Horizon Scanning COVID-19 Supplement High Impact Report Volume 2, Issue 1

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

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

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Statement of Funding and Purpose

This report incorporates data collected during implementation of the Patient-Centered Outcomes Research Institute (PCORI) Health Care Horizon Scanning System COVID-19 Supplement, operated by ECRI under contract to PCORI (Contract No. MSA-HORIZSCAN-ECRI-ENG-2018.7.12). The findings and conclusions herein 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 it did not provide opinions on the potential impact of interventions.

Financial Disclosure Statement

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

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Preface

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

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

In early 2020, the COVID-19 pandemic created a fast-moving, widespread public health crisis. In May 2020, PCORI expanded its HCHSS to elucidate the landscape of potentially impactful applications for COVID-19. The HCHSS COVID-19 Supplement scans for, identifies, monitors, and reports on emerging and available COVID-19-related treatments, diagnostics, preventive measures, management strategies, and systems changes with potential 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 means 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 them 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 their understanding of the currently available evidence or, in the absence of hard evidence, their 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 (e.g., 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 (e.g., 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 and/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 (i.e., 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 (i.e., insurers), or health care providers.

A preselected 3-member panel of PCORI HCHSS senior team members rapidly reviews and votes on each proposed topic for inclusion; 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 (e.g., 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 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 their 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 largely 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. A senior horizon scanning reviewer and a medical copyeditor then check each chapter before all chapters are 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.

To ensure that content is current, analysts update topics as new information arises. 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 5000 information leads has led to the identification of 202 COVID-19-related topics across 6 content areas. As of April 16, 2021, after subjecting potential topics to our inclusion criteria and selection process, we have selected 186 topics as having potential for impact. Of them, 75 are being actively monitored in the system; 111 topics have been archived. The 186 total topics span the 6 COVID-19-related content areas as follows (Figure 1):

- Devices: 23 topics (12%)
- Identifiable risk factors and prognostic indicators: 9 topics (5%)
- Screening and diagnostics: 45 topics (24%)
- Systems and management: 35 topics (19%)
- Treatments: 60 topics (32%)
- Vaccines and prophylaxis: 14 topics (8%)

**Figure 1. Percentage of Topics by Content Area**
Of the 75 actively monitored topics, we have selected—based on the procedures described in High-Impact Topic Selection and Reporting Methods—29 topics for inclusion in this report, distributed across 5 COVID-19-related content areas as follows (Figure 2):

- Devices: 1 topic (3%)
- Screening and diagnostics: 5 topics (17%)
- Systems and management: 8 topics (28%)
- Treatments: 7 topics (24%)
- Vaccines and prophylaxis: 8 topics (28%)

Figure 2. Percentage of Topics Selected for Report by Content Area
Chapter 1. Devices

Chapter Summary

As of March 12, 2021, we were monitoring or had recently archived 6 COVID-19-related device topics. These topics are listed in the January 2021 PCORI Health Care Horizon Scanning System: Horizon Scanning COVID-19 Supplement Status Report, Volume 2, Issue 1. All 6 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 March 11, 2021. Additional ratings and comments might also have been received after March 11, 2021.

Topics Considered for Inclusion in This Report

Table 1.1 lists the topic selected for inclusion in this High Impact Report. The included topic received, on average, moderately high impact ratings and demonstrated considerable consensus among stakeholders, as evident in the ratings and comments.

Table 1.1. Included Device Topics

<table>
<thead>
<tr>
<th>Topic title</th>
<th>Potential impact score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative-pressure tents to limit airborne transmission of coronavirus</td>
<td>3.2</td>
</tr>
</tbody>
</table>

Table 1.2 lists 5 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 arranged 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

<table>
<thead>
<tr>
<th>Topic title</th>
<th>Potential impact score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extracorporeal blood filtration to treat COVID-19*</td>
<td>3.0</td>
</tr>
<tr>
<td>Transvenous phrenic nerve stimulation to improve ventilator weaning*</td>
<td>3.0</td>
</tr>
<tr>
<td>Decontamination systems for reprocessing of single-use N95 respirators</td>
<td>2.8</td>
</tr>
<tr>
<td>Nickel foam air filter to reduce the risk of coronavirus transmission</td>
<td>2.8</td>
</tr>
<tr>
<td>Reusable silicone respirators to protect against COVID-19 infection</td>
<td>2.3</td>
</tr>
</tbody>
</table>

* Topic was recently archived.
Topic Summaries

We present below a summary on a topic deemed to have moderately high to high impact potential.

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 enclosed air—including droplets exhaled by the patient—using an attached vacuum motor and filter it through a high-efficiency particulate air filter before releasing the air into the surrounding 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 hospitals and could improve patient throughput.
- In August 2020, FDA rescinded a general Emergency Use Authorization (EUA) for passive protective barrier enclosures (ie, non–negative-pressure tents) to treat COVID-19 cases, citing risks to both providers and patients. FDA recommends using negative-pressure barriers instead.
- 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 negative-pressure tents cost less than full-sized rooms, the resources needed to set up these tents and increased vaccine uptake might limit their use.

Description

Negative-pressure rooms can effectively contain the spread of airborne pathogens, but the number of COVID-19 cases can overload this resource. Portable negative-pressure tents might reduce the need for negative-pressure rooms, decrease the risk of airborne transmission to frontline health care providers, and increase patient throughput.1

Compact tents are placed over the patient’s head and shoulders.2−4 Larger designs enclose the entire patient bed.5,6 Tents are constructed of either clear, rigid plastic or clear, soft plastic over a reusable frame. Providers reach patients through hand-access ports or slits in the walls. A
vacuum hose connected to the hospital air-evacuation system creates the negative-pressure environment.\textsuperscript{1}

As of March 15, 2021, FDA had granted 6 EUAs for negative-pressure tents—4 compact tents\textsuperscript{2-4} and 2 whole-bed tents\textsuperscript{5,6}—to enhance personal barrier protection for providers during airway management, medical procedures, or transport of patients with COVID-19. Of added significance, on August 20, 2020, FDA revoked an umbrella EUA issued on May 1, 2020, that authorized use of passive protective barrier enclosures (ie, without negative pressure) when treating patients with confirmed or suspected COVID-19.\textsuperscript{7,8} FDA cited recent research of simulated intubations using passive barriers, which suggested they might not reduce and could increase provider exposure to airborne particles (eg, tearing personal protective equipment, escape of airborne particles).\textsuperscript{9,10} Further, passive barriers might increase patient risk by restricting providers’ mobility in performing procedures quickly or accurately on first attempts.\textsuperscript{9,10} Thus, FDA recommended using only negative-pressure protective barrier enclosures, noting it granted EUAs for multiple negative-pressure tents.\textsuperscript{7,8}

**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, enhancing 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 April 20, 2021, seven 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-size 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. However, use of the tents is expected to decrease with increased vaccine uptake.
- 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 those of standard rooms, which might prevent hospitals from using these tents.
- Health care delivery and process

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 enclosed air—including droplets exhaled by the patient—using an attached vacuum motor and high-efficiency particulate air filter, before releasing the air into the surrounding 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 hospitals and could improve patient throughput.
In August 2020, FDA rescinded a general Emergency Use Authorization (EUA) for passive protective barrier enclosures (ie, non–negative pressure tents) to treat COVID-19 cases, citing risks to both providers and patients. FDA recommends using negative-pressure barriers instead.

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 negative-pressure tents cost less than full-sized rooms, the resources needed to set up these tents might still limit their widespread adoption.

**Description**

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

Compact tents are placed over the patient’s head and shoulders.⁹⁻¹¹ Larger designs enclosure the entire patient bed.¹²,¹³ Tents are constructed of either clear, rigid plastic or clear, soft plastic over a reusable frame. Providers reach patients through hand-access ports or slits in the walls. A vacuum hose connected to the hospital air-evacuation system creates the negative-pressure environment.⁸

As of mid-November 2020, FDA had granted 5 EUAs for negative-pressure tents—3 compact tents⁹⁻¹¹ and 2 whole-bed tents¹²,¹³—to enhance personal barrier protection for providers during airway management, medical procedures, or transport of patients with COVID-19. Of added significance, on August 20, 2020, FDA revoked an umbrella EUA issued on May 1, 2020, that authorized use of passive protective barrier enclosures (ie, without negative pressure) when treating patients with confirmed or suspected COVID-19.¹⁴,¹⁵ FDA cited recent research of simulated intubations using passive barriers, which suggested they might not reduce and could increase provider exposure to airborne particles (eg, tearing personal protective equipment, escape of airborne particles).¹⁶,¹⁷ Further, passive barriers might increase patient risk by restricting providers’ mobility in performing procedures quickly or accurately on first attempts.¹⁶,¹⁷ Thus, FDA recommended using only negative-pressure protective barrier enclosures, noting it granted EUAs for multiple negative-pressure tents.¹⁴,¹⁵

**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, enhancing 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 and July 24, 2020, five ECRI stakeholders—reflecting allied health, health systems, physician, and research perspectives—offered comments and ratings on this topic. The list below summarizes 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 those of standard rooms, which might prevent hospitals from using these tents.
Chapter 2. Identifiable Risk Factors and Prognostic Indicators

Chapter Summary

As of March 12, 2021, we were not monitoring any COVID-19-related identifiable risk factor and prognostic indicator topics. We had previously been monitoring 7 topics, which are listed in the January 2021 PCORI Health Care Horizon Scanning System: Horizon Scanning COVID-19 Supplement Status Report, Volume 2, Issue 1. The topics were sent for comment to internal ECRI stakeholders and received at least 5 sets of ratings and comments from stakeholders between May 18, 2020, and March 11, 2021. Additional ratings and comments might also have been received after March 11, 2021.

Internal ECRI stakeholders did not think that any of the 7 topics had moderately high to high impact potential relative to COVID-19-related patient-oriented health care in the United States within the next 12 months. All 7 topics have been archived.

Topics Considered for Inclusion in This Report

Because all 7 COVID-19-related identifiable risk factor and prognostic indicator topics had been previously archived, no topics were considered for inclusion in this report.
Chapter 3. Screening and Diagnostics

Chapter Summary

As of March 12, 2021, we were monitoring or had recently archived 22 COVID-19-related screening and diagnostics topics. Seventeen of these topics are listed in the January 2021 PCORI Health Care Horizon Scanning System: Horizon Scanning COVID-19 Supplement Status Report, Volume 2, Issue 1; the remaining 5 topics were added to the system subsequent to that report. All 22 topics were sent for comment to internal ECRI stakeholders and received at least 5 sets of ratings and comments from stakeholders between May 18, 2020, and March 11, 2021. Additional ratings and comments might also have been received after March 11, 2021.

Five topics included in the previous High Impact Report were excluded from this report after stakeholders re-reviewed the topics and rated them as having low potential for impact (see ratings in Table 3.2):

- Accula SARS-CoV-2 point-of-care test to diagnose COVID-19 (incorporated into Point-of-care nucleic acid–based assays to diagnose COVID-19)
- Employee SARS-CoV-2 testing programs to reopen businesses
- Next-generation sequencing assays to diagnose COVID-19 (2.8)
- Point-of-care rapid breath tests to detect COVID-19 (2.8)
- QIAstat-Dx Respiratory SARS-CoV-2 Panel test to diagnose COVID-19

Of the 22 topics, 5 have been selected for inclusion because internal ECRI stakeholders thought they 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.
Topics Considered for Inclusion in This Report

Table 3.1 lists 5 topics selected for inclusion in this High Impact Report. Included topics received, on average, moderately high to high impact ratings and demonstrated considerable consensus among stakeholders, as evident in the ratings and comments. Topics are arranged 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

<table>
<thead>
<tr>
<th>Topic title</th>
<th>Potential impact score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lucira COVID-19 All-In-One Test Kit at-home assay to diagnose COVID-19a</td>
<td>3.5</td>
</tr>
<tr>
<td>Population-wide antibody testing to quantify coronavirus infection rates</td>
<td>3.4</td>
</tr>
<tr>
<td>Saliva-based nucleic acid assays to diagnose COVID-19</td>
<td>3.4</td>
</tr>
<tr>
<td>Dual point-of-care nucleic acid assays to diagnose COVID-19 and influenza</td>
<td>3.2</td>
</tr>
<tr>
<td>Existing FDA-authorized nucleic acid–based tests with potential to help identify the SARS-CoV-2 B.1.1.7 varianta</td>
<td>3.2</td>
</tr>
</tbody>
</table>

Table 3.2 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 arranged 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

<table>
<thead>
<tr>
<th>Topic title</th>
<th>Potential impact score</th>
</tr>
</thead>
<tbody>
<tr>
<td>3D-printed nasopharyngeal swabs for COVID-19 testing</td>
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</tr>
<tr>
<td>Ellume over-the-counter and at-home assay to diagnose COVID-19</td>
<td>3.0</td>
</tr>
<tr>
<td>Assure COVID-19 IgG/IgM Rapid Test Device point-of-care test to detect antibodies against SARS-CoV-2</td>
<td>2.8</td>
</tr>
<tr>
<td>Employee SARS-CoV-2 testing programs to reopen businessesa</td>
<td>2.8</td>
</tr>
<tr>
<td>Multigene expression tests to predict COVID-19 before symptom onset</td>
<td>2.8</td>
</tr>
<tr>
<td>Next-generation sequencing assays to diagnose COVID-19a</td>
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<tr>
<td>Point-of-care antigen assays to diagnose COVID-19</td>
<td>2.8</td>
</tr>
<tr>
<td>Point-of-care nucleic acid–based assays to diagnose COVID-19a</td>
<td>2.8</td>
</tr>
<tr>
<td>Point-of-care rapid breath tests to detect COVID-19</td>
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</tr>
<tr>
<td>Serology test kits for quantitative detection of anti-SARS-CoV-2 antibodiesa</td>
<td>2.8</td>
</tr>
<tr>
<td>COVID-19 diagnostic test at-home self-collection kits</td>
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</tr>
<tr>
<td>Topic title</td>
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<tr>
<td>---------------------------------------------------------------------------</td>
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<tr>
<td>CRISPR-based assays to diagnose COVID-19*</td>
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<tr>
<td>College and university SARS-CoV-2 testing programs to prevent COVID-19 spread among returning students*</td>
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</tr>
<tr>
<td>QIAstat-Dx Respiratory SARS-CoV-2 Panel test to diagnose COVID-19</td>
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<tr>
<td>Artificial intelligence blood test analysis to rule out COVID-19*</td>
<td>2.2</td>
</tr>
<tr>
<td>cPass SARS-CoV-2 test to detect neutralizing antibodies against SARS-CoV-2*</td>
<td>2.2</td>
</tr>
<tr>
<td>T-cell assay (T-Detect COVID) to identify past COVID-19 infection</td>
<td>1.8</td>
</tr>
</tbody>
</table>

* Topic was recently archived.

**Topic Summaries**

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

**Lucira COVID-19 All-In-One Test Kit At-Home Assay to Diagnose COVID-19**

**Potential Impact Score**

Stakeholders reviewing this topic thought that Lucira COVID-19 All-In-One Test Kit at-home assay to diagnose 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**

- The Lucira COVID-19 All-In-One Test Kit is the first COVID-19 test granted Emergency Use Authorization (EUA) by FDA for use in the home setting as well as in point-of-care (POC) settings.
- The test requires a prescription from a health care provider for home use in patients aged 14 years or older who are suspected of having COVID-19. Patients testing positive should follow up with their health care provider and are recommended to self-quarantine.
- Lucira costs about $50 per test and includes a single-use, battery-operated unit; a nasal swab; a sample vial; and a plastic disposal bag. Based on results from 51 samples, the manufacturer claims that the test yields laboratory-quality results in about 30 minutes.
- If Lucira shows comparable accuracy to standard-of-care tests, it might lower the burden on testing centers and shift care to an at-home setting, which might also expand to airports, long-term health care facilities, schools, and workplaces.
Description

The Lucira COVID-19 All-In-One Test Kit (Lucira Health, Inc, Emeryville, California) is the first coronavirus test granted EUA for use in the home setting by FDA.\(^{11}\) It is a low-complexity, portable loop-mediated isothermal amplification assay that amplifies and detects viral nucleic acids.\(^ {12}\)

A health care provider prescribes the test for home use in patients aged 14 years or older who are suspected of having COVID-19. The test is also intended for use in POC settings, including temporary screening facilities, physician offices, laboratories, urgent care, and long-term nursing facilities.\(^ {13,14}\) The Lucira COVID-19 test includes a single-use, battery-operated testing unit; a nasal swab; a sample vial; and a plastic disposal bag.\(^ {14}\)

According to Lucira Health, Lucira COVID-19 requires a small sample volume to yield laboratory-quality results in about 30 minutes and is expected to cost about $50 per kit.\(^ {15}\) Patients who test positive are recommended to self-quarantine and follow up with their health care provider.

