
- Patient outcomes

Possible Future Impacts

Widespread antibody testing might clarify actual infection rates and help more accurately track the spread of the coronavirus. However, it might misinform public health guidance if the tests generate high levels of false-positive or false-negative results. False-negative results might lead people to think that they no longer require masks or need to conform to other public health guidance, which might increase infection rates. The COVID-19 antibody testing studies might misrepresent true infection rates by depending on blood donors, who are disproportionately healthy and may not be the ideal population in which to evaluate the spread of the coronavirus infection.

Key Stakeholder Perspectives

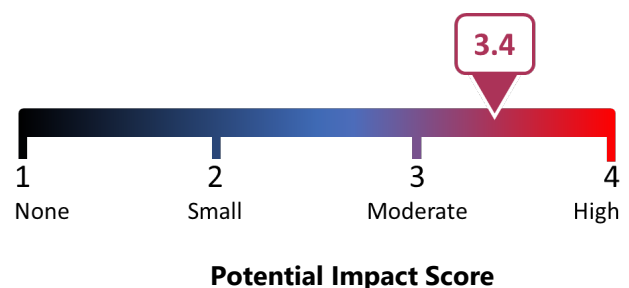
Between June 25, 2020, and July 6, 2020, five ECRI stakeholders, reflecting health care generalist, health systems, nursing, and research perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- Serology tests could provide useful information about the spread of COVID-19 and how long the antibodies prevent reinfection.
- Widespread testing might guide reopening policies and procedures, which might help boost the economy and reduce stress and anxiety in people.
- Because both symptomatic and asymptomatic individuals can spread coronavirus, reliable and accurate tests are needed to guide suitable public health infection prevention policies.
- Population-wide testing might increase legal, privacy, and security concerns if test results influence travel restrictions or if employment decisions affect specific individuals in the population.

Rapid Point-of-Care Breath Test to Detect COVID-19

Potential Impact Score

Stakeholders reviewing this topic thought that a rapid point-of-care breath test to detect COVID-19 could have a moderately high impact on patient-oriented health care relative to COVID-19 in the United States within the next 12 months.



Highlights

- A point-of-care test for detecting coronavirus in breath samples, based on the detection of viral particles using terahertz spectroscopy, is being developed by researchers at Ben-Gurion University of the Negev in Israel.
- The test purportedly takes less than a minute to perform, and initial studies demonstrated about 90% concordance with results generated by gold-standard nucleic acid testing.
- Test developers have indicated that the test could be commercially available as early as fall 2020.
- Stakeholders commenting on this topic thought that an accurate point-of-care breath test for detecting the coronavirus could help reduce the spread of coronavirus by informing infected patients of their need to self-isolate.

Description

Researchers at Ben-Gurion University of the Negev (Beer-Sheva, Israel) are developing a point-of-care test that purportedly detects COVID-19 in breath samples from both symptomatic and asymptomatic carriers in less than 1 minute.⁴⁰ The test is intended to detect electroacoustic properties specific to coronavirus viral particles using terahertz spectroscopy, which has been proposed as a technology capable of detecting various microbial agents.^{41,42}

To test for COVID-19, a subject breathes into a whistle-like tube that holds a removable capsule with an electronic chip containing thousands of electro-optical sensors. After breath sample collection, the capsule is placed in a small spectrometer connected to a laptop computer that transmits data for cloud-based analysis. Results are automatically recorded into a database that public health authorities can use to track viral spread. In preliminary tests, the breath test matched polymerase chain reaction–based swab test results in more than 90% of tests performed. Researchers estimate that test kits will cost between \$50 and \$100 and could be commercially available by fall 2020.^{40,43}

Coronavirus breath tests using various alternative detection methods are also under study by other research groups. Approaches include detection of COVID-19-specific metabolic profiles⁴⁴⁻⁴⁷ and direct detection of viral nucleic acid or protein.^{48,49}

Possible Areas of Impact

- Health care costs
- Health care delivery
- Patient outcomes
- Population health

Possible Future Impacts

A point-of-care breath test for coronavirus infection might allow for a testing regimen that incorporates more frequent testing as well as decreased turnaround time for results, potentially improving on 2 shortcomings of existing diagnostic testing. If deployed in community settings such as schools, nursing homes, and airports, it might more rapidly identify potentially infectious individuals, allowing their quarantine and disrupting coronavirus spread. However, given the early developmental status of the technology, questions remain regarding its accuracy in

detecting coronavirus and the ability of developers to scale it to the extent needed for widespread deployment.

Key Stakeholder Perspectives

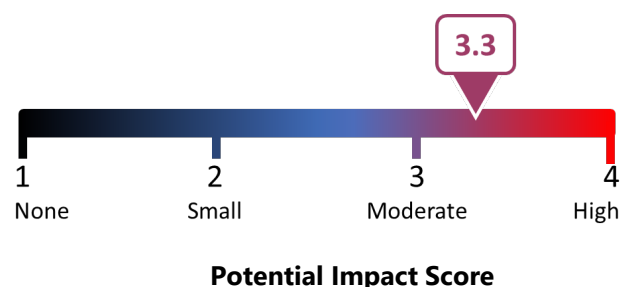
Between July 21, 2020, and July 29, 2020, nine ECRI stakeholders, reflecting allied health, clinical engineering, health systems, health care generalist, nursing, physician, and research perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- The rapidity and ease of testing provided by a point-of-care breath test could have a substantial impact on coronavirus testing. Such a test could facilitate testing patients scheduled for inpatient procedures at health care facilities, provide a means of widespread disease surveillance, reduce the testing volume at central laboratories, and provide a test with potential to be used in community settings. These effects would be possible only if the system is shown to work and can be made widely available.
- The accuracy of the detection method is uncertain. For example, individuals who have recovered from COVID-19 might continue to produce noninfective viral particles that could be detected as false-positive results by such a system.
- Uploading results for review by public health authorities could raise privacy concerns regarding the implementation of such a system.
- Reported high costs of the test could be prohibitive if the system were to be applied in widespread, frequent testing, potentially inhibiting its uptake and potential impact.

Employee Coronavirus Testing Programs to Reopen Businesses

Potential Impact Score

Stakeholders reviewing this topic thought that employee coronavirus testing programs to reopen businesses could have a moderately high impact on patient-oriented health care relative to COVID-19 in the United States within the next 12 months.



Highlights

- Employee COVID-19 testing programs offered by clinical laboratories are intended to limit coronavirus spread in the workplace, where employees are in close proximity to one another.
- The testing programs incorporate a range of methods, from less reliable (eg, health questionnaires, temperature screening) to more reliable (eg, molecular and/or antibody testing for coronavirus).
- Stakeholders commenting on this topic thought employee testing programs are an important strategy to help mitigate coronavirus spread, but there will inevitably be shortcomings and challenges (eg, false negatives, missed symptoms).
- Stakeholders also agreed that offering widespread testing to employees could be costly and might reduce overall population testing capacity.

Description

Employee COVID-19 testing programs offered by clinical laboratories are intended to limit novel coronavirus spread in the workplace and boost confidence that employees can return to a safe work environment.⁵⁰⁻⁵³ The programs emphasize operating under simple and streamlined conditions that allow COVID-19 cases to be caught early and prevent disease spread. COVID-19 testing programs might incorporate less reliable screening methods, including health questionnaires and temperature screening, or more reliable screening methods requiring sample collection, such as molecular and/or antibody testing either at the employer site or offsite using an at-home self-collection kit. Pilot programs have used tests performed at central laboratories that provide results within 2 to 3 days after receiving the sample.⁵⁴ The employer and employee can access test results through an online platform.

While point-of-care tests offer same-day test results, they are currently not being used because of recent concerns about higher false-positive and false-negative rates compared with central laboratory tests.⁵⁵

Possible Areas of Impact

- Patient outcomes
- Population health
- Health care disparities
- Health care costs

Possible Future Impacts

Employee COVID-19 testing programs might reduce the spread of coronavirus in the workplace and enable employees to feel safer and work more productively; however, they might produce a false sense of safety if shortcomings in their design or execution do not mitigate the risk of coronavirus spread and infection as employees return to the workplace.

Population health might be improved if employee testing programs do not divert testing and timeliness of results away from the general public. However, frequent testing of large groups of employees might be costly to organizations paying for such services. It is unknown how these program costs might compare to potential revenue lost by businesses that otherwise would not reopen or resume normal business operations, or health care costs saved by reducing employee coronavirus infection and disease, such as costs of hospitalization, treatments, and intensive care resources.

Key Stakeholder Perspectives

Between July 1, 2020, and July 6, 2020, six ECRI stakeholders, reflecting health care generalist, health systems, nursing, physician, and research perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- Employee COVID-19 testing programs could help mitigate the spread of coronavirus in the workplace, although these programs might have the most impact when outbreaks are more contained and remote work is still encouraged when possible.
- These testing programs are not perfect and pose many challenges stemming from false-positive and false-negative results, uncertainty and potentially unsafe exposure while test

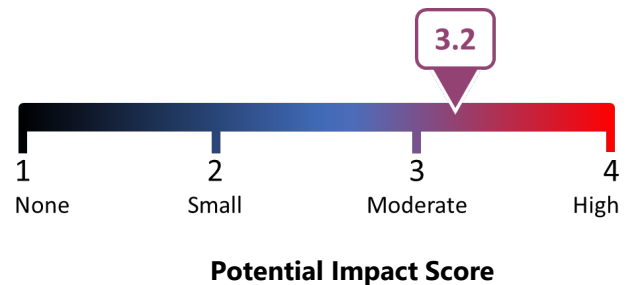
results are pending, difficulties identifying early symptoms of COVID-19, unreliable temperature check results, and incomplete reporting of recent travel/exposure.

- Testing large groups of employees will be expensive and could reduce overall population testing capacity.

QIAstat-Dx Respiratory SARS-CoV-2 Panel Test to Diagnose COVID-19

Potential Impact Score

Stakeholders reviewing this topic thought that the QIAstat-Dx Respiratory SARS-CoV-2 Panel test to diagnose COVID-19 could have a moderately high impact on patient-oriented health care relative to COVID-19 in the United States within the next 12 months.