The Lucira COVID-19 package insert claims that the test’s performance was evaluated in 51 samples also tested with an FDA-authorized coronavirus test.\(^ {13,14}\) Compared to this reference standard, Lucira COVID-19 showed a positive percent agreement of 94% and a negative percent agreement of 98%.\(^ {14}\)

Possible Areas of Impact

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

Possible Future Impacts

As the pandemic continues, communities are beginning to accept that they will have to coexist with COVID-19 to prevent complete lockdowns. In addition to safety measures, such as mask wearing and social distancing, regular and on-demand testing is used to identify infected and uninfected individuals. Reliable home COVID-19 testing has been sought since the pandemic started, to quickly and conveniently identify infected individuals while limiting exposure to others. Lucira offers fast turnaround times, convenient at-home testing, reliable accuracy, and a competitive price.\(^ {14,15}\)

While testing at central laboratories is standard of care, people have to wait several days to receive test results. For many, waiting for results in self-isolation is not feasible; thus, rapid and reliable tests are needed. Similar to rapid POC tests, Lucira might reduce the testing burden on central laboratories. However, Lucira’s at-home testing feature allows individuals to test for COVID-19 and receive a result within 30 minutes without exposing health care workers to the virus. People might also use Lucira before joining large crowds such as those in airports, concerts, stadiums, or movie theaters.\(^ {16}\)
Key Stakeholder Perspectives

Between November 25, 2020, and December 4, 2020, six ECRI stakeholders—reflecting health care generalist, health systems, and research perspectives—provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- Lucira will increase access to testing and might shift COVID-19 management to an at-home setting by providing purportedly faster results with comparable accuracy to standard-of-care tests performed at health centers and central laboratories.
- Even though Lucira COVID-19 was validated in a trial that used a small number of samples (n = 51), as use of the test expands, it might reduce demands on testing centers, and testing might extend to airports, long-term health care facilities, schools, and workplaces.
- Despite Lucira’s $50-per-test cost, frequent and widespread testing might increase health care costs and worsen disparities for low-income individuals who lack financial assistance.
- At-home testing requires that people voluntarily report positive results to a provider and that they self-isolate. Some people might not report positive results, fearing social or economic consequences from isolation protocols.

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 Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH) are conducting population-wide antibody studies using samples from volunteer blood donors and commercial laboratories to better understand prevalence of exposure to 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 guidance (eg, wearing masks, social distancing).
Stakeholders also raised legal, privacy, and security concerns of coronavirus antibody test results being used to influence policies on 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. Testing for coronavirus-specific antibodies has potential to serve as a population health screening tool to identify individuals who have been exposed to the virus regardless of whether they developed symptoms. Widespread serosurveys could 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 reinfection.\(^{17,18}\) Serosurveys could also help identify individuals who can give convalescent plasma or donate blood or platelets needed for some COVID-19 patients.\(^{19}\)

Several large, government agency–sponsored antibody studies are ongoing. The CDC is collaborating with commercial laboratories to test blood samples submitted for reasons unrelated to COVID-19. The CDC is also conducting a countrywide COVID-19 study that plans to test samples from up to 325,000 blood donors in 25 selected cities over 18 months.\(^{20}\) Additionally, the NIH has launched a similar study of 15,000 participants with no known coronavirus infection or exposure.\(^{21}\) Results from an antibody positivity (ie, seroprevalence) study in 9028 blood samples from individuals who had not been diagnosed with COVID-19 showed that there were nearly 5 undiagnosed cases for every individual diagnosed with COVID-19 as of August 2020.\(^{22}\)

In addition to these large-scale government agency–sponsored studies, results from a large range of US and international seroprevalence studies have been published.\(^{23}\) Of note, a January 2021 study of the prevalence of coronavirus antibodies in 21,424 patients receiving dialysis across the United States identified a seroprevalence of 18.7% when standardized to the US adult population.\(^{24}\)

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

Widespread antibody testing might clarify actual infection rates and help more accurately track the spread of the coronavirus. These data may inform public health efforts surrounding disease surveillance and management by being incorporated into models of coronavirus spread, revealing patterns of transmission dynamics, aiding in calculation of the case fatality rate, and tracking the persistence of coronavirus antibodies over time.

However, seroprevalence studies might misinform public health guidance if the tests generate high levels of false-positive or false-negative results. In particular, patients who had mild or
asymptomatic disease may not have mounted a large antibody response to treatment and, therefore, test negative for coronavirus antibodies. Additionally, antibody testing studies using samples from blood donors or other potentially biased populations might misrepresent true infection rates if infection rates are different in the targeted population than they are in the population as a whole.

Key Stakeholder Perspectives

Between June 25, 2020, and July 6, 2020, five ECRI stakeholders—reflecting health care generalist, health systems, nursing, and research perspectives—gave comments and ratings on this topic. The list below summarizes key stakeholder perspectives.

- Serology tests could provide useful information about the spread of COVID-19 and how long the antibodies prevent reinfection.
- Widespread testing to determine rates of coronavirus infection 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.
- If results are relayed to study volunteers, 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.

Saliva-Based Nucleic Acid Assays to Diagnose COVID-19

Potential Impact Score

Stakeholders reviewing this topic thought that saliva-based nucleic acid 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

- Saliva-based nucleic acid assay sampling can be performed at home or in health centers to detect coronavirus nucleic acids in a patient-collected saliva sample—a less invasive and less costly method than standard nasopharyngeal swab sample collection.
- Results from 2 systematic reviews and 2 published studies found that saliva-based nucleic acid tests were comparable to nasopharyngeal swab–based testing.
- As of March 2021, FDA has granted Emergency Use Authorization (EUA) to 16 saliva-based nucleic acid tests for use in laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA). The EUAs for most tests allow patients to collect samples at home.
• Stakeholders commenting on this topic indicated that, compared with nasopharyngeal swab–based tests, saliva-based tests have similar accuracy, are more convenient to use, cost less, and reduce the exposure of health care workers to infected patients.

**Description**

Saliva-based nucleic acid assays use a process known as polymerase chain reaction (PCR) to diagnose COVID-19 by detecting coronavirus nucleic acids in a patient’s saliva sample. Stakeholders evaluated the potential impacts of these saliva-based assays as a single topic because such tests use similar methods and are expected to yield relatively indistinguishable results. Compared with nasopharyngeal swab sampling, which is considered the standard of care, saliva sampling is less invasive, less costly, and can be performed at home or at a health center without the supervision of a health care worker. Some saliva-based assays have been validated to use minimally processed saliva samples, obviating the need for a nucleic acid extraction step, which might save time and testing supplies.25

Results from 2 systematic reviews suggest that saliva-based tests yield similar outcomes to nasopharyngeal swab–based tests for detecting coronavirus nucleic acids.25 We also identified 2 recently published studies that compared COVID-19 positivity on paired saliva samples and nasopharyngeal swabs tested by PCR. The studies reported that saliva samples had an overall agreement between 94% and 99% for detecting coronavirus nucleic acids when compared with simultaneously collected nasopharyngeal swab samples.26,27

As of March 2021, FDA has granted EUA to 16 saliva-based nucleic acid assays for use in CLIA-certified laboratories to diagnose COVID-19:

- Advanta Dx SARS-CoV-2 (Fluidigm Corp, South San Francisco, California)28
- Ambry COVID-19 (Ambry Genetics, Aliso Viejo, California)29
- Clarifi COVID-19 (Quadrant Biosciences, Inc, Syracuse, New York)30
- covidSHIELD (University of Illinois, Urbana, Illinois)31
- CRL Rapid Response (Clinical Reference Laboratory, Inc, Lenexa, Kansas)32
- DxTerity SARS-CoV-2 (DxTerity Diagnostics, Inc, Rancho Dominguez, California)33
- Express Gene 2019-nCoV (Express Gene, LLC, Palmetto Bay, Florida)34
- Gravity Diagnostics SARS-CoV-2 (Gravity Diagnostics, LLC, Covington, Kentucky)35
- Infinity Biologix TaqPath SARS-CoV-2 (Infinity Biologix, LLC, Piscataway, New Jersey)36
- NeuMoDx SARS-CoV-2 (NeuMoDx Molecular, Inc, Ann Arbor, Michigan)37
- P23 TaqPath SARS-CoV-2 (P23 Labs, LLC, Little Rock, Arkansas)38
- Phosphorus COVID-19 (Phosphorus Diagnostics, LLC, Secaucus, New Jersey)39
- Rheonix COVID-19 MDx (Rheonix, Inc, Grand Island, New York)40
- SalivaDirect (Yale School of Public Health, New Haven, Connecticut)41
- TRUPCR SARS-CoV-2 (3B Blackbio Biotech India, Ltd, Somerset, New Jersey)42
- Wren Laboratories COVID-19 (Wren Laboratories, Inc, Branford, Connecticut)43
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

Even though nasopharyngeal swab testing is considered the standard of care, mass testing requires a large quantity of supplies and trained personnel, which results in an economic and planning burden at testing sites. Swabbing also causes discomfort to patients, and significant septum deviation is a contraindication that might discourage some people from getting tested. Saliva is a viable noninvasive specimen because it contains liquid, cells, oral bacteria, and viruses from the oral mucosa and upper airways; however, its occasional stringy and thick consistency might interfere with test results.

Similar to nasopharyngeal swab–based tests, saliva–based tests might help triage patients. For most EUA tests, saliva samples can be collected at home without the supervision of a health care worker. This might reduce the risk of transmitting the coronavirus to medical staff and other patients while easing the burden at centers with limited testing supplies and personal protective equipment. The adoption of saliva–based tests might improve patient willingness to undergo testing, thus increasing testing rates, including among infected patients who are not yet showing symptoms.

Key Stakeholder Perspectives

Between August 31, 2020, and October 5, 2020, five ECRI stakeholders—reflecting allied health, health care generalist, health systems, nursing, and research perspectives—provided comments and ratings on this topic. The list below summarizes key stakeholder perspectives.

- A clear advantage that saliva–based tests offer over nasopharyngeal swab–based tests is that allowing patients to collect a specimen at home reduces the exposure of health care workers to infected patients.
- Because collecting a saliva sample is noninvasive and more convenient than collecting a nasopharyngeal swab sample, saliva–based testing could improve patient outcomes by increasing testing rates and reducing COVID–19 spread.
- Although similar in accuracy, saliva–based tests are expected to cost less than nasopharyngeal swab–based tests, which might reduce disparities and improve care process and delivery.
- The adoption of saliva–based tests might be hampered by numerous authorized tests and public test fatigue. It is also unknown whether the assays can detect viral nucleic acids at all stages of infection.
Dual Point-of-Care Nucleic Acid Assays to Diagnose COVID-19 and Influenza

Potential Impact Score

Stakeholders reviewing this topic thought that dual point-of-care nucleic acid assays to diagnose COVID-19 and influenza 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 infection symptoms that the coronavirus and influenza virus initially cause can be similar, yet clinicians must be able to differentiate between the 2 respiratory infections to properly manage patients.

• Point-of-care (POC) nucleic acid–based assays (ie, tests that detect RNA and DNA) have been developed to diagnose COVID-19 and influenza within an hour.

• FDA has granted Emergency Use Authorization (EUA) to cobas SARS-CoV-2 & Influenza A/B Nucleic Acid Test and Xpert Xpress SARS-CoV-2/Flu/RSV under a Clinical Laboratory Improvement Amendments of 1988 (CLIA) certificate of waiver, which allows these tests to be performed outside of CLIA-certified laboratories.

• Stakeholders commenting on this topic thought that dual POC tests that can rapidly rule out or identify COVID-19 and influenza could help health care workers manage patients soon after testing, leading to improved health outcomes.

Description

The flu season in the Northern Hemisphere usually begins in the fall, peaks between December and February, and tapers around May. Because symptoms for coronavirus and influenza virus infection can be similar, clinicians must be able to differentiate between the two to properly manage patients.44

Dual reverse transcription polymerase chain reaction (RT-PCR) assays have been developed that can diagnose both COVID-19 and influenza. FDA has granted EUA to cobas SARS-CoV-2 & Influenza A/B Nucleic Acid Test (Roche Molecular Systems, Inc, Branchburg, New Jersey)45 and Xpert Xpress SARS-CoV-2/Flu/RSV (Cepheid, Inc, Sunnyvale, California).46 These assays are intended for use in POC settings, including temporary screening facilities, physician office laboratories, urgent care, and long-term nursing facilities.

A patient’s nasal or nasopharyngeal sample is loaded into a single-use cartridge or tube that contains the reagents needed for nucleic acid extraction, amplification, and detection of coronavirus and influenza virus. The cartridge or tube is placed in an analyzer that controls the reaction and reports whether viral nucleic acids have been detected. The manufacturers claim that their assays require a small sample volume and minimal hands-on time to yield accurate results in less than an hour.47,48
In a study conducted in 375 nasopharyngeal samples, the dual cobas test had a positive percent agreement (PPA) of 100% and a negative percent agreement (NPA) of 97.4% compared with a standard-of-care RT-PCR test.49

Although we found no data specific to the performance of Xpert Xpress SARS-CoV-2/Flu/RSV, we identified 2 multicenter studies suggesting that single-virus and multipanel versions of Xpert Xpress perform with similar accuracy. These studies compared Xpert Xpress SARS-CoV-2 with several standard-of-care RT-PCR tests in 483 nasopharyngeal and 88 upper respiratory tract samples and reported a PPA of 99.5% to 100% and an NPA of 95.8% to 100%.50,51

Possible Areas of Impact
- Health care delivery
- Health care costs
- Health care disparities
- Patient outcomes
- Population health

Possible Future Impacts

Even before the beginning of the COVID-19 pandemic, respiratory infections caused by influenza virus and respiratory syncytial virus (RSV) were the leading causes of sickness and death worldwide in young children, pregnant women, older adults, and patients with other illnesses.52 As the pandemic continues to overlap with the flu season, it is extremely important to correctly identify the virus causing a respiratory infection because this will help clinicians determine a patient’s optimal management.44

Rapid detection of respiratory viruses using POC tests has the potential to decrease the overall time it takes to receive test results, testing costs, and number of hospitalizations. Accurate identification of the infectious agent might also decrease the need for follow-up diagnostic imaging and treatment for opportunistic infections.46 More importantly, rapid testing might allow health centers to triage infected and uninfected patients on the same day they are tested and promote early isolation to prevent further spread of the viruses.52-54

Key Stakeholder Perspectives

Between October 20, 2020, and October 27, 2020, five ECRI stakeholders—reflecting clinical engineering, health care generalist, health systems, physician, and research perspectives—provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- Even though mask wearing and social distancing have the potential to lower respiratory infections, there was an uptick in COVID-19 cases congruent with the beginning of the flu season. Dual POC tests to distinguish between coronavirus and influenza virus are critical tools for triaging patients soon after being tested.
• Dual POC tests can pinpoint the infectious agent responsible for a patient’s respiratory symptoms. This identification might have an enormous impact on population health because early treatment for the appropriate virus might lead to improved management of symptoms and fewer hospitalizations.

• Because RSV is responsible for many respiratory infections in children, Xpert Xpress’s ability to also detect RSV might lead to appropriate care in this cohort. Clear test results might reduce anxiety in children who might otherwise worry that they have COVID-19 while waiting for subsequent follow-up test results.

• Some concerns exist that manufacturing delays or constraints might limit the availability of these dual POC tests to a few larger health centers. The adoption of these tests might also be limited by pandemic fatigue and the availability of many other COVID-19 tests.

Existing FDA-Approved Nucleic Acid-Based Tests With Potential to Help Identify the SARS-CoV-2 B.1.1.7 Variant

Potential Impact Score
Stakeholders reviewing this topic thought that existing FDA-approved nucleic acid–based tests with potential to help identify the SARS-CoV-2 B.1.1.7 variant 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 SARS-CoV-2 B.1.1.7 variant, initially identified in the United Kingdom, might be more infectious than previous coronavirus strains and might avoid immune responses.

• FDA has identified 2 nucleic acid–based tests with potential to identify individuals likely to be infected with B.1.1.7. However, possible B.1.1.7 infections will have to be confirmed by using extensive genetic sequencing.

• Tests that screen for B.1.1.7 infections assess multiple viral genes, but positive cases with loss of the S gene signal might suggest the presence of the variant.

• Stakeholders commenting on this topic thought that the use of tests to identify possible B.1.1.7 outbreaks might help health departments prevent spread and guide vaccination efforts. However, manufacturing capability of these tests is limited, which might decrease their effect on current testing and prevention measures.
Description

In December 2020, a genetic variant of SARS-CoV-2 with higher transmissibility, B.1.1.7, was identified in the United Kingdom. It has subsequently been detected in countries around the world.\(^55\)

Eight of the 17 mutations accumulated in B.1.1.7 occur in the spike protein–encoding S gene. Two of these mutations raise potential health concerns: N501Y might increase infectivity, and 69-70del might help the strain evade immune responses. Only sequencing can detect B.1.1.7, but no tests have been specifically developed to detect B.1.1.7.\(^55\,56\) FDA has identified 2 authorized nucleic acid–based tests (Linea COVID-19 Assay Kit [Applied DNA Sciences, Inc, Stony Brook, New York]\(^57\) and TaqPath COVID-19 Combo Kit [Rutgers University, Piscataway, New Jersey]\(^58\)) with the potential to identify possible B.1.1.7 infections.\(^59\)

The S gene mutations in B.1.1.7 lead to loss of an S gene signal from these tests. However, because the tests assess multiple viral genes, they produce positive signals from other viral sequences and appropriately detect SARS-CoV-2. This pattern of results (negative for S gene, positive for other genes) might serve as an indicator of a potential B.1.1.7 infection.\(^60\) However, because variants affecting S gene amplification are not unique to B.1.1.7 (eg, B.1.351 variant identified in South Africa, P.1 variant identified in Brazil), follow-up testing by more extensive genetic sequencing is required to confirm the presence of B.1.1.7.\(^56\,60\)

Possible Areas of Impact

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

Possible Future Impacts

Even though the B.1.1.7 variant was first described in December 2020, evidence suggests that it had been spreading through the United Kingdom since September 2020. These data, together with computer modeling, suggest that B.1.1.7 is 70% more transmissible than previous dominant SARS-CoV-2 strains. The mutations B.1.1.7 has accumulated do not appear to significantly affect the performance of most FDA-authorized tests. However, proper identification might be pivotal for preventing B.1.1.7 from spreading and becoming the coronavirus’s dominant strain.\(^60\,61\)

Early evidence suggests that B.1.1.7 is associated with an increased risk of COVID-19-related death.\(^62\) The use of Linea and TaqPath and similar COVID-19 tests that report the loss of S gene signal in positive cases to screen for, but not confirm, B.1.1.7 might help suppress the spread of this variant by predicting possible outbreaks, thereby decreasing COVID-19-related hospitalizations and deaths. This approach to screen for B.1.1.7 might also cost less than more extensive sequencing.\(^59\)
**Key Stakeholder Perspectives**

Between January 18, 2021, and February 2, 2021, five ECRI stakeholders—reflecting health care generalist, health systems, physician, and research perspectives—provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- Tests such as Linea and TaqPath provide an easy and quick way to identify individuals who are likely to be infected with B.1.1.7, which will allow time-consuming full sequencing to be allocated to these specific cases.

- Screening for B.1.1.7 might help local and state health departments provide guidance to prevent its spread. Identifying possible B.1.1.7 outbreaks might also help direct vaccination efforts in communities surrounding the outbreak to contain the virus and prevent it from mutating into new variants.

- The Linea and TaqPath assays are 2 of many tests central laboratories use to diagnose COVID-19. The companies that manufacture and distribute these tests might have limited production capabilities, meaning they will be unable to supply laboratories with enough tests to meet the demand.

- As vaccines continue to roll out, current testing and prevention measures are unlikely to shift dramatically toward the use of tests that can screen and subsequently confirm infections with the B.1.1.7 variant.
Chapter 4. Systems and Management

Chapter Summary

As of March 12, 2021, we were monitoring or had recently archived 25 COVID-19-related systems and management topics. Twelve of these topics are listed in the January 2021 PCORI Health Care Horizon Scanning System: Horizon Scanning COVID-19 Supplement Status Report, Volume 2, Issue 1; the remaining 13 topics were added to the system subsequent to that report. All 25 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 March 12, 2021.

One topic included in the previous High Impact Report, Contact tracing software systems to mitigate coronavirus epidemic scenarios, was archived after stakeholders re-reviewed the topic and rated it as having low potential for impact; the topic was not considered for inclusion in this report. From among the remaining 24 topics, 8 topics have been selected that internal ECRI stakeholders thought 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.

Topics Considered for Inclusion in This Report

Table 4.1 lists 8 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 arranged 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

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<thead>
<tr>
<th>Topic title</th>
<th>Potential impact score</th>
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<tbody>
<tr>
<td>Post-COVID-19 recovery programs</td>
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<tr>
<td>COVID-19 vaccine allocation planner</td>
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<tr>
<td>Drive-through COVID-19 vaccination clinics</td>
<td>3.4</td>
</tr>
<tr>
<td>Mobile health clinics to increase access to COVID-19 health services</td>
<td>3.4</td>
</tr>
<tr>
<td>Statewide surge line for patient load management during the coronavirus pandemic</td>
<td>3.3</td>
</tr>
<tr>
<td>Multidose vials to strengthen vial supply chain during COVID-19</td>
<td>3.2</td>
</tr>
<tr>
<td>Phone applications to manage COVID-19 vaccine communications and scheduling</td>
<td>3.2</td>
</tr>
<tr>
<td>Surveillance programs to identify and follow the spread of emerging SARS-CoV-2 variants</td>
<td>3.2</td>
</tr>
</tbody>
</table>
Table 4.2 lists 12 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 or were not considered by most stakeholders to be likely to have an impact within the next 12 months. Topics are arranged 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

<table>
<thead>
<tr>
<th>Topic title</th>
<th>Potential impact score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Artificial intelligence (AI)-assisted radiographic image assessment for determining COVID-19 prognosis&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3.2</td>
</tr>
<tr>
<td>Drive-through prenatal care model to reduce COVID-19 exposure</td>
<td>3.1</td>
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<tr>
<td>3D-printed face shields to protect against COVID-19 infection</td>
<td>3.0</td>
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<tr>
<td>COVID-19 Testing Impact Calculator</td>
<td>3.0</td>
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<tr>
<td>Emotional PPE Project to facilitate health care worker access to mental health services</td>
<td>3.0</td>
</tr>
<tr>
<td>Machine learning to predict the spread of COVID-19</td>
<td>3.0</td>
</tr>
<tr>
<td>Pandemic response strategies to mitigate mental health effects of the COVID-19 pandemic</td>
<td>3.0</td>
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<tr>
<td>Support phone lines to alleviate emotional burden on health care workers&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.8</td>
</tr>
<tr>
<td>Waived insurance copayments, coinsurance, and deductibles to facilitate patient access to mental health services&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.8</td>
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<tr>
<td>Machine learning algorithm to predict spikes in COVID-19 cases&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.7</td>
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<tr>
<td>Mental health applications to alleviate mental health effects of COVID-19&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.7</td>
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<tr>
<td>Public-private partnerships to fast-track COVID-19 treatment and vaccine development&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.7</td>
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<tr>
<td>Recharge rooms to reduce stress in frontline health care workers&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.7</td>
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<tr>
<td>Temporary field hospitals to increase capacity during the COVID-19 pandemic&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.7</td>
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<tr>
<td>Pediatric-specific risk scoring systems to prioritize surgical procedures&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.4</td>
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<tr>
<td>Contact-tracing software systems to mitigate coronavirus epidemic scenarios&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.0</td>
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<tr>
<td>SMART Health Cards to provide digital COVID-19 immunization records&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.0</td>
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</table>

<sup>a</sup> 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.

<sup>b</sup> Topic was recently archived.
Topic Summaries

We present below 8 summaries on topics deemed to have moderately high to high impact potential. Topics are arranged first in descending order by potential impact score; topics with the same score are listed alphabetically by topic title.

Post-COVID-19 Recovery Programs

Potential Impact Score

Stakeholders reviewing this topic thought that post-COVID-19 recovery programs 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

- Multidisciplinary clinical rehabilitation programs might help facilitate recovery from the long-term effects of COVID-19.
- Several hospitals across the country are setting up post-COVID-19 recovery programs to accommodate the growing need for continued care in patients experiencing postacute sequelae of SARS-CoV-2 infection.
- Some programs provide recovery from specific side effects (eg, neurological effects); other programs have multidisciplinary teams comprising primary care physicians, pulmonologists, neurologists, mental health professionals, and others.
- Stakeholders commenting on this topic thought that these recovery programs, if carried out correctly, might improve patient outcomes and provide data for better managing growing cases of long-term effects of COVID-19.
- Stakeholders expressed concern that these recovery programs may not be covered by insurance, which might increase financial burden on patients with long-term effects and their caregivers.

Description

Some individuals who have recovered from COVID-19 have an increased risk of long-term health problems because of permanent damage to their lungs, heart, kidneys, and brain. Even with no detectable damage to these organs, some patients still report lingering and debilitating symptoms months after clearing the infection. The National Institutes of Health has launched an initiative to study postacute sequelae of SARS-CoV-2 infection.

Many hospitals across America are setting up post-COVID-19 recovery programs to accommodate the growing need for continued care in patients experiencing long-term side effects from COVID-19. As of March 2021, more than 67 million people have recovered from COVID-19. Ongoing post-COVID-19 medical, psychological, and rehabilitation programs may help ensure a full recovery from COVID-19.
Patients who have cleared the viral infection but are still experiencing symptoms can go to postinfection programs with or without a referral, where they will be screened to identify their clinical needs and establish a therapeutic plan. The programs consist of multidisciplinary teams comprising primary care physicians, pulmonologists, neurologists, mental health professionals, physical/occupational/speech therapists, and others. Some recovery programs address specific areas such as neurological effects, long-term symptoms in pediatric populations, or respiratory recovery. Some programs have implemented new therapeutic approaches to accommodate the precautions needed to minimize the risk of viral spread, such as negative-pressure rooms for patients in need of inpatient rehabilitation and isolation as well as therapy through telemedicine.

**Possible Areas of Impact**

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

**Possible Future Impacts**

Post-COVID-19 recovery programs might improve management of long-term sequelae from COVID-19 while increasing knowledge about the long-term effects of COVID-19. These programs might increase health care costs if clinic visits are not covered by insurance. Patients might face long wait times due to the lack of recovery programs and increased demand for these services.

**Key Stakeholder Perspectives**

Between November 10, 2020, and November 17, 2020, six ECRI stakeholders, reflecting health systems and research perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- Post-COVID-19 recovery programs might improve health outcomes for patients who continue to have persistent symptoms after the main course of COVID-19.
- Centralized data collection at these recovery centers can improve understanding of the long-term effects of COVID-19 and help assess the effectiveness of various treatments.
- Insurance coverage might not be available for patients with postacute sequelae of COVID-19, which could significantly increase health care costs for patients who may be unable to work at their previous capacity and their families or caregivers.
- Health care disparities might be reduced if the multidisciplinary recovery programs help manage various postacute symptoms in one center; however, disparities might increase due to the lack of recovery programs across the United States.
- Although full recovery from COVID-19 is an important goal for those who have had the disease, many more recovery programs are desired to expand access to basic care (eg, maternal health care, mental health) in the general population.
COVID-19 Vaccine Allocation Planner

Potential Impact Score
Stakeholders reviewing this topic thought that the COVID-19 Vaccine Allocation Planner 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 COVID-19 Vaccine Allocation Planner was created to help state and local officials and health care leaders plan and implement fair vaccine distribution plans with limited vaccine availability.
- The standardized tool lets users estimate achievable local vaccine coverage based on vaccine supplies, vulnerability of local populations, and other variables.
- Some large information technology companies are also starting to offer their own vaccine allocation planning tools, which could complicate a coordinated national vaccine rollout strategy if multiple approaches take hold.
- Stakeholders reviewing this topic thought the COVID-19 Vaccine Allocation Planner could offer a valuable tool for equitable vaccine distribution at the state and local level, provided that local leaders embrace the planning tool and put its recommendations into practice.
- Stakeholders also thought the usefulness of this planning tool has diminished over time as vaccine production and distribution has improved since the shortages seen during the early vaccine rollout phase.

Description
Early supplies of COVID-19 vaccines are limited. To help with orderly and equitable early distribution of coronavirus vaccines, researchers at Ariadne Labs (Boston, Massachusetts) and the Surgo Foundation (Washington, DC) developed the COVID-19 Vaccine Allocation Planner. It is intended to help state and county decision makers distribute early vaccines to the 13 priority populations identified in the Framework for Equitable Allocation of COVID-19 Vaccine guidelines, created by the National Academies of Sciences, Engineering, and Medicine. The vaccine planning tool purportedly lets users obtain estimates of the size of high-priority populations in their respective geographic regions and consider other factors, such as community vulnerability, to assign relative weights to groups when considering which groups should have the highest priority. The allocation planner also helps users estimate the number of vaccine doses available and the percentage of vaccine coverage achievable under different scenarios.

Several large information technology companies, including Google (Mountain View, California), Microsoft (Redmond, Washington), and IBM (Armonk, New York), are reportedly launching their own digital tools intended to support users with COVID-19 disease forecasting,
vaccine allocation planning, and supply chain logistics.\textsuperscript{77,78} Multiple approaches could complicate a smooth national vaccine rollout if a lack of coordination produces overlap or confusion.

In a related report that has not yet undergone peer review, Massachusetts Institute of Technology researchers developed a computational model suggesting that optimized COVID-19 vaccine allocation could reduce US deaths by 10\% to 25\%, or 10 000 to 20 000 deaths, over 3 months.\textsuperscript{79}

**Possible Areas of Impact**

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

**Possible Future Impacts**

The COVID-19 Vaccine Allocation Planner might improve equitable distribution of vaccines to vulnerable populations by giving local officials tools to implement a more standardized approach. By providing more transparency early in the vaccine distribution process, the COVID-19 Vaccine Allocation Planner might increase public acceptance of vaccine distribution plans. If the allocation planner can help provide for fair distribution during initial vaccine rollouts to highest-risk groups, the tool might offer a foundation for continued equitable vaccine distribution among the wider population.

**Key Stakeholder Perspectives**

Between November 10, 2020, and April 20, 2021, ten ECRI stakeholders, reflecting physician, research, health systems, and health care generalist perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- A standardized tool to equitably distribute limited vaccine supplies is highly desirable and could help alleviate disparities, provided the data informing the system are timely, verifiable, and reliable.
- Comprehensive and effective planning is imperative for equitable and efficient vaccination efforts that maximize patient access and minimize waste.
- State governments and health care leaders will need to take ownership of the process to ensure accountability for entering data into the system, using the tools effectively, and acting accordingly on the results.
- Pressure from outside groups seeking vaccine preference or expressing vaccine reluctance could complicate vaccine rollout efforts despite good planning.
- With increased vaccine production and distribution after early shortages, the usefulness for such a planning tool has diminished, especially as eligibility has expanded to age 16 years. However, this model might be helpful for the COVID-19 booster vaccinations likely needed in the coming months.
Drive-through COVID-19 Vaccination Clinics

Potential Impact Score

Stakeholders reviewing this topic thought that drive-through COVID-19 vaccination clinics 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

- Drive-through vaccination sites could accelerate the effort to vaccinate all eligible and interested individuals now that multiple COVID-19 vaccines are being distributed across the country after receiving Emergency Use Authorization (EUA) from FDA.
- Several states have begun constructing drive-through vaccine clinics, and some have already begun administering COVID-19 vaccines to individuals based on their risk allocation determined by local guidelines.
- Different storage and handling guidelines for the authorized COVID-19 vaccines could contribute to vaccination site errors, leading to efficacy concerns and poor population health outcomes.
- Stakeholders thought that drive-through vaccination clinics would speed up vaccination rates while promoting social distancing to reduce the risk of transmitting COVID-19.
- Stakeholders shared concerns about the limited supply of vaccines, inadequate staffing, bottlenecks due to a 30-minute postvaccination observation period to monitor adverse effects, and traffic congestion.