Highlights

- The QIAstat-Dx Respiratory SARS-CoV-2 Panel is a real-time polymerase chain reaction (RT-PCR) assay to detect coronavirus nucleic acids (ie, building blocks of RNA and DNA) in a patient sample to diagnose COVID-19.
- The test is performed in a laboratory certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA). It provides results in about 1 hour from nasopharyngeal swabs and can differentiate the coronavirus from 20 other respiratory infectious agents.
- FDA granted the QIAstat-Dx test Emergency Use Authorization (EUA) in March 2020.
- Stakeholders commenting on this topic thought that QIAstat-Dx has potential to accurately diagnose COVID-19 and distinguish it from other respiratory infections and, therefore, to help reduce the spread of the disease by informing infected patients of their need to self-isolate.

Description

The QIAstat-Dx Respiratory SARS-CoV-2 Panel is an RT-PCR assay developed by Qiagen, NV (Hilden, Germany), to diagnose COVID-19 and differentiate it from 20 other causes of respiratory infection. The test is authorized to be used in CLIA-certified laboratories, which include central laboratories and others located in hospitals, health centers, and research institutions.⁵⁶

The panel consists of a single-use cartridge that includes all the chemicals needed for nucleic acid extraction, nucleic acid amplification, and detection of 3 bacteria and 18 viruses, including coronavirus, that cause respiratory symptoms. A nasopharyngeal swab sample is added into the cartridge, which is then placed in the QIAstat-Dx Analyzer 1.0. The RT-PCR assay should be performed only by laboratory professionals trained in the use of the QIAstat-Dx Analyzer 1.0. When the amplification reaction is complete, the test result indicating whether viral nucleic acids have been detected is displayed on the analyzer's screen.^{56,57}

The manufacturer claims that QIAstat-Dx requires a small sample volume and minimal hands-on time to yield accurate results in approximately 1 hour.⁵⁶ In March 2020, FDA granted the QIAstat-Dx Respiratory SARS-CoV-2 Panel EUA.^{58,59}

A published study evaluated the performance of the panel in 69 samples previously tested by an RT-PCR test recommended by the World Health Organization (Geneva, Switzerland). QIAstat-Dx had a sensitivity of 100%, a specificity of 93%, and an overall agreement of 97%.⁵⁷ Another study reported that, while variations in the nucleic acid sequence of the coronavirus decrease the accuracy of some standard of care tests, they do not decrease the performance of QIAstat-Dx.⁶⁰

Possible Areas of Impact

- Health care delivery
- Health care costs
- Health care disparities
- Patient outcomes
- Population health

Possible Future Impacts

Nucleic acid–based tests performed in central laboratories are considered the standard of care to diagnose COVID-19. However, most tests take between 3 and 6 hours to provide test results, a process that is further limited by transporting samples to the laboratory and having to test samples in large batches.¹⁸ This delay increases the risk of patients transmitting COVID-19 to other individuals. Because the QIAstat-Dx test can be performed in laboratories at some hospitals and health centers and provide results in about 1 hour, it might help clinicians triage infected and uninfected patients and reduce the spread of COVID-19.^{56,57,59}

As the COVID-19 pandemic continues, it will overlap with the flu season, caused by an influenza virus. Both COVID-19 and influenza initially manifest with similar respiratory symptoms, but patient management depends on which virus is causing the disease.¹⁸ QIAstat-Dx might help clinicians determine whether symptoms are caused by the coronavirus or a different infectious agent.^{56,57} Testing with a panel might also cost less than individually testing for each infectious agent.⁵⁷

Key Stakeholder Perspectives

Between June 1, 2020, and June 10, 2020, five ECRI stakeholders, reflecting health systems, nursing, and physician perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- Because the QIAstat-Dx test is performed in a CLIA-certified laboratory within an hour, it has potential to help clinicians reduce the spread of coronavirus by distinguishing between infected and noninfected individuals.
- QIAstat-Dx also has potential to help clinicians determine whether a symptomatic patient has COVID-19 or another respiratory infection. This will be particularly helpful during the flu season because patient management will be guided according to whether the test detects the coronavirus or an influenza virus.

-
- Unlike several point-of-care tests that have not had their performance fully validated, the QIAstat-Dx test is performed in a CLIA-certified laboratory, where it is more likely to undergo quality control to deliver accurate results.
 - Because some health centers do not have CLIA-certified laboratories, there are concerns that having to send patient samples to be tested at a central laboratory will increase the time for confirming a COVID-19 diagnosis, which may delay isolation and contact tracing practices.

Chapter 4. Systems and Management

Chapter Summary

As of July 30, 2020, we were monitoring 10 COVID-19-related systems and management topics. Eight of these topics are listed in the July 2020 *PCORI Health Care Horizon Scanning System: Horizon Scanning COVID-19 Supplement Status Report, Volume 1, Issue 1*. The remaining 2 topics will be listed in the October 2020 edition of the *COVID-19 Supplement Status Report*. All 10 topics were sent for comment to internal ECRI stakeholders, and each received at least 5 sets of ratings and comments from stakeholders between May 18, 2020, and July 29, 2020.

Topics Considered for Inclusion in This Report

Table 4.1 lists 3 topics selected for inclusion in this High Impact Report. Included topics received, on average, moderately high to high impact ratings and demonstrated high consensus among stakeholders, as evident in the ratings and comments. Topics are ordered first in descending order by potential impact score and second in ascending order alphabetically by topic title.

Table 4.1. Included Systems and Management Topics

Topic title	Potential impact score
Statewide surge line for patient load management during the coronavirus epidemic	3.8
Contact tracing software systems to mitigate coronavirus epidemic scenarios	3.7
Rapid expansion of telemedicine driven by widespread COVID-19 response	3.6

Table 4.2 lists 7 topics considered, but not selected, for inclusion in this High Impact Report. Excluded topics received, on average, low to moderate impact ratings and were not considered by most stakeholder reviewers to have high impact potential. Topics are ordered first in descending order by potential impact score; topics with the same score are listed alphabetically by topic title.

Table 4.2. Systems and Management Topics Considered but Not Included

Topic title	Potential impact score
Artificial intelligence (AI)–assisted radiographic image assessment for determining COVID-19 prognosis	3.2
Drive-through prenatal care model	3.1
3D-printed face shields to protect against COVID-19 infection	3.0
Machine learning to predict the spread of COVID-19	3.0
Expanded availability of digital health therapeutic devices for psychiatric conditions during COVID-19 public health emergency ^a	2.7
Disinfecting spray (Clyraguard) to prevent personal protective equipment (PPE) contamination ^a	2.6
Immunity certification to set public health directives for individuals previously infected with SARS-CoV-2	2.2

^a Topic was archived. A description of the topic and the archive reason can be found in the July 2020 *PCORI Health Care Horizon Scanning System: Horizon Scanning COVID-19 Supplement Status Report, Volume 1, Issue 1*.

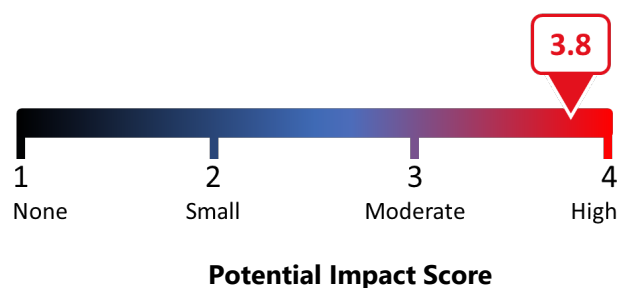
Topic Summaries

We present below 3 summaries on topics deemed to have moderately high to high impact potential. Topics are ordered first in descending order by potential impact score; topics with the same score are listed alphabetically by topic title.

Statewide Surge Line for Patient Load Management During the Coronavirus Pandemic

Potential Impact Score

Stakeholders reviewing this topic thought that the statewide surge line for patient load management could have a high impact on patient-oriented health care relative to COVID-19 in the United States within the next 12 months.



Highlights

- A statewide patient load balancing system (ie, a surge line), such as the Arizona Surge Line, can facilitate interfacility transfer of critically ill patients with presumed or confirmed COVID-19.
- The Arizona system comprises a 24/7 toll-free call line with transfer agents who review critical care availability for each hospital in the state and transfer calls to a site with appropriate bed and ventilator capacity. It might also assist with effectively distributing new staffing placements from out of state.

- Public health authorities might use the knowledge acquired from implementing these strategies to enhance statewide emergency protocols in the future.
- Stakeholders commenting on this topic thought that the surge line system had potential to significantly improve patient load management in hospitals.
- Stakeholders also thought that some transfers might not be covered by insurance, which could prevent optimal use of the system and increase costs of care for some patients.

Description

The Arizona Department of Health Services (ADHS) has launched a statewide patient load balancing system (ie, surge line) to help with transferring patients between facilities during the COVID-19 public health emergency.⁶¹ ADHS hopes that the system will help accommodate potential surges in the number of COVID-19 cases, which have led some hospitals to cancel or postpone elective procedures.⁶²

The Arizona Surge Line is a 24/7 toll-free call line for health care providers. For each call, a surge line transfer agent reviews critical care availability for each hospital in the state and transfers the call to the appropriate destination, thereby assisting with interfacility transfer of patients with presumed or confirmed COVID-19 or transfer of patients to postacute care facilities.⁶¹ It can assist with effectively distributing new staffing placements from out of state.⁶³ The surge line may also provide clinical consultation if a transfer is declined or delayed.⁶¹

The Oregon Health Authority has also developed a statewide hospital capacity system using a real-time data-tracking tool to efficiently manage the surge in COVID-19 patients.⁶⁴ These efforts might encourage 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.

Possible Areas of Impact

- Clinician and/or caregiver safety
- Health care costs
- Health care delivery and process
- Health care disparities
- Patient outcomes
- Population health

Possible Future Impacts

A statewide surge line might help optimize interfacility transfer of presumed or confirmed COVID-19 patients and could enable health care staff to manage time more effectively by reducing time to find the right level of care for their patients. These systems might also lead to improved patient outcomes if patients are able to receive appropriate care in a timely manner.