Description

Multiple COVID-19 vaccines have received EUA from FDA and are being distributed across the United States. Drive-through vaccination sites could accelerate the vaccination effort to meet the nation’s goal of vaccinating all persons who want to be vaccinated. This model was previously utilized during the swine flu (H1N1) outbreak in 2009 to deliver about 19,000 vaccine shots in 1.5 days in Louisville, Kentucky. The Centers for Disease Control and Prevention has published considerations for planning drive-through clinics for routine vaccinations, which may also be useful for distribution of COVID-19 vaccines.

Several states have begun constructing drive-through clinics. For example, a site in Montgomery County, Pennsylvania, has a 10-lane carport and has retrofitted shipping containers for vaccine and medical equipment storage. Some other sites across the country have already begun administering COVID-19 vaccines to individuals based on their risk allocation in mass drive-through clinics. For example, states like Texas and California have been adding mass drive-through sites as vaccines are made available.
Possible Areas of Impact

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

Possible Future Impacts

Drive-through vaccination sites might increase access to vaccination, potentially contributing to reaching the threshold for herd immunity faster. They might ease the burden on health care facility resources (e.g., personal protective equipment needs) and medical staff since these drive-through centers would have a different staff pool. There might be efficacy concerns due to the lack of consistency in storage and handling requirements for the authorized COVID-19 vaccines. If these vaccination centers are not run well, inefficiencies or errors might lead to poor population health outcomes.

Key Stakeholder Perspectives

Between March 4, 2021, and March 8, 2021, five ECRI stakeholders, reflecting health systems and research perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- Drive-through vaccination clinics, if run well, could streamline vaccine administration; however, the limited supply of vaccines, inadequate staffing, and the 30-minute adverse effects observation period after vaccine delivery could create bottlenecks.
- This initiative could reduce the risk of COVID-19 transmission since people will not need to stand in lines, which could reduce health care costs by lowering incidence of severe illness.
- Drive-through vaccination centers might also decrease health disparities and increase access for the elderly or those with disabilities who are unable to walk into indoor vaccination sites.
- These sites may be more feasible to run even in poor weather conditions and might help reduce appointment cancellations or no-shows, limiting wasted vaccine doses.
- Drive-through clinics would supplement current vaccination centers rather than replace them and could be useful for disseminating variant boosters; however, they might not be practical for routine vaccinations after the pandemic.
Mobile Health Clinics to Increase Access to COVID-19 Health Services

Potential Impact Score

Potential Impact Score

Stakeholders reviewing this topic thought that mobile health clinics to increase access to COVID-19 health services 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

- Mobile health clinics—customized motor vehicles that travel to communities to provide health care—might help meet shortages in COVID-19 health services, including access to testing, vaccinations, and treatment.
- Aardvark’s health vehicles have 2 to 4 testing windows where staff can administer up to 400 tests a day, comparable to drive-through testing facilities, which are inaccessible for some people.
- Ease of movement and setup of mobile health clinics might improve implementation of testing and vaccination initiatives in scattered or harder-to-reach populations.
- Stakeholders commenting on this topic thought that mobile health clinics might benefit rural areas where COVID-19 cases are surging and health facilities are lacking.
- Stakeholders also thought that the use of mobile clinics depends on the availability of health care workers to staff these units, costs associated with running the clinics, and the decision makers who select which areas to serve.

Description

As the COVID-19 pandemic continues, many underserved and rural communities in the United States still face challenges surrounding access to testing and vaccination. An estimated 2000 mobile clinics (customized motor vehicles that travel to communities to provide health care) are active and may be able to help meet needs for COVID-19 health services.86

In addition to the existing mobile clinic infrastructure, various companies are offering mobile clinics. For example, Aardvark Mobile Tours, LLC (Conshohocken, Pennsylvania), offers mobile health trucks that are equipped with both positive and negative air pressure and the ability to be Certified Laboratory Improvement Amendments of 1988–certified up to biosafety level 2.87 The vehicles can be used for rapid testing, vaccinations, and health screenings. The trucks offer a self-contained space with air conditioning and heating that takes 15 minutes to set up. The easily sterilized areas and partitions, which separate the nurses conducting the tests from the individuals receiving them, help maintain the safety of all involved.87 Two to 4 testing windows allow nurses to administer up to 400 tests a day, similar to drive-through testing facilities, which are inaccessible to people relying on public transportation. The company supplies an experienced driver, maintenance, insurance, logistics management, and a program manager so the states maintain focus on delivering care.87
Additionally, a mobile vaccination clinic in North Carolina expanded its vaccination efforts to include farmworkers who do not reside in that state.\(^8^8\) Other pilot programs (eg, Curbside Care) have also begun vaccinating eligible individuals in mobile clinics in rural parts of Michigan.\(^8^9\)

**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**

Mobile health clinics might increase access to COVID-19 testing in underserved hot spots and rural communities, which would improve patient and population health outcomes while reducing disparities. These clinics might lead to faster implementation of testing initiatives in hot spots and rural communities, which would inform future public health guidelines. Although the mobile health clinics would benefit harder-to-reach populations, they might lead to long wait times if the mobile testing/vaccination site is overwhelmed.

**Key Stakeholder Perspectives**

Between December 10, 2020, and January 6, 2021, seven ECRI stakeholders, reflecting health systems, nursing, physician, and research perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- Such direct-to-consumer services might add convenience for populations they serve and help boost the economy by reducing missed school days, lost wages, and other factors.
- Mobile health clinics might increase access to COVID-19 health services; however, the usability of mobile clinics hinges on the availability of health care workers to staff these units, who are at risk of shortages and burnout.
- Economic incentives or resistance to unconventional medical care in rural areas might influence decision makers’ views on promoting the use of mobile health units in urban areas, increasing disparities in rural areas.
- These mobile health centers may be able to supplement the shortfalls of the health care system during the COVID-19 pandemic; however, they may not be sustainable post-pandemic because of operational costs.
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 moderately 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. It might also assist with effectively distributing new staffing placements from out of state.
- 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.
- Statewide hospital resource utilization hubs might inform public health authorities on strategies to enhance emergency protocols in future hospital crisis situations.
- Stakeholders commenting on this topic thought that the surge line system had potential to significantly improve patient care while avoiding staff burnout during COVID-19 surges.
- 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. 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.

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 post–acute care facilities. The surge line can assist with effectively distributing new staffing placements from out of state. It may also provide clinical consultation if a transfer is declined or delayed.

Other states (eg, Illinois, Minnesota, Oregon) have created similar statewide hubs with real-time visibility into bed and ventilator availability across health care systems.

As of December 2020, the Arizona Surge Line had transferred more than 4000 COVID-19 cases to higher levels of care across more than 130 hospitals in Arizona. A 4-month satisfaction
survey suggested that the program successfully expedited transferring patients with COVID-19, load-balanced patients across Arizona hospitals, improved patient outcomes, and safeguarded the state’s health care system. These results might encourage other states to create similar programs.

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 lead to improved patient outcomes if patients are able to receive appropriate care in a timely manner. Statewide surge systems might also enhance government policies and public health emergency guidelines.

Key Stakeholder Perspectives

Between February 10, 2021, and April 5, 2021, nine ECRI stakeholders—reflecting allied health, engineering, health care generalist, health systems, physician, and research perspectives—provided comments and ratings on this topic. The list below summarizes 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 optimal care of COVID-19 patients in critical condition and could therefore improve patient outcomes and reduce risk of death.
- This system might reduce health care disparities since patients from underserved locations would have the ability to receive care as well as transportation assistance postdischarge.
- Interfacility transfer might increase financial burden on families based on insurance coverage for in-network vs out-of-network hospitals.
- Similar statewide hubs can be developed for improved resource utilization for future public health emergencies or other situations when the health care system is strained.
Multidose Vials to Strengthen Vial Supply Chain During COVID-19

Potential Impact Score
Stakeholders reviewing this topic thought that multidose vials to strengthen the vial supply chain during 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 global demand for vaccinations, combined with an anticipated shortage of medical-grade glass vials, has prompted vaccine developers to package COVID-19 vaccines in multidose glass vials containing 8 to 15 doses each.
- Some health experts caution that switching to multidose vials during mass vaccination programs may increase safety risks for patients and health care providers who administer vaccinations.
- Stakeholders commenting on this topic thought use of multidose vials increases risk of infection and improper dosing to patients and risk of injury to providers delivering vaccinations.
- Stakeholders also thought many providers would likely require refresher training on safe use of multidose vials since use of these vials for vaccinations has largely been abandoned in the US health care system.

Description
Drug developers are quickly advancing coronavirus vaccine candidates through clinical trials and, in parallel, readying manufacturing to prepare for deployment if their candidate proves to be safe and effective. In the early months of the pandemic, news articles highlighted a shortage of the medical-grade glass vials needed to distribute vaccines. A shortage of these glass vials or syringes could create vaccine access issues for millions of people. Currently, the industry has decided to use 10-milliliter vials that are capable of holding 8 to 15 doses of coronavirus vaccine to conserve glass supply. Corning Inc will receive funding from the Biomedical Advanced Research and Development Authority to accelerate the manufacturing of glass vials for COVID-19 vaccines and treatments. Some health experts have expressed concerns about the safety of multidose vaccine vials, both for patients and for providers giving the vaccinations. Single-dose vaccine vials have a higher per-unit cost than multidose vials, but single-dose vials can lower risk of cross-contamination and vaccine wastage from improper dosing or storage.

As of early 2021, further news reports have provided mixed messages from glass manufacturers regarding the current supply of medical-grade glass vials for vaccines relative to demand, as more vaccines are now in use in several countries.
Possible Areas of Impact

- Population health
- Health care delivery process
- Health care disparities

Possible Future Impacts

Use of multidose vaccine vials during the pandemic might increase access to COVID-19 vaccination for a larger share of the population, potentially shortening the time to achieve herd immunity to control disease spread. The need to quickly revert to multidose vaccine vials due to material shortages might change standards for quality and manufacturing throughput in pharmaceutical packaging. The experience of pivoting between single-dose and multidose vaccine vials might improve understanding of supply chain management and help inform preparations for future public health emergencies. Finally, the use of multidose vaccine vials might increase the risk of treatment-related illness due to cross-contamination of multidose vaccine vials during mass vaccinations.

Key Stakeholder Perspectives

Between August 13, 2020, and August 28, 2020, six ECRI stakeholders, reflecting physician, nursing, research, and allied health perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- In the US health care system, single-dose vaccine vials or prefilled, single-use syringes have largely replaced multidose vials for infection control, medication safety, and convenience purposes. Thus, many providers will likely require refresher training on infection prevention and proper draw to measure correct vaccine doses.
- For safety reasons, multidose vials are generally restricted to delivery of multiple doses of medications to a single patient.
- Beyond the risk of cross-contamination, the use of multidose vaccine vials raises concerns about proper vaccine handling and storage techniques.
- Shortages of medical-grade glass are likely to affect more than mass vaccination efforts, since medical-grade glass is used across multiple clinical areas.
- Multidose vials can increase the risk of injury to health care personnel who administer vaccinations.
- Prefilled, single-dose syringes are the safest option for health care providers and patients because they create the lowest risk of needlestick injuries, cross-contamination, and improper dosing.
Phone Applications to Manage COVID-19 Vaccine Communications and Scheduling

Potential Impact Score
Stakeholders reviewing this topic thought that phone applications to manage COVID-19 vaccine communications and scheduling 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 recent availability of multiple COVID-19 vaccines has created a need for broad campaigns to improve vaccine education, safety and efficacy monitoring, and appointment scheduling.
- Multiple smartphone apps are in development to educate the public about vaccines and help health professionals communicate and schedule COVID-19 vaccinations, thus ensuring an orderly vaccine rollout.
- The GetWellNetwork app communicates locally with users through phones, smartwatches, and computers to provide information about vaccines and schedule appointments. Other apps operating at a national level, such as V-Safe, keep track of any vaccine-related side effects, remind users about second doses, and recommend follow-up protective measures.
- Stakeholders commenting on this topic thought that if these apps are convenient and use technology similar to that of other health apps, they might improve vaccine uptake. But if a large number of apps with limited features and accessibility become available, they might increase disparities and slow down vaccine rollout.

Description
The availability of multiple FDA-authorized COVID-19 vaccines has created a need for large public vaccine initiatives that include education campaigns, effectiveness monitoring, appointment scheduling, and reporting of side effects. Several applications are in development to help government agencies and health care professionals communicate about COVID-19 vaccines and schedule appointments. Some apps are intended to operate at a local and statewide level, while others are intended for broader use across the country.

LifeBridge Health, a regional health system in the Baltimore metropolitan area, commissioned GetWellNetwork (Bethesda, Maryland) to develop an app that supports vaccine distribution, education, and guidance for health care organizations within the state. The app delivers patient communications through smartphones, smartwatches, and computers. It allows users to schedule vaccine appointments, report side effects, learn more about the vaccines, and receive reminders about second doses. Other vaccine-management app developers include Skedulo Holdings, Inc (San Francisco, California), Mozzaz Corp (Philadelphia, Pennsylvania), and RSVPify LLC (Chicago, Illinois).
The Centers for Disease Control and Prevention is providing vaccine recipients access to V-Safe, a nationwide smartphone app that uses text messages and web surveys to keep track of any side effects experienced by COVID-19 vaccine recipients. Additionally, the app can notify patients when it is time to go back for a second dose and remind users to remain engaged in protective measures even after receiving their vaccinations. Information provided by users remains confidential and private.107

**Possible Areas of Impact**

- Data privacy
- Health care delivery and process
- Population health

**Possible Future Impacts**

With an initial absence of federal protocols for managing COVID-19 vaccinations, state and local governments have developed their own policies and procedures, using online tools to educate the public and help administer vaccines. As vaccine rollout continues, additional smartphone apps have been developed to manage COVID-19 vaccine communications and scheduling.107,112

Widespread use of smartphone apps might increase public knowledge about these initiatives, which could, in turn, improve adherence to COVID-19 vaccine dosing schedules. However, the widespread use of smartphone apps for vaccine scheduling and follow-up could raise concerns about patient data confidentiality.108,112

If vaccination apps are able to provide unbiased information about the risks and benefits of vaccination, they might also help engage vaccine-hesitant communities. However, some apps that lack transparency might support preconceived distrust of vaccines.112

**Key Stakeholder Perspectives**

Between January 12, 2021, and January 19, 2021, ten ECRI stakeholders—reflecting allied health, health systems, nursing, physician, and research perspectives—provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- Implementation of these apps with COVID-19 vaccine rollout programs could improve vaccine uptake, if well timed and convenient for users.
- The public might be open to adopting familiar technology for COVID-19 vaccination efforts because similar apps (eg, appointment reminders, symptom checkers) are increasingly common across health care networks.
- The usefulness of these apps could be limited if users disregard recommendations or instructions. Single-language-only apps might limit vaccination efforts and increase disparities in some communities.
- The use of multiple vaccine-related apps by different health systems or municipalities might fragment vaccine rollout efforts and slow overall progress compared with more centralized national health systems.
Surveillance Programs to Identify and Follow the Spread of Emerging SARS-CoV-2 Variants

Potential Impact Score

Stakeholders reviewing this topic thought that surveillance programs to identify and follow the spread of emerging SARS-CoV-2 variants 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

- In December 2020, three genetic variants of SARS-CoV-2 with higher transmissibility were identified in the United Kingdom (B.1.1.7), South Africa (B.1.351), and Brazil (P.1). These variants were subsequently detected in locations around the world.
- The variants appear to be more transmissible than the previously dominant variant, which might lead to an increase in infections and subsequent COVID-19-related deaths. Concerns remain that these or future variants might compromise COVID-19 vaccine efficacy.
- The CDC is working with clinical and national laboratories, state and local health departments, and genomic sequencing companies to expand the national surveillance infrastructure for detecting and tracking new variants.
- Stakeholders commenting on this topic thought that surveillance programs for emerging variants might help prevent their spread, thus improving population health, reducing costs, and decreasing hospitalizations. However, such programs might not be established before novel variants emerge and spread.

Description

In December 2020, three genetic variants of SARS-CoV-2 with higher transmissibility were identified in the United Kingdom (B.1.1.7), South Africa (B.1.351), and Brazil (P.1).55,113 They have subsequently been detected in countries around the world. The higher transmissibility of B.1.1.7, B.1.351, and P.1 than the previously dominant coronavirus strain might lead to more hospitalizations and an increase in COVID-19-related deaths.56,61,62 Moreover, available vaccines might offer less-than-robust protection against other variants. One such variant is B.1.351, which contains at least 1 mutation in a region of the spike protein that serves as a key target for neutralizing antibodies.113 P.1 also harbors mutations in the spike protein that allow the reinfection of individuals who have recovered from COVID-19.114

Surveillance programs are needed to support public health responses to these emerging variants. This will require expanded testing and genomic sequencing to identify where the variants are starting to spread, followed by contact tracing and quarantine programs to decrease transmission.56 With support from the CDC, the genomic sequencing companies Illumina (San Diego, California) and Helix (San Mateo, California) will expand the national surveillance infrastructure to track the emergence and prevalence of new variants.115 The CDC has also
partnered with clinical laboratories, national laboratories, state and local health departments, and universities to ramp up sequencing-based surveillance and contact tracing.\textsuperscript{56}

**Possible Areas of Impact**

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

**Possible Future Impacts**

The pandemic has strained health care facilities, caused financial hardship, and increased anxiety. The emergence of variants that are more transmissible than previous SARS-CoV-2 strains might cause even more burden. Early detection of emerging coronavirus strains in communities might help suppress their spread.\textsuperscript{56} Working side by side with vaccination campaigns, surveillance programs can identify variant outbreaks and direct vaccination efforts in surrounding communities to contain the spread of variants.\textsuperscript{56,116}

Early characterization of these variants suggests that some shared spike protein mutations might help the coronavirus avoid immune responses in previously infected and vaccinated individuals.\textsuperscript{114,116} If vaccination efforts are not sufficient to slow the spread of variants, surveillance programs might trigger lockdowns and broader restrictions to contain the spread of variants.\textsuperscript{116}

**Key Stakeholder Perspectives**

- Surveillance programs might help provide officials with data to direct the creation of new public health guidelines that can be applied to prevent the new variants from becoming dominant coronavirus strains. If these programs help limit coronavirus spread, they might improve population health, decrease hospitalizations, and reduce health care costs.
- Surveillance programs combined with vaccine monitoring might help determine the efficacy of vaccines against emergent strains and so direct the plans for targeted vaccination campaigns.
- Stakeholders noted that the success of these programs relies on having reporting systems that share information at a national level among the CDC, its partners, and health officials. However, well-structured systems might not be established before novel variants arise.
- Surveillance programs might also use resources that are already limited in the overburdened testing process.
Chapter 5. Treatments

Chapter Summary

As of March 12, 2021, we were monitoring or had recently archived 34 COVID-19-related treatment topics. Of these topics, 21 are listed in the January 2021 PCORI Health Care Horizon Scanning System: Horizon Scanning COVID-19 Supplement Status Report, Volume 2, Issue 1; the remaining 13 topics were added to the system subsequent to that report. All 34 topics were sent for comment to internal ECRI stakeholders and received at least 5 sets of ratings and comments from stakeholders between May 18, 2020, and March 11, 2021. Additional ratings and comments might also have been received after March 11, 2021.

Six topics included in the previous High Impact Report were excluded from this report after stakeholders re-reviewed the topics and rated them as having low potential for impact (see ratings in Table 5.2):

- **Anakinra (Kineret) for treating COVID-19 with acute respiratory distress syndrome and hyperinflammation**
- **Aviptadil (Zyesami, formerly RLF-100) for treating COVID-19**
- **Convalescent plasma for treating COVID-19**
- **GM-CSF–inhibiting monoclonal antibodies for treating COVID-19**
- **Losartan for treating COVID-19**
- **Remdesivir (Veklury) for treating COVID-19**

From among the 34 topics, 7 topics have been selected that internal ECRI stakeholders thought 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.
Topics Considered for Inclusion in This Report

Table 5.1 lists 7 topics selected for inclusion in this High Impact Report. Included topics received, on average, moderately high to high impact ratings and demonstrated considerable consensus among stakeholders. Topics are arranged 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

<table>
<thead>
<tr>
<th>Topic title</th>
<th>Potential impact score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamethasone for treating severe COVID-19</td>
<td>3.5</td>
</tr>
<tr>
<td>Monoclonal antibodies targeting SARS-CoV-2 spike protein receptor binding domain for treating nonhospitalized patients with COVID-19</td>
<td>3.3</td>
</tr>
<tr>
<td>Nitazoxanide (NT-300) to treat mild to moderate COVID-19&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3.3</td>
</tr>
<tr>
<td>CD24Fc (MK-7110) for treating severe COVID-19&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3.2</td>
</tr>
<tr>
<td>Dociparstat for treating acute lung injury in severe COVID-19</td>
<td>3.2</td>
</tr>
<tr>
<td>Proteomics to identify human protein targets for treating COVID-19</td>
<td>3.2</td>
</tr>
<tr>
<td>TD-0903 for treating acute lung injury in COVID-19</td>
<td>3.2</td>
</tr>
</tbody>
</table>

<sup>a</sup> Topic appears for the first time in this High Impact Report.

Table 5.2 lists 27 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 arranged 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

<table>
<thead>
<tr>
<th>Topic title</th>
<th>Potential impact score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tranexamic acid for treating COVID-19</td>
<td>3.1</td>
</tr>
<tr>
<td>ANG-3777 to treat patients hospitalized with COVID-19 pneumonia</td>
<td>3.0</td>
</tr>
<tr>
<td>Auxora to treat severe COVID-19-associated pneumonia</td>
<td>3.0</td>
</tr>
<tr>
<td>Colchicine to treat COVID-19</td>
<td>3.0</td>
</tr>
<tr>
<td>CYT107 for treating hospitalized patients with COVID-19-related lymphopenia</td>
<td>3.0</td>
</tr>
<tr>
<td>EIDD-2801 for treating COVID-19</td>
<td>3.0</td>
</tr>
<tr>
<td>Hyperimmune immunoglobulin for treatment of COVID-19</td>
<td>3.0</td>
</tr>
<tr>
<td>Leronlimab for treating COVID-19</td>
<td>3.0</td>
</tr>
<tr>
<td>Lowering testosterone levels to treat coronavirus infection</td>
<td>3.0</td>
</tr>
<tr>
<td>MultiStem for treating COVID-19-induced ARDS</td>
<td>3.0</td>
</tr>
<tr>
<td>Pulmonary surfactant to treat respiratory distress in COVID-19</td>
<td>3.0</td>
</tr>
</tbody>
</table>
### Topic Summaries

We present below 7 summaries on topics deemed to have moderately high to high impact potential. Topics are arranged 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.

<table>
<thead>
<tr>
<th>Topic title</th>
<th>Potential impact score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Losartan for treating COVID-19</td>
<td>2.8</td>
</tr>
<tr>
<td>Machine learning to identify drug candidates to treat COVID-19</td>
<td>2.8</td>
</tr>
<tr>
<td>Aviptadil (Zyesami, formerly RLF-100) to treat COVID-19</td>
<td>2.6</td>
</tr>
<tr>
<td>Combination baricitinib and remdesivir to treat COVID-19</td>
<td>2.6</td>
</tr>
<tr>
<td>Fenofibrate to treat COVID-19</td>
<td>2.6</td>
</tr>
<tr>
<td>Prophylactic rivaroxaban anticoagulation for nonhospitalized patients with COVID-19*</td>
<td>2.6</td>
</tr>
<tr>
<td>Quellor (XPro1595) for treating immune-mediated complications due to COVID-19*</td>
<td>2.6</td>
</tr>
<tr>
<td>Recombinant plasma gelsolin (rhu-pGSN) for treating COVID-19 pneumonia*</td>
<td>2.6</td>
</tr>
<tr>
<td>SPI-1005 to treat moderate to severe COVID-19*</td>
<td>2.6</td>
</tr>
<tr>
<td>rNAPc2 (AB201) for treating COVID-19*</td>
<td>2.4</td>
</tr>
<tr>
<td>Remdesivir (Veklury) to treat COVID-19*</td>
<td>2.2</td>
</tr>
<tr>
<td>Anti-interleukin-6 monoclonal antibodies for treating patients hospitalized with severe COVID-19*</td>
<td>2.0</td>
</tr>
<tr>
<td>GM-CSF–inhibiting monoclonal antibodies for treating COVID-19*</td>
<td>2.0</td>
</tr>
<tr>
<td>Peginterferon lambda-1A (Lambda) for treating COVID-19*</td>
<td>2.0</td>
</tr>
<tr>
<td>Anakinra (Kineret) for treating COVID-19 with acute respiratory distress syndrome and hyperinflammation*</td>
<td>1.8</td>
</tr>
<tr>
<td>Convalescent plasma for treating COVID-19*</td>
<td>1.8</td>
</tr>
</tbody>
</table>

* Topic was recently archived.
Highlights

- Dexamethasone is a corticosteroid, given orally or intravenously, that has become the standard of care to treat severe or critical COVID-19.
- Clinical trial data suggest dexamethasone lowers 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 significant potential to improve patient outcomes by reducing risk of death and is having an impact in our health care system now.
- Stakeholders thought dexamethasone is likely to be widely used, considering it is relatively inexpensive, already widely available, and already familiar to prescribers.

Description

Dexamethasone is an orally or intravenously administered corticosteroid that has become a standard-of-care treatment in patients with severe or critical COVID-19. It is an immunosuppressant that might mitigate hyperinflammation observed in patients with severe COVID-19, which is thought to contribute to acute respiratory distress syndrome, multiorgan failure, and death.\(^\text{117}\)

The National Institutes of Health COVID-19 treatment guidelines recommend the use of dexamethasone in hospitalized patients with various disease severity levels, including patients requiring increasing amounts of supplemental oxygen, patients requiring high-flow oxygen or noninvasive ventilation, and patients requiring mechanical ventilation or extracorporeal membrane oxygenation.\(^\text{118}\) The World Health Organization (WHO) similarly recommends the use of dexamethasone in patients with severe or critical COVID-19.\(^\text{119}\) These guidelines were based on findings from multiple trials. Data from the 6424-patient phase 2/3 RECOVERY trial found that dexamethasone significantly lowered 28-day mortality among those who were receiving either invasive mechanical ventilation or oxygen alone, but not among those who were not receiving respiratory support.\(^\text{120}\) A meta-analysis performed by the WHO before publication of the RECOVERY data showed that systemic corticosteroids in those critically ill with COVID-19 were associated with lower 28-day all-cause mortality in 1703 patients across 7 randomized trials.\(^\text{121}\)

In addition, several clinical trials of dexamethasone are ongoing (eg, phase 3 ACCT-4 trial,\(^\text{122}\) phase 4 trial\(^\text{123}\)).

Based on available clinical trial dosing information and dexamethasone pricing, a course of COVID-19 treatment with dexamethasone is likely to cost between $9 and $21 per patient.\(^\text{124}\)

Possible Areas of Impact

- Patient outcomes
- Population health
- Health care costs
Possible Future Impacts

Dexamethasone reduces the risk of death in patients with severe or critical disease who require mechanical ventilation and supplemental oxygen and might help decrease the need for intensive care 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 (e.g., masks, ventilators). At an estimated cost of less than $21 per treatment course, dexamethasone might result in overall health care cost savings if hospitalization times are shortened and fewer intensive care resources are needed.

Key Stakeholder Perspectives

Between February 9, 2021, and February 26, 2021, eight ECRI stakeholders—reflecting health systems, nursing, and research perspectives—provided comments and ratings on this topic. The list below summarizes key stakeholder perspectives.

- Dexamethasone has become a standard-of-care treatment for severe and critical COVID-19 and is having an impact now.
- The drug is highly likely to improve patient outcomes by reducing death, supported by data published thus far on the intervention.
- Dexamethasone is a relatively inexpensive, widely available, and clinically known drug, offering potential advantages compared with other treatments (such as cost savings and prescriber familiarity) that might increase its clinical use.
- Dexamethasone might be the most promising COVID-19 treatment currently available for improving survival.

Monoclonal Antibodies Targeting SARS-CoV-2 Spike Protein Receptor Binding Domain for Treating Nonhospitalized Patients With COVID-19

Potential Impact Score

Stakeholders reviewing this topic thought that monoclonal antibodies targeting SARS-CoV-2 spike protein receptor binding domain for treating nonhospitalized 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

- Monoclonal antibodies targeting coronavirus spike protein (anti-spike monoclonal antibodies) purportedly treat COVID-19 by interfering with the interaction between the viral spike protein and its receptor on host cells.
- Multiple randomized controlled trials of anti-spike monoclonal antibody products have demonstrated their ability to reduce viral loads, reduce rates of hospitalization/emergency room visits, and/or reduce death rates among nonhospitalized patients.
• Based on these data, FDA has granted Emergency Use Authorization (EUA) to 3 anti-spike monoclonal antibody products for use in nonhospitalized patients.

• Stakeholders commenting on this topic thought that, based on initial data indicating that anti-spike monoclonal antibodies reduce the hospitalization rate in patients with mild to moderate COVID-19, these therapies had the potential to both improve patient health outcomes and mitigate systemic burdens related to COVID-19 hospitalizations.

• Stakeholders commenting on this topic thought that logistical issues concerning administering intravenous infusions to coronavirus-infected persons in the outpatient setting would cause substantial disruption to health care systems and could limit uptake of these therapies.

**Description**

Coronavirus cellular entry depends on an interaction between the viral surface spike protein and a host cell-surface protein, angiotensin-converting enzyme 2 (ACE2). Anti-spike monoclonal antibodies are intended to disrupt this interaction, potentially neutralizing the virus. Investigational anti-spike monoclonal antibody products currently under study include both single-antibody (e.g., bamlanivimab [Lilly, Indianapolis, Indiana], VIR-7831 [Vir Biotechnology, San Francisco, California, and GlaxoSmithKline, Brentford, United Kingdom]) and dual-antibody (e.g., casirivimab/imdevimab [Regeneron, Tarrytown, New York], bamlanivimab/etesevimab [Lilly]) agents.

Multiple randomized, placebo-controlled trials of anti-spike monoclonal antibody products have demonstrated efficacy in treating nonhospitalized patients with mild to moderate COVID-19. Bamlanivimab reduced the rate of hospitalizations or emergency department visits from 10% to 3% in a 465-patient trial. Casirivimab/imdevimab reduced the rate of COVID-19-related medical visits from 9% to 3% in a 799-patient trial. Bamlanivimab/etesevimab reduced the rate of COVID-19-related hospitalizations or death from 7% to 2% in a 1035-patient trial. VIR-7831 reduced the rate of hospitalization or death by 85% in a 583-patient trial.

Based on these data, FDA has granted EUA to 3 anti-spike monoclonal antibody products (bamlanivimab, casirivimab/imdevimab, and bamlanivimab/etesevimab). These EUAs cover the administration of these products as a single intravenous infusion for treating patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older and who are at high risk for progressing to severe COVID-19 and/or hospitalization. The products are not authorized for patients who are hospitalized or require oxygen therapy due to COVID-19. GlaxoSmithKline and Vir Biotechnology have indicated that they intend to submit an EUA application for VIR-7831 in the near future.

**Possible Areas of Impact**

• Patient outcomes
• Population health
• Health care delivery and process
• Health care costs
• Health care disparities
**Possible Future Impacts**

Anti-spike monoclonal antibodies have substantial potential to improve patient health outcomes by reducing the rate at which mild to moderate COVID-19 progresses to more severe, potentially life-threatening, disease. In addition to these direct effects on patient health, the potential for these therapies to reduce the number of patients who require hospitalization could have a positive effect at the population health level by reducing hospital occupancy levels, potentially allowing for improved care of patients still requiring hospitalization.

Logistical issues surrounding the identification of eligible patients early in the course of their disease and the intravenous administration of these drugs have the potential to require substantial changes to health care delivery and processes. Additionally, while the US government has purchased substantial supplies of these antibodies and is covering their approximately $1250 to $1500 cost during initial rollout, patients may still be required to cover the cost of the infusion procedure. These factors may have contributed to a perceived underuse of anti-spike monoclonal antibodies.

**Key Stakeholder Perspectives**

Between February 9, 2021, and February 27, 2021, nine ECRI stakeholders, reflecting 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.

- Anti-spike monoclonal antibodies have substantial potential to improve health outcomes in nonhospitalized patients at high risk of developing more severe disease. However, the data are preliminary and may not reflect all potential treatment-related adverse events or the treatments’ efficacy against newly emerging coronavirus variants.

- The requirement for anti-spike monoclonal antibodies to be administered by intravenous infusion will be disruptive for health care systems. A shortage of appropriately trained staff and/or a lack of appropriate physical spaces for isolation of a COVID-19-infected person during treatment may limit health care facilities’ ability to offer these treatments.