Key Stakeholder Perspectives

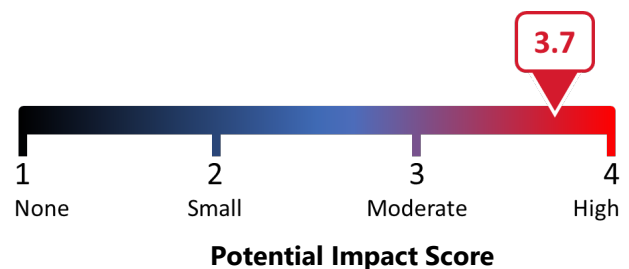
Between May 28, 2020, and May 29, 2020, five ECRI stakeholders, reflecting allied health, health systems, nursing, and research perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- Surge line systems could significantly improve patient load management in hospitals, streamline critical care operations, and enable effective coordination and resource management among hospitals.
- A statewide surge line system would support timely care of COVID-19 patients in critical condition and could therefore improve patient outcomes and reduce risks of death.
- Patient transport to other facilities might increase health risk for some patients who are already coping with COVID-19 and increase infection risks to others during the transfer.
- Interfacility transfer might increase financial burden on families because of insurance coverage restrictions and transportation costs, which might prevent patients from getting appropriate care in a timely manner.

Contact Tracing Software Systems to Mitigate Coronavirus Epidemic Scenarios

Potential Impact Score

Stakeholders reviewing this topic thought that contact tracing software systems to mitigate coronavirus epidemic scenarios could have a high impact on patient-oriented health care relative to COVID-19 in the United States within the next 12 months.



Highlights

- Contact tracing software systems using Bluetooth- or location service-enabled devices (eg, smartphones) can track proximity between people, notify someone who was near an infected person, and provide advice on what to do next.
- These systems require users to opt in and report a COVID-19 diagnosis, allowing for contact tracing and data access to public health systems.
- Public health authorities might use data from these systems to track the spread of coronavirus or provide advice to individuals on next steps (eg testing or isolation).
- Stakeholders commenting on this topic thought contact tracing software systems might help significantly reduce transmission of coronavirus; however, they noted data security and privacy concerns, which might discourage some individuals from using the systems.

Description

Contact tracing enables public health agencies to identify, evaluate, and monitor individuals who may have been exposed to coronavirus.⁶⁵ Although many public health organizations use manual contact tracing processes (eg, individuals making phone calls), software developers are collaborating to create contact tracing tools that can inform governments and public health agencies about the spread of coronavirus and help individuals know if they have been near an infected person.

Apple and Google have launched exposure notification systems using Bluetooth-enabled devices (eg, smartphones) to track physical proximity between people.⁶⁶ Users can opt to report a

COVID-19 diagnosis, thereby allowing for efficient contact tracing by alerting users whose devices come near their own. Additionally, access to the data can be granted to public health systems, which can provide advice on next steps for potentially exposed users.⁶⁶ The wireless networking company EnGenius Technologies has developed a new feature for its cloud platform that uses Wi-Fi to detect proximity of user devices.⁶⁷ The state governments of North Dakota, South Dakota, and Utah are already using mobile applications for contact tracing, namely Care19 and Healthy Together, which use Bluetooth and Global Positioning System data to track person-to-person transmission and transmission zones in their states.^{68,69}

Possible Areas of Impact

- Health care delivery and process
- Patient outcomes
- Population health
- Health care disparities

Possible Future Impacts

Contact tracing software systems might help reduce burden on public health organizations that would otherwise manually gather relevant information from individuals. Timely contact tracing might help reduce transmission of the coronavirus and might improve population health outcomes while protecting vulnerable individuals such as older adults and cancer patients. The systems might also help governments and health agencies develop policies to reduce the spread of COVID-19.

Contact tracing might not be enough to reduce transmission if individuals are not taking appropriate safety measures such as getting tested and practicing quarantine. In addition, because the software can alert a user only to a self-identified COVID-19 carrier, overreliance on these software tools could encourage some individuals to engage in unsafe behaviors. A breach of security could lead to violations of personal privacy, unlawful surveillance, or illegal or improper use of personal data and medical information.

Key Stakeholder Perspectives

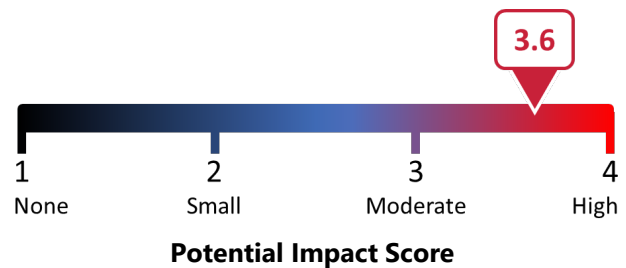
Between May 27, 2020, and May 29, 2020, six ECRI stakeholders, reflecting allied health, health care generalist, information technology, nursing, and research perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- Contact tracing software systems might be an effective strategy to mitigate the spread of coronavirus because data gathered from smartphones could inform public health policies and quarantine measures that could help slow or stop the spread of infection.
- Despite assurances from software developers, significant privacy concerns exist about the potential of data retention for wider surveillance, as well as the potential for intentionally or inadvertently revealing individuals' identities or health status.
- Developers and public health departments should be transparent about all data usage, security risks, and concerns to reassure all stakeholders and promote reporting of COVID-19 diagnoses using software systems.

Rapid Expansion of Telemedicine Driven by Widespread COVID-19 Response

Potential Impact Score

Stakeholders reviewing this topic thought that rapid expansion of telemedicine driven by the widespread COVID-19 response could have a moderately high to high impact on patient-oriented health care relative to COVID-19 in the United States within the next 12 months.



Highlights

- In response to the COVID-19 pandemic, many health care providers have shifted patient encounters for some acute and chronic diseases to a telemedicine environment to avoid risks associated with person-to-person contact.
- Regulators and insurers have modified policies to permit broader telemedicine use during the pandemic. Whether such changes will endure after the pandemic remains uncertain.
- Stakeholders reviewing this topic thought that, although telemedicine demonstrates clear benefits for health care providers and patients during the pandemic, broad telemedicine adoption might have some negative impacts on patient care and might not fill all gaps in care delivery created by the response to the pandemic.
- Stakeholders also noted that many patients who could benefit from telemedicine might lack adequate access to this service due to cost or technical issues, such as lack of high-speed internet, software, or necessary equipment, thereby creating or increasing disparities.

Description

The dramatic, widespread response to the COVID-19 pandemic has disrupted traditional physician-patient encounters across all clinical specialties treating acute and chronic conditions unrelated to COVID-19. Stay-home orders, strict social distancing guidelines, and other measures have prompted many health care providers to implement or expand their use of telemedicine to maintain patient care plans while protecting patients and clinical staff.^{70,71} Telemedicine offers providers and patients multiple ways to hold virtual visits that attempt to compensate for the lack of in-person contact.

In response to the increased need for telemedicine during the pandemic, many regulators and insurers have temporarily loosened regulations and reimbursement restrictions that traditionally limited telemedicine to rural areas with limited access to providers.^{72,73} 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 practice. However, the need to rapidly adopt telemedicine systems can present obstacles to a smooth transition in patient care for providers without telemedicine experience. Some experienced centers have offered guidance for quickly implementing a telemedicine system in clinical practice.⁷⁴ Other experts have noted that the broad expansion of health care information technology (IT) use prompted by the COVID-19 pandemic 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.⁷⁵

Possible Areas of Impact

- Clinician or caregiver safety
- Health care delivery process
- Health care disparities
- Patient outcomes

Possible Future Impacts

Increased telemedicine use might help alleviate care disruptions for patients with non-COVID-19 conditions (eg, heart failure, cancer) for which frequent monitoring is needed to identify changes requiring prompt intervention. Wider telemedicine use might also enable health care providers to remotely monitor patients with mild COVID-19 symptoms without increasing care burden on hospitals treating high volumes of severe cases. Telemedicine could also protect providers and other patients from exposure to asymptomatic, undiagnosed coronavirus carriers. However, rapid telemedicine adoption could present technical and operational obstacles to health care providers without telemedicine experience. Health care disparities could develop or increase because not all patients who could benefit from telemedicine may have access to the required broadband internet or associated home-monitoring technology.

Once the COVID-19 pandemic wanes, stakeholders might evaluate the benefits and risks of widespread telemedicine implementation, potentially shaping its future use. Health care providers might assess which physician-patient interactions can safely continue remotely and which should return to in-person visits. Third-party payers might compare outcomes of in-person and telemedicine-assisted patient management. Surveys of patient satisfaction with telemedicine could also shape policies of regulators, payers, and providers.

Key Stakeholder Perspectives

Between May 21, 2020, and May 29, 2020, eleven ECRI stakeholders, reflecting physician, nursing, research, health care generalist, health systems, and clinical engineering perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- Greater use of telemedicine could improve safety for patients and providers by reducing risks of COVID-19 infection.
- Widespread, rapid adoption of telemedicine might help restore some level of care delivery that the COVID-19 pandemic has disrupted, particularly for chronic health conditions.
- However, video encounters might hinder health care providers from observing subtle clues that patients might not mention or recognize but that could inform treatment decisions, thereby potentially negatively affecting patient outcomes.
- In some instances, the rapid shift toward telemedicine could create or widen disparities in care for patients unable to have telemedicine visits due to technical or socioeconomic barriers to access. The lack of a national health care IT infrastructure could exacerbate such disparities, particularly during lockdown conditions.
- If implemented effectively and widely available to all patients, greater telemedicine use could help shift care delivery to a more patient-centric and less provider-centric model.

Chapter 5. Treatments

Chapter Summary

As of July 30, 2020, we were monitoring 33 COVID-19-related treatment topics. Of these topics, 24 are listed in the July 2020 *PCORI Health Care Horizon Scanning System: Horizon Scanning COVID-19 Supplement Status Report, Volume 1, Issue 1*. The remaining 9 topics will be listed in the October 2020 edition of the *COVID-19 Supplement Status Report*. All 33 topics were sent for comment to internal ECRI stakeholders; 25 received at least 5 sets of ratings and comments from stakeholders between May 18, 2020, and July 29, 2020. The following 8 topics had received fewer than 5 sets of ratings and comments by July 29, 2020, and were not considered for inclusion in this report:

- ANG-3777 to treat patients hospitalized with COVID-19-associated pneumonia
- Auxora to treat severe COVID-19-associated pneumonia
- CYT107 for treating hospitalized patients with COVID-19-related lymphopenia
- Dapagliflozin to reduce risk of complications from mild to moderate COVID-19
- Garadacimab (CSL312) for treating respiratory distress caused by COVID-19
- Opaganib to treat pneumonia associated with COVID-19
- Pamrevlumab for treating hospitalized patients with acute COVID-19
- Sargramostim (Leukine) for treating patients with COVID-19-associated respiratory illness

Topics Considered for Inclusion in This Report

Table 5.1 lists 5 topics selected for inclusion in this High Impact Report. Included topics received, on average, moderately high to high impact ratings and demonstrated high consensus among stakeholders, as evident in their ratings and comments. Topics are ordered first in descending order by potential impact score; topics with the same score are listed alphabetically by topic title.

Table 5.1. Included Treatment Topics

Topic title	Potential impact score
Dexamethasone for treating severe COVID-19	3.6
Anakinra (Kineret) for treating COVID-19 with acute respiratory distress syndrome and hyperinflammation	3.4
Remdesivir (Veklury) for treating COVID-19	3.4
Convalescent plasma for treating COVID-19	3.3
TD-0903 for treating acute lung injury in patients with COVID-19	3.2

Table 5.2 lists 20 topics considered, but not selected, for inclusion in this High Impact Report. Excluded topics received, on average, low to moderate impact ratings and were not considered by most stakeholder reviewers to have high impact potential. Topics are ordered first in descending order by potential impact score; topics with the same score are listed alphabetically by topic title.

Table 5.2. Treatment Topics Considered but Not Included

Topic title	Potential impact score
Canakinumab [Ilaris] for treating COVID-19 ^a	3.4
RLF-100 (aviptadil) for treating COVID-19-induced nonacute lung injury and acute respiratory distress syndrome ^a	3.3
Anti-GM-CSF monoclonal antibodies for treating COVID-19 ^a	3.2
Dociparstat for treating COVID-19 ^a	3.2
Losartan for treating COVID-19 ^a	3.2
Proteomics to identify human protein targets for treating COVID-19 ^a	3.2
Anti-interleukin-6 monoclonal antibodies for treating hospitalized patients in respiratory distress	3.1
Tranexamic acid for treating COVID-19	3.1
EIDD-2801 for treating COVID-19	3.0
Leronlimab for treating COVID-19	3.0
Lowering testosterone levels to treat COVID-19 infection	3.0
Monoclonal antibodies targeting coronavirus spike protein receptor binding domain for treating COVID-19	3.0
Baricitinib (Olumiant) for treating COVID-19	2.8
Bruton's tyrosine kinase inhibitors for treating COVID-19 ^b	2.8
Tissue plasminogen activator for treating COVID-19 ^b	2.8
Chloroquine/hydroxychloroquine for treating COVID-19 ^b	2.7
Anti-C5 monoclonal antibodies for treating COVID-19 ^b	2.6
Ruxolitinib (Jakafi) for treating COVID-19 ^b	2.6
Famotidine (Pepcid) for treating COVID-19 ^b	2.3
Lopinavir/ritonavir for treating COVID-19 ^b	1.8

^a Although this topic received a moderately high impact score, it was not included because stakeholders agreed that it would not likely have an impact in the next 12 months. This topic will be reconsidered for the next report.

^b Topic has been archived. A description of the topic and the archive reason can be found in the July 2020 *PCORI Health Care Horizon Scanning System: Horizon Scanning COVID-19 Supplement Status Report, Volume 1, Issue 1*.

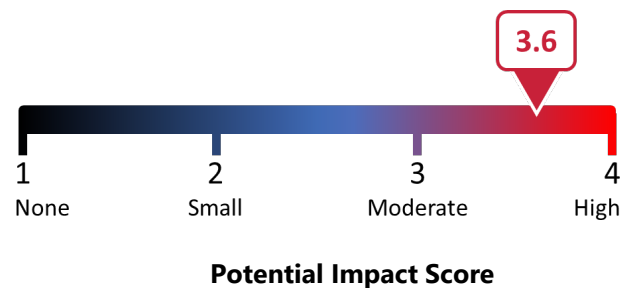
Topic Summaries

We present below 5 summaries on topics deemed to have moderately high to high impact potential. Topics are ordered first in descending order by potential impact score; topics with the same score are listed alphabetically by topic title.

Dexamethasone for Treating Severe COVID-19

Potential Impact Score

Stakeholders reviewing this topic thought that dexamethasone for treating severe COVID-19 could have a moderately high to high impact on patient-oriented health care relative to COVID-19 in the United States within the next 12 months.



Highlights

- Dexamethasone is a corticosteroid, given orally or intravenously, that is intended to reduce inflammation in patients with severe COVID-19.
- Clinical trial data suggest it can lower risk of death in patients who require mechanical ventilation and, to a lesser degree, in patients who require supplemental oxygen.
- Stakeholders commenting on this topic agreed that dexamethasone has potential to reduce risk of death in some patients, slow disease progression, and prevent some intensive care unit (ICU) admissions.

Description

Dexamethasone is a corticosteroid being investigated as an intravenous or oral treatment to reduce inflammation in severe COVID-19. It might be beneficial because an extreme inflammatory condition (hyperinflammation) and cytokine storm are thought to contribute to acute respiratory distress syndrome (ARDS) in patients with COVID-19.⁷⁶ Data were published from a large, randomized, phase 3 clinical trial in the United Kingdom.⁷⁷ In the study, 2104 hospitalized patients with COVID-19 were treated with dexamethasone. Compared with 4321 patients who received standard care, there were one-third fewer deaths in the subset of study participants who were ventilated and a one-fifth decrease in deaths in the subset who received oxygen only; no benefit was seen in the subset that did not require respiratory support.⁷⁸ In the United States, a phase 2 trial of dexamethasone to treat moderate to severe ARDS versus placebo is ongoing, with an estimated primary completion date of December 2020.⁷⁹

Concerns exist regarding the risk of corticosteroid immunosuppression-related coronavirus replication. A brief report published July 22, 2020, on the use of glucocorticoids (a class of corticosteroids) to treat hospitalized patients with COVID-19 suggested that early intervention with glucocorticoids is not associated (positively or negatively) with mortality or the need for mechanical ventilation.⁸⁰ However, the report suggested that glucocorticoids might provide some benefit for patients with markedly elevated levels of a biomarker of inflammation, C-reactive protein (CRP), but could cause harm for those with lower CRP levels.

Based on available clinical trial dosing and pricing information, a course of COVID-19 treatment with dexamethasone will likely cost between \$9 and \$21.⁸¹

Possible Areas of Impact

- Patient outcomes
- Population health
- Health care delivery and process
- Health care costs

Possible Future Impacts

Dexamethasone might reduce risk of death in patients with severe disease requiring mechanical ventilation and supplemental oxygen and might help decrease the need for intensive resources such as mechanical ventilation. In turn, population health outcomes might be improved if better individual patient outcomes translate to lower overall burden on the health care system and fewer supply shortages (eg, masks, ventilators). At an estimated cost of less than \$21 per treatment course, dexamethasone might reduce costs if hospitalization times are shortened and fewer intensive care resources are needed.

Key Stakeholder Perspectives

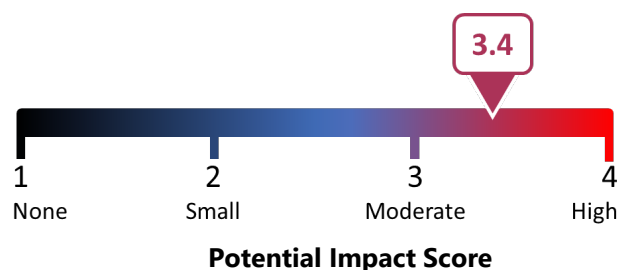
Between June 18, 2020, and June 23, 2020, five ECRI stakeholders, reflecting allied health, health care generalist, nursing, and research perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- Dexamethasone shows promise in treatment of patients with severe COVID-19.
- The drug might significantly reduce risk of death in patients with severe respiratory symptoms; it might also slow disease progression and reduce ICU admissions.
- Dexamethasone is a relatively inexpensive, widely available drug used to treat inflammation.
- More data are needed to define which patients might benefit most from treatment with dexamethasone and to determine whether it might increase viral load or cause adverse events.

Anakinra (Kineret) for Treating COVID-19 With Acute Respiratory Distress Syndrome and Hyperinflammation

Potential Impact Score

Stakeholders reviewing this topic thought that anakinra (Kineret) for treating COVID-19 with acute respiratory distress syndrome and hyperinflammation could have a moderately high impact on patient-oriented health care relative to COVID-19 in the United States within the next 12 months.



Highlights

- Anakinra is an interleukin 1 (IL-1) receptor antagonist that is FDA approved for treating rheumatoid arthritis and is being repurposed for treating COVID-19.
- IL-1 can cause a systemic inflammatory response to coronavirus that can lead to poor outcomes or death; therefore, blocking the action of IL-1 might lead to better outcomes in patients with COVID-19.
- Initial retrospective studies suggest that anakinra treatment might improve clinical outcomes for patients with hyperinflammatory respiratory failure related to COVID-19; randomized controlled trials (RCTs) to confirm these benefits are ongoing.
- Stakeholders commenting on this topic thought that initial results for anakinra to treat COVID-19 were promising; however, they thought that results from the RCTs are needed to fully determine the drug's safety and effectiveness for treating COVID-19.