- These therapies are likely to be less readily available in resource-poor communities and, therefore, have potential to widen health disparities.

- Treatment with anti-spike monoclonal antibodies will impose a substantial cost burden on the health care system. While these costs may be offset partially by reduced rates of hospitalizations and associated costs, the impact of these offsets will be constrained by the large number of patients needing to be treated to prevent a single patient from developing more severe disease that requires hospitalization.
Nitazoxanide (NT-300) to Treat Mild to Moderate COVID-19

Potential Impact Score
Stakeholders reviewing this topic thought that nitazoxanide (NT-300) to treat mild to moderate 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
- Nitazoxanide is an FDA-approved oral antiparasitic drug in development as a repurposed treatment for mild to moderate COVID-19 in the outpatient setting.
- Stakeholders commenting on this topic thought nitazoxanide has significant potential to prevent COVID-19 progression to severe disease, thus potentially improving patient outcomes, reducing hospitalization and associated costs, decreasing health disparities, and improving clinician safety.
- Stakeholders also thought nitazoxanide is likely to diffuse clinically given its relatively low cost, established safety profile, and simple storage and administration requirements.

Description
Nitazoxanide is an antiparasitic drug approved by FDA for treating diarrhea caused by Cryptosporidium parvum and Giardia lamblia (“traveler’s diarrhea”). An extended-release oral formulation, NT-300 (Romark, LC, Tampa, Florida), is being developed to treat mild to moderate COVID-19 in the outpatient setting.

Preclinical research suggests nitazoxanide exhibits broad-spectrum antiviral activity against multiple respiratory viruses, including SARS-CoV-2, and that it suppresses the production of proinflammatory cytokines. Excessive release of proinflammatory cytokines is thought to lead to hyperinflammation in COVID-19 and correlate with severe disease and poor outcomes.

No clinical data have been reported yet. NT-300 is being investigated in a developer-sponsored phase 3, randomized, placebo-controlled clinical trial of 1092 participants with mild or moderate COVID-19, which had an estimated primary completion date in February 2021. In clinical trials, NT-300 is taken by mouth twice daily for 5 days. Based on available clinical trial dosing and pricing information for 500-mg tablets (300-mg tablets are taken in trials but are commercially unavailable), we estimate a course of nitazoxanide to treat COVID-19 might cost less than $1300.
Possible Areas of Impact

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

Possible Future Impacts

Nitazoxanide could be the first oral treatment authorized to treat mild to moderate COVID-19 in the outpatient setting. It might improve patient outcomes by preventing severe COVID-19, which is associated with poor outcomes and risk of death. It might reduce health disparities among groups that face disproportionately high rates of progression to severe disease. Less progression to severe disease might help keep patients with COVID-19 out of the hospital and thus reduce clinician exposure to the virus, decrease burden on the health care system, and reduce health care costs associated with hospitalization and intensive care resources.

Key Stakeholder Perspectives

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

- Nitazoxanide’s purported antiviral and anti-inflammatory mechanisms of action are promising and have significant potential to improve patient outcomes by treating COVID-19 early and preventing disease progression.
- The drug could be an important COVID-19 treatment option, considering current standard treatment focuses largely on treating patients already hospitalized with moderate to severe disease rather than preventing disease progression in outpatients with mild symptoms.
- Nitazoxanide could reduce hospitalizations, thus reducing transmission risk of the coronavirus to health care personnel and reducing health care costs associated with hospitalization.
- Aspects of nitazoxanide, including its relatively low cost, established safety profile, and simple storage and administration requirements, are favorable for potential clinical uptake.
CD24Fc (MK-7110) for Treating Severe COVID-19

Potential Impact Score

Stakeholders reviewing this topic thought that MK-7110 for treating severe 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

- CD24Fc (MK-7110) is a first-in-class fusion protein that purportedly targets an immune system checkpoint to modulate the aberrant inflammatory response in patients with severe COVID-19.
- Clinical trial data suggest that CD24Fc has the potential to reduce time to clinical recovery and reduce the risk of respiratory failure and death.
- Stakeholders commenting on this topic thought that initial data on CD24Fc suggested it had substantial potential to improve patient health outcomes in patients with severe COVID-19.

Description

CD24Fc (MK-7110) is an investigational recombinant fusion protein that consists of the extracellular domain of mature human CD24 linked to the human immunoglobulin G1 protein.\(^{139}\) It purportedly targets a novel immune pathway checkpoint involving the innate immune system and is intended to modulate the aberrant inflammatory response to SARS-CoV-2 that is thought to contribute to disease pathology.\(^{140,141}\)

A phase 3, randomized, placebo-controlled trial studying the safety and efficacy of CD24Fc enrolled 243 patients hospitalized with severe or critical COVID-19.\(^{142}\) In this trial, patients received an intravenous infusion of CD24Fc or placebo at day 1 in addition to standard of care, which could include remdesivir and/or dexamethasone. Preliminary data from 203 patients indicated that, compared with placebo, treatment with CD24Fc improved the likelihood of clinical recovery by 60%, decreased median time to recovery from 10 days to 6 days, and reduced the risk of death or respiratory failure by more than 50%.\(^{143}\)

CD24Fc is being developed by Merck (Kenilworth, New Jersey), which acquired CD24Fc’s original developer, Oncoimmune (Rockville, Maryland), in late 2020.\(^{144}\) In December 2020, Merck entered into a supply agreement with the US government to supply 60,000 to 100,000 doses of the drug during the first half of 2021.\(^{145}\) However, in February 2021, Merck announced that FDA had indicated a potential Emergency Use Authorization application would need data beyond those provided by the completed phase 3 trial, likely delaying availability of the drug.\(^{146}\)
Possible Areas of Impact

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

Possible Future Impacts

CD24Fc might reduce risk of death in patients with severe disease and might help reduce the need for intensive care 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. As a novel biologic drug, CD24Fc is likely to be highly costly; however, direct drug costs might be offset by reducing the length of hospital stay for some patients and/or avoiding the need for costly mechanical ventilation.

Key Stakeholder Perspectives

Between November 5, 2020, and November 16, 2020, five ECRI stakeholders, reflecting health systems, physician, and research perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- If the signs of efficacy demonstrated in the initial phase 3 data are confirmed by further study, CD24Fc has substantial potential to provide an alternative treatment option for patients with severe COVID-19 and improve outcomes for these patients.
- The signs of efficacy that CD24Fc demonstrated when used in addition to standard-of-care treatments (eg, dexamethasone, remdesivir), in addition to its ability to be used as a combination therapy, could promote more widespread use of CD24Fc.
- Availability of a treatment with potential to reduce time to recovery and duration of hospital stays would have a positive effect on health systems, freeing up resources and reducing costs associated with hospitalization.
- Further study is needed to confirm the initial signs of efficacy and to identify any potential adverse effects of the treatment.

Dociparstat for Treating Acute Lung Injury in Severe COVID-19

Potential Impact Score

Stakeholders reviewing this topic thought that dociparstat for treating acute lung injury in severe 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.
High Impact Report: Highlights

- Dociparstat is a derivative of the anticoagulant heparin that is being investigated as an intravenous treatment for patients hospitalized with acute lung injury in severe COVID-19.
- Dociparstat purportedly reduces excessive inflammation, immune cell infiltration, and hypercoagulability associated with poor outcomes in severe COVID-19.
- Initial reported clinical data suggest treatment with dociparstat, compared with placebo, might be associated with lower laboratory measures of inflammation and coagulability, decreased thromboembolic events, and increased survival.
- Stakeholders commenting on this topic thought dociparstat has significant potential to improve patient outcomes in those with acute lung injury in severe COVID-19 and might be safer than heparin, which carries significant risk for bleeding.
- Stakeholders also thought dociparstat might be used in combination with other COVID-19 treatments.

Description

Dociparstat is a derivative of the anticoagulant heparin that is being investigated by Chimerix (Durham, North Carolina) as an intravenous treatment for hospitalized adult patients who have acute lung injury associated with severe COVID-19. Hypercoagulability is commonly observed in patients who have severe COVID-19 and is associated with worse outcomes.\textsuperscript{147} It might occur due to damage to endothelial cells from infection with SARS-CoV-2.\textsuperscript{148} Treatment with anticoagulants such as heparin has been linked to improved clinical outcomes and increased survival in patients who have severe COVID-19 with coagulopathy.\textsuperscript{149,150} Dociparstat purportedly reduces excessive inflammation, immune cell infiltration, and hypercoagulability associated with worse outcomes in COVID-19.\textsuperscript{151} Dociparstat purportedly has less anticoagulant activity than heparin, allowing it to be given at higher doses for larger anti-inflammatory effects.\textsuperscript{152}

Dociparstat is in an ongoing phase 2/3 clinical trial enrolling more than 500 hospitalized adults who have acute lung injury in COVID-19 requiring supplemental oxygen or noninvasive ventilation.\textsuperscript{153} Chimerix reported initial topline data in February 2021 from the first cohort of 12 patients (6 dociparstat, 6 placebo).\textsuperscript{154} Two deaths were reported in the placebo group (at day 2 and post day 28) compared with no deaths reported in the dociparstat group. Normal coagulation and inflammatory laboratory parameters were observed in the dociparstat group. Two patients in the placebo group demonstrated significant elevations in these parameters by day 5; one patient experienced pulmonary embolism with subsequent recovery and the other developed acute respiratory disease syndrome resulting in death.

Possible Areas of Impact

- Health care costs
- Patient outcomes
- Population health
Possible Future Impacts

Dociparstat might improve patient health outcomes by reducing risk of thromboembolic events and improving survival. It might reduce hospitalization length and intensive care resource use, thus decreasing the burden on the health care system and resulting in health care cost savings. Population health might be improved from better individual patient outcomes and overall decreased burden on the health care system. The development of dociparstat for treating COVID-19 might aid in understanding anticoagulation in the treatment of COVID-19 and better help the formulation of COVID-19 clinical guidelines.

Key Stakeholder Perspectives

Between June 12, 2020, and June 25, 2020, five ECRI stakeholders, reflecting health systems, nursing, physician, and research perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- Dociparstat has significant potential to improve patient outcomes, considering its purported mechanisms of action and promising preclinical data.
- If efficacious, dociparstat has potential to decrease health care costs associated with hospitalization and COVID-19 testing and treatment.
- Dociparstat is likely to be safer and easier to titrate than heparin, which carries significant risk for bleeding, and might have larger anti-inflammatory effects.
- Dociparstat might be used clinically in combination with medications in other drug classes, such as biologic immune-modifying agents or antiviral drugs.

Proteomics to Identify Human Protein Targets for Treating COVID-19

Potential Impact Score

Stakeholders reviewing this topic thought that proteomics to identify human protein targets 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

- University of California, San Francisco, researchers have developed a protein map that helps identify which human proteins interact with proteins in SARS-CoV-2. This tool might make it easier and faster to identify drugs approved or in development for other indications that could be repurposed to treat COVID-19.
- Initial findings suggest that several existing drugs, including the hormone progesterone, antipsychotic drugs, and antihistamines, might warrant clinical trials as COVID-19 treatments.
To further promote this drug-repurposing approach, researchers in China have created a publicly accessible web server to explore potential COVID-19 treatments using proteomics.

Stakeholders reviewing this topic thought proteomics and protein mapping was a promising approach to assess the repurposing of existing drugs that might dramatically shorten the timeline for clinical testing and making new COVID-19 treatments available to patients.

Stakeholders also anticipated a large, continuing need for new COVID-19 treatments because of the high vaccine refusal rates and the emergence of new treatment-resistant coronavirus variants.

**Description**

Researchers at the University of California, San Francisco, have developed a protein interaction map for SARS-CoV-2. The map might facilitate the repurposing of drugs approved or in development for other indications to treat COVID-19. The team identified 66 druggable human proteins or host factors targeted by 69 compounds (29 FDA-approved drugs, 12 drugs in clinical trials, and 28 preclinical compounds). The team then tested a subset of these compounds for their activity against SARS-CoV-2 in the laboratory. Researchers identified 2 drug classes with antiviral activity: messenger RNA translation inhibitors (including the investigational cancer drugs zotatifin and ternatin-4) and predicted regulators of the sigma1 and sigma2 receptors (including the hormone progesterone, antipsychotic drugs haloperidol and chlorpromazine, the antianxiety drug siramesine, and the antihistamines clemastine and cloperastine). Researchers suggest these agents could result in new therapeutic approaches to treat COVID-19 that warrant further testing, leading to clinical trials.

In related work, Chinese Academy of Sciences researchers have created a publicly available web server to explore potential COVID-19 treatments. The web server has 2 goals: to predict protein targets for drugs or compounds observed in clinical or laboratory studies and to identify lead compounds against potential drug targets via molecular docking. Further, University of Virginia (Charlottesville) researchers proposed a computational model to predict protein interactions between novel viruses and humans using only protein sequence information, dramatically shortening the discovery process compared with conventional techniques.

**Possible Areas of Impact**

- Patient outcomes
- Health care costs

**Possible Future Impacts**

Identifying drugs approved for other indications that might also treat coronavirus could speed the development of new COVID-19 treatments and benefit patients sooner. Screening existing drugs for potential benefit against COVID-19 might also reduce drug development costs for the new indications. Further, the protein interaction maps could expand the potential treatment targets for new therapeutic agents in development for other indications.
Key Stakeholder Perspectives

Between June 5, 2020, and April 19, 2021, seven ECRI stakeholders—reflecting physician, research, health systems, and health care generalist perspectives—provided comments and ratings on this topic. The list below summarizes key stakeholder perspectives.

- The protein mapping approach could help shorten drug development time by years, by identifying which existing drugs have clinically important effects on COVID-19 and warrant further clinical testing. The proteomics approach might also help identify compounds that could work in combination against COVID-19.
- Proteomics is well suited to help researchers learn how to neutralize viruses, because viruses basically consist of DNA or RNA enclosed in a protein outer shell.
- Shortening the development pipeline by using available drugs with established safety profiles could ultimately improve patient outcomes by making more treatment options available sooner and to more patients globally.
- Repurposing approved drugs to treat COVID-19 could help alleviate supply issues that can sometimes affect new investigational treatments.
- High rates of vaccine refusal combined with new and future coronavirus variants that are resistant to available treatments will increase the importance of and need for rapid discovery and testing of effective new COVID-19 therapeutics.

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

Potential Impact Score

Stakeholders reviewing this topic thought that TD-0903 for treating acute lung injury in 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 inhaled janus kinase (JAK) inhibitor being investigated as a treatment for patients with acute lung injury in COVID-19 to prevent disease progression to acute respiratory distress syndrome (ARDS).
- Compared with placebo, initial reported phase 2 clinical data suggest numerical improvements in several clinical outcomes in patients treated with TD-0903.
- Stakeholders commenting on this topic thought TD-0903 has potential to improve patient outcomes and improve survival in patients with severe COVID-19 with lung inflammation.
- Stakeholders also thought it might lead to health care cost savings from reduced hospitalizations, intensive care resource usage, and health complications, even though it is likely to be used in combination with other COVID-19 therapies, thus increasing up-front treatment costs.
Description

TD-0903 (Theravance Biopharma, Dublin, Ireland) is an investigational, inhaled JAK inhibitor intended to treat COVID-19 by preventing the progression of acute lung injury to life-threatening ARDS. ARDS in COVID-19 is thought to be caused, in part, by a rapid influx of inflammatory proteins called cytokines into the lungs (ie, cytokine storm). Excessive release of proinflammatory cytokines is thought to lead to hyperinflammation in COVID-19 and correlate with severe disease and poor outcomes. Intervening early to block cytokine storm in COVID-19 pneumonia might be critical for survival. TD-0903 purportedly broadly inhibits the activity of JAKs that play a central role in cytokine signaling. It is taken in a nebulized form to directly target hyperinflammation in the lungs and limit systemic suppression of the immune system.

A phase 2 study enrolling 222 hospitalized COVID-19 patients is ongoing. Primary completion is expected in April 2021. In February 2021, Theravance Biopharma reported initial clinical data from part 1 of the trial. The developer reported TD-0903 was generally well tolerated, was related to no serious adverse events, and demonstrated numerical improvements in outcomes, including all-cause mortality by day 28 of hospitalization, clinical status worsened during the 7-day treatment period, survival with no respiratory failure on day 28, and average time to hospital discharge. Data from part 2 of the trial are anticipated in the second quarter of 2021.