Description

Anakinra is an IL-1 receptor antagonist that is FDA approved for treating rheumatoid arthritis and cryopyrin-associated periodic syndromes and is under study as a treatment for patients with COVID-19.^{82,83} Some patients with COVID-19 develop an inflammatory response that can lead to acute lung injury, respiratory insufficiency, and multisystem organ dysfunction. Investigators are studying existing anti-inflammatory drugs such as anakinra as COVID-19 treatments.⁸⁴ Anakinra acts as a competitive antagonist of the cytokine receptor IL-1R1, which drives proinflammatory signaling.⁸³

Several small, retrospective studies have suggested that anakinra treatment improves clinical outcomes in patients with COVID-19-related respiratory distress.⁸⁵⁻⁸⁷ In the largest of these studies, Huet et al reported that, for patients with severe COVID-19-related bilateral pneumonia, 25% of patients (n = 52) who received subcutaneous anakinra (200 mg/d on days 1 to 3, 100 mg/d on days 4 to 10) required mechanical ventilation or died compared with 73% of patients (n = 44) in a historical control group.⁸⁶ Multiple randomized studies involving anakinra treatment for patients with COVID-19 are registered at the National Library of Medicine trial registry, including a 240-patient French trial⁸⁸ and a 7100-patient, multiarm, international trial.⁸⁹

Cost estimates for anakinra treatment are complicated by differences in dosing used across trials. In addition, while anakinra is supplied as 100-mg prefilled syringes for subcutaneous injection,⁸² some trials have reported using intravenous administration of anakinra to treat COVID-19, further complicating estimates of cost.⁸⁵ At the dosing level reported by Huet et al,⁸⁶ a 10-day anakinra treatment course would cost about \$2600 to \$3200, with higher costs incurred by more intensive dosing regimens.⁹⁰

Possible Areas of Impact

- Patient outcomes
- Health care delivery and process
- Health care costs

Possible Future Impacts

Despite the emergence of the antiviral remdesivir and the use of corticosteroids (eg, dexamethasone) as an immunomodulatory therapy, outcomes for many patients with severe COVID-19 remain poor and additional treatments are needed.

By modulating the maladaptive systemic inflammatory response, anakinra has the potential to improve patient outcomes in patients with severe COVID-19. However, anakinra's immunosuppressive effects could also lead to an increase in opportunistic infections, for which patients would require monitoring. In addition to direct effects on patient outcomes, an effective treatment might reduce demand within a health care facility for limited resources, such as spaces in the intensive care unit (ICU) or ventilators.

Anakinra is a relatively expensive drug and would increase the direct costs of treating patients with COVID-19; however, these costs could be offset by reductions in costs associated with mechanical ventilation, ICU occupancy, or treatment of downstream sequelae.

Key Stakeholder Perspectives

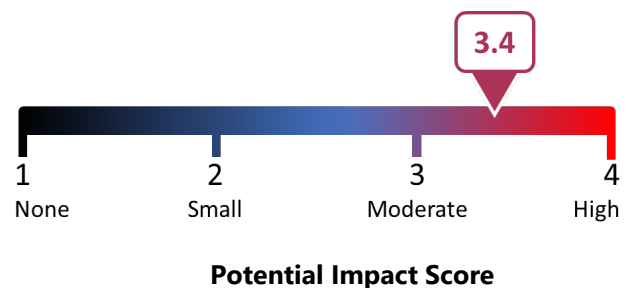
On May 19, 2020, twelve ECRI stakeholders, reflecting allied health, clinical engineering, health systems, health care generalist, nursing, physician, and research perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- Targeting the deleterious inflammatory response to COVID-19 is an important approach to treatment, and initial data on anakinra look promising in terms of improving survival rates; avoiding mechanical ventilation and ICU admission could have positive downstream effects on long-term recovery of COVID-19 survivors.
- Anakinra could be rapidly deployed in treating COVID-19 because it is a commercially available drug with a known safety profile; however, it is usually administered subcutaneously, and intravenous use could affect its safety profile.
- Although the initial studies show promise, they were poorly controlled and performed in the background of potentially active therapies (hydroxychloroquine, lopinavir/ritonavir); results from RCTs are needed to fully determine anakinra's safety and efficacy.
- The cost of anakinra will likely be substantial; however, stakeholders also noted that direct drug costs might be offset by avoiding costly ICU admissions for some patients.

Remdesivir (Veklury) for Treating COVID-19

Potential Impact Score

Stakeholders reviewing this topic thought that remdesivir (Veklury) for treating COVID-19 could have a moderately high impact on patient-oriented health care relative to COVID-19 in the United States within the next 12 months.



Highlights

- Remdesivir is an intravenously administered antiviral drug that might treat COVID-19 by stopping coronavirus from replicating (ie, multiplying) in a patient's body.
- It is currently the only drug to have Emergency Use Authorization (EUA) from FDA and is permitted for use in hospitalized adults and children who have COVID-19.
- Clinical trial data from several global studies suggest a 5-day course of remdesivir is effective in shortening recovery time compared with placebo and might reduce mortality.
- Stakeholders commenting on this topic thought that remdesivir has the potential to positively impact patient outcomes, health care delivery/process, and costs.
- Stakeholders agreed that clinical trial data demonstrated that remdesivir could lead to quicker recovery from COVID-19 and suggested that it might improve patient health outcomes and reduce hospitalization time and health care costs.

Description

Remdesivir (Gilead Sciences, Foster City, California) is an intravenously delivered antiviral prodrug (ie, it converts to a drug in the patient's body) intended to inhibit the replication of multiple RNA coronaviruses that has demonstrated in vitro activity against the novel coronavirus.⁹¹ On May 1, 2020, FDA issued EUA for the use of remdesivir to treat severe COVID-19 based on data from 2 global clinical trials.⁹² FDA expanded the EUA on August 28, 2020, to include the treatment of all hospitalized adults and children with suspected or confirmed COVID-19, irrespective of disease severity.⁹³ The manufacturer is seeking full approval and submitted a New Drug Application to FDA on August 28, 2020.⁹⁴ If approved, it would be the first FDA-approved treatment for COVID-19.

Mounting clinical trial data suggest remdesivir is effective in reducing time to recovery and risk of death in patients with moderate to severe COVID-19. Data published May 22, 2020, from a phase 3 trial⁹⁵ in 1023 people with moderate and severe disease found that a 10-day course of remdesivir improved recovery time compared with placebo (11 and 15 days, respectively) as well as mortality estimates at 14 days (7.1% and 11.9% for remdesivir and placebo, respectively).⁹⁶ Data published May 27, 2020, from a developer-sponsored phase 3 trial⁹⁷ in 6000 people with severe disease suggested similar outcomes between 5-day and 10-day dosing.⁹⁸ Additional data, released July 10, 2020, compared outcomes against retrospective world cohort data and suggested a 62% reduction in risk of mortality compared with standard of care treatment, improvement in clinical recovery at day 14 (74.4% versus 59.0%, respectively), and similar outcomes among various racial and ethnic patient subgroups.⁹⁹ Data published August 21, 2020, from a second developer-sponsored phase 3 trial¹⁰⁰ in 584 people with moderate disease demonstrated that patients who received a 5-day course of remdesivir had significantly greater clinical improvement at day 11 compared with the control group (standard of care). However, no differences were found between patients given a 10-day treatment course and the control group.¹⁰¹

Gilead announced in June 2020 that the cost of remdesivir to the US government would be \$2340 per 5-day treatment course and the list price would be \$3120 per 5-day treatment course.^{102,103}

Possible Areas of Impact

- Health care costs
- Health care delivery and process
- Population health
- Patient outcomes

Possible Future Impacts

Remdesivir might improve patient outcomes by reducing time to clinical recovery and risk of death. There are no FDA-approved treatments for COVID-19, and remdesivir is the only treatment to currently have EUA from FDA to treat COVID-19. Its use might increase as it replaces treatment with hydroxychloroquine, for which FDA revoked EUA over concerns about its safety and efficacy.¹⁰⁴ Further, remdesivir production increased significantly over the past few months to enable greater and sustainable availability of the drug.¹⁰⁵ Population health might improve if the overall burden on the health care system is reduced. Remdesivir might impact health care delivery and process by decreasing length of hospitalization and reducing need for invasive interventions such as endotracheal intubation and mechanical ventilation. It might impact health care costs if cost savings from shorter hospitalization and use of fewer health care resources outweigh the cost of treatment. Remdesivir might pave the way for developing additional antiviral treatments and the understanding of antivirals to treat COVID-19.

Key Stakeholder Perspectives

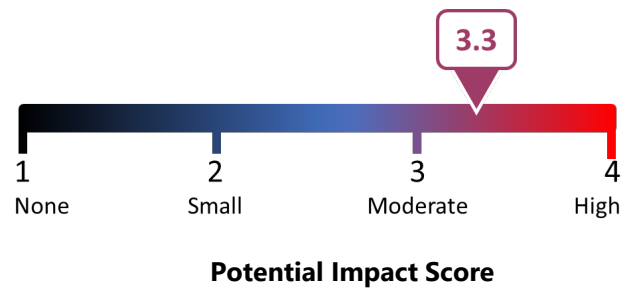
Between May 22, 2020, and June 15, 2020, eight ECRI stakeholders, reflecting physician, nursing, health systems, and research perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- Remdesivir might improve patient and population health outcomes, considering that (1) early clinical trial data suggested it reduces time to recovery, (2) it is already being used clinically under EUA, and (3) it is widely and readily available.
- Use of remdesivir will likely increase following recent findings that hydroxychloroquine has significant adverse effects, although other treatments, such as those that reduce risk of cytokine storm, might emerge and prove more efficacious in the long term.
- More data are needed to assess long-term efficacy in different patient populations (eg, varying severity of disease) and efficacy in reducing mortality.
- Initial reports of serious adverse effects are concerning, and more data on adverse effects are needed.

Convalescent Plasma for Treating COVID-19

Potential Impact Score

Stakeholders reviewing this topic thought that convalescent plasma for treating COVID-19 could have a moderately high impact on patient-oriented health care relative to COVID-19 in the United States within the next 12 months.



Highlights

- Plasma collected from patients who have recovered from COVID-19 (ie, convalescent plasma [CP]) can contain high levels of antibodies that neutralize the virus and has the potential to improve outcomes in patients when used therapeutically.
- CP reduced mortality in hospitalized patients with severe acute COVID-19 who were given CP earlier in the treatment course or CP samples containing higher levels of coronavirus antibodies.
- FDA granted Emergency Use Authorization (EUA) for CP products in hospitalized patients based on scientific evidence from an expanded access program (EAP).
- Stakeholders commenting on this topic thought that CP showed potential to improve patient health outcomes, but larger controlled trials are needed to determine CP's safety and efficacy.
- Stakeholders also thought that implementation of CP therapy on a large scale would require significant logistics, and a limited supply of CP might increase health care disparities.