Possible Areas of Impact

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

Possible Future Impacts

TD-0903 to treat acute lung injury in COVID-19 might improve patient outcomes by preventing disease progression to ARDS, thus potentially preventing disease complications or death. Preventing ARDS is likely to shorten length of hospitalization and reduce intensive care resource use (eg, mechanical ventilation), thus reducing the burden on the health care system and potentially resulting in health care cost savings related to hospitalization and intensive care resources. Population health outcomes might improve as a result of improved individual patient outcomes and reduced burden on local health care systems.

Key Stakeholder Perspectives

Between June 1, 2020, and April 19, 2021, six ECRI stakeholders, reflecting health systems, nursing, physician, and research perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- TD-0903 to treat acute lung injury in COVID-19 might significantly improve patient outcomes and reduce mortality in patients who have severe COVID-19 with lung inflammation.
• TD-0903’s route of administration (ie, inhalation) is promising since it targets the lungs directly, and it might be easier to use in the acute care setting.
• TD-0903 might increase treatment cost since it is likely to be used in combination with other drug therapies, but its cost might be offset by health care cost savings from reduced intensive care hospital stays, mechanical ventilation, and health complications.
• If efficacious, it might change the health care delivery process by reducing the need for mechanical ventilation for severe COVID-19 treatment.
Chapter 6. Vaccines and Prophylaxis

Chapter Summary

As of March 12, 2021, we were monitoring or had recently archived 10 COVID-19-related vaccine and prophylaxis topics. Eight of these topics are listed in the January 2021 PCORI Health Care Horizon Scanning System: Horizon Scanning COVID-19 Supplement Status Report, Volume 2, Issue 1; the remaining 2 topics were added to the system subsequent to that 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 March 11, 2021. Additional ratings and comments might also have been received after March 11, 2021.

One topic included in the previous High Impact Report, AZD1222 (ChAdOx1 nCoV-19) vaccine for preventing coronavirus infection, was excluded from this report after stakeholders re-reviewed the topic and rated it as having only moderate potential for impact.

From among the 10 topics, 8 topics have been selected that internal ECRI stakeholders thought 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.

Topics Considered for Inclusion in This Report

Table 6.1 lists 8 topics selected for inclusion in this High Impact Report. Included topics received, on average, high impact ratings and demonstrated considerable consensus among stakeholders. Topics are arranged 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

<table>
<thead>
<tr>
<th>Topic title</th>
<th>Potential impact score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderna COVID-19 vaccine for preventing coronavirus infection</td>
<td>3.8</td>
</tr>
<tr>
<td>Novavax COVID-19 vaccine (NVX-CoV2373) for preventing SARS-CoV-2 infectiona</td>
<td>3.7</td>
</tr>
<tr>
<td>Variant-specific vaccines for preventing COVID-19a</td>
<td>3.7</td>
</tr>
<tr>
<td>ARCT-021 (LUNAR-COV19) vaccine for preventing SARS-CoV-2 infection</td>
<td>3.6</td>
</tr>
<tr>
<td>JNJ-78436735 (Ad26.COV2-S) vaccine for preventing coronavirus infection</td>
<td>3.4</td>
</tr>
<tr>
<td>Pfizer-BioNTech COVID-19 vaccine for preventing coronavirus infection</td>
<td>3.4</td>
</tr>
<tr>
<td>Sanofi-GSK SARS-CoV-2 vaccine for preventing SARS-CoV-2 infectiona</td>
<td>3.4</td>
</tr>
<tr>
<td>CoVLP vaccine for preventing SARS-CoV-2 infectiona</td>
<td>3.2</td>
</tr>
</tbody>
</table>

* Topic appears for the first time in this High Impact Report.
Table 6.2 lists 2 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 arranged 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

<table>
<thead>
<tr>
<th>Topic title</th>
<th>Potential impact score</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZD1222 (ChAdOx1 nCoV-19) vaccine for preventing SARS-CoV-2 infection</td>
<td>3.0</td>
</tr>
<tr>
<td>Monoclonal antibodies targeting coronavirus spike protein receptor binding domain for preventing COVID-19a</td>
<td>2.8</td>
</tr>
</tbody>
</table>

**Topic Summaries**

We present below 8 summaries on topics deemed to have high impact potential. Topics are arranged first in descending order by potential impact score; topics with the same score are listed alphabetically by topic title.

**Moderna COVID-19 Vaccine for Preventing Coronavirus Infection**

**Potential Impact Score**

Stakeholders reviewing this topic thought that the Moderna COVID-19 vaccine (mRNA-1273) 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**

- The Moderna vaccine is an investigational vaccine intended to generate a protective immune response against the coronavirus spike protein expressed on the surface of the virus.
- The Moderna vaccine is in phase 3 development, with primary completion expected in October 2022.
- FDA granted the Moderna vaccine Emergency Use Authorization (EUA) for preventing COVID-19 in individuals aged 18 years and older.
- Stakeholders commenting on this topic thought that the Moderna vaccine was safe and effective, with widespread immunization efforts pushing population health toward achieving herd immunity; however, there is concern over the vaccine’s ability to create an effective immune response against emerging variants.
Description

The Moderna vaccine (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. 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.

Published primary efficacy data from the phase 3 randomized trial found that the Moderna vaccine had an efficacy of 94.1%. Of the 196 confirmed cases of COVID-19 included in the analysis, 185 cases were observed in the placebo group vs 11 cases observed in the vaccine group, resulting in a point estimate of vaccine efficacy of 94.1%. There were 30 severe cases of COVID-19, all of which occurred in the placebo group, leading to a point estimate of vaccine efficacy of 100% against severe COVID-19.

Initial studies of the vaccine’s efficacy against SARS-CoV-2 variants of concern, compared with prior variants, found no significant impact on neutralization of B.1.1.7, first identified in the United Kingdom. However, a 6-fold, but still significant, decrease was observed in neutralization of B.1.351, first identified in South Africa, compared with prior variants.

On December 18, 2020, FDA granted the Moderna COVID-19 vaccine EUA for preventing COVID-19 in individuals aged 18 years and older. A phase 3 trial in 30 000 individuals is in progress, with full data expected by October 2022. The vaccine is part of the US government’s Operation Warp Speed. The company purportedly remains on track to be able to deliver approximately 500 million doses per year beginning in 2021.

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

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

In ongoing trials, the Moderna vaccine has proven effective against SARS-CoV-2. 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 regarding the benefits of immunization might be necessary to minimize vaccine hesitancy and concerns.\textsuperscript{170,171}

**Key Stakeholder Perspectives**

Between February 25, 2021, and March 2, 2021, five ECRI stakeholders—reflecting health systems and research perspectives—provided comments and ratings on this topic. The list below summarizes key stakeholder perspectives.

- The Moderna vaccine might substantially improve patient and population health outcomes by preventing coronavirus infection or reducing case severity in some patients.
- The emergence of new variant strains of COVID-19 might result in lower efficacy as well as the need for a booster or modified vaccine; however, specific vaccines against these variants might be able to be developed in a few months due to the advancements and funding put into RNA technology.
- Availability of the Moderna vaccine might help relax social-distancing guidelines and economic disruptions, which could result in an improvement in overall population psychological health.
- While analysis of the phase 3 trial said that the vaccine was safe, the long-term safety profile is yet to be completely determined; additional adverse events are being reported in the general population vaccinated after the vaccine was authorized.
- Since the Moderna vaccine does not require extreme refrigeration, the vaccine might be more accessible in rural and underserved areas than other authorized COVID-19 vaccines, allowing for improved access and reduced disparities.

**Novavax COVID-19 Vaccine (NVX-CoV2373) for Preventing Coronavirus Infection**

**Potential Impact Score**

Stakeholders reviewing this topic thought that the Novavax COVID-19 vaccine (NVX-CoV2373) 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 Novavax vaccine is an investigational vaccine intended to generate a protective immune response against coronavirus by mimicking the structure of the coronavirus spike protein expressed on the surface of the virus.
The Novavax vaccine is in phase 3 development, with primary completion expected in March 2021.

Novavax has begun a rolling review of NVX-CoV2373 with FDA for Emergency Use Authorization (EUA).

Stakeholders commenting on this topic thought that NVX-CoV2373’s efficacy data are promising, especially against B.1.1.7, the COVID-19 variant first identified in the United Kingdom, but there is concern regarding the vaccine’s ability to generate an immune response that is protective against other emerging variants such as B.1.351, a variant first identified in South Africa.

**Description**

The Novavax vaccine (Gaithersburg, Maryland) is a vaccine against coronavirus that uses recombinant nanoparticles that mimic the structure of a full-length SARS-CoV-2 spike protein, the protein expressed on the surface of the virus that is responsible for viral fusion and entry. Immune cells in the body react to the spike nanoparticles, resulting in a host immune response against the virus to prevent future infection. The vaccine is coadministered with Novavax’s Matrix-M1 adjuvant to help enhance the immune response.\(^{172}\)

Primary efficacy data of a phase 3 randomized trial involving 15,000 adults in the United Kingdom, announced through a company press release, found that the Novavax vaccine had an efficacy of 96.4% against the original strain of the virus and 86.3% against the B.1.1.7 variant, first identified in the United Kingdom. Phase 2 efficacy results from the South Africa trial, where a majority of the COVID-19 strains were the B.1.351 variant (first identified in South Africa), found vaccine efficacy to be 55.4% among 2,665 HIV-negative participants. The vaccine has an overall efficacy of 100% against severe disease.\(^{173}\)

NVX-CoV2373 is currently in a phase 3, randomized trial in the United States that is enrolling 30,000 participants, with primary completion expected in March 2021.\(^{174}\) The vaccine is part of the US government’s Operation Warp Speed, and the manufacturer announced plans to produce up to 150 million doses per month globally by the third quarter of 2021.\(^{175,176}\) Novavax has begun a rolling review process with FDA for EUA of NVX-CoV2373.\(^{177}\)

**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 the Novavax vaccine 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 February 2, 2021, and February 26, 2021, six ECRI stakeholders, reflecting health systems, physician, and research perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- NVX-CoV2373 might substantially improve patient and population health outcomes by preventing coronavirus infection or reducing case severity in some patients.
- The Novavax vaccine’s use of nanoparticles adds a different approach to immunization than the authorized messenger RNA (mRNA) vaccines, which might help patients who are unable to develop immune responses from certain vaccine platforms.
- If NVX-CoV2373 is authorized, the availability of another vaccine against COVID-19 might help ease the current production and distribution bottlenecks, pushing society toward achieving herd immunity and ending the pandemic.
- The Novavax vaccine’s high efficacy against the rapidly spreading COVID-19 UK variant is promising, but there is concern over the vaccine’s effectiveness against the South African and other emerging variants.
- Since the Novavax vaccine is not limited by the need for cold chain infrastructure, the vaccine might be more accessible in rural and underserved areas than other authorized COVID-19 vaccines, allowing for improved access and reduced disparities. However, the 2-dose regimen required by this vaccine might limit widespread use in rural and hard-to-access areas compared with a single-dose option.

**Variant-Specific Vaccines for Preventing COVID-19**

**Potential Impact Score**

Stakeholders reviewing this topic thought that variant-specific vaccines for preventing 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

- Variant-specific vaccines are investigational vaccines intended to generate a protective immune response against emerging coronavirus variants that may render current COVID-19 vaccines ineffective.
- The variant-specific vaccines are in phase 1/2 development, with primary completion of mRNA-1273.351 expected in August 2022.
- Variant-specific vaccines might be used to immunize individuals who have not received any COVID-19 vaccine or be used as booster shots after vaccination with currently authorized COVID-19 vaccines.
- Stakeholders commenting on this topic thought that variant-specific vaccines, if effective, might be able to control emerging variants quickly, thereby preventing spikes in transmission, hospitalization, and death rates caused by the disease; however, there was concern that these vaccines might increase health disparities due to lack of timely vaccine delivery in underserved and rural populations.

Description

Mutations in viruses are inevitable, leading to viral variants that can emerge and persist around the world. These variants can result in faster spread and increased transmission, helping the disease persist in the population. Due to the emergence of certain SARS-CoV-2 variants, vaccines specific to these variants might be necessary to protect individuals from contracting COVID-19.

Of particular concern are variants harboring mutations in the SARS-CoV-2 spike protein, which the virus uses to attach itself to the surface of human cells and gain entry. Since the S protein is the target of many of the currently available COVID-19 vaccines, changes to this protein may affect the efficacy of these vaccines. Initial studies have found that the mRNA-1273 vaccine has a 6-fold reduced neutralization against the B.1.351 variant, first identified in South Africa. Neutralization of B.1.351 by BNT162b2 was reduced by two-thirds when compared with early COVID-19 isolates.

Moderna, the developer of mRNA-1273, has announced a phase 1 trial in 210 participants to determine the neutralizing ability of a vaccine (mRNA-1273.351) specific for B.1.351. Moderna has also amended its phase 2 study of mRNA-1273 to give 60 participants previously vaccinated with mRNA-1273 a single booster dose of either mRNA-1273.351 or a multivalent booster candidate, mRNA-1273.111. Pfizer and BioNTech, the developers of BNT162b2, are discussing the start of a study using a messenger RNA (mRNA) vaccine with a variant sequence, which would lead to an adaptable vaccine for use against B.1.351 or other emerging variants.

Possible Areas of Impact

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

Possible Future Impacts

If the variant-specific vaccines are proved effective against emerging coronavirus variants, they might improve patient outcomes as well as clinician or caregiver safety by preventing or mitigating adverse health events caused by infection. They 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. They might also help decrease the overall cost burden to governments and the health care system. Effective vaccines against current and emerging variants of coronavirus could also enable more relaxed social-distancing protocols.

Although most expected outcomes from effective variant-specific vaccines are positive, a vaccine shortage could lead to increased disparities if certain populations are unable to access the vaccines. 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 vaccines are brought to market prematurely (ie, before full safety data are available). Misinformation about vaccines might result in the need for proactive information campaigns highlighting the benefit of immunizations against COVID-19 variants to minimize vaccine hesitancy in the public.

Key Stakeholder Perspectives

Between March 1, 2021, and March 9, 2021, six ECRI stakeholders, reflecting health systems and research perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

• Variant-specific vaccines might substantially improve patient and population health outcomes by preventing coronavirus infection or reducing case severity in some patients, especially if authorized vaccines are unable to effectively protect individuals and slow infection.

• Public misinformation over the variant strains’ ability to escape the vaccine’s protection and antivaccination campaigns, as well as mistakes in initial vaccine rollout, might affect compliance of variant-specific vaccine programs.

• Since vaccine platforms that use RNA technology are new, RNA variant-specific vaccines might cause long-term safety concerns and adverse effects by exposing recipients to multiple doses of lipid nanoparticles.

• Variant-specific vaccines might be able to address new pathogenic variants quickly to control transmission before the variant virus begins to spread; however, the distribution of new variant-specific vaccines might increase health disparities for individuals living in rural or underserved areas if they are not able to constantly obtain new or updated vaccines.
ARCT-021 (LUNAR-COV19) Vaccine for Preventing SARS-CoV-2 Infection

**Potential Impact Score**

Stakeholders reviewing this topic thought that the ARCT-021 (LUNAR-COV19) vaccine for preventing SARS-CoV-2 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**

- ARCT-021 is a messenger RNA (mRNA) vaccine intended to generate a protective immune response against the coronavirus spike protein expressed on the surface of the virus.
- ARCT-021 is under study in a randomized phase 2 trial, and the developer intends to initiate a phase 3 trial in the first half of 2021.
- Based on the low dose of vaccine required to induce immune responses, the manufacturer claims that only a single dose might be needed for protection and plans to be able to produce hundreds of millions of doses in 2021, if authorized by FDA.
- Stakeholders commenting on this topic thought that, if effective, ARCT-021 could improve patient and population health while also decreasing health care disparities due to low doses of the vaccine being easily mass produced; however, more clinical data on its safety and efficacy are needed.

**Description**

ARCT-021 (Arcturus Therapeutics, San Diego, California) is a lipid nanoparticle–encapsulated mRNA vaccine that encodes a full-length viral spike protein responsible for host receptor binding and cellular entry. The vaccine purportedly enters host antigen-presenting cells and induces expression of the viral spike protein, which elicits a host immune response that prevents future coronavirus infection. The mRNA component of the vaccine is self-amplifying, which purportedly increases immunogenicity. Additionally, the manufacturer has produced a lyophilized (ie, freeze-dried) version of the vaccine that would purportedly reduce cold chain storage requirements compared with existing mRNA vaccines that are shipped as a frozen liquid.