Description

Plasma (ie, the cell-free liquid component of blood) obtained from patients who have recovered from COVID-19 (ie, CP) is under study as a COVID-19 treatment.¹⁰⁶ Plasma contains high levels of blood proteins. If CP contains high levels of coronavirus-neutralizing antibodies, it might confer passive immunity against the virus. CP is collected from recovered COVID-19 patients by apheresis, with each donation providing sufficient plasma to treat up to 4 patients of matching blood type.¹⁰⁷

An interim analysis of a prospective, propensity score-matched study of 316 COVID-19 patients found a significant reduction in mortality in patients transfused within 3 days of admission, compared with 251 control COVID-19 patients not transfused with CP.¹⁰⁸

Additional studies of CP are ongoing, including about 50 randomized controlled trials (RCTs) that are being fed into a living systematic review.¹⁰⁹

FDA has opened an EAP for CP treatment for COVID-19, and more than 50 000 patients have been treated through the program.¹¹⁰ A multicenter study across 2807 acute care facilities found that, at 7 and 30 days after treatment, 35 322 patients hospitalized with severe acute COVID-19 and transfused with CP under the EAP within 3 days of diagnosis had significantly lower mortality rates than patients given CP at 4 days or more after diagnosis.¹¹¹ However, a small RCT in 103 patients with severe or life-threatening COVID-19 in Wuhan, China, found CP

with standard treatment did not significantly improve time to clinical improvement within 28 days compared with standard treatment alone.¹¹² Among the first 20 000 CP-treated patients, program investigators have reported a serious adverse event rate of less than 1%, suggesting that CP is safe in hospitalized patients with COVID-19.^{113,114}

Based on the success of CP in these and other studies, FDA granted EUA for CP products, stating that the benefits of CP outweigh the known and potential risks.¹¹⁵

Possible Areas of Impact

- Health care costs
- Health care delivery and process
- Health care disparities
- Patient outcomes

Possible Future Impacts

Despite the emergence of the antiviral remdesivir and the use of corticosteroids (eg, dexamethasone) as immunomodulatory therapy, outcomes for many patients with COVID-19 remain poor and additional treatments are needed. By providing a potential source of coronavirus-neutralizing antibodies, CP might improve outcomes in patients with COVID-19. While the initial use of CP focused on treating patients with severe or critical COVID-19, CP is being used increasingly in patients with less severe disease with the hope of preventing disease progression.¹¹⁶ CP is a promising approach to treating COVID-19; however, completion of RCTs to determine its efficacy has been hampered by declining infection rates in initial disease hotspots where the trials were begun and the widespread availability of the treatment through compassionate use and EAPs.¹¹⁶

Establishing a system to provide CP would involve a substantial logistical undertaking to identify recovered patients while antibody titers are sufficiently high and to collect, test, store, and distribute plasma. These infrastructure requirements could lead to high costs for CP, which could exacerbate existing health care disparities based on socioeconomic status. Concerns exist regarding the appropriate use of CP, including the risk-benefit ratio (eg, bloodborne disease risk) from widespread administration of plasma products if other, better-controlled options are available. Additionally, the high demand for CP could create additional health care disparities based on access to the treatment.

Key Stakeholder Perspectives

Between May 23, 2020, and May 29, 2020, eight ECRI stakeholders, reflecting clinical engineering, health systems, health care generalist, nursing, physician, and research perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

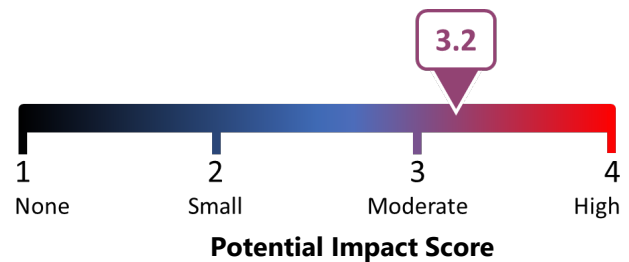
- CP is a promising approach for treating COVID-19 based on its purported mechanism of action and likely safety; however, the evidence base for the efficacy of CP is lacking and a need exists for RCTs and comparisons to other COVID-19 treatments.
- COVID-19-directed CP therapy could be rapidly available; however, whether enough donors would exist to meet demand is unclear.

- The supply of CP might be limited by logistical issues involved in implementing CP therapy on a large scale, including a narrow time window for collecting CP and the resource-intensive process required to recruit, screen, and coordinate donations.
- Limited availability of CP might increase health care disparities.

TD-0903 for Treating Acute Lung Injury in Patients With COVID-19

Potential Impact Score

Stakeholders reviewing this topic thought that TD-0903 for treating acute lung injury in patients with COVID-19 could have a moderately high impact on patient-oriented health care relative to COVID-19 in the United States within the next 12 months.



Highlights

- TD-0903 is an investigational drug intended to reduce hyperinflammation and stop acute lung injury from progressing to acute respiratory distress syndrome (ARDS) in patients with COVID-19.
- Patients take the drug via a nebulizer, an inhaler that helps deliver the drug directly to lung tissue; this route might reduce unintended immunosuppression in other body tissues.
- Stakeholders commenting on this topic thought that using TD-0903 to treat acute lung injury in patients with COVID-19 and prevent cytokine storm is theoretically sound and, therefore, might provide benefits for patients; however, more clinical trial data are needed to assess its efficacy and safety.
- Stakeholders also thought that TD-0903 would likely be one of many immunomodulatory drugs investigated for COVID-19 and might be used in combination with other treatments.

Description

TD-0903 (Theravance Biopharma, Dublin, Ireland) is an investigational, inhaled Janus kinase inhibitor intended to prevent the progression of acute lung injury to ARDS in patients with COVID-19. ARDS associated with 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 influx causes severe inflammation, leads to fluid accumulation and impaired oxygen exchange, and often results in the need for mechanical ventilation. Intervening early to block cytokine storm in COVID-19-associated pneumonia might improve survival.¹¹⁷ TD-0903 purportedly broadly inhibits the activity of enzymes called Janus kinases that play a central role in cytokine signaling. It is administered in a nebulized formulation to target hyperinflammation in the lungs, thereby limiting its action of suppressing the immune system in the rest of the body. A developer-sponsored phase 2 study (n = 159) has begun in the United Kingdom and is planned to expand to include US clinical sites.^{118,119} The trial has an expected primary completion date of October 2020.

Possible Areas of Impact

- Health care costs
- Health care delivery and process
- Population health
- Patient outcomes

Possible Future Impacts

TD-0903 might positively impact patient health outcomes if it successfully and safely prevents progression of acute lung injury to ARDS in patients with COVID-19 and reduces the use of intensive resources such as mechanical ventilation. In turn, population health outcomes might be improved if better individual patient outcomes translate to less overall burden on the health care system and fewer supply shortages (eg, masks, ventilators). TD-0903 might increase drug treatment costs, especially if it is used in combination with other drugs, but it might contribute to overall cost savings if health care resource costs are reduced because of improved outcomes. TD-0903 might increase knowledge about using immune system–modulating drugs to treat COVID-19 and inform the development of future treatments. Nebulized formulation of drugs to treat COVID-19 might be increasingly pursued in the future if ongoing clinical trials with TD-0903 demonstrate clinically meaningful efficacy and safety.

Key Stakeholder Perspectives

Between June 1, 2020, and June 8, 2020, five ECRI stakeholders, reflecting physician, nursing, health systems, and research perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- The nebulized formulation of this drug seems promising for delivering the drug directly to the lungs, although it might increase coughing and subsequent coronavirus exposure risk to health care personnel.
- More data on the safety and efficacy of TD-0903 are needed, although the purported mechanism of action of the drug is theoretically promising, considering that preventing or reducing cytokine storm in patients with COVID-19 is thought to be critical for survival.
- It remains to be seen how TD-0903 fits into the growing landscape of immune system–modulating drugs being investigated to treat COVID-19, as some candidates are more likely than others to be successful in demonstrating safety and efficacy.
- TD-0903 is likely to be used in combination with other drugs, which might increase the overall cost of drug treatment, but other health care cost savings gained from successful treatment might outweigh potential drug costs.

Chapter 6. Vaccines and Prophylaxis

Chapter Summary

As of July 30, 2020, we were monitoring 7 COVID-19-related vaccine and prophylaxis topics. Three of these topics are listed in the July 2020 *PCORI Health Care Horizon Scanning System: Horizon Scanning COVID-19 Supplement Status Report, Volume 1, Issue 1*. The remaining 4 topics will be listed in the October 2020 edition of the *COVID-19 Supplement Status Report*. All 7 topics were sent for comment to internal ECRI stakeholders, and each received at least 5 sets of ratings and comments from stakeholders between May 18, 2020, and July 29, 2020.

Topics Considered for Inclusion in This Report

Table 6.1 lists 4 topics selected for inclusion in this High Impact Report. Included topics received, on average, high impact ratings and demonstrated high consensus among stakeholders, as evident in the ratings and comments. Topics are ordered first in descending order by potential impact score; topics with the same score are listed alphabetically by topic title.

Table 6.1. Included Vaccine and Prophylaxis Topics

Topic title	Potential impact score
mRNA-1273 vaccine for preventing coronavirus infection	3.9
AZD1222 (ChAdOx1 nCoV-19) vaccine for preventing coronavirus infection	3.8
JNJ-78436735 (Ad26.COV2-S) vaccine for preventing coronavirus infection	3.8
BNT162b2 mRNA vaccine for preventing coronavirus infection	3.7

Table 6.2 lists 3 topics considered, but not selected, for inclusion in this High Impact Report. Excluded topics received, on average, low to moderate impact ratings and were not considered by most stakeholder reviewers to have high impact potential. Topics are ordered first in descending order by potential impact score and second in ascending order alphabetically by topic title.