Preliminary immunogenicity data from a randomized phase 1/2 study in 106 participants given either 1 or 2 doses of ARCT-021 (1-10 μg per injection) or placebo showed that participants receiving doses in the range of 5 to 7.5 μg achieved neutralizing antibodies at the low end of the range of levels found in serum from patients who recovered from COVID-19. Participants also developed T-cell responses against the spike protein and receptor binding domain. The vaccine had a favorable safety and tolerability profile in participants and resulted in no moderate or severe fevers.
ARCT-021 is in phase 2 development in a 600-patient trial in the United States and Singapore. The manufacturer has announced that it expects to initiate a phase 3 trial of the vaccine using both single-shot and prime-boost (ie, 2-shot) dosing strategies in the first half of 2021. Pending regulatory authorization, the manufacturer plans to be able to produce hundreds of millions of doses before the end of 2022.

**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 ARCT-021 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 in vulnerable populations, thereby decreasing negative COVID-19-related outcomes and improving individual and population health outcomes over time. If effective after a single dose, the vaccine might confer protection quicker and easier and aid patients with limited access to care. It might also help decrease the overall cost burden to governments and the health care system for implementation of a vaccination program. An effective vaccine against coronavirus could also enable more relaxed social-distancing protocols.

Although most potential impacts of 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 August 31, 2020, and April 19, 2021, six ECRI stakeholders—reflecting health care generalist, health systems, nursing, physician, and research perspectives—provided comments and ratings on this topic. The list below summarizes key stakeholder perspectives.

- ARCT-021 might substantially improve patient and population health outcomes by preventing coronavirus infection; however, more safety and efficacy data are needed to determine if the vaccine is adequate and effective at a low dose.
- A low-dose vaccine might allow for mass production, which could prevent health care disparities if underserved communities and at-risk populations are given ARCT-021 at no cost.
• Availability of an additional coronavirus vaccine might be significant in alleviating vaccine shortages and in halting or slowing down the coronavirus pandemic.

• An accelerated development timeline of ARCT-021 might result in data that do not accurately determine the extent of long-term immunity conferred by the vaccine.

• If the vaccine efficacy and safety profile of ARCT-021 is favorable, it might aid in decreasing public vaccine hesitancy surrounding adverse events experienced with other COVID-19 vaccines.

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 moderately high impact on patient-oriented health care relative to COVID-19 in the United States within the next 12 months.

HNIGRS

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 3 development, with full data expected in March 2023.

• The manufacturer hopes to produce and distribute up to 1 billion doses of the vaccine globally beginning in 2021.

• Stakeholders commenting on this topic thought that because JNJ-78436735 was developed using a traditional vaccine platform, it might provide a more familiar alternative for individuals hesitant to receive COVID-19 vaccines developed through novel mechanisms.

• Although JNJ-78436735 is an effective COVID-19 vaccine, stakeholders were concerned regarding its ability to effectively protect against newly emerging COVID-19 variants.

Description

JNJ-78436735 (Ad26.COV2-S; Johnson & 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 the genetic material induces the production of 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.¹⁹⁰

Topline efficacy and safety data from the randomized phase 3 ENSEMBLE trial, announced through a company press release, found that JNJ-78436735 was 66% effective at preventing
moderate to severe disease and 85% effective at preventing severe disease 28 days after a single
dose of vaccine, with no significant safety concerns. Efficacy in preventing moderate to severe
disease across geographic regions was 72% in the United States, 66% in Latin America, and 57% in South Africa. A 2-dose protocol is also being studied in the phase 3 ENSEMBLE 2 trial, with primary completion expected in May 2022.

On February 27, 2021, FDA granted the Johnson & Johnson COVID-19 vaccine Emergency Use Authorization for preventing COVID-19 in individuals aged 18 years and older. JNJ-78436735 is in a large phase 3 trial in 40,000 people. Full 12-month results on its safety and effectiveness against coronavirus are not expected until March 2023. Effective April 23, 2021, the CDC and FDA recommended that the use of the vaccine resume in the United States. However, the agencies warn that women with low platelets younger than 50 years especially should be aware of the rare risk of blood clots after vaccination. The US government has agreed to purchase 100 million doses for about $10 per dose. The company plans to manufacture 100 million doses for the United States by end of June 2021.

### 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 (e.g., 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 (i.e., before full safety data are available).

### Key Stakeholder Perspectives

Between June 25, 2020, and July 6, 2020, five ECRI stakeholders—reflecting research, nursing, and systems perspectives—provided comments and ratings on this topic. The list below summarizes key stakeholder perspectives.
• ARCT-021 might substantially improve patient and population health outcomes by preventing coronavirus infection; however, more safety and efficacy data are needed to determine if the vaccine is adequate and effective at a low dose.

• A low-dose vaccine might allow for mass production, which could prevent health care disparities if underserved communities and at-risk populations are given ARCT-021 at no cost.

• Availability of a coronavirus vaccine might be significant in halting or slowing down the coronavirus pandemic.

• An accelerated development timeline of ARCT-021 might result in data that do not accurately determine the extent of long-term immunity conferred by the vaccine.

Pfizer-BioNTech COVID-19 Vaccine for Preventing Coronavirus Infection

Potential Impact Score
Stakeholders reviewing this topic thought that the Pfizer-BioNTech COVID-19 vaccine (BNT162b2) for preventing coronavirus infection 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 Pfizer-BioNTech vaccine is a messenger RNA (mRNA) vaccine intended to generate a protective immune response against the coronavirus spike protein expressed on the surface of the virus.

• The Pfizer-BioNTech vaccine is in phase 2/3 development, with primary completion expected on August 3, 2021.

• FDA granted the Pfizer-BioNTech vaccine Emergency Use Authorization (EUA) for preventing COVID-19 in individuals aged 16 years and older.

• 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 and immune response duration of the mRNA vaccine against COVID-19 and emerging variants must continue to be evaluated in clinical trials.

Description
The Pfizer-BioNTech vaccine (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. 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.
Primary safety and efficacy analysis of the phase 2/3 trial stated that the Pfizer-BioNTech vaccine was found to be 95% effective in preventing COVID-19 in participants without evidence of prior infection. The data also reported that the vaccine was well tolerated across all populations, with the most common adverse events being fatigue and headache, experienced at a frequency of 3.8% and 2%, respectively. FDA granted the Pfizer-BioNTech vaccine EUA on December 11, 2020, for preventing COVID-19 in individuals aged 16 years and older.

A retrospective cohort study from Israel of 596,618 vaccinated people found that estimated vaccine efficacy against documented infection at days 14 through 20 after the first dose or at 7 or more days after the second dose was 46% and 92%, respectively. Initial studies of the vaccine’s efficacy against SARS-CoV-2 variants of concern demonstrated a 3-fold decrease in neutralization of B.1.351, a variant first identified in South Africa, compared with earlier variants.

The Pfizer-BioNTech vaccine is also in a large phase 2/3 trial in more than 43,000 people. Full results on its safety and effectiveness against coronavirus are not expected until August 2021. Under an agreement as part of Operation Warp Speed, the US government has purchased 300 million doses.

**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**
In ongoing trials, the Pfizer-BioNTech vaccine has proven effective against SARS-CoV-2. 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, and headache) occurred in more than half of the study participants, a proactive information campaign regarding the benefits of immunization might be necessary to minimize vaccine hesitancy and concerns.
Key Stakeholder Perspectives

Between February 25, 2021, and March 8, 2021, five ECRI stakeholders—reflecting health care generalist, health systems, and research perspectives—provided comments and ratings on this topic. The list below summarizes key stakeholder perspectives.

- The Pfizer-BioNTech vaccine might significantly improve patient and population health outcomes by preventing infection with coronavirus, mitigating disease spread, and conferring immunity to much of the population; however, more information is needed regarding the duration of immunogenicity as well as the vaccine’s ability to protect against emerging variants.
- Boosters or new formulations of the Pfizer-BioNTech vaccine might need to be made to protect against virus variants, and large-scale immunization efforts would be necessary to prevent further outbreaks.
- The accelerated development timeline for the Pfizer-BioNTech vaccine might pose unforeseen safety and efficacy risks when manufacturing and distributing the vaccine.
- The Pfizer-BioNTech vaccine’s temperature storage requirements might have contributed to health disparities in areas where the vaccine could not be easily stored and administered. However, the company has recently validated the vaccine in storage conditions that would make the vaccine more available at a community-wide level.

Sanofi-GSK SARS-CoV-2 Vaccine for Preventing SARS-CoV-2 Infection

Potential Impact Score

Stakeholders reviewing this topic thought that the Sanofi-GSK SARS-CoV-2 vaccine for preventing SARS-CoV-2 infection 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 Sanofi-GSK SARS-CoV-2 vaccine uses a recombinant version of the SARS-CoV-2 spike protein to generate a protective immune response against COVID-19.
- The Sanofi-GSK SARS-CoV-2 vaccine does not have the same deep-cold storage requirements of some other COVID-19 vaccines, potentially easing distribution challenges.
- A vaccine formulation error in early trials caused a lower than desired immune response in older adults, slowing vaccine development and delaying possible US regulatory authorization until at least late 2021.
- Stakeholders commenting on this topic thought that, if safe and effective, the Sanofi-GSK SARS-CoV-2 vaccine could reduce disparities and help improve access to vaccinations in underserved populations domestically and globally because it has less burdensome cold-storage requirements than other available COVID-19 vaccines.
Description

GlaxoSmithKline (GSK) plc (Brentford, United Kingdom) and Sanofi (Paris, France) are jointly developing an adjuvanted, recombinant protein–based vaccine that is intended to generate a protective immune response against SARS-CoV-2. The Sanofi-GSK SARS-CoV-2 vaccine consists of a recombinant SARS-CoV-2 spike protein, which is expressed on the surface of SARS-CoV-2 and is responsible for viral fusion and entry. The vaccine is expected to engage the immune system in a manner similar to that of other recombinant protein vaccines (eg, hepatitis B vaccine, human papillomavirus vaccine). The recombinant protein vaccine is formulated with an adjuvant intended to boost the immune response to the vaccine, thereby requiring less antigen to stimulate a response. Using less antigen per dose potentially allows more total vaccine doses to be produced in less time. In clinical trials, the vaccine is given as 2 injections spaced 21 days apart.

The vaccine is part of the US government’s Operation Warp Speed and is in a phase 1/2 randomized trial in 440 adults with estimated completion in November 2021. Due to inadequate results in older adults caused by a vaccine formulation error in the phase 1/2 trial, the company has pushed back its target date of a request for regulatory authorization to the second half of 2021. Unlike vaccines further in development that are based on messenger RNA (mRNA) platforms and need to be kept frozen before use, the Sanofi-GSK vaccine is intended to be stable in liquid form at refrigerator temperatures.

Possible Areas of Impact

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

Possible Future Impacts

The Sanofi-GSK SARS-CoV-2 vaccine might reduce the general risk of coronavirus infection and lessen the need for social distancing if it is authorized for clinical use. If safe and effective at reducing infections, the vaccine could improve patient outcomes and reduce costs for treating severe COVID-19 infections. Distributing the Sanofi-GSK vaccine might be easier and less costly since the vaccine can be stored at normal refrigerator temperatures, thus lowering the cold chain burden for vaccine providers. As with other vaccines during the pandemic, limited production capacity of the Sanofi-GSK vaccine might result in vaccine shortages, depending on its demonstrated level of effectiveness and market demand. However, the accelerated approval process might mean that the vaccine does not achieve the desired level of protection against COVID-19. Further, rapid approval also raises concerns that unexpected or undetected adverse events related to the vaccine could arise after the vaccine reaches widespread use.
Key Stakeholder Perspectives

Between November 20, 2020, and January 20, 2021, five ECRI stakeholders, reflecting physician, nursing, research, and health systems perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- A COVID-19 vaccine that does not have the deep-cold storage requirements of some other COVID-19 vaccines could improve vaccine access to underserved populations domestically and globally.
- If safe and effective at preventing COVID-19, another vaccine option might help overcome global shortages, potentially reducing disparities. Broad access to and acceptance of vaccination globally could speed economic recovery, possibly restoring employment opportunities in hard-hit industrial sectors.
- Proposed proof-of-vaccination requirements for travel or large gatherings could encourage more individuals to seek COVID-19 vaccinations. The availability of more vaccine options could make such vaccination requirements somewhat less burdensome.

Large-scale vaccination programs could be very costly to implement. However, the benefits of a healthy population and economy unhindered by pandemic fears could offset the costs of widespread vaccinations.

CoVLP Vaccine for Preventing SARS-CoV-2 Infection

Potential Impact Score

Stakeholders reviewing this topic thought that the Coronavirus Virus-Like Particle (CoVLP) vaccine for preventing SARS-CoV-2 infection 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 CoVLP vaccine is designed to mimic the shape of the SARS-CoV-2 virus to stimulate an immune system response without using infectious genetic material from the virus.
- The 2-dose CoVLP vaccine is in phase 2/3 trials scheduled for completion in December 2021, and it has FDA Fast Track designation.
- Results of a phase 1 trial suggested patients vaccinated with CoVLP vaccine showed neutralizing antibody responses up to 50 times higher than those seen in individuals who had recovered from COVID-19 infection.
- Stakeholders commenting on this topic thought that if safe and effective at reducing COVID-19, the CoVLP vaccine could be an important addition to expand global vaccination programs, helping to end the pandemic and improve global public health.
• Stakeholders also thought the CoVLP vaccine might require special handling and shipping requirements because virus-like particles (VLPs) tend to be more fragile than whole viral particles.

Description

GlaxoSmithKline (GSK) plc (Brentford, United Kingdom) and Medicago Inc (Quebec City, Quebec, Canada) are jointly developing the adjuvanted, plant-based CoVLP vaccine against the novel coronavirus. The CoVLP vaccine mimics the shape and dimensions of the virus, displaying the SARS-CoV-2 spike protein on the surface of VLPs (assemblies of viral proteins that present antigens in a manner similar to the native virus but do not incorporate genetic material and, therefore, are noninfectious). By presenting viral antigens in a manner similar to the virus, VLPs purportedly elicit a balanced immune response that is both antibody- and cell-mediated.

FDA has granted the CoVLP vaccine Fast Track designation. CoVLP is in a phase 2/3 randomized trial in 30,918 adults, with estimated completion in December 2021. Participants will receive 2 doses of placebo or 3.75 µg of CoVLP with AS03 adjuvant given 21 days apart. Results from a phase 1 randomized trial found that almost all of the patients receiving both doses of adjuvanted CoVLP developed neutralizing antibody responses that were 10- to 50-fold higher than levels seen in individuals recovering from COVID-19 infection. Pain at the injection site, headache, and fatigue were the most common reactions, and most adverse events were mild to moderate and of short duration.

Possible Areas of Impact

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

Possible Future Impacts

If found to be safe and effective for preventing COVID-19, the CoVLP vaccine might reduce infection risk and improve health outcomes in the general population. If the vaccine helps prevent severe COVID-19 infections, it could also reduce costs arising from treatment of severe infections and related complications.

More broadly, another effective vaccine option could allow local leaders and health officials to relax social-distancing protocols. If found to be safe and effective at preventing COVID-19, the CoVLP vaccine could expand the knowledge base regarding the effectiveness of plant-based manufacturing technology. Depending on its effectiveness and subsequent demand, shortages of the CoVLP vaccine could emerge due to limited production capacity.
Key Stakeholder Perspectives

Between January 25, 2021, and February 26, 2021, six ECRI stakeholders, reflecting nursing, research, health systems, health care generalist, and clinical engineering perspectives, provided comments and ratings on this topic. The list below provides a summary of key stakeholder perspectives.

- The availability of several safe, effective COVID-19 vaccines both domestically and globally is a major requirement for successful vaccination programs intended to slow and then halt the pandemic.
- Although funding worldwide vaccination programs will remain a challenge, the emergence of more safe and effective COVID-19 vaccines could shorten global wait times to receive a vaccine, potentially reducing disparities and improving global population health.
- Long-term safety concerns about CoVLP remain because its specific development technology has not been used before to produce vaccines.
- VLPs tend to be more fragile than whole viral particles, potentially making them more susceptible to constant movement and drastic temperature changes that can occur during transit. Thus, safe transportation and handling of CoVLP vaccine might require additional precautions.
References