Table 6.2. Vaccine and Prophylaxis Topics Considered but Not Included

Topic title	Potential impact score
Monoclonal antibodies targeting coronavirus spike protein receptor binding domain for preventing COVID-19	3.0
Hydroxychloroquine for preventing COVID-19 ^a	2.8
Bacille Calmette-Guérin vaccine for reducing COVID-19 incidence or severity in health care workers	2.6

^a Topic has been archived. A description of the topic and the archive reason can be found in the July 2020 *PCORI Health Care Horizon Scanning System: Horizon Scanning COVID-19 Supplement Status Report, Volume 1, Issue 1*.

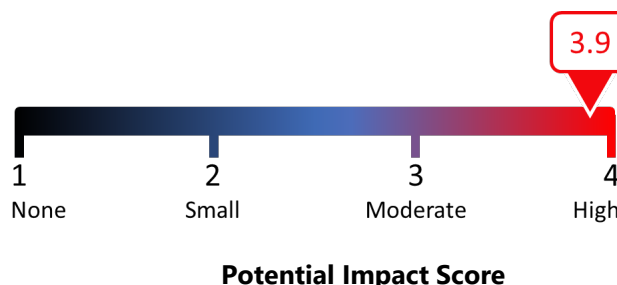
Topic Summaries

We present below 4 summaries on topics deemed to have high impact potential. Topics are ordered first in descending order by potential impact score; topics with the same score are listed alphabetically by topic title.

mRNA-1273 Vaccine for Preventing Coronavirus Infection

Potential Impact Score

Stakeholders reviewing this topic thought that the mRNA-1273 vaccine for preventing coronavirus infection could have a high impact on patient-oriented health care relative to COVID-19 in the United States within the next 12 months.



Highlights

- mRNA-1273 is an investigational vaccine intended to generate a protective immune response against the coronavirus spike protein expressed on the surface of the virus.
- mRNA-1273 is in phase 3 development, with primary completion expected in October 2022.
- Beginning in 2021, the manufacturer expects to deliver between about 500 million and 1 billion doses per year.
- Stakeholders commenting on this topic thought that mRNA-1273's early immune response data were encouraging and that, if the vaccine is effective, it could have substantial patient and population health benefits; however, additional studies are needed to determine vaccine efficacy, including in populations hardest hit by COVID-19 and those with comorbidities.

Description

mRNA-1273 (Moderna, Cambridge, Massachusetts) is a vaccine against coronavirus that uses messenger RNA (mRNA) to encode the viral spike protein expressed on the surface of the virus.¹²⁰ The vaccine purportedly enters host antigen-presenting cells and induces expression of

the viral spike protein, which acts to elicit a host immune response against the virus to prevent future infection.

Results from a phase 1, nonrandomized dosing study in 45 healthy adults given 1 of 2 doses of vaccine (25 µg or 100 µg) at days 1 and 28 showed that, by day 43, the 100-µg group had 15 times more antibodies to the viral protein than people who received only convalescent serum (serum from people who recovered from infection).¹²¹ Patients also developed strong helper T-cell responses against the spike protein. Adverse events occurred in more than half the participants and included chills, fatigue, headache, injection site pain, and myalgia.

On May 12, 2020, FDA granted mRNA-1273 Fast Track designation. A phase 3 trial in 30 000 individuals is in progress, with full data expected by October 2022.¹²² The vaccine is part of the US government's Operation Warp Speed, which could allow limited use of the vaccine by the end of 2020. The company purportedly remains on track to be able to deliver approximately 500 million doses per year beginning in 2021.¹²³

Moderna has agreed to set the preorder price of mRNA-1273 between \$32 and \$37 per dose for small quantities of the vaccine.¹²⁴

Possible Areas of Impact

- Patient outcomes
- Population health
- Clinicians and/or caregiver safety
- Health care delivery and process
- Health care disparities
- Health care costs

Possible Future Impacts

If mRNA-1273 is proved effective against coronavirus, it might improve patient outcomes as well as clinician or caregiver safety by preventing or mitigating adverse health events caused by infection. It might also aid the development of “herd immunity” among vulnerable populations, thereby decreasing negative COVID-19-related outcomes and improving individual and population health outcomes over time. It might also help decrease the overall cost burden to governments and the health care system. An effective vaccine against coronavirus could also enable more relaxed social distancing protocols.

Although most expected outcomes from an effective vaccine are positive, a vaccine shortage could lead to increased disparities if certain populations are unable to access the vaccine. Facilities that administer vaccines (eg, hospitals, clinics, pharmacies) might experience a transient increase in patient volume as people seek vaccinations. In addition, currently unknown adverse events might come to light if the vaccine is brought to market prematurely (ie, before full safety data are available). Considering that adverse events resembling coronavirus-like symptoms (chills, fatigue, headache, and myalgia) occurred in more than half the study participants, a proactive information campaign similar to for influenza vaccines might be necessary to inform the public that the vaccine does not cause COVID-19.^{121,125}

Key Stakeholder Perspectives

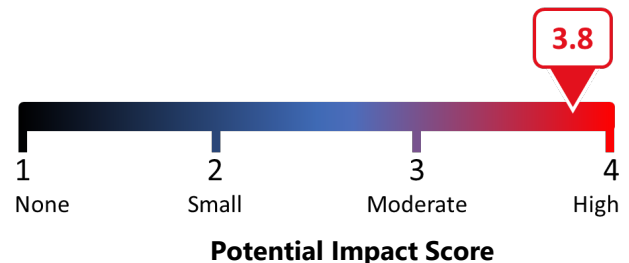
Between May 22, 2020, and July 29, 2020, seven ECRI stakeholders, reflecting health care generalist, health systems, nursing, physician, and research perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- mRNA-1273 might substantially improve patient and population health outcomes by preventing coronavirus infection or reducing case severity in some patients; however, more data are needed to determine if and what level of neutralizing antibodies are needed for protection and how long the effects of the vaccine might last.
- Availability of mRNA-1273 might help relax social distancing guidelines and economic disruptions, which could result in an improvement in overall population psychological health.
- mRNA-1273 has been tested only in healthy participants. More studies are needed in high-risk populations, such as those with comorbidities and other risk factors, to determine effectiveness and impact potential.

AZD1222 (ChAdOx1 nCoV-19) Vaccine for Preventing Coronavirus Infection

Potential Impact Score

Stakeholders reviewing this topic thought that the AZD1222 vaccine for preventing coronavirus infection could have a high impact on patient-oriented health care relative to COVID-19 in the United States within the next 12 months.



Highlights

- AZD1222 is a vaccine intended to generate a strong immune response against the coronavirus spike protein expressed on the surface of the virus.
- AZD1222 is in phase 2/3 development, with full data expected in August 2021.
- Beginning in September 2020, the manufacturer is preparing to produce and distribute the first doses of AZD1222 in the United States as part of Operation Warp Speed.
- Stakeholders commenting on this topic thought that AZD1222, if effective, could have significant impacts on population health and in supporting recovery from the pandemic.
- Stakeholders were concerned that the accelerated development timeline might pose safety risks related to bringing a vaccine to market before it has been properly tested.

Description

AZD1222 (ChAdOx1 nCoV-19; AstraZeneca, licensed from the University of Oxford, United Kingdom) is a recombinant (ie, genetically engineered) adenoviral vector vaccine against coronavirus. AZD1222 uses a shortened, weakened form of a “common cold” virus to carry genetic material into special antigen-presenting cells in the patient’s body, where it produces the viral spike protein normally found on the surface of the coronavirus.¹²⁶ The spike protein then moves to the cell’s surface, where it stimulates an immune response intended to prevent future infection by coronavirus.

In a phase 1/2 randomized trial of more than 1000 healthy volunteers, 543 participants received a single dose of AZD1222 and 534 received a single dose of meningococcal conjugate vaccine, which acted as a control for the study.¹²⁷ Participants who received AZD1222 reportedly developed T-cell responses against the spike protein that peaked at day 14. A small subset (ie, 10 participants) of those who received AZD1222 also received a booster dose of AZD1222 at day 28 and had neutralizing antibody (ie, against coronavirus spike protein) levels that were 4 times higher at day 56 compared with those who received only a single dose of AZD1222. The most commonly reported adverse reactions among study participants included chills, feeling feverish, headache, malaise, muscle ache, and pain. On September 9, 2020, AstraZeneca announced a voluntary temporary pause of all AZD1222 trials due to a single event of a [neurological illness](#) that occurred in the UK phase 3 trial. This triggered a preplanned review process by an independent committee to review the safety data.¹²⁸

AZD1222 is also in a large phase 2/3 trial in more than 10 000 people. Full 6-month results on its safety and effectiveness against coronavirus are not expected until August 2021¹²⁹; however, because the vaccine is part of the US government’s Operation Warp Speed, if early results seem promising, the manufacturer claims it may be able to begin limited distribution of the vaccine by the end of 2020.^{123,130} The US government has purportedly agreed to purchase 300 million doses of the vaccine for \$4 per dose.^{131,132}

Possible Areas of Impact

- Clinician and/or caregiver safety
- Health care costs
- Health care delivery and process
- Health care disparities
- Patient outcomes
- Population health

Possible Future Impacts

If AZD1222 is proved effective against coronavirus, it might improve patient outcomes as well as clinician or caregiver safety by preventing or mitigating adverse health events caused by infection. It might also aid the development of “herd immunity” among vulnerable populations, thereby decreasing negative COVID-19-related outcomes and improving individual and population health outcomes over time. It might also help decrease the overall cost burden to governments and the health care system. An effective vaccine against coronavirus could also enable more relaxed social distancing protocols.

Although most expected outcomes from an effective vaccine are positive, a vaccine shortage could lead to increased disparities if certain populations are unable to access the vaccine. Facilities that administer vaccines (eg, hospitals, clinics, pharmacies) might experience a transient increase in patient volume as people seek vaccinations. In addition, currently unknown adverse events might come to light if the vaccine is brought to market prematurely (ie, before full safety data are available). Considering that adverse events resembling coronavirus-like symptoms (chills, feeling feverish, headache, malaise, muscle ache, and pain) occurred in more than half the study participants, a proactive information campaign similar to for influenza vaccines might be necessary to inform the public that the vaccine does not cause COVID-19.^{125,127}

Key Stakeholder Perspectives

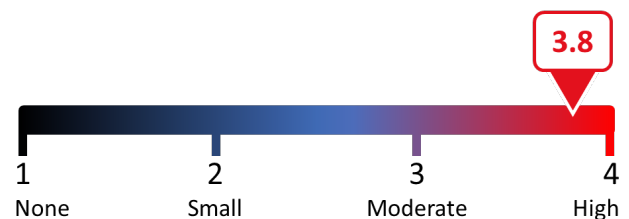
Between June 23, 2020, and July 9, 2020, five ECRI stakeholders, reflecting health systems, nursing, and research perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- AZD1222 might substantially improve patient, caregiver, and population health by reducing infection rates and disease severity, as well as by improving mental health and anxiety about fear of contracting coronavirus.
- If effective, AZD1222 might reduce strain on the health care system and health care workers due to fewer hospitalizations.
- Availability of a coronavirus vaccine might prompt a return to normalcy in society as well as help restore the economy and job functions.
- AZD1222 might reduce health care disparities if essential workers and populations that are most severely affected or at high risk are able to receive the vaccine.
- The accelerated development timeline for AZD1222, which could allow distribution of the vaccine before trial completion, might pose safety risks related to unknown adverse events. The aggressive timeline might also decrease public acceptance of the vaccine.

JNJ-78436735 (Ad26.COV2-S) Vaccine for Preventing Coronavirus Infection

Potential Impact Score

Stakeholders reviewing this topic thought that the JNJ-78436735 vaccine for preventing coronavirus infection could have a high impact on patient-oriented health care relative to COVID-19 in the United States within the next 12 months.



Potential Impact Score

Highlights

- JNJ-78436735 is an investigational vaccine intended to generate a protective immune response against the coronavirus spike protein expressed on the surface of the virus.
- JNJ-78436735 is in phase 1/2 development, with full data expected in September 2021; a phase 3 trial began in September 2020.

- The manufacturer hopes to produce and distribute up to 1 billion doses of the vaccine globally beginning in 2021.
- If the vaccine receives FDA Emergency Use Authorization, the US government has agreed to purchase 100 million doses for about \$10 per dose.
- Stakeholders commenting on this topic thought that, if effective, JNJ-78436735 could improve patient and population health and might enable governments to relax social distancing protocols; however, clinical data supporting its effectiveness are not yet available.

Description

JNJ-78436735 (Ad26.COV2-S; Johnson and Johnson [New Brunswick, New Jersey]) is a recombinant (ie, genetically engineered) adenoviral vector vaccine against coronavirus. JNJ-78436735 uses a shortened, weakened form of a “common cold” virus to carry genetic material into special antigen-presenting cells in the patient’s body, where it produces the viral spike protein normally found on the surface of the coronavirus. The spike protein then moves to the cell’s surface, where it stimulates an immune response intended to prevent future infection by coronavirus.¹³³

The developer claims to be using the same platform that it uses for its Ebola vaccine (Zabdeno; Ad26.ZEBOV), which is in phase 3 development.^{134,135}

JNJ-78436735 is in a phase 1/2 trial in 1045 people, with primary results expected in September 2021.¹³⁶ The manufacturer has also announced plans to start a phase 3 trial in September 2020.¹³⁴ The vaccine is part of the US government’s Operation Warp Speed, which could allow use of the vaccine by 2021.^{123,134} If the vaccine receives FDA Emergency Use Authorization, the US government has agreed to purchase 100 million doses for about \$10 per dose.¹³²

Possible Areas of Impact

- Clinician and/or caregiver safety
- Health care costs
- Health care delivery and process
- Health care disparities
- Patient outcomes
- Population health

Possible Future Impacts

If JNJ-78436735 is proved effective against coronavirus, it might improve patient outcomes as well as clinician or caregiver safety by preventing or mitigating adverse health events caused by infection. It might also aid the development of “herd immunity” among vulnerable populations, thereby decreasing negative COVID-19-related outcomes and improving individual and population health outcomes over time. It might also help decrease the overall cost burden to governments and the health care system. An effective vaccine against coronavirus could also enable more relaxed social distancing protocols.

Although most expected outcomes from an effective vaccine are positive, a vaccine shortage could lead to increased disparities if certain populations are unable to access the vaccine.

Facilities that administer vaccines (eg, hospitals, clinics, pharmacies) might experience a transient increase in patient volume as people seek vaccinations. In addition, currently unknown adverse events might come to light if the vaccine is brought to market prematurely (ie, before full safety data are available).

Key Stakeholder Perspectives

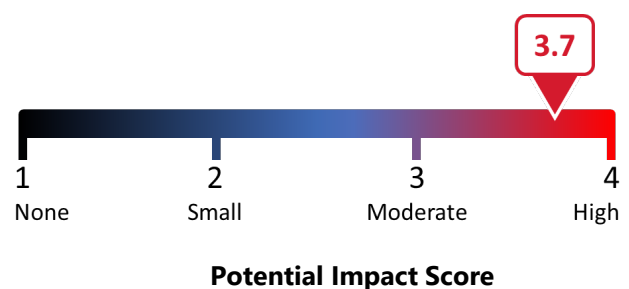
Between June 25, 2020, and July 10, 2020, five ECRI stakeholders, reflecting research, nursing, and systems perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- JNJ-78436735 might substantially improve patient and population health outcomes by preventing coronavirus infection or reducing case severity in key populations, including essential workers and severely affected populations.
- Availability of JNJ-78436735 might enable governments to relax social distancing guidelines.
- JNJ-78436735 has no clinical data reported and an aggressive timeline for the availability of the first doses to patients; data are too early to determine if and what level of immune responses are needed for protection and how long the effects of the vaccine might last.
- Concerns exist regarding the accelerated development timeline, which might bring a vaccine to market before full safety data are available.

BNT162b2 mRNA Vaccine for Preventing Coronavirus Infection

Potential Impact Score

Stakeholders reviewing this topic thought that the BNT162b2 mRNA vaccine for preventing coronavirus infection could have a high impact on patient-oriented health care relative to COVID-19 in the United States within the next 12 months.



Highlights

- BNT162b2 is a messenger RNA (mRNA) vaccine intended to generate a protective immune response against the coronavirus spike protein expressed on the surface of the coronavirus.
- BNT162b2 is in phase 2/3 development, with primary completion expected on April 16, 2021.
- By late 2020, the developers hope to begin producing and distributing 100 million doses globally and to expand production and distribution to 1.3 billion doses by the end of 2021.
- Stakeholders commenting on this topic thought that early data on the vaccine platform's safety and ability to simulate an immune response were promising; however, the effectiveness of mRNA vaccine technology has not yet been established in clinical trials.

Description

BNT162b2 (Pfizer [New York, New York] and BioNTech [Cambridge, Massachusetts]) is a lipid nanoparticle–encapsulated mRNA vaccine that encodes the entire viral spike protein responsible for receptor binding and cellular entry.^{137,138} The vaccine purportedly enters host antigen-presenting cells and induces expression of the viral spike protein, which acts to elicit a host immune response against the virus to prevent future infection. The manufacturers had been pursuing 4 vaccine candidates to accelerate vaccine development (BNT162a, BNT162b1, BNT162b2, and BNT162c2) and, in late July 2020, chose to proceed with BNT162b2 as their phase 3 candidate.¹³⁸

Early immunogenicity data reported on BNT162b1, which could provide some context for BNT162b2, showed a tolerability and safety profile consistent with other mRNA-based vaccines given to healthy adults.^{139,140} Participants (45 healthy adults) receiving 2 doses of 10 µg or 30 µg produced coronavirus-neutralizing antibody responses almost 2 to 3 times higher, respectively, than levels found in serum from patients who recovered from COVID-19. Common adverse reactions reported by participants included chills, fatigue, and headaches, but no severe adverse events were reported.

The manufacturers have started a phase 2/3 trial (n = 30 000) that is expected to be completed in April 2021.¹⁴⁰ Under an agreement as part of Operation Warp Speed, the US government has prepurchased 100 million doses for \$1.95 billion, if approved by FDA, and will offer BNT162b2 for free.^{123,141}

Possible Areas of Impact

- Clinician and/or caregiver safety
- Health care costs
- Health care delivery and process
- Health care disparities
- Patient outcomes
- Population health

Possible Future Impacts

If BNT162b2 is proved effective against coronavirus, it might improve patient outcomes as well as clinician or caregiver safety by preventing or mitigating adverse health events caused by infection. It might also aid the development of “herd immunity” among vulnerable populations, thereby decreasing negative COVID-19-related outcomes and improving individual and population health outcomes over time. It might also help decrease the overall cost burden to governments and the health care system. An effective vaccine against coronavirus could also enable more relaxed social distancing protocols.

Although most expected outcomes from an effective vaccine are positive, a vaccine shortage could lead to increased disparities if certain populations are unable to access the vaccine. Facilities that administer vaccines (eg, hospitals, clinics, pharmacies) might experience a transient increase in patient volume as people seek vaccinations. In addition, currently unknown adverse events might come to light if the vaccine is brought to market prematurely (ie, before full safety data are available). Considering that adverse events resembling coronavirus-like symptoms (chills, fatigue, fever, and headache) occurred in more than half of the study

participants, a proactive information campaign similar to for influenza vaccines might be necessary to inform the public that the vaccine does not cause COVID-19.^{125,138}

Key Stakeholder Perspectives

Between June 12, 2020, and June 16, 2020, seven ECRI stakeholders, reflecting clinical engineering, health care generalist, health systems, nursing, and research perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- BNT162b2 might significantly improve patient and population health outcomes by preventing infection with coronavirus, mitigating disease spread, and conferring immunity to much of the population.
- If effective, BNT162b2 might enable governments to relax social distancing protocols, which could help mitigate some adverse economic effects of economic shutdowns, severe coronavirus hospitalizations, and the need for personal protective equipment and testing.
- The accelerated development timeline for BNT162b2 and plans to produce millions of doses by the end of 2020, which could allow distribution of vaccine before trial completion, might pose the risk of manufacturing an ineffective vaccine.
- New formulations of BNT162b2 might need to be made if different strains of coronavirus emerge, and large-scale immunization efforts would be necessary to prevent further outbreaks.

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